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Some addition reactions of chalcones

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SOME ADDITION REACTIONS OF CHALCONES

by

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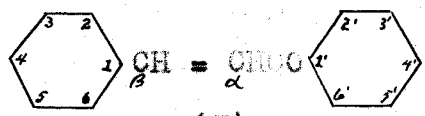
I. INTRODUCTION

The chalcones[1] (from the Greek, χαλκός, ore or bronze, particularly copper) represent a large group of synthetic organic compounds derived from benzalacetophenone (I)[2].



(I)

Since the preparation of the parent compound (benzalacetophenone, commonly called chalcone) by Claisen and Claparede[3] in 1881, the properties and reactions of this α,β-unsaturated ketone and its derivatives have been thoroughly investigated. Their structural relationship to certain synthetic and naturally occurring chromogens has been widely illustrated, and their use in the syntheses of the flavone pigments has been studied extensively.

Of special interest, however, are the addition reactions of the chalcones. From a consideration of formula (I),

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1. The name "chalcone" was first used by Kostanecki and Tambor, Ber., 32, 1921 (1889).

2. The Chemical Abstracts system of numbering has been used throughout this study, /C.A., 39, 5931 (1945)/.

3. Claisen and Claparede, Ber., 14, 2463 (1881).

it is evident that the addition of reagents to chalcones may take place by means of four possible mechanisms. Some reagents add to the 1,2-unsaturated carbonyl group, while others add to the 3,4-olefinic linkage. There are those groups of compounds which react exclusively with the 1,4-conjugated system, and finally, those which are capable of adding to both the 1,2- and 1,4-systems. In the present investigation, emphasis has been placed, as far as possible, on those reactions involving the 1,4-addition of various classes of compounds to α- or β-unsubstituted chalcones.

Although certain chalcones have been reported to possess bactericidic and fungicidic properties[4], information concerning like properties as well as the pharmacological activity of their addition products is relatively limited. It was, therefore, the purpose of this investigation to synthesize a number of these types of compounds for pharmacological testing, and, also, during the course of this work, to extend our present knowledge of reactions involving α,β-unsaturated ketones.

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4. Geiger and Conn, J. Am. Chem. Soc., 67, 112 (1945).

II. HISTORICAL

A. Sulfur-Containing Compounds

The ease with which mercaptans, sulfinic acids and related types of sulfur-containing compounds add to chalcones has been extensively illustrated in the chemical literature. These investigations were begun by Posner[5] in 1901. In connection with a study of the condensation of mercaptans with unsaturated carbonyl compounds, he obtained a trimercapto compound (II) when chalcone was condensed with ethyl mercaptan in the presence of gaseous hydrogen chloride and/or zinc chloride in ethanol or acetic acid. In addition to the union of two molecules of the mercaptan with the carbonyl oxygen, one molecule of the compound had added to the ethylenic linkage, the mercapto group occupying the α-position according to Posner.

$$C_6H_5CH = CHCOC_6H_5 + 3C_2H_5SH \longrightarrow C_6H_5CH_2CH(SC_2H_5)C(SC_2H_5)_2C_6H_5 \qquad \text{(II)}$$

The oil obtained was oxidized to the corresponding sulfone for identification. However, the resulting product was not the expected 1,1,2-triethylsulfonyl-1,3-diphenylpropane but

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5. Posner, Ber., 34, 1395 (1901).

the ketomonosulfone (IV) assumed to have been formed by the initial loss of two molecules of the thiol and the subsequent oxidation of the intermediary ketomonosulfide (III) as represented by the following equation.

$$C_6H_5CH_2CH(SC_2H_5)C(SC_2H_5)_2C_6H_5 \xrightarrow{-2C_2H_5SH} [O]$$

$$C_6H_5CH_2CH(SC_2H_5)COC_6H_5 \longrightarrow C_6H_5CH_2CH(SO_2C_2H_5)COC_6H_5$$

(III) (IV)

After further investigation of these reactions, Posner[6] was of the opinion that in the addition of the mercaptan to the ethylenic linkage of chalcone the mercapto group occupied the β-position. Hence, from the unsaturated ketone and amyl mercaptan there was obtained a mixture which upon oxidation yielded the monosulfone, β-amylsulfonyl-β-phenylpropiophenone. Two compounds (V) and (VI) were obtained from the oxidation of the product formed from the condensation of benzyl mercaptan with the ketone.

$$C_6H_5CH(SO_2C_7H_7)CH_2C(SO_2C_7H_7)_2C_6H_5 \quad (V)$$

$$C_6H_5CH(SO_2C_7H_7)CH_2COC_6H_5 \quad (VI)$$

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6. Posner, ibid., 35, 799 (1902).

Thiophenol, however, added exclusively to the ethylenic system giving rise to the monosulfide which was readily oxidized to β-phenylsulfonyl-β-phenylpropiophenone*. Identical monosulfones resulted from the addition of the corresponding alkyl- or arylsulfinic acid to chalcone.

In a further and more general study of this work, Posner[7] explained the mechanism of these reactions on the basis of Thiele's theory of partial valence. This has been adequately summarized by Fullhart[8]. Because of the general application of the theory to reactions involving the addition of other reagents to the 1,4-conjugated system of chalcones, the above mentioned resumé will, in part, be presented at this point of the present review.

> According to Thiele's theory, the unsaturated linkage is considered as being made up of four valences which have united to form a double bond. However, two of the valences are mutually and completely saturated while the second pair is held together by only a fraction of the unit of affinity, leaving a residue of affinity, which was termed "partial valency" by

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*Posner (loc. cit.) reported this compound as the oxidation product of the corresponding α-ketomonosulfide.

7. Posner, ibid., 37, 502 (1904).

8. Fullhart, L., Doctoral Dissertation, Iowa State College, 1946, page 11.

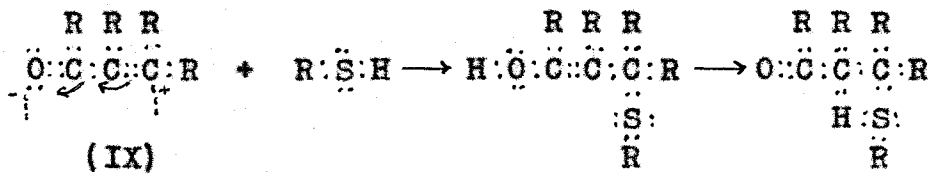
Thiele. When the unsaturated group becomes a part of the conjugated system, there arises what is called an "inactive double bond" which can be illustrated in the following manner.

(VII)

(VIII)

If figure (VII) represents a conjugated system, the dotted lines represent the partial valences. The behavior of the system can be explained on the basis that the partial valences on atoms 2 and 3 mutually saturate each other giving rise to the so-called "inactive double bond" represented by figure (VIII). The ease of 1,4-addition is apparent on the basis of the above considerations.

The addition of mercaptans to α,β-unsaturated ketones can be explained by means of electronic formulae. Figure (IX) represents an intermediate state in which the electrons are shifted in the direction of the oxygen atom resulting in a loss of negativity about the β-carbon atom.



(IX)

The equilibrium is reëstablished by the attachment of the negative thiol residue to this position.

As a result of the reinvestigation of Posner's work[5,6,7] it was revealed that mercaptans combine with olefinic ketones in the presence of the basic catalysts piperidine or sodium ethoxide yielding exclusively the 1,4-addition product in which the mercapto group occupies the β-position with respect to the carbonyl linkage[9]. β-Isoamylmercapto-β-phenylpropiophenone, $C_6H_5CH(SC_5H_{11})CH_2COC_6H_5$, and β-phenylmercapto-β-phenylpropiophenone, $C_6H_5CH(SC_6H_5)CH_2COC_6H_5$, were prepared in this manner from chalcone and isoamyl mercaptan and thiophenol, respectively[10]. The action of piperidine on a mixture of β-bromochalcone and thiophenol unexpectedly gave rise to β-phenylmercapto-β-phenylpropiophenone.

In a more recent study of the reaction, Nicolet[11] has indicated that the addition of sulfhydryl compounds to unsaturated ketones is reversible, the equilibrium as represented in the following equation being shifted far to the left in the presence of alkalies.

$$C_6H_5CH = CHCOC_6H_5 + p\text{-}C_7H_7SH \rightleftharpoons C_6H_5CH(SC_7H_7\text{-}p)CH{=}C(OH)C_6H_5 \rightleftharpoons C_6H_5CH(SC_7H_7\text{-}p)CH_2COC_6H_5$$

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9. Ruhemann, J. Chem. Soc., 87, 17 (1905).
10. Ruhemann, ibid., 461 (1905).
11. Nicolet, J. Am. Chem. Soc., 53, 3066 (1931).

Thus, benzalacetophenone-β-thioglycolic acid, $C_6H_5CH(SCH_2COOH)CH_2COC_6H_5$, prepared from chalcone and thioglycolic acid did not dissolve in caustic alkali because of the ease with which the unsaturated ketone was liberated. The product was slowly decomposed at room temperature by a 0.1 N solution of sodium carbonate. β-(p-Tolylmercapto)-β-phenylpropiophenone was hydrolyzed into its original components on standing at room temperature in a 0.1 N alcoholic solution of sodium hydroxide. When the ketosulfide was warmed with a slight excess of phenylhydrazine in acetic acid, a sulfur-free 1,3,5-triphenylpyrazoline was formed.

A later investigation revealed that p-thiocresol and benzyl mercaptan add smoothly to chalcone without the aid of the basic catalysts[12].

An interesting and related type of reaction in which p-tolylmercaptomagnesium iodide was added to chalcone was reported by Gilman and King[13].

$$C_6H_5CH = CHCOC_6H_5 + p\text{-}C_7H_7SMgI \longrightarrow C_6H_5\underset{SC_7H_7\text{-}p}{CH}CH = \overset{OMgI}{\underset{|}{C}}\text{-}C_6H_5 \xrightarrow{/HOH/}$$

$$C_6H_5\underset{SC_7H_7\text{-}p}{CH}CH = \overset{OH}{\underset{|}{C}}\text{-}C_6H_5 \xrightarrow{\text{Rearr.}} C_6H_5\underset{SC_7H_7\text{-}p}{CH} - CH_2COC_6H_5$$

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12. Nicolet, ibid., 57, 1098 (1935).

13. Gilman and King, ibid., 47, 1136 (1925).

The resulting ketosulfide was identified by oxidation to the corresponding sulfone.

Kohler and Reimer[14] reported the addition of arylsulfinic acids to chalcone. The resulting β-arylsulfonylketones were stable and well crystallized substances which were smoothly cleaved by alkalies to the sulfinic acid and the unsaturated ketone. β-(p-Toluenesulfonyl)-β-phenylpropiophenone was prepared from p-toluenesulfinic acid and chalcone. Benzenesulfinic acid reacted smoothly with the ketone giving β-benzenesulfonyl-β-phenylpropiophenone[6,15] also obtained by Vorländer and Friedberg[16] from the reaction of benzene and sulfur dioxide with chalcone in the presence of anhydrous aluminum chloride. 4-Methoxychalcone formed an analogous addition compound by this procedure.

By the simple addition of the appropriate sulfinic acid to chalcone, Martin[17] prepared β-phenyl-β-(2-chloro-5-nitrobenzenesulfonyl)propiophenone and β-phenyl-β-methanesulfonylpropiophenone.

The condensation of benzyl p-tolyl sulfone with chalcone in the presence of sodium ethoxide was reported by Con-

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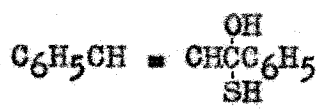
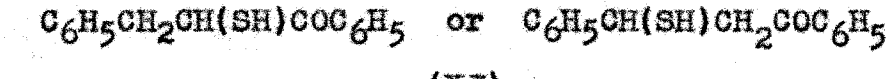
14. Kohler and Reimer, Am. Chem. J., 31, 163 (1904).
15. Kohler and Larson, J. Am. Chem. Soc., 58, 1518 (1936).
16. Vorländer and Friedberg, Ber., 56, 1144 (1923).
17. Martin, G. A., Doctoral Dissertation, Iowa State College, 1945.

nor, Flemming, and Clayton[18]. This reaction was, however, classified as of the Michael condensation type rather than simple addition to the 1,4-unsaturated system of the ketone.

Fromm and his students[19] have made a thorough study of the reaction of hydrogen sulfide with unsaturated ketones under varying conditions. When hydrogen sulfide was passed into an alcoholic solution of chalcone containing a small amount of potassium hydroxide and cooled to 0°C, benzalacetophenonehydrosulfide was obtained. Of the two possible structures for the compound resulting from this reaction, the sulfhydryl configuration (X) rather than the mercaptan arrangement (XI) was preferred since the corresponding sulfonic acid was not obtained on oxidation.



(X)



(XI)

The product was easily converted into its S-benzoyl deriva-

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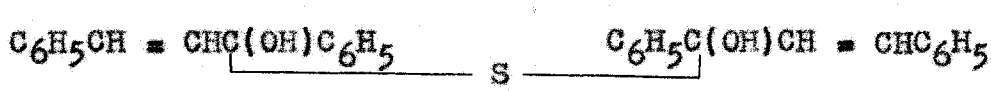
18. Connor, Flemming, and Clayton, J. Am. Chem. Soc., 58, 1386 (1936).

19. Fromm and Hubert, Ann., 394, 301 (1912); Fromm and Lambricht, Ber., 41, 3646 (1908).

tive by treatment with benzoyl chloride and was oxidized to the disulfide by iodine. 1,3,5-Triphenylpyrazoline was obtained on treatment of the compound with phenylhydrazine in acetic acid.

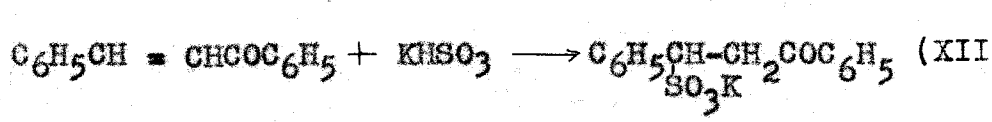
A complex sulfide of structure (XII) resulted from the action of ammonia on benzalacetophenonehydrosulfide, or, more directly, from the action of hydrogen sulfide on a solution of chalcone in ethanol containing ammonia.



(XII)

The smooth addition of hydrogen sulfide to chalcone in the absence of a base has been reported by Nicolet[12]. No details were given on the identification of the product, however.

Generally, sulfurous acid and alkali bisulfites add to α,β-unsaturated ketones yielding the corresponding β-ketosulfonic acid or the alkali β-ketosulfonate (XIII).



According to Knoevenagel[20] only the sulfonate could be obtained from chalcone. Potassium 1-phenyl-2-benzoylethane-

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20. Knoevenagel, Ber., 37, 4038 (1904).

sulfonate (XIII) prepared in this manner was unstable toward base and decomposed at its melting point of 155°C.

Recently, Kratzl and Däubner[21] in attempting to explain the mechanism involved in the sulfitation of lignin and related products through sulfite cooking have investigated the addition of sodium bisulfite to chalcones. Nearly quantitative yields of the sulfonate was obtained by boiling the chalcone with an aqueous solution of sodium bisulfite. The yields were considerably lower when the process of sulfite cooking was employed. The substituted sodium 2-benzoyl-1-phenylethenesulfonates were converted into their respective benzylthiuronium or to the 2-naphthylamine salts for identification. A summary of the experimental results obtained from this investigation is given in Table I.

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21. Kratzl and Däubner, ibid., 77, 519 (1944) [C. A., 40, 4697 (1946)].

Table I

Formation of β-Ketosulfonic Acids from Chalcones

Chalcone	Yield of Sulfonic Acid (%)		Melting Point Salt °C	
	By sulfite cooking[a]	From addn. of $NaHSO_3$	Benzylthiuronium	2-Naphthylamine
2-Hydroxy-	21	--	192	191 dec.
4-Hydroxy-3-methoxy-	52	100	181-2	--
4-Hydroxy-3,3',4'-trimethoxy	98	98	107[b]	156

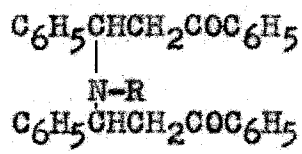
(a) The general procedure consisted of shaking the chalcone with sodium bisulfite and 100 ml. of 4% sulfurous acid for 19 hours at 135° in a sealed tube.
(b) Evolution of gas.

B. Nitrogen Compounds

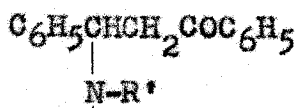
The general nature of the addition of amines and ammonia to α,β-unsaturated ketones has been known since the rather early beginnings of structural organic chemistry. This review, however, will consider only those reactions involving chalcones having no substituent other than hydrogen in either the α- or β-position. The addition of these reagents to α- or β-substituted chalcones has been reviewed by Cromwell[22].

22. Cromwell, Chem. Rev., 38, 83 (1946).

In 1898, Tambor and Wildi[23] reported the addition of ammonia and primary aromatic amines to chalcones. These reactions proceeded with ease either in the presence or absence of a basic catalyst. Secondary aromatic or mixed secondary aromatic-aliphatic bases failed to undergo the reaction. One molecule of the amine reacted exclusively with one or two moles of chalcones to give β-ketoamines of the structure (XIV) or (XV), respectively.



(XIV)



(XV)

R = H
= $-C_6H_3(CH_3)(NO_2)$-o,p-
= $-C_6H_4NO_2$-o,-m, or -p-
= $-C_{10}H_7$-α-

R' = $-C_6H_5$
= $-C_{10}H_7$-β
= $-C_6H_4CH_3$-p

No attempt was made to explain these differences in reactions among the amines indicated above.

In connection with a study of the three isomeric 4'-methylchalcones, Weygand and Mathes[24] observed that this un-

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23. Tambor and Wildi, Ber., 31, 349 (1898).

24. Weygand and Mathes, ibid., 59, 2247 (1926).

saturated ketone added one molecule of aniline yielding an addition product identical to that obtained by the addition of p-methylacetophenone to benzalaniline. Similar products resulted from the addition of aniline to 4'-ethylchalcone and 4'-propylchalcone and from the addition of p-toluidine to 4'-methoxychalcone.

β-Piperidinobenzylacetophenone was originally prepared by Georgi and Schwyzer[25] by the addition of piperidine to chalcone. The compound formed a stable hydrochloride and picrate but decomposed into the original ketone and piperidine when heated with water. More recently, Stewart and Pollard have reported the addition of piperazine[26] and morpholine[27] to a series of chalcones. These reactions were effected by heating the reagents together in ethanol or in hydrocarbon solvents. One molecule of the chalcone reacted with a molecule of morpholine while the bis-compound was obtained from one mole of piperazine and two moles of the ketone. 3,4-Methylenedioxychalcone and 2-nitrochalcone failed to undergo the reaction with piperazine while morpholine formed no addition product with 4-methoxy-4'-bromochalcone, 4-methoxy-4'-chlorochalcone, and 4,4'-dimethyl-

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25. Georgi and Schwyzer, J. prakt. Chem., 86, 273 (1912).
26. Stewart and Pollard, J. Am. Chem. Soc., 58, 1980 (1936).
27. Stewart and Pollard, ibid., 59, 2702 (1937).

chalcone[27]. According to Stewart[28], it is entirely possible that in these cases a product may have been formed but was too unstable to isolate.

In an effort to synthesize compounds of possible pharmacological value[29a,b] Cromwell, Wiles and Schroeder[29b] prepared β-amino-α-hydroxy- and α,β-diaminopropane derivatives by the reduction of the oximes obtained from these previously prepared β-aminoketones. Useful intermediates in the preparation of pharmaceuticals were obtained through the addition of tetrahydroisoquinoline to chalcone[30] and by the addition of a molecule of methylamine to two molecules of the ketone[31].

In contrast to the smooth 1,4-addition of amines to chalcones, the behavior of amino derivatives, commonly considered as carbonyl reagents, toward this unsaturated ketone is much more complex[32a,b]. Besides reactions involving 1,2-, 1,4-, and 3,4-additions, secondary products result

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28. Stewart and Pollard, ibid., 2006 (1937).

29. (a) Cromwell and Hoeksemm, ibid., 67, 1658 (1945); (b) Cromwell, Wiles and Schroeder, ibid., 64, 2432 (1942).

30. Cromwell and Burch, ibid., 66, 872 (1944).

31. Cromwell and Caughlin, ibid., 67, 2235 (1945).

32. (a) Gilman, "Organic Chemistry", John Wiley and Sons, Inc., New York, 1943, p. 678; (b) Reference 22 p. 121.

from oxidation-reduction reactions and from condensation reactions involving active hydrogen atoms in the primary addition product. In an acid medium, these reagents usually form phenylhydrazones, hydrazones, semicarbazones, and oximes, whereas alkaline media favor the formation of side products.

Blatt[33], however, has reported the reversible addition of methoxyamine to chalcone and a number of its 4- or 4'-substituted derivatives. Saturated β-methoxyaminoketones of the type (XVI) or, in some instances, methoxyamino-bis-propiophenones corresponding to the structure (XVII) were obtained.

1. $C_6H_5CH = CHCOC_6H_5 + CH_3ONH_2 \rightleftharpoons C_6H_5\underset{NHOCH_3}{CH}-CH_2COC_6H_5$

(XVI)

2. $C_6H_5\underset{NHOCH_3}{CH}-CH_2COC_6H_5$

$+$

$C_6H_5CH = CHCOC_6H_5 \longrightarrow C_6H_5\underset{NOCH_3}{CH}CH_2COC_6H_5$

$C_6H_5CHCH_2COC_6H_5$

(XVII)

These products exhibited weakly basic properties forming salts with the halogen acids and the corresponding acetyl

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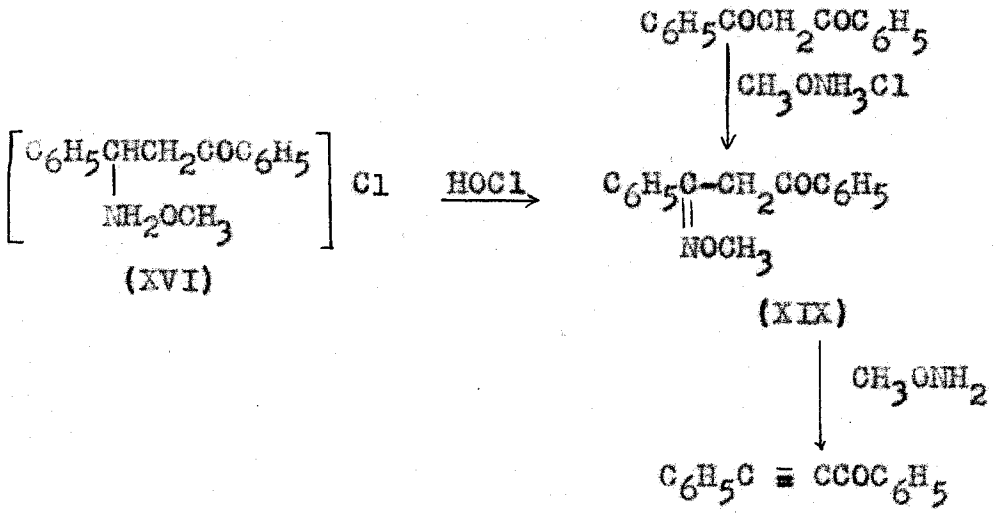
33. Blatt, J. Am. Chem. Soc., 61, 3494 (1939).

derivatives on treatment with acetic anhydride. They were unstable in the presence of aldehydes ("methoxyamine acceptors") and were decomposed by heating under ordinary pressure. The treatment of the β-methoxyaminoketone with strong alkali led to an interesting rearrangement in which the unsaturated α-aminoketone (XVIII) was formed through the loss of methanol and the subsequent shift of the nitrogen from the β- to the α-carbon atom.

$$\underset{\substack{\text{NHOCH}_3\\ \text{(XVI)}}}{\text{C}_6\text{H}_5\text{CHCH}_2\text{COC}_6\text{H}_5} \xrightarrow{\text{NaOCH}_3} \underset{\substack{\text{NH}_2\\ \text{(XVIII)}}}{\text{C}_6\text{H}_5\text{CH} = \text{CCOC}_6\text{H}_5} + \text{CH}_3\text{OH}$$

When β-phenyl-β-methoxyaminopropiophenone (XVI) as its hydrochloride was oxidized by hypochlorous acid, there was obtained the monoxime methyl ether of dibenzoylmethane (XIX) also synthesized independently from dibenzoylmethane and by the addition of methoxyamine to benzoylphenylacetylene, thus establishing the mechanism of 1,4-addition.



The mechanism of the addition of amines to α,β-unsaturated ketones has been excellently summarized by Cromwell[22] and is worthy of reproduction at this point of the discussion. He stated that α,β-unsaturated ketones,

$$\overset{4}{C}=\overset{3}{C}-\overset{2}{C}=\overset{1}{O}$$

in general, undergo 1,2-, 3,4-, and 1,4-additions. The position favored depends on three factors: (1) the groups attached to the conjugated systems, (2) the experimental conditions, and (3) the nature of the addenda. In the addition of amines, factors (1) and (3) are more important. The highly polar carbonyl group would be expected to confer electrophilic character on the olefinic carbon atom 4 by electromeric relay in such conjugated systems.

$$\overset{4}{C}=\overset{3}{C}\leftarrow\overset{2}{C}=\overset{1}{O}$$

Since bases are also known to add to the carbonyl double bond, carbon atoms 2 and 4 must be expected to be in competition as electrophilic centers. However, the product of addition to such systems is not always determined by the relative rates of the two competing reactions. It seems probable in this case, that the relative stability of the products resulting from competing reactions is of major importance. That is, $-\underset{\underset{N<}{|}}{C}-C-C=O$ is more stable and less susceptible to reversal than $-C=C-\underset{\underset{OH}{|}}{C}-N<$. Furthermore, resonance would be expected to favor the attack by the base at carbon atom 4. Although the carbonyl group activates the ethylenic double bond of the conjugated system, this group itself is less reactive toward bases when it occurs isolated.

In conclusion, Cromwell calls attention to the transition state for the addition of a base to the conjugated systems as described by Branch and Calvin*, and states that the driving force for such reactions may be logically assumed to be the attraction of the electrophilic carbon atom 4 for the unshared electrons of the amino nitrogen, keeping in mind, however, that the ability of amines to form C-N bonds is related to their basic strengths. Strong bases are strongly nucleophilic toward carbon, whereas, weaker bases retain a more than proportional activity toward carbon. The

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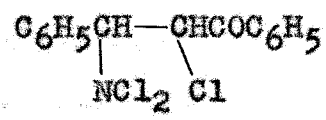
*Branch and Calvin, "The Theory of Organic Chemistry" Prentice-Hall, Inc., New York (1941).

factor of stability of the product and the steric factor of ease of approach of the nitrogen atoms to carbon atom 4 are of major importance.

The mode of migration of the hydrogen from the oxygen atom to carbon atom 3 may possibly be through the formation of an intermediate six-membered chelate-ring structure.

The addition of nitrogen trichloride to chalcone was reported by Coleman and Craig[34]. As in other addition reactions of chalcones not involving the carbonyl group, the negative part, $-NCl_2$, of the adding molecule was attached to the β-carbon atom of the unsaturated system whereas the chlorine atom was joined to the carbon adjacent to the carbonyl group. Hence, the compound β-(N-dichloroamino)-α-chloropropiophenone (XX) was formed.



(XX)

These investigators stated that while it might be possible to explain the formation of the product by a series of reactions following a 1,4-addition to the conjugated system, it seems more probable that the addition involves only the ethylenic linkage as in typical addition to unsaturated hy-

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34. Coleman and Craig, ibid., 49, 2593 (1927).

drocarbons.

The addition of nitrosyl chloride to chalcone has been reported[35] to take place at room temperature and in good yields. The resulting nitrosochloride yielded hydroxylamine on hydrolysis and formed a stable nitrolamine with piperidine.

Wieland[36] observed that three different reactions could occur when nitrous gases (a mixture of N_2O_3 and N_2O_4) acted upon chalcones. (1) An unstable β-nitroso-α-nitro derivative (XXI) capable of forming an oxazole (XXIII) through rearrangement and subsequent dehydration could be formed:

$$C_6H_5CH{=}CHCOC_6H_5 + N_2O_3 \longrightarrow C_6H_5CH(NO)CH(NO_2)COC_6H_5 \longrightarrow$$

(XXI)

$$C_6H_5C(=NOH)C(NO_2){=}C(OH)C_6H_5 \longrightarrow C_6H_5C\underset{\underset{N}{\|}}{-}C(NO_2){=}C\underset{\underset{O}{|}}{C}C_6H_5$$

(XXII) (XXIII)

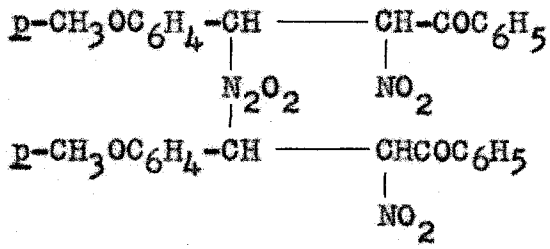
(2) A nitronitrite, $C_6H_5CH(ONO)CH(NO_2)COC_6H_5$ (XXIV), could result; or (3) the nitration of the p-position of a phenyl nucleus could occur. Actually, there was isolated from the reaction β-p-dinitrochalcone, $p\text{-}NO_2C_6H_4C{=}\underset{NO_2}{C}HCOC_6H_5$, the

35. Perrot, Compt. rend., 203, 329 (1936).

36. Wieland, Ann., 328, 154 (1903).

nitronitrite (XXIV), and a complex anhydride, $C_{30}H_{24}O_{13}N_6$.

In contrast to the action of nitrogen tetroxide, N_2O_4, on chalcone, 4-methoxychalcone formed the pseudonitrosite[37] (XXV) which was converted into the isooxazole by boiling with alcohol.



(XXV)

4-Methoxychalcone-α-nitro-β-nitrite was also a product of the reaction. In a further study of the reaction Bauer and Seyfarth[38] obtained only 4-dimethylamino-3-nitrochalcone when the addition of nitrous oxide to 4-dimethylaminochalcone was attempted. They suggested that the influence exerted by the phenyl group on the ease of addition of reagents to the conjugated system was offset by the basic group in the p-position.

The action of absolute nitric acid on 3,3'-dinitrochalcone and 4,3'-dinitrochalcone was studied by Van der Lee[39].

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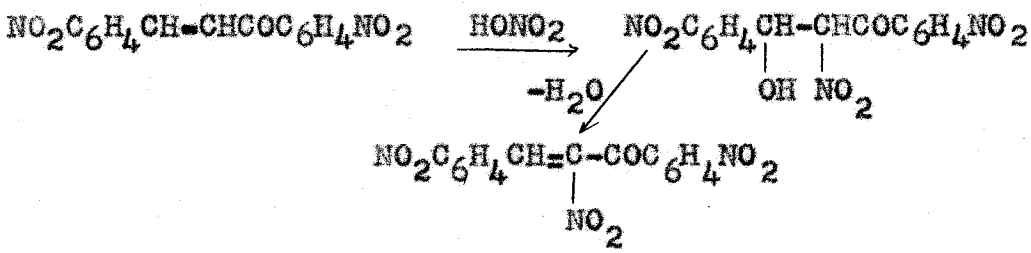
37. Wieland and Bloch, ibid., 340, 63 (1905).

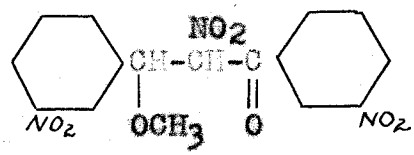
38. Bauer and Seyfarth, Ber., 63, 2691 (1930).

39. Van der Lee, Rec. trav. chim., 47, 920 (1928).

In each case, an additional nitro group entered the α-position of the chalcone.



The products were stable toward base at room temperature and formed ethers of the type (XXVI) on recrystallization from methanol or ethanol.



(XXVI)

The addition of diazo compounds to chalcones has been reported by Kohler and Steele[40] and by Smith and Pings[41]. Ethyl 4-phenyl-5-benzoylpyrazolinecarboxylate-3 (XXVII) resulted from the addition of ethyl diazoacetate to chalcone. This ketonic pyrazoline was decomposed on heating to the corresponding pyrone (XXVIII)[40].

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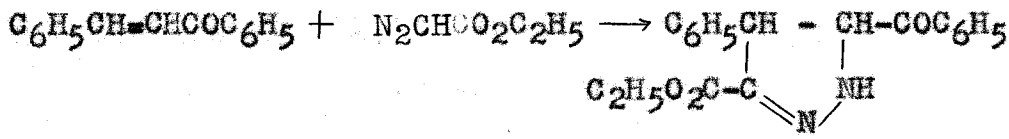
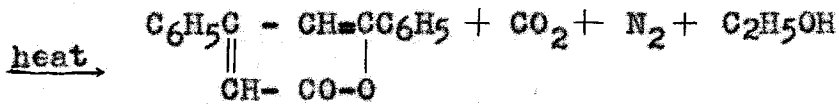
40. Kohler and Steele, J. Am. Chem. Soc., 41, 920 (1919).

41. Smith and Pings, J. Org. Chem., 2, 23 (1939).

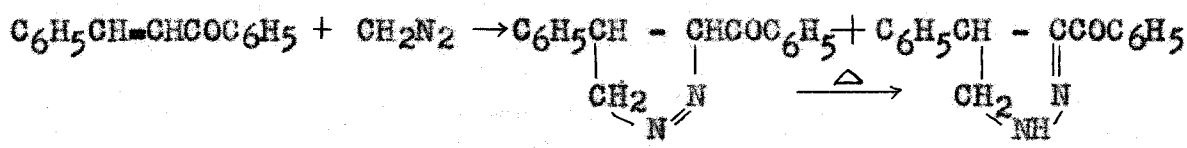


(XXVII)



(XXVIII)

Two isomeric pyrazolines (melting at 92-93° and 127-129°, respectively) were obtained from the addition of diazomethane to chalcone[41]. The conversion of the lower melting product (XXIX) into its isomer (XXX) was effected by the gentle heating above its melting point.



(XXIX) (XXX)

Although the addition of aliphatic nitro compounds to chalcones does not directly involve the nitrogen atom or the nitro group, these types of reactions will be discussed here. Much of this work was carried out by Kohler and his students[42-45] in connection with a study of the syntheses of

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42. Kohler, J. Am. Chem. Soc., 38, 889 (1916).

43. Kohler and Englebrecht, ibid., 41, 1379 (1919).

44. Kohler and Williams, ibid., 1644 (1919).

certain cyclopropane derivatives. They found that these compounds readily added to chalcone[42], 4'-bromochalcone[44], and 4'-methylchalcone[45] in the presence of a secondary base or sodium methoxide.

$$C_6H_5CH{=}CHCOC_6H_5 + CH_3NO_2 \xrightarrow[(2)HCl]{(1)NaOCH_3} C_6H_5\underset{\displaystyle CH_2NO_2}{\underset{|}{CH}}\text{-}CH_2COC_6H_5$$

The reaction was general for most primary and secondary nitro compounds. However, the addition was much slower in the case of the secondary compounds. The addition of β-nitropropane to chalcone required several weeks' standing at room temperature after which time a 92 percent yield of the corresponding tertiary nitroketone was obtained. These reaction differences were explained on the basis of steric hindrance[42]. Phenylnitromethane was also found to undergo the reaction.

Analogous reactions were observed to take place between nitroesters and chalcones[42]. A mixture of products resulted except in the case of the secondary compounds. In this instance, the sole product was a lactone of the structure (XXXI).

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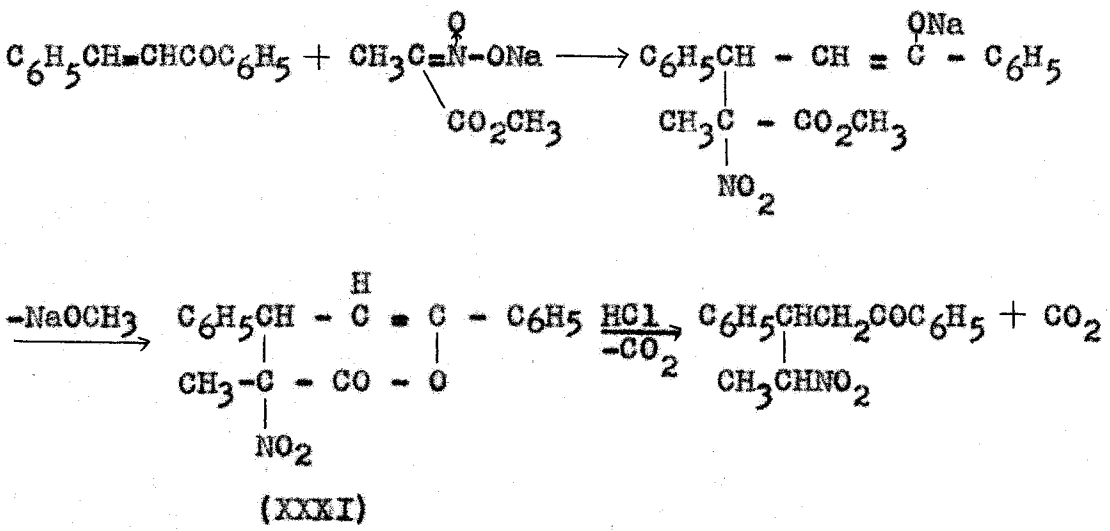
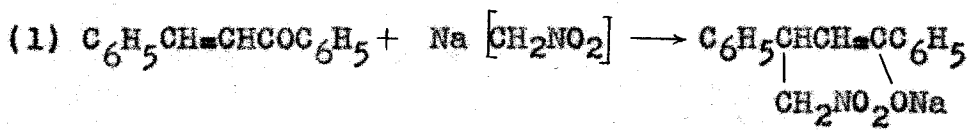
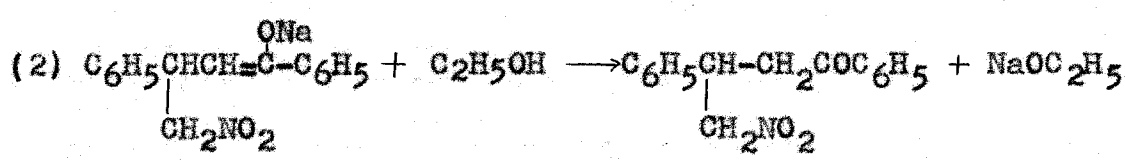
45. Kohler and Allen, ibid., 50, 884 (1928).



(XXXI)

In summarizing the mechanism of the reaction, Kohler pointed out that lactone formation indicated that the 1,4-addition of the sodium salt of aliphatic nitro-compounds to the conjugated system, -C=C-C=O, follows the same pattern as the addition of Grignard reagents (see page 30) in which the metallic residue unites with the oxygen and the remainder of the molecule goes to the β-carbon atom. The complete picture of the reaction may be represented in the following manner[42].





More recently, Worrall and Bradway[46] reported a similar

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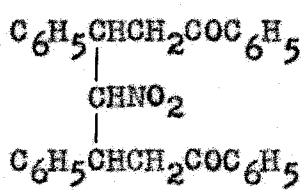
46. Worrall and Bradway, ibid., 58, 1607 (1936); Kloetzel, J. Am. Chem. Soc., 69, 2271 (1947).

reaction in which nitromethane was added to chalcone in the presence of alcoholic ammonia. They postulated that the nitroketone resulted from the 1,4-addition of the ammonium salt of nitromethane and the subsequent spontaneous decomposition of the primary addition product. The trimolecular compound (XXXII) was also obtained by this method.



(XXXII)

C. Organometallic Compounds

The study of the addition of organometallic compounds to chalcones is of cardinal importance. "With the Grignard reagent, the mechanism of 1,4-addition has been established and the effect of substituents on the mode of addition has been determined. Furthermore, from information concerning the addition of the Grignard reagent, it is often possible to predict the mode in which other reagents might add and to draw reasonable inferences about the mechanism of addition"[47].

These classical studies were begun by Kohler[48] in 1903.

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47. Reference 32(a), p. 672.

48. Kohler, Am. Chem. J., 29, 342 (1903).

In an attempt to prepare diphenylstyrylcarbinol from chalcone and phenylmagnesium bromide, he obtained the saturated ketone, α,β-diphenylpropiophenone. The mechanism of this anomalous reaction required the intermediate formation of either the bromomagnesium derivative (XXXIII) as a result of the 3,4-addition of the Grignard reagent to chalcone or the bromomagnesium enolate (XXXIV) formed through the 1,4-addition[49] of phenylmagnesium bromide to the unsaturated ketone.

$(C_6H_5)_2CHCHCOC_6H_5$ (XXXIII)
|
MgBr

$(C_6H_5)_2CHCH{=}CC_6H_5$ (XXXIV)
|
OMgBr

Since the direct addition of Grignard reagents to isolated olefinic systems is highly improbable and since the newly formed magnesium derivative did not yield a tertiary alcohol when treated with an active ketone, the mechanism involving the intermediate formation of (XXXIII) was promptly discarded. The fact that the corresponding ester was obtained on treating the compound with benzoyl chloride was accepted at that time[49] as the conclusive proof for the intermediate formation of the enolate, (XXXIV). This proof of structure based on the benzoylation of the magnesium enolate was later shown to be invalid[50].

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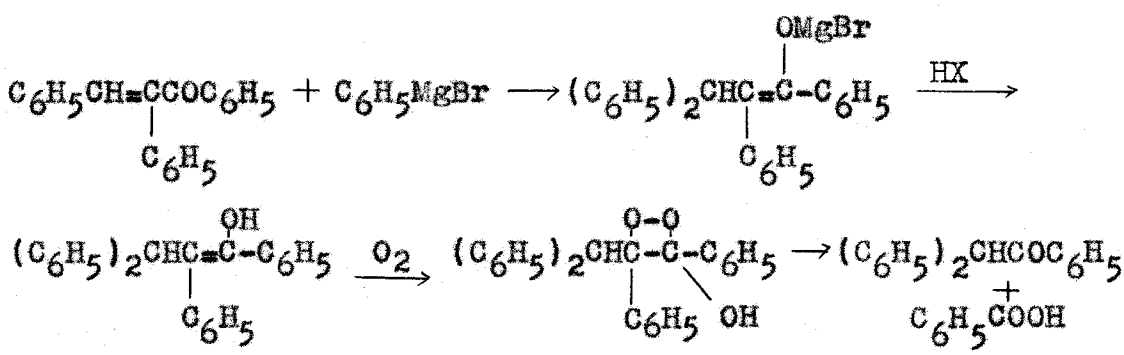
49. Kohler, ibid., 31, 642 (1904).

50. Kohler and Tishler, J. Am. Chem. Soc., 54, 1594 (1932).

Later Kohler and his students[51] presented conclusive proof for the 1,4-addition of the Grignard reagent to α,β-unsaturated ketones. Phenylmagnesium bromide was added to a derivative of chalcone in which the carbonyl group was highly hindered, for example, benzalacetomesitylene or α-phenylchalcone. The product was an enolate in which the magnesium halide group was joined to oxygen and was sufficiently stable to permit isolation. The structure of the 1,4-addition product was established by the conversion of this enolate into its peroxide and identification of the decomposition products obtained therefrom.



The formation of secondary products from the interaction of phenylmagnesium bromide and chalcone has been shown to take place also through 1,4-addition according to the following scheme[52].

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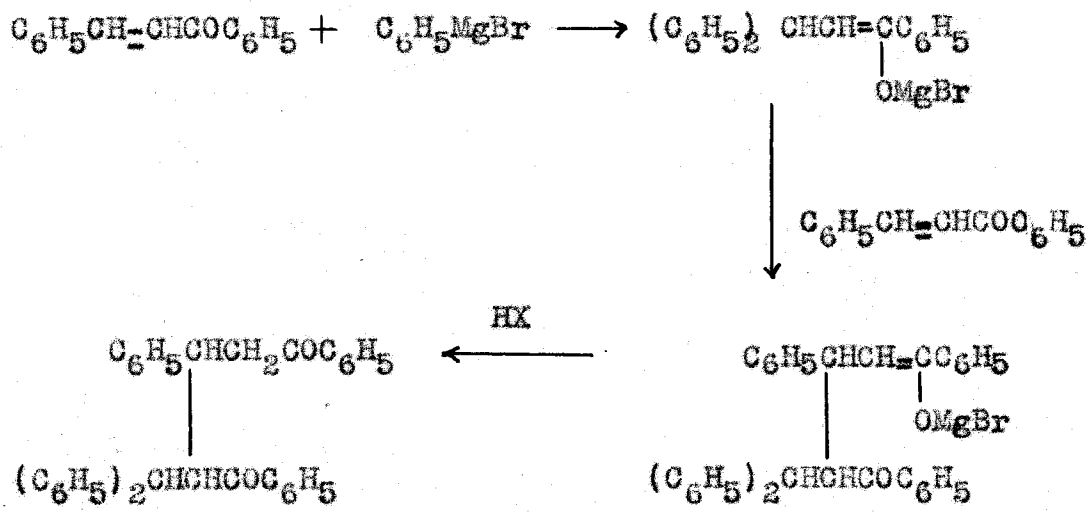
51. Kohler and Mydans, ibid., 4667 (1932); Kohler, Tishler, and Potter, ibid., 57, 2517 (1935).

52. Kohler and Peterson, ibid., 55, 1073 (1933).

53. Kohler, Am. Chem. J., 38, 514, 548 (1907).



The results of an early series of investigations (see Table II) in which both the Grignard reagent and the chalcone were varied indicate no differences in the mode of addition.

In this connection, however, MacClean and Widdows[54] have reported the 1,2-addition of phenylmagnesium bromide to 4-dimethylaminochalcone. Gilman and Kirby[55] were unable to confirm these results. They obtained the 1,4-addition product exclusively.

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54. MacClean and Widdows, J. Chem. Soc., 105, 2169 (1914).

55. Gilman and Kirby, J. Am. Chem. Soc., 63, 2046 (1941).

Table II

The Addition of Grignard Reagents to Chalcone

Ketone	RMgBr	Yield 1,4-product (%)	Ref.
4-Methoxychalcone	C_6H_5-	96	53
	C_2H_5-	98	"
Chalcone	C_6H_5-	94	"
	C_2H_5-	98	"
	C_6H_{11}-	95	56
	α-$C_{10}H_7$	--	57

Recently, interesting applications of the reaction involving the addition of Grignard reagents to chalcones have been reported. Fuson and others[58] have added arylmagnesium halides to certain polyalkylated chalcones. The resulting magnesium enolates were sufficiently stable to permit their

56. Kohler and Burnley, Am. Chem. J., 43, 412 (1910).

57. Kohler and Heritage, ibid., 33, 21 (1905).

58. Fuson, Maynert, and Shenk, ibid., 67, 1939 (1945); Fuson and Rachlin, ibid., 2055 (1945).

conversion into the peroxide from which was obtained the corresponding vinyl alcohol through thermal decomposition. The reaction has also been used by Tallman and Stuart[59] in the syntheses of estrogenic substances. 4,4'-Dimethoxychalcone when treated with ethylmagnesium bromide gave rise to 1,3-bis(p-methoxyphenyl)-1-pentanone. The catalytic hydrogenation of this compound yielded the corresponding hydrocarbon derivative which after the hydrolysis of the methoxy groups was converted into the dipalmitate. The dipalmitate of 2,4-bis(p-hydroxyphenyl)-3-ethylhexane prepared according to this procedure exhibited estrogenic properties.

Significant studies relating the reactivities of organometallic compounds to their mode of addition to chalcone have been carried out in these laboratories[55,60]. Generally the manner in which phenylmetallic compounds add to the unsaturated ketone depends upon their relative reactivities. The lesser reactive compounds of beryllium, magnesium, zinc, aluminum, and manganese show predominantly 1,4-addition whereas the highly active compounds of calcium and potassium

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59. Tallman and Stuart, U. S. Patent 2,400,033 (1946) /C. A., 40, 4484 (1946)/.

60. (a) Gilman and Bailie, J. Org. Chem., 2, 84 (1937); (b) Gilman and Jones, J. Am. Chem. Soc., 61, 1513 (1939); (c) Gilman and Jones, ibid., 62, 2353 (1940); (d) Gilman and Jones, ibid., 980 (1940); see also reference 32(a), page 511.

show 1,2-addition. Those organometallic compounds of intermediate activity--phenyllithium[61] and phenylsodium--show both 1,2- and 1,4-addition.

Gilman and Kirby[55] have suggested the application of the reaction between phenylmetallic compounds and chalcone as a means of establishing metal-metal interconversions of the following type:

$$BeCl_2 + 2C_6H_5Li \longrightarrow (C_6H_5)_2Be + 2LiCl \quad (1)$$

$$MnI_2 + C_6H_5Li \longrightarrow C_6H_5MnI + LiI \quad (2)$$

$$MgI_2 + p\text{-}(CH_3)_2NC_6H_4Li \longrightarrow p\text{-}(CH_3)_2NC_6H_4MgI + LiI \quad (3)$$

Thus, when an equimolar mixture of magnesium iodide and p-dimethylaminophenyllithium react with chalcone, only the 1,4-addition product should be obtained.

1,4-Addition products have also been obtained by Bergmann[62a] from the addition of benzhydrylsodium to chalcone and to 4-methoxychalcone and by Michael and Saffer[62b] from the reaction between triphenylmethylsodium and chalcone.

Kohler and Heritage[63] obtained the corresponding β-hy-

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61. The exclusive 1,2-addition of phenyllithium was reported earlier by Luttringhaus, Ber., 67, 1602 (1934). A revision of this work in which both 1,2- and 1,4-addition products were obtained has been published recently. Luttringhaus and Scholtis, Ann., 557, 70 (1945).

62. (a) Bergmann, J. Chem. Soc., 412 (1936); (b) Michael and Saffer, J. Org. Chem., 8, 60 (1943).

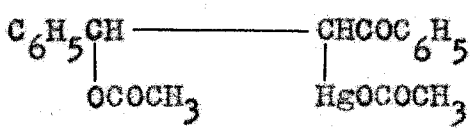
63. Kohler and Heritage, Am. Chem. J., 43, 475 (1910).

droxyester when chalcone was treated with an α-bromoester and zinc. 2',4',6'-Trimethylchalcone in which the carbonyl group is highly hindered did not undergo the reaction.

$$C_6H_5CH{=}CHCOC_6H_5 + BrZnCH_2CO_2CH_3 \longrightarrow$$

$$C_6H_5CH{=}CHC(OZnBr)(CH_2CO_2CH_3)C_6H_5 \longrightarrow C_6H_5CH{=}CH{-}C(OH)(CH_2CO_2CH_3){-}C_6H_5$$

Although not an organometallic compound, mercuric acetate has been observed to add to chalcone as $-OCOCH_3$ and $-HgOCOCH_3$. The resulting product (XXXV) was believed to have been formed by way of addition to the 3,4-ethylenic system[64].



(XXXV)

D. Compounds Containing Active Methylene Groups

The condensation of chalcones with compounds containing a hydrogen atom activated by an adjacent unsaturated group has been quite generally studied. Reactions of this type take place in the presence of small amounts of a secondary

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64. Middleton, J. Am. Chem. Soc., 45, 2763 (1923).

amine or inorganic base and are in many cases reversible.

$$C_6H_5CH{=}CHCOC_6H_5 + CH_3COCH_2CO_2C_2H_5 \xrightarrow{NaOCH_3} C_6H_5\underset{\displaystyle CH_3COCHCO_2C_2H_5}{\underset{|}{CH}}\text{-}CH_2COC_6H_5$$

Some typical examples of this general reaction are summarized in Table III.

Within recent years, several papers have been published on the mechanism and products of the Michael condensation with chalcones and active methylene compounds. In general, these investigations have been concerned with the structural nature and reactions of the adding molecule rather than the general reactions of chalcones. For information on this particular aspect of the reaction the reader is referred to the series of studies indicated in reference 82.

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65. Vorländer, Ann., 294, 332 (1897).

66. Knoevenagel and Speyer, ibid., 35, 397 (1902).

67. Kohler, Am. Chem. J., 37, 385 (1907).

68. Kohler, J. Am. Chem. Soc., 44, 842 (1922).

69. Borsche, Ber., 42, 4497 (1909).

70. Meerwein, J. prakt. Chem., 97, 271, 284 (1918).

71. Knoevenagel, Ann., 281, 25 (1894).

72. Abell, J. Chem. Soc., 83, 360 (1903).

73. Kostanecki, Ber., 29, 240 (1896); Kostanecki and Rossbach, ibid., 1488 (1896).

74. Georgi and Holland, J. prakt. Chem., 86, 232 (1912).

Table III

Condensation Products from Chalcones and Active Methylene Compounds

Acceptor	Addendum	Product[a]	Ref.
Chalcone	Diethyl malonate	β-Phenyl-γ-benzoylbutyric acid	66
"	Acetoaceticester	Ethyl α-(1-phenyl-2-benzoylethyl)acetoacetate[b]	66, 67
"	"	1,3-Diphenyl-4-carboethoxy-4-cyclohexanone-5	66
"	Diethyl methylmalonate	Methyl β-phenyl-γ-benzoylethylmethylmalonate	68
4'-Bromochalcone	"	Methyl β-phenyl-γ-(4-bromobenzoyl)-ethylmethylmalonate	"
4'-Methoxychalcone	"	Methyl β-phenyl-γ-(4-methoxybenzoyl)-ethylmethylmalonate	"
Chalcone	Ethyl phenylacetate	Ethyl α,β-diphenyl-γ-benzoylbutyrate	69
"	Phenylacetaldehyde	δ-Hydroxy-α,β,δ-triphenylvaleric acid[c]	70
"	Desoxybenzoin	1,2-Diphenyl-1,3-dibenzoylpropane	71
"	Propiophenone	1,3-Dibenzoyl-2-phenyl-1-methylpropane 1,3,5-Tribenzoyl-2,4-diphenyl-1-methylpentane	72

Table III (continued)

Acceptor	Addendum	Product[a]	Ref.
Chalcone	Acetophenone	Dibenzalacetophenone	73
"	Cyclopentanone	α-Benzoyl-β-phenyl-β-cyclopentanonylethane	74 75a,c
4'-Methoxychalcone	"	α-Benzoyl-β-anisyl-β-cyclopentanonylethane	76
Chalcone	3-Methylcyclohexanone	α-Benzoyl-β-phenyl-β-(3-methylcyclohexanonyl)ethane[b]	77a,b
4-Methoxychalcone	"	α-Benzoyl-β-anisyl-β-(3-methylcyclohexanonyl)ethane[b]	77a,c
Chalcone	Dihydroresorcinol	2-(1-Phenyl-2-benzoylethyl)cyclohexane-2,6-dione	78
"	Fluorene[d]	β-(9-Fluorenyl)-β-phenylpropiophenone[e]	79
"	Cyclopentadiene	β-Phenyl-β-cyclopentadienylpropiophenone	79
"	Anthrone	β-Anthronyl-β-phenylethylphenyl ketone	70
"	Benzalaniline hydrocyanide	γ-Cyano-α-benzoyl-γ-anilino-βγ-diphenylpropane	80
4'-Methoxychalcone	Benzylcyanide	α,β-Diphenyl-γ-(p-methoxybenzoyl)butyronitrile	81

(a) The nomenclature is that employed by the original investigator. (b). Sterioisomeric compounds were obtained. (c). The intermediate α,β,δ-triphenyl-δ-keto-n-valeraldehyde could not be isolated. (d). The compound did not add to 3- or 4-nitrochalcone. (e). The reaction did not take place in the presence of a secondary base.

E. Aromatic Hydrocarbons

Aromatic hydrocarbons add to chalcones in the presence of anhydrous aluminum chloride[16,83] or sulfuric acid[49].

$$C_6H_5CH{=}CHCOC_6H_5 + C_6H_6 \xrightarrow{AlCl_3} (C_6H_5)_2CHCH_2COC_6H_5$$

The mechanism of the reaction is not too clear at present. However, Vorländer and Friedberg[16] have suggested that the usual Friedel and Crafts reaction between the hydrocarbon and the intermediately formed hydrogen halide addition product of the chalcone takes place when aluminum chloride

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75. (a) Stobbe and Volland, Ber., 35, 3973 (1902); (b) Stobbe, J. prakt. Chem., 86, 209 (1912); (c) Stobbe, Ber., 35, 1445 (1902).

76. Stiegler, J. prakt. Chem., 86, 241 (1912).

77. (a) Stobbe, ibid., 218 (1912); (b) Rosenberg, ibid., 250 (1912); (c) Cruikshanks, ibid., 269, (1912); (d) Stiegler, ibid., 257 (1912).

78. Mikhailov, J. Gen. Chem. (U.S.S.R.), 7, 2950 (1937) /C. A., 32, 5402 (1938)/.

79. Taylor and Connor, J. Org. Chem., 6, 696 (1941).

80. Clark and Lapworth, J. Chem. Soc., 91, 704 (1907).

81. Allen, J. Am. Chem. Soc., 49, 1112 (1927).

82. Holden and Lapworth, J. Chem. Soc., 2368 (1931); Michael and Ross, J. Am. Chem. Soc., 55, 1632 (1933); Connor and Andrews, ibid., 56, 2713 (1934); Breslow and Hauser, ibid., 62, 2389 (1940); Hauser and Abramovitch, ibid., 1763 (1940); deBenneville, Clagett, and Connor, J. Org. Chem., 6, 690 (1941); Taylor and Connor, ibid., 696 (1941); Connor and McClellan, ibid., 3, 570 (1939).

is used as the catalyst. They showed that the stable hydrochloride of chalcone reacts with benzene and aluminum chloride in the usual manner yielding the same product which can be obtained directly from the chalcone in the manner indicated by the above equation. On the other hand, 4-methoxychalcone does not undergo the reaction since it forms no stable addition product with the halogen acids. As further support for their viewpoint, they showed that an exchange of radicals takes place between the benzenesulfonyl group, $C_6H_5SO_2$-, and the phenyl radical when β-phenyl-β-phenylsulfonylpropiophenone (page 9) is refluxed with a mixture of benzene and aluminum chloride. β-Phenyl-β-(p-methoxyphenylsulfonyl)propiophenone is stable under these conditions.

Eaton, Black and Fuson[83] have reported the reversible addition of aromatic hydrocarbons to chalcones. They found that generally chalcones of the type XC_6H_4-CH=CHCOC_6H_5 (XXXVI) (X = o, m, or p-Cl; m and p-Br; p-CH_3) react with benzene in the presence of aluminum chloride and hydrogen chloride yielding β,β-diphenylpropiophenone (XXXVII) as the exclusive product.

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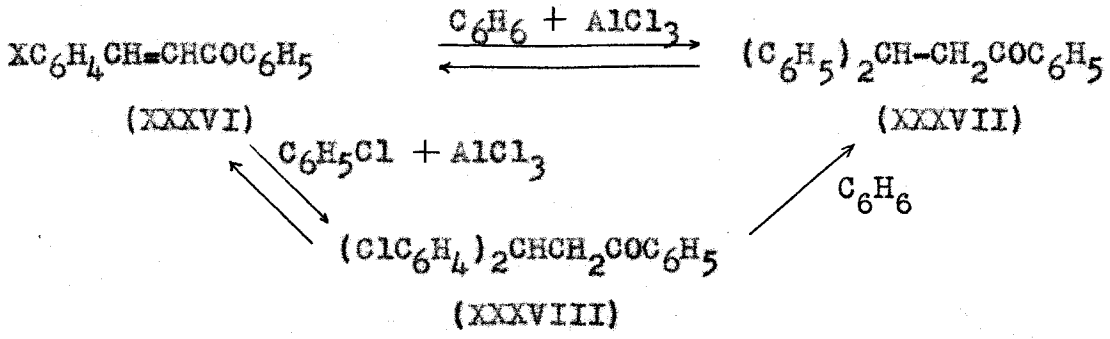
83. Eaton, Black, and Fuson, J. Am. Chem. Soc., 56, 687 (1934); Alexander, Jacoby, and Fuson, ibid., 57, 2208 (1935).



One product, β,β-di(p-chlorophenyl)propiophenone (XXXVIII) was obtained from chalcones of the type (XXXVI) (X is a halogen atom) and chlorobenzene regardless of the nature or position of the substituent X. Furthermore, the compound (XXXVIII) could be converted into the compound (XXXVII) by refluxing with benzene. On the basis of these experimental results, Fuson and his colleagues[83] concluded that as a necessary consequence of assuming the reversibility of the reaction, any halophenyl radical can be replaced by any other aromatic group.

F. Phosphorus Halides

The addition of phosphorus trichloride to chalcone is unique in that it represents a case in which a single atom by increasing its valence unites with the conjugated system of the α,β-unsaturated ketone[84]. This type of reaction was

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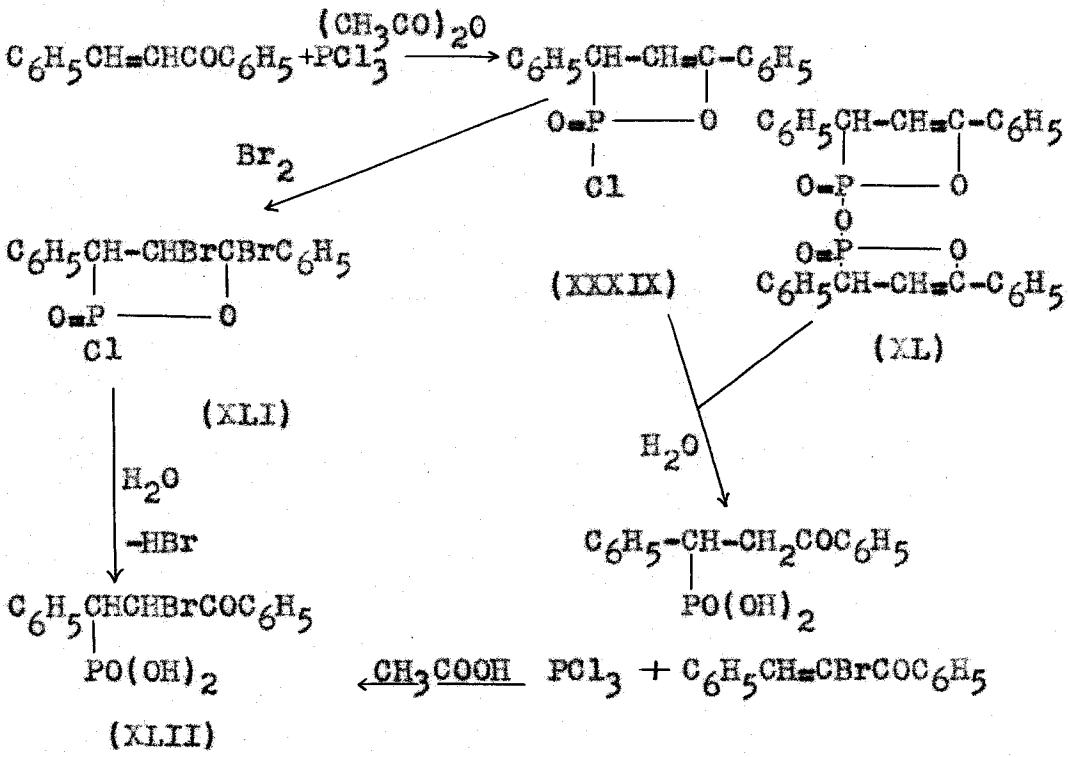
84. Conant and Cook, ibid., 42, 830 (1920).

85. Conant, ibid., 39, 2679 (1917).

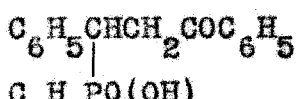
first reported by Conant[85] who obtained the corresponding β-ketophosphonic acid from the action of phosphorus trichloride on 4-methoxychalcone in glacial acetic acid. Upon using acetic anhydride as the solvent Conant and Cook[84] were able to obtain an intermediate cyclic acid chloride (XXXIX) and the anhydride (XL) which upon hydrolysis yielded the β-ketophosphonic acid (XLI). The fact that these intermediate products added a molecule of bromine established their structure and conclusively proved their formation by 1,4-addition.



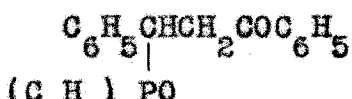
After a comparative study of the reactions of phosphorous trichloride[84,85], phenyldichlorophosphine[86], and diphenyl-

86. Conant and Pollack, ibid., 43, 1665 (1921).

chlorophosphine, respectively, with chalcone, Conant and his colleagues concluded that the behavior of these three halides was completely parallel. The final product from the reaction with phenyldichlorophosphine was the β-ketophenylphosphonic acid (XLIII)[87]; the β-ketodiphenylphosphine oxide (XLIV)[88] was obtained from diphenylchlorophosphine and



(XLIII)



(XLIV)

chalcone. In concluding these investigations it was shown that mono- and diphenoxychlorophosphines add to chalcones giving the mono- or diphenylester of the phosphonic acid also obtainable from the corresponding acid and phenol.

Drake and Marvel[89] successfully applied these reactions to the syntheses of β-ketophosphonic esters of long-chained aliphatic alcohols. They were unable to effect a similar addition to chalcones with arsenic trichloride.

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87. Conant, Braverman, and Hussey, ibid., 45, 165 (1923).

88. Conant, Wallingford, and Candheker, ibid., 43, 762 (1921); Conant and Jackson, ibid., 46, 1003 (1924).

89. Drake and Marvel, J. Org. Chem., 2, 387 (1939)

C. Miscellaneous Compounds

The general mode of the addition of halogens to chalcones is the one common to most olefinic compounds. In certain cases, however, isomeric dihalides of chalcones have been isolated[90]. Also anomalous reactions in which no addition takes place have been reported[38] as in the case of 4-dimethylaminochalcone.

The mechanism of the addition of halogen acids to chalcones probably involves an initial 1,4-addition followed by ketonization.

$$C_6H_5CH{=}CHCOC_6H_5 + HCl \longrightarrow C_6H_5\underset{Cl}{CH}\text{-}C{=}\underset{OH}{C}\,C_6H_5 \longrightarrow C_6H_5\underset{Cl}{CH}\text{-}CH_2COC_6H_5$$

The β-halogenated ketone is invariably the resulting product. In some instances, however, this addition takes place with difficulty, e.g., with 4-methoxy- and 4-hydroxychalcone, and the products dissociate with unusual ease[16,91] (see page 40).

Chalcones can be reduced catalytically or by metal combinations to the corresponding saturated ketones. In the

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90. Pond, York, and Moore, J. Am. Chem. Soc., 23, 789 (1901); Abell, J. Chem. Soc., 101, 998 (1912).

91. (a) Vorländer and Mumme, Ber., 36, 1470 (1903); (b) Vorländer and Tubant, ibid., 37, 1644 (1904); (c) Vorländer, Ann., 341, 1 (1905); (d) Vorlander, Ber., 58, 118 (1925).

latter case, however, bimolecular compounds often result[92]. The work of Kohler and Thompson[93] points out that catalytic hydrogenation possibly involves the 1,4-addition of hydrogen to the conjugated system and proves conclusively that reduction by metal combinations proceeds by this mechanism. According to these investigators, 1,2- and 1,4-addition are competing reactions in the catalytic reduction of α,β-unsaturated ketones, and the outcome depends on the same factors that control the mode of addition of Grignard reagents. Thus, when phenylbenzalacetomesitylene was reduced with hydrogen and palladium on calcium carbonate, the product was a mixture of 88 percent benzhydrylacetomesitylene and 12 percent of its enol. These results proved that at least 12 percent of the product was due to 1,4-addition but left doubt as to whether the remainder resulted from 1,2-addition or from the ketonization of the enol. The product obtained from the reduction of the chalcone with zinc and hydrochloric acid yielded the same amount of peroxide formed from the addition product of benzalacetomesitylene and phenylmagnesium bromide. This proved conclusively that the reduction of α,β-unsaturated ketones with metal combinations involves the

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92. Harries and Hübner, Ann., 296, 295 (1897); Conant and Cutter, J. Am. Chem. Soc., 48, 1020 (1926).

93. Kohler and Thompson, ibid., 59, 887 (1937).

94. Weidlich and Meyer-Delius, Ber., 74, 1195 (1941).

1,4-addition of hydrogen to the conjugated system.

Weidlich and Meyer-Delius[94] have attacked the problem of the reduction of α,β-unsaturated ketones from the standpoint of two possible basic mechanisms--the "ionic" and the "atomic." By the former mechanism which appears to predominate in acid medium, they postulated the formation of a mesomeric cation with which hydrogen reacts as H H, the H anion going either to the carbenium C of the limiting for-

$$R_2C{=}CHCOR + HX \rightleftarrows \underset{\text{"a"}}{\left[R_2C{=}C\overset{R}{H}C{=}\overset{(+)}{\underset{}{O}}\right]} \longrightarrow H \longleftrightarrow \underset{\text{"b"}}{R_2C{=}CH\overset{(+)}{C}R{-}\bar{O}H} \longleftrightarrow$$

$$\underset{\text{"c"}}{\left[R_2\overset{(+)}{C}CH{=}\overset{R}{C}{-}\bar{O}H\right]}\ X^-$$

mula "b" or to the β-carbon atom of the limiting formula "c", while the H cation combines with X to form HX. However, "b" by polarization of the double bond, induced by the charge on the carbenium carbon atom, may react in the following manner:

$$\left[R_2\underset{+(-)}{C}\bar{C}H{-}\overset{+}{C}R{-}\bar{O}H\right]X^- + H^+H^- \longrightarrow \left[R_2\overset{(+)}{\underset{H}{C}}{-}\underset{H}{C}{-}\overset{(+)}{C}R{-}\bar{O}H\right]X^- \longrightarrow R_2CHCH_2COR + HX$$

Hence, in acid medium in addition to the saturated ketone, R_2CHCH_2COR, the carbinol, $R_2CHCH_2CH(OH)R$ should be formed.

An alkaline medium favors the "atomic" mechanism in which the hydrogen reacts in the form of single hydrogen atoms. The OH anion of the alkaline solvent takes posses-

sion of the nucleus of a hydrogen atom with the formation of water while the electron of the hydrogen atom is taken up by the electrophilic oxygen of the carbonyl group. From the ketone there is then formed a radical-like anion with an isolated electron:

$$R_2C{=}CHCR{=}O + Na^+ OH^- + H \longrightarrow [R_2C{=}CHCR\bar{O}] \longleftrightarrow [R_2CCH{=}CR\bar{O}]^- Na^+ + H_2O$$

A carbinol, $R_2C{=}CHCH(OH)R$, or an enol, $R_2CHCH{=}C(OH)R$, depending on the position of the mesomerism is then formed as a result of the combining of a second atom of hydrogen with the radical-like anion. In an alkaline medium, mesomerism favors 1,4-addition--the formation of the enol or saturated ketone. On the basis of these theoretical considerations, the authors concluded that the products of the catalytic hydrogenation of chalcone in an acid medium result from 1,2- or 3,4-addition while those in an alkaline medium result from the 1,4-addition to the conjugated system. Their experimental results were in agreement with the theoretical predictions.

Examples of the selective catalytic reduction of chalcones using ferric chloride[95a], ferrous sulfate, or zinc acetate[95b] as promoters have been reported. No theories in-

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95. (a) Weygand and Werner, Ber., 71, 2469 (1938); Weygand and Meusel, ibid., 76, 498 (1943); (b) Csuros, Zech, and Geczy, Hung. acta chim., 1, 1 (1946) /C. A., 41, 109 (1947)/

volving the addition of hydrogen to the unsaturated system were presented, however.

The addition of hydrocyanic acid to chalcones affords an excellent method for synthesizing substituted β-ketobutyronitriles or β-ketobutyric acids. In this connection, Hann and Lapworth[96] made a study of the experimental factors affecting the addition of hydrogen cyanide to chalcone. They found that the reaction proceeded smoothly and almost quantitatively without the formation of secondary condensation products if both potassium cyanide and free hydrocyanic acid were present and if the alkalinity of the medium was not too high. Their product was identical with that previously obtained by Rupe and Schneider[97] from β-chloro-β-phenylpropiophenone and potassium cyanide. More recently, the mechanism of this addition reaction has been clarified by Michael and Weiner[98]. They were able to show that when chalcone is boiled with potassium isocyanide in methanol, the condensation product, $C_{31}H_{25}ON$ (also obtained by previous investigators[96,97]), results. The first stage of the reaction was assumed to result in the formation of the enol-

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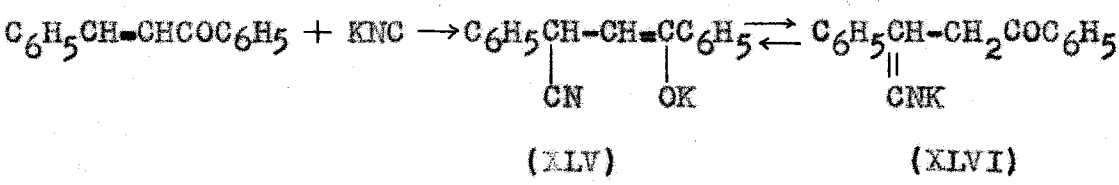
96. Hann and Lapworth, J. Chem. Soc., 85, 1355 (1904); Lapworth and Wechsler, ibid., 97, 38 (1910).

97. Rupe and Schneider, Ber., 28, 960 (1895).

98. Michael and Weiner, J. Am. Chem. Soc., 59, 744 (1937).

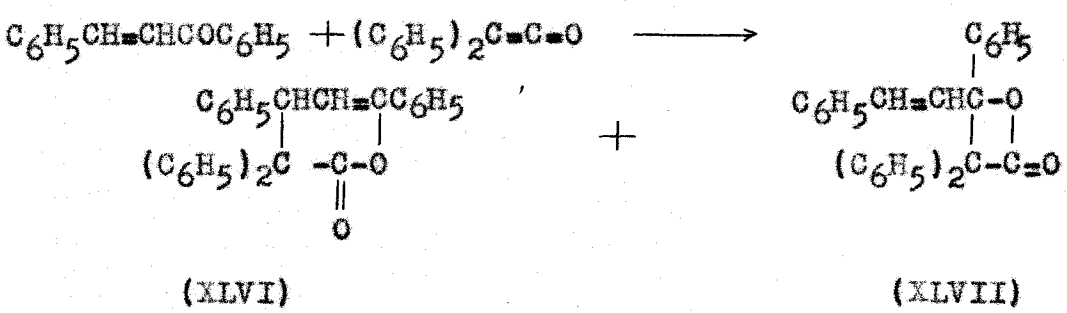
ate (XLV), in which the metal is poorly neutralized and which should rearrange to a mixture containing the still imperfectly neutralized iminolate (XLVI).



(XLV) (XLVI)

The potassium enolate (XLV) can attain a better neutralization by reacting with another molecule of chalcone, but the iminolate cannot do so. Accordingly the reaction proceeds by way of 1,4-addition through the formation of the enolate (XLV).

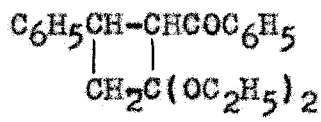
Ketene derivatives react with chalcones yielding either 1,2- or 1,4-addition products. Staudinger[99] noted that diphenylketone adds to chalcone, 4-methoxychalcone, and to 4-dimethylaminochalcone yielding the corresponding δ-lactone (XLVI) by 1,4-addition and a small percentage of the β-lactone (XLVII) by 1,2-addition.



(XLVI) (XLVII)

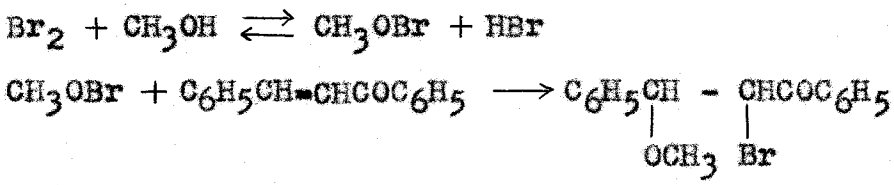
99. Staudinger, "Die Ketene," Enke, Stuttgart, 1912, p. 64.

From chalcone and ketene diethylacetal there was formed 1,1-diethoxy-2-benzoyl-3-phenylcyclobutane (XLVIII), apparently by the addition of the acetal to the ethylenic system of the ketone[100].



(XLVIII)

α-Halogen-β-methoxypropiophenone derivatives were prepared in good yields by the addition of methyl hypobromite[101] or methyl hypochlorite[102] to chalcones in methanol at 0° or at room temperature.



Methyl hypoiodite did not undergo the reaction.

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100. McElvain and Cohen, J. Am. Chem. Soc., 64, 260 (1942).

101. Conant and Jackson, ibid., 46, 1727 (1924).

102. Jackson, ibid., 48, 2166 (1926).

III. EXPERIMENTAL

Unless otherwise specified all compounds were of the highest purity commercially obtainable. All melting and boiling points are uncorrected. The sulfur and chlorine analyses were made by the macro Parr bomb procedure. All analyses for nitrogen were performed by the micro Dumas method.

General Procedure for the Addition of Sulfinic Acids to Chalcones.- Three methods were employed in the preparation of the ketosulfones: (A)[17]. The pulverized alkali sulfinate was suspended in absolute ethanol. A slight excess of concentrated hydrochloric acid was added, and after shaking vigorously, the sodium chloride was removed by filtration. The filtrate was immediately mixed with an ethanolic solution containing an equivalent amount of the chalcone. In most cases, the addition product began to crystallize out of solution after standing at room temperature for ten minutes.

(B). Equivalent amounts of the chalcone and alkali sulfinate were suspended in 50 to 60 ml. of absolute ethanol. A slight excess of glacial acetic acid was added and the mixture shaken or warmed until a uniform solution was obtained. The reaction was allowed to stand at room temperature until the crystallization of the addition product was complete. In most cases, the product was formed instantly.

(C). In the case of certain chalcones which were difficultly soluble in absolute ethanol, the reaction was carried out as in (B) using glacial acetic acid as the solvent. Essentially the same technique was used in working up the products. The solid material was filtered off and recrystallized from an appropriate solvent. In most cases ethyl acetate was satisfactory.

β-Benzenesulfonyl-*β*-phenylpropiophenone.[6,15] Four and one-tenths grams (0.025 mole) of sodium benzenesulfinate was suspended in 100 ml. of absolute ethanol. After the addition of 2 ml. of concentrated hydrochloric acid, the mixture was shaken vigorously and filtered. In the clear solution there was dissolved 5.2 g. (0.025 mole) of benzalacetophenone and the solution set aside at room temperature for crystallization. Approximately forty minutes were required for the completion of the reaction. The product was recrystallized from ethanol. The yield was 7.1 g. (76%); m.p. 156° (decomp.).

β-(p-Toluenesulfonyl-*β*-phenylpropiophenone.[14] The compound was prepared in the manner described above from 4.5 g. (0.025 mole) of sodium p-toluenesulfinate and 5.2 g. (0.025 mole) of benzalacetophenone. The yield was 8.0 g. (84%); m.p. 168-9° (decomp.). This melting point corresponded to that given by Kohler and Reimer[14]. When the specimen was

heated rapidly, a value of 174° (decomp.) was obtained.

4-Methoxy-4'-chlorochalcone.-[103] To a solution of 18.5 g. (0.14 mole) of p-chloroacetophenone in 50 ml. of absolute ethanol there was added with shaking 10 ml. of a 10 percent solution of sodium methoxide in methanol. The flask was allowed to stand at room temperature for two hours and then in the cold for twelve hours. The solid material was filtered off and washed with cold 80 percent methanol. The crude yield was 34 g. (93%). After recrystallization from ethanol, the yield of the pure product was 33 g. (90%); m.p. 122°.

p-Chloro-α-(p-toluenesulfonyl)-β-(4-methoxyphenyl)propiophenone.- To a warm solution of 1.5 g. (0.0055 mole) of 4-methoxy-4'-chlorochalcone in 25 ml. of glacial acetic acid there was added 1 g. (0.0055 mole) of sodium p-toluenesulfinate. The product began to form upon cooling to room temperature. The yield after recrystallization from glacial acetic acid was 1.8 g. (72%); m.p. 158° (decomp.).

Anal. Calcd. for $C_{23}H_{21}O_4ClS$: S, 7.5. Found: S, 7.4 and 7.5.

4-Dimethylamino-4'-chlorochalcone.-[104] To a solution of

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103. Straus and Blankenhorn, Ann., 415, 253 (1918).

104. Pfeiffer and Kleu, Ber., 66, 1706 (1933).

15 g. (0.1 mole) of p-dimethylaminobenzaldehyde and 15 g. (0.1 mole) of p-chloroacetophenone in 150 ml. of absolute ethanol there was gradually added 10 ml. of 10 percent sodium methoxide in methanol. After standing at room temperature for twelve hours, a solid mass of yellow crystals was obtained. The product was filtered and washed with 80 percent methanol. The yield was 27.5 g. (94%). The product was purified by recrystallization from ethyl acetate; m.p. 140-141°.

4-Dimethylamino-4'-methoxychalcone.[104] The compound was prepared according to the above procedure from 18 g. (0.12 mole) of p-dimethylaminobenzaldehyde and 18 g. (0.12 mole) of p-methoxyacetophenone. The yield of the crude product was 32.2 g. (94%). Recrystallization from a 50 percent mixture of ethanol and ethyl acetate gave 28.5 g. (87%) of the pure product; m.p. 127°.

p-Chloro-β-(p-toluenesulfonyl)-β-(4-dimethylaminophenyl)propiophenone.- One and seven-tenths grams (0.0055 mole) of 4-dimethylamino-4'-chlorochalcone was dissolved in 20 ml. of warm glacial acetic acid. To the deep red solution there was added 1 g. (0.0055 mole) of sodium p-toluenesulfinate. The addition product crystallized from the solution after standing at room temperature for forty-five minutes. The solid was filtered off and recrystallized from an ethanol-

ethyl acetate mixture. The yield was 1.4 g. (53%); m.p. 153-156° (decomp.).

Anal. Calcd. for $C_{24}H_{24}O_3NClS$: S, 7.02. Found: S, 7.36 and 7.24.

p-Methoxy-β-(p-toluenesulfonyl)-β-(4-dimethylaminophenyl)propiophenone.- In a warm solution of 5.5 g. (0.02 mole) of 4-dimethylamino-4'-methoxychalcone in 50 ml. of glacial acetic acid was dissolved 5 g. (0.028 mole) of sodium p-toluenesulfinate. The product was formed after standing at room temperature for twelve hours. After filtering and recrystallization from ethyl acetate, the yield of the pure product was 2.8 g. (30%); m.p. 149° (decomp.).

Anal. Calcd. for $C_{25}H_{27}O_4NS$: S, 7.32. Found: S, 7.34.

2-Mercaptoquinoline.[105] A solution of 15.7 g. (0.1 mole) of 2-chloroquinoline and 7.8 g. (0.1 mole) of thiourea in 75 ml. of absolute ethanol was refluxed for one hour. To the cooled solution there was added with stirring 15 g. of sodium carbonate and 50 ml. of water. After stirring for fifteen minutes, the crude product was filtered and washed with cold water. The pure product was obtained by recrystallization from absolute ethanol. The yield was 12 g. (78%); m.p.

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105. Rosenhauer, Hoffmann, and Heuser, Ber., 62, 2733 (1929).

175-176°.

Attempted Addition of 2-Mercaptoquinoline to Benzalacetophenone.- Attempts to add the thiol to benzalacetophenone resulted in the recovery of the starting materials. The addition product was not obtained after refluxing an alcoholic solution of the two reactants for twenty-four hours. The addition of piperidine or sodium ethoxide failed to catalyze the reaction.

p-Chloro-β-(p-toluenemercapto)-β-(4-dimethylaminophenyl)propiophenone.- A solution of 2.9 g. (0.01 mole) of 4-dimethylamino-4'-chlorochalcone and 1.2 g. (0.01 mole) of p-thiocresol in 50 ml. of absolute ethanol was refluxed in a nitrogen atmosphere for twelve hours. The light yellow crystalline solid was filtered from the cooled solution and recrystallized from ethyl acetate. The yield of the pure product was 2.9 g. (70%); m.p. 148-149.5°.

Anal. Calcd. for $C_{24}H_{24}ONClS$: S, 7.83. Found: S, 7.82.

p-Acetamidobenzenesulfinic Acid.- This compound was prepared according to the directions given in the literature[106]. The crude sulfonyl chloride prepared[107] from an ex-

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106. Smiles and Bere, Org. Syn., Coll. Vol. I, 7 (1941).

107. Smiles and Stewart, ibid., 8 (1941).

cess of chlorosulfonic acid and 75 g. (0.55 mole) of acetanilide was reduced by shaking with 500 ml. of a slightly alkaline solution containing 252 g. (1.0 mole) of crystallized sodium sulfite. The crude yield of the acid was 65.3 g. (60%); m.p. 145-148° (decomp.). The product was preserved in the form of the sodium salt.

β-(4-Acetaminobenesulfonyl)-*β*-phenylpropiophenone.- To a stirred suspension of 25 g. (0.12 mole) of benzalacetophenone and 25 g. (0.12 mole) of sodium p-acetamidobenzenesulfinate in 350 ml. of absolute ethanol was added 15 ml. of glacial acetic acid. The addition product began to form immediately after all of the sulfinate had dissolved. The reaction was allowed to stir for an additional hour then cooled and the product filtered. The compound was insoluble in most of the common organic solvents and was purified by digesting with a mixture of glacial acetic acid and ethyl acetate. The yield was 41 g. (80%); m.p. 176-178° (decomp.).

Anal. Calcd. for $C_{23}H_{21}O_4NS$: N, 3.44; S, 7.85. Found: N, 3.59; S, 7.85.

p-Chloro-*β*-(4-acetamidobenzenesulfonyl)-*β*-(4-methoxyphenyl)propiophenone.- Three and five-tenths grams (0.018 mole) of sodium p-acetamidobenzenesulfinate was dissolved in a solution of 4.5 g. (0.018 mole) of 4-methoxy-4'-chlorochalcone in 50 ml. of glacial acetic acid. After warming

for a few minutes on the steam bath, the solid addition product began to form. The crude yield was 6.2 g. (78%). The product was purified by digesting with 50 ml. of hot ethyl acetate. The yield of the pure product was 5.7 g. (71%); m.p. 159-160° (decomp.).

Anal. Calcd. for $C_{24}H_{22}O_5NClS$: N, 2.97; Cl, 7.5; S, 6.79. Found: N, 3.16; Cl, 7.2 and 7.3; S, 6.72 and 6.77.

Ethyl Picolinate.- Picolinic acid hydrochloride was prepared from 200 g. (2.15 moles) of α-picoline and 680 g. (4.5 moles) of potassium permanganate according to the directions of Singer and McElvain[108]. The crude acid hydrochloride was esterified directly by refluxing for twenty-four hours with 1500 ml. of ethanol previously saturated with anhydrous hydrogen chloride. The excess ethanol was removed by distillation under diminished pressure, and the solid residue was dissolved in water and cautiously poured into an excess of a sodium carbonate solution. The ester was extracted from the basic solution with ether and dried over anhydrous sodium sulfate. The product was distilled at 133-134° (20 mm.). One hundred and forty-two and five-tenths grams (47.5% based on the α-picoline) of the pure material was obtained. The unesterified acid was precipitated as the copper salt (33 g.) by the addition of copper

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108. Singer and McElvain, Org. Syn., 20, 79 (1940).

sulfate to the slightly acidified aqueous solution.

Methyl α-Pyridyl Ketone.- The method of preparation was a modification of that described by Kolloff and Hunter[109a] as reported by Gilman, Tolman, and Massie[109b]. To a stirred refluxing suspension of 27.6 g. (1.2 g. atoms) of sodium sand in one liter of dry benzene was gradually added 55.2 g. (1.2 moles) of repurified absolute ethanol. Stirring and refluxing were continued for four hours. To the white suspension was added a solution of 140.8 g. (1.16 moles) of ethyl acetate and 120.2 g. (0.8 mole) of ethyl picolinate at such a rate as to maintain continuous refluxing. The thick, light yellow emulsion was heated with stirring for nine hours.

After cooling, the contents of the flask were poured into a beaker containing 40 g. of sodium hydroxide dissolved in 800 ml. of water. The solution was filtered and the two liquid layers separated. The organic portion was washed with two 400 ml. portions of water and the washings combined with the aqueous extract. To this was added the yellow precipitate and the whole acidified with 400 ml. of concentrated hydrochloric acid.

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109. (a) Kolloff and Hunter, J. Am. Chem. Soc., 63, 490 (1941); (b) Gilman, Tolman, and Massie, ibid., 68, 2399 (1946).

After refluxing for three hours the solution was cooled, neutralized with sodium carbonate and extracted with ether. After drying over anhydrous sodium sulfate, the ether was removed, and the product distilled under reduced pressure. The yield was 70 g. (72%); b.p. 85-86° (20 mm.).

α-Pyridyl Styryl Ketone.[110] To a suspension of 2 g. (0.0165 mole) of 2-pyridyl methyl ketone and 2 g. (0.018 mole) of benzaldehyde in 100 ml. of water there was added 5 ml. of a 10 percent sodium hydroxide solution. A light yellow solid was formed after stirring the mixture for two hours. After cooling in the ice box, the product was filtered off and recrystallized from ethanol. The yield was 1.5 g. (44%); m.p. 73°. Engler[110] reported a melting point of 75° for the compound.

β-(p-Toluenesulfonyl)-β-phenylethyl α-Pyridyl Ketone.- A mixture of 5 g. (0.024 mole) of α-pyridyl styryl ketone, 4 g. (0.024 mole) of sodium p-toluenesulfinate and 2 ml. of glacial acetic acid in 50 ml. of absolute ethanol was warmed on the steam bath until a clear solution was obtained. The addition product crystallized immediately from the cooled solution. After recrystallization from ethyl acetate, the yield was 7.8 g. (86%); m.p. 172-174° (decomp.).

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110. Engler and Engler, Ber., 35, 4061 (1902).

Anal. Calcd. for $C_{21}H_{19}O_3NS$: N, 4.06; S, 8.75. Found: N, 4.02; S, 8.4.

The Reaction of Lithium Benzenesulfinate with Chalcone.- Anhydrous sulfur dioxide was passed into an ethereal solution of phenyllithium prepared from 15.8 g. (0.1 mole) of bromobenzene and 1.4 g. (0.2 g. atom) of lithium until the Color Test No. I[111] for the organometallic compound was negative. The light gray solid obtained was filtered and washed with fresh ether then dried at 100°. Eleven grams (74%) of the material was obtained.

To a suspension of 1 g. (0.007 mole) of the crude sulfinate and 1 g. (0.005 mole) of benzalacetophenone in 20 ml. of absolute ethanol was added 0.6 ml. of glacial acetic acid. The mixture was shaken to obtain a uniform solution and set aside for crystallization. The yield of the addition product was 0.5 g. (30%); m.p. 156°. The product was identical with that obtained from sodium benzenesulfinate and benzalacetophenone (mixed m.p.).

2-Chloro-4'-methoxychalcone.[112] The chalcone was prepared in the usual manner from 14.1 g. (0.1 mole) of o-

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111. Gilman and Schulze, J. Am. Chem. Soc., 47, 2002 (1925).

112. Pfeiffer, Kalckbrenner, Kunze, and Levin, J. prakt. Chem., 119, 109 (1928).

chlorobenzaldehyde and 15.0 g. (0.1 mole) of p-methoxyacetophenone. The yield was 26.3 g. (96%); m.p. 91-92° (from ethanol).

p-Methoxy-β-(4-acetamidobenzenesulfonyl-β-(2-chlorophenyl)propiophenone.- A solution of 8.2 g. (0.03 mole) of 2-chloro-4'-methoxychalcone and 6.6 g. (0.03 mole) of sodium p-acetamidobenzenesulfinate in 75 ml. of glacial acetic acid was warmed on the steam bath for one hour. After standing at room temperature for several hours, the crystalline product was filtered off and digested with warm 95 percent ethanol. The yield of the pure product was 12 g. (81%); m.p. 160-161° (decomp.).

Anal. Calcd. for $C_{24}H_{22}O_5NClS$: S, 6.78. Found: S, 6.46.

β-(4-Acetamidobenzenesulfonyl)-β-(3,4-methylenedioxyphenyl)propiophenone.- A solution of 7.6 g. (0.13 mole) of piperonalacetophenone and 6.6 g. (0.03 mole) of sodium p-acetamidobenzenesulfinate in 60 ml. of glacial acetic acid was warmed on the steam bath for one hour. The product crystallized from the solution only after seeding and cooling to 10°. The yield of the pure compound after recrystallization from glacial acetic acid was 9.7 g. (68.5%); m.p. 150-153° (decomp.).

Anal. Calcd. for $C_{24}H_{21}O_6NS$: S, 7.1. Found: S, 7.32.

2-Quinolinealdehyde.[113] In a one-liter, three-necked, round-bottomed flask equipped with a dropping funnel, a reflux condenser and a mechanical stirrer there was placed a solution of 27 g. (0.24 mole) of freshly sublimed selenium dioxide in 240 ml. of dioxane containing 10 ml. of water. To the stirred refluxing solution was added over a period of one and one-half hours a solution of 50 g. (0.19 mole) of quinaldine in 50 ml. of dioxane. Refluxing and stirring were continued for two and one-half hours, and the coagulated selenium and insoluble decomposition products filtered from the warm solution. The solvent was removed by distillation under reduced pressure and the residue was dissolved in 400 ml. of ether. After chilling in the ice-box for twelve hours, the solution was filtered and the excess solvent removed. The viscous red oil was extracted with four 50 ml. portions of boiling petroleum ether (b.p. 60-68°) and the combined extract boiled with Norite and filtered. The aldehyde crystallized from the chilled filtrate yielding 17.1 g. (65%) of the pure product; m.p. 67-69°. Recrystallization from petroleum ether (b.p. 60-68°) gave 15.2 g. (51%) of a product which melted at 68-69°. The aldehyde was distilled at 93-95° (0.5 mm.).

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113. Kaplan, J. Am. Chem. Soc., 63, 2654 (1941).

1-(4-Methoxyphenyl)-3-(2-quinolyl)-2-propen-1-one.* To a solution of 15.7 g. (0.1 mole) of 2-quinolinealdehyde and 14.0 g. (0.1 mole) of p-methoxyacetophenone in 60 ml. of absolute ethanol there was gradually added 10 ml. of a 10 percent solution of sodium methoxide in methanol. The condensation took place at once producing a light yellow crystalline product. The yield on recrystallization from ethanol was 24.5 g. (88%); m.p. 133-134°.

Anal. Calcd. for $C_{19}H_{15}O_2N$: N, 4.84. Found: N, 4.61.

1,3-Diphenyl-3-benzenesulfonylpropen-1-ol.- A mixture of 12 g. (0.034 mole) of β-benzenesulfonyl-β-phenylpropiophenone, 10.2 g. (0.05 mole) of aluminum isoproxide (Eastman Kodak Co., practical grade) and 250 ml. of isopropyl alcohol (distilled from sodium) was placed in a 500 ml. distilling flask equipped with a twelve-inch Vigreux column. The flask was heated by means of an oil bath regulated to maintain a fairly slow rate of distillation. After a negative test for acetone was obtained in the distillate, the ex-

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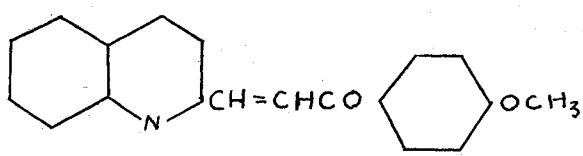

cess solvent was removed under reduced pressure. The residue was hydrolyzed by means of an ice-hydrochloric acid mixture, and the solid material was filtered and recrystallized from ethyl acetate. The yield was 4.5 g. (38%); m.p. 175-176° (decomp.).

Anal. Calcd. for $C_{21}H_{20}O_3S$: S, 9.09. Found: S, 9.26 and 9.22.

2-Acetyldibenzothiophene.[114] In a one-liter, three-necked, round-bottomed flask equipped with a reflux condenser, a mechanical stirrer and a solid addition funnel there was placed 60 g. (0.32 mole) of dibenzothiophene and 450 ml. of carbon disulfide. One hundred and twenty grams (0.9 mole) of anhydrous aluminum chloride was gradually added to the solution with stirring. To the resulting dark purple mixture was added dropwise 26 g. (0.32 mole) of acetyl chloride. The reaction was stirred and heated on the steam bath for four hours. After cooling, the complex was hydrolyzed by the usual method, the organic layer was separated, washed with water, and dried over anhydrous calcium chloride. After removing the excess solvent, the residue was distilled at 175-179° (0.4 mm.). Twenty and four-tenths grams (56%) of the crude product melting over a range of 89-107° resulted from the recrystallization of the distillate from absolute ethanol. The product

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114. Gilman and Jacoby, J. Org. Chem., 3, 108 (1938); Burger, Wartmann and Lutz, J. Am. Chem. Soc., 60, 2628 (1938).

was further purified by extracting the solid material with boiling ether. The 2-acetyl derivative was insoluble in the solvent. From 55.2 g. of the crude mixture there was obtained 25.5 g. (46%) of the 2-acetyldibenzothiophene; m.p. 110-112°.

1-(2-Dibenzothienyl)-3-phenyl-2-propen-1-one.- To a solution of 2.3 g.(0.01 mole) of 2-acetyldibenzothiophene and 1.1 g. (0.01 mole) of benzaldehyde in 30 ml. of absolute ethanol there was added 1.5 ml. of a 10 percent solution of sodium methoxide in methanol. The solution was warmed to 40° in order to prevent the crystallization of the ketone from the solution. An oil separated out which gradually solidified on standing. The crude product was filtered and recrystallized from ethyl acetate. The yield was 2 g. (62%); m.p. 154.5-155.5°.

Anal. Calcd. for $C_{21}H_{14}OS$: S, 10.19. Found: S, 10.04 and 9.97.

3-(p-Toluenesulfonyl)-1-(2-dibenzothienyl)-3-phenylpropanone-1.- A suspension of 3 g. (0.015 mole) of sodium p-toluenesulfinate, 5 g. (0.015 mole) of 1-(2-dibenzothienyl)-3-phenyl-2-propen-1-one, 5 ml. of glacial acetic acid and 50 ml. of ethyl acetate was refluxed until a uniform solution was obtained. The addition product crystallized from the solution after standing twenty-four hours at room temperature. The product was purified by digesting with warm

ethyl acetate. The yield was 5.4 g. (68%); m.p. 180-182° (decomp.).

Anal. Calcd. for $C_{18}H_{22}O_3S$: S, 13.66. Found: S, 12.86 and 12.75.

Recrystallization of the product from glacial acetic acid failed to give a product of higher analytical purity.

3-(3-Acetamido-4-methoxybenzenesulfonyl)-1-(2-dibenzothienyl)-3-phenylpropanone-1.- The compound was prepared in the usual manner by the addition of 5 g. (0.018 mole) of sodium 2-acetamidoanisole-4-sulfinate to 5 g. (0.016 mole) of 1-(2-dibenzothienyl)-3-phenyl-2-propen-1-one in 50 ml. of glacial acetic acid. The product was purified by digesting with boiling ethyl acetate. The yield was 5.6 g. (56%); m. p. 175-177.5° (decomp.).

Anal. Calcd. for $C_{30}H_{25}O_5NS_2$: S, 11.80. Found: S, 11.48.

1-(2-Dibenzothienyl)-3-(p-dimethylaminophenyl)-2-propen-1-one.- To a warm solution (40°) of 8.4 g. (0.037 mole) of 2-acetyldibenzothiophene and 6.6 g. (0.037 mole) of p-dimethylaminobenzaldehyde in 50 ml. of absolute ethanol there was added 10 ml. of a 10 percent sodium methoxide solution in methanol. After standing at room temperature for two hours a light orange oil which crystallized on cooling was obtained. The product was recrystallized from a 50 percent solution of ethanol and ethyl acetate. The yield was 8 g. (57%); m.p. 163-164°.

Anal. Calcd. for $C_{23}H_{19}ONS$: S, 8.96. Found: S, 9.02

p-Methoxy-β-(4-acetamidobenzenesulfonyl)-β-(4-dimethylaminophenyl)propiophenone.- A mixture of 6.2g. (0.02 mole) of 4-dimethylamino-4' -methoxychalcone, 4.8 g. (0.02 mole) of sodium p-acetamidobenzenesulfinate and 75 ml. of glacial acetic acid was warmed on the steam bath until a clear solution was obtained. After standing at room temperature for twelve hours the crystalline product was filtered from the solution and recrystallized from ethyl acetate. The yield was 4.6 g. (42%); m.p. 155-156° (decomp.).

Anal. Calcd. for $C_{26}H_{28}O_5N_2S$: S 6.67. Found: S, 6.65.

p-Chloro-β- (4-acetamidobenzenesulfonyl)-β-(4-dimethylaminophenyl)propiophenone.- The compound was prepared by the above procedure from 6.2g. (0.02 mole) of 4-dimethylamino-4' -chlorochalcone and 4.8 g. (0.02 mole) of sodium p-acetamidobenzenesulfinate. The product was purified by digesting with ethyl acetate. The yield of the pure product was 3.6 g. (32%); m.p. 158° (decomp.).

Anal. Calcd. for $C_{25}H_{25}O_4N_2ClS$; S, 6.61. Found: S, 6.66.

p-Methoxy-β- (p-toluenesulfony)-β- (2-chlorophenyl)propiophenone.- A mixture of 7 g. (0.025 mole) of 2-chloro-4'-methoxychalcone, 4.5 g. (0.025 mole) of sodium p-toluenesulfinate, 5 ml. of glacial acetic acid, and 75 ml. of absolute ethanol was refluxed until a uniform solution was obtained. After

cooling and allowing to stand at room temperature for six hours, the addition product crystallized from the solution. The yield after recrystallization from ethyl acetate was 9.5 g. (82.5%); m.p. 149-150° (decomp.).

Anal. Calcd. for $C_{23}H_{21}O_4ClS$: S, 7.47. Found: S, 7.2.

p-Chlorobenzenesulfinic Acid.[115] The acid was prepared by the reduction of p-chlorobenzenesulfonyl chloride[116] by sodium sulfite in an alkaline solution. Into a 500 ml. three-necked, round-bottomed flask equipped with a mechanical stirrer, a dropping funnel and a thermometer was introduced 165 ml. (295 g., 2.5 moles) of redistilled chlorosulfonic acid. The flask was cooled by an ice bath and, while stirring, 56 g. (0.5 mole) of chlorobenzene was added at such a rate that the temperature did not rise above 5°. The reaction was stirred at low temperature for one hour and at 50° for three hours. After cooling, the mixture was cautiously poured over cracked ice and the white solid was filtered off and washed with cold water. The yield of the crude material (m.p. 43-45°) was quantitative. (The reported melting point for the compound is 53°).

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115. German Patent 224,019 (1910) /Chem. Zentr., 81, II, 513 (1910); Frdl. 10, 115 (1910)/.

116. Ullmann and Korsett, Ber., 40, 642 (1907).

To a solution of 126 g. (1.0 mole) of anhydrous sodium sulfite in 650 ml. of water was added the crude sulfonyl chloride. The suspension was stirred vigorously for three and one-half hours. A basic reaction was maintained by the frequent addition of small amounts of a 50 percent sodium hydroxide solution. The insoluble material was removed by filtration and the filtrate acidified to Congo red by 40 percent sulfuric acid. The yield of the sulfinic acid was 16 g. (20%); m.p. 94-95°. From the alkali-insoluble material there was obtained 30 g. (42%) of p,p'-dichlorodiphenyl sulfone; m.p. 145-147°.

o-Anisidine-4-sulfonic Acid.[117] Sixty-two grams (0.5 mole) of o-anisidine was cautiously dissolved in 100 ml. of concentrated sulfuric acid. One hundred milliliters of fuming sulfuric acid (20% oleum) was added and the solution heated at 80° for one-half hour. After cooling to room temperature, the liquid was poured over crecked ice. The acid settled out of the solution in the form of fine white crystals. The crude product was dissolved in 700 ml. of water, boiled with Norite and filtered. The product crystallized out of the chilled solution. The yield was 70.5 g. (70%).

2-Chloroanisole-4-sulfonic Acid.[117] Seventy and five-tenths grams (0.345 mole) of o-anisidine-4-sulfonic acid was

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117. Child, J. Chem. Soc., 715 (1932).

dissolved in 300 ml. of an aqueous solution containing 13.7 g. (0.345 mole) of sodium hydroxide. There was then added 24.2 g. (0.345 mole) of sodium nitrite and the resulting solution cooled to 0°. The diazotization was carried out by gradually adding 120 ml. of concentrated hydrochloric acid at such a rate that the temperature did not rise above 5°. A light brown precipitate formed but redissolved as the reaction neared completion. The solution of the diazonium salt was then allowed to run into a well stirred, boiling 0.4 N solution of cuprous chloride in 300 ml. of concentrated hydrochloric acid. Stirring was continued as the solution cooled to room temperature. The acid was isolated as its sodium salt by the addition of 1800 ml. of a saturated brine solution. The solid was filtered and dried at 100°; 61.6 g. (73.5%) was obtained.

2-Chloroanisole-4-sulfonyl Chloride.[117] A mixture of 61.6 g. (0.252 mole) of sodium 2-chloroanisole-4-sulfonate and 103 g. (0.5 mole) of phosphorus pentachloride was triturated until the mass had completely liquified. The reaction was allowed to remain at room temperature for two hours and then poured into ice water. The heavy oil obtained solidified on standing yielding 57.1 g. (95%) of the crude product; m.p. 77-79°. The product was purified further by recrystallization from petroleum ether (b.p. 60-68°); m.p. 81-82°. (This value agreed with that reported by

Child)[117].

2-Chloroanisole-4-sulfinic Acid.- The crude sulfonyl chloride, 57.1 g. (0.24 mole), obtained from the above reaction was reduced to the sulfinic acid by a slightly alkaline solution of 126 g. (0.5 mole) of crystallized sodium sulfite in 500 ml. of water. Thirty-eight grams (76%) of the sulfinic acid was obtained from the acidified solution. The product formed an opaque glass at 99-100° but melted sharply to a clear green liquid at 110-111°.

Anal. Calcd. for $C_7H_7O_3ClS$: S, 15.48. Found: S, 15.25.

2-Acetamidoanisole-4-sulfinic Acid.[117] To 165 ml. (2.5 moles, 295 g.) of redistilled chlorosulfonic acid cooled to 0° there was added with stirring 54.5 g. (0.33 mole) of o-acetanisidide at such a rate that the reaction temperature did not exceed 10°. After stirring at 50° for three hours, then cooling, the mixture was poured over cracked ice. The crude product was filtered off, washed with cold water and immediately reduced to the sulfinic acid by stirring vigorously with 500 ml. of a slightly alkaline solution containing 252 g. (1.0 mole) of sodium sulfite heptahydrate. The resulting solution was filtered and acidified with 40 percent sulfuric acid. The yield of the product was 58 g. (77%); m.p. 100-105° (decomp.). The acid was converted to

its sodium salt and stored in that form. According to the literature[117], the acid begins to decompose at 100° and melts at 117-119°.

Cumenesulfinic Acid.- Cumenesulfonyl chloride was prepared in the usual manner from 200 ml. (353 g., 3 moles) of redistilled chlorosulfonic acid and 120 g. (1 mole) of cumene. The crude product was reduced by stirring vigorously for three hours with a solution of 504 g. (2 moles) of sodium sulfite heptahydrate in one liter of water. Small portions of a 50 percent sodium hydroxide solution were frequently added in order to maintain a slightly basic reaction. This solution was filtered and acidified with 40 percent sulfuric acid. The product separated from the solution as an oil and was removed by ether extraction, and the ether extract was washed with 20 percent sodium bicarbonate. The oil was again obtained by acidifying the basic extract. The yield of the crude product after ether extraction, drying and removing the solvent in vacuo was 44.5 g. (24%). The acid was dissolved in 20 percent aqueous sodium hydroxide and precipitated from the solution as the sodium sulfinate by the addition of a saturated salt solution.

Anal. Calcd. for $C_9H_{11}O_2Na \cdot 2H_2O$: S, 13.22. Found: S, 13.00.

1-(p-Chlorophenyl)-3-(2-quinolyl)-2-propen-1-one*.- To a solution of 14 g. (0.089 mole) of 2-quinolinealdehyde and 14.8 g. (0.089 mole) of p-chloroacetophenone in 150 ml. of absolute ethanol there was added 10 ml. of a 10 percent solution of sodium methoxide in methanol. The product crystallized from the solution on standing at room temperature. The pure product was obtained after several recrystallizations from a 50 percent ethanol-ethyl acetate mixture. The yield was 8 g. (30%); m.p. 165°.

Anal. Calcd. for $C_{18}H_{12}ONCl$: Cl, 11.94. Found: Cl, 11.77 and 11.91.

p-Chloro-β-(2-quinolyl)-β-(3-acetamido-4-methoxybenzenesulfonyl)propiophenone (Attempted).- A suspension of 5 g. (0.02 mole) of sodium 2-acetamidoanisole-4-sulfinate and 5.9 g. (0.02 mole) of 1-(p-chlorophenyl)-3-(2-quinolyl)-2-propen-1-one in 60 ml. of glacial acetic acid was warmed on the steam plate until a homogeneous solution was obtained. The reaction was allowed to stand at room temperature for twelve hours after which time the product was precipitated from the solution by the addition of an equal volume of ethanol. The original unsaturated ketone was recovered quantitatively from the reaction; m.p. 165° (mixed m.p.).

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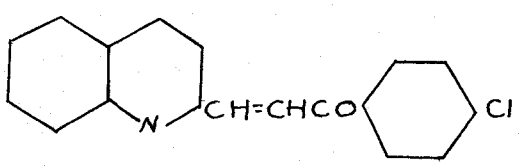
* 

β-(4-Chlorobenzenesulfonyl)-*β*-phenylpropiophenone.- A mixture of 5.2 g. (0.025 mole) of benzalacetophenone, 5 g. (0.025 mole) of sodium p-chlorobenzenesulfinate, 5 ml. of glacial acetic acid and 50 ml. of absolute ethanol was refluxed until a uniform solution was obtained. The addition product began to crystallize from the solution immediately on cooling to room temperature. After filtration and recrystallization from ethyl acetate, the yield was 9.1 g. (89%); m.p. 175-176° (decomp.).

Anal. Calcd. for $C_{21}H_{17}O_3ClS$: S, 8.31. Found: S, 8.26.

β-(3-Chloro-4-methoxybenzenesulfonyl)-*β*-phenylpropiophenone.- The compound was prepared according to the above procedure from 5.2 g. (0.025 mole) of benzalacetophenone and 5.7 g. (0.025 mole) of sodium 2-chloroanisole-4-sulfinate. The product was purified by recrystallization from ethyl acetate. The yield was 10.2 g. (94%); m.p. 172-174° (decomp.).

Anal. Calcd. for $C_{22}H_{19}O_4ClS$: S, 7.72. Found: S, 7.75.

β-(3-Acetamido-4-methoxybenzenesulfonyl)-*β*-phenylpropiophenone.- This compound was prepared according to the above procedure from 5.3 g. (0.025 mole) of benzalacetophenone and 6.2 g. (0.025 mole) of sodium 2-acetamidoanisole-4-

sulfinate. After crystallization from glacial acetic acid, the yield was 4.4 g. (39%); m.p. 155-156° (decomp.).

Anal. Calcd. for $C_{24}H_{23}O_5NS$: S, 7.32. Found: S, 7.38.

p-Methoxy-β-(4-chlorobenzenesulfonyl)-β-(4-dimethylaminophenyl)propiophenone.- The compound was prepared by the addition of 4 g. (0.02 mole) of sodium p-chlorobenzenesulfinate to 5.6 g. (0.02 mole) of 4-dimethylamino-4'-methoxychalcone in 60 ml. of glacial acetic acid. The pure product was obtained after recrystallization from ethyl acetate. The yield was 4.5 g. (45%); m.p. 149-150° (decomp.).

Anal. Calcd. for $C_{24}H_{24}O_4NClS$: S, 7.00. Found: S, 7.06.

p-Chloro-β-(3-acetamido-4-methoxybenzenesulfonyl)-β-(4-dimethylaminophenyl)propiophenone.- A suspension of 5 g. (0.02 mole) of sodium 2-acetamidoanisole-4-sulfinate, 5.7 g. (0.02 mole) of 4-dimethylamino-4'-chlorochalcone, 100 ml. of absolute ethanol and 5 ml. of glacial acetic acid was refluxed until a uniform solution was obtained. The chalcone was recovered from the cooled solution. The reaction was repeated using 60 ml. of glacial acetic acid as the solvent; the yield of the pure addition product was 4.2 g. (39%); m.p. 176° (decomp.) (recrystallized from ethyl acetate).

Anal. Calcd. for $C_{26}H_{27}O_5N_2ClS$: S, 6.42. Found: S,

6.33.

p-Methoxy-β-(4-acetamidobenzenesulfonyl)-β-(2-quinolyl)-propiophenone*.- The reactions between 1-(4-methoxyphenyl)-3-(2-quinolyl)-2-propen-1-one and the sulfinic acids usually resulted in the quantitative recovery of the unsaturated ketone when ethanol was used as the solvent. The following modification was employed. Seven and two-tenths grams (0.025 mole) of the ketone and 5.5 g. (0.025 mole) of sodium p-acetamidobenzenesulfinate was dissolved in 60 ml. of warm glacial acetic acid. The addition product did not crystallize from the solution on standing at room temperature overnight but was obtained after diluting the solution with an equal volume of ethanol and chilling in the ice box. The crude product was filtered from the solution and purified by digesting the boiling ethanol. The yield of the pure product was 6.4 g. (53%); m.p. 170-172° (decomp.).

Anal. Calcd. for $C_{27}H_{24}O_5N_2S$: S, 6.56. Found: S, 6.81.

p-Methoxy-β-(4-chlorobenzenesulfonyl)-β-(2-quinolyl)-propiophenone.- The compound was prepared by the method described above from 5.0 g. (0.017 mole) of 1-(4-methoxyphenyl)-

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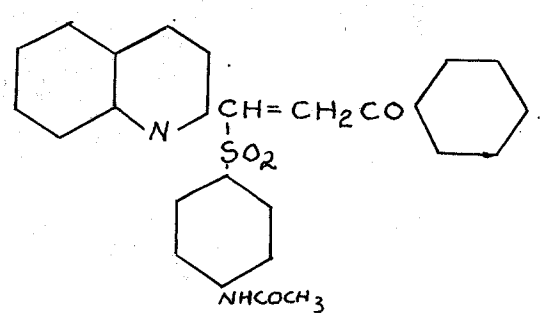
* 

3-(2-quinolyl)-2-propen-1-one and 4.0 g. (0.02 mole) of sodium p-chlorobenzenesulfinate in 60 ml. of glacial acetic acid. The yield of the product, purified by digesting with boiling with absolute ethanol was 5.4 g. (64%); m.p. 158-160° (decomp.).

Anal. Calcd. for $C_{25}H_{20}O_4NClS$: S, 6.88. Found: S, 6.83.

p-Methoxy-α-benzenesulfonyl-β-(2-quinolyl)propiophenone.- The product was obtained by the above method from 5 g. (0.0173 mole) of 1-(4-methoxyphenyl)-3-(2-quinolyl)-2-propen-1-one and 3.3 g. (0.02 mole) of sodium benzenesulfinate in 60 ml. of glacial acetic acid. The yield of the pure product was 4.6 g. (59%); m.p. 150-152° (decomp.).

Anal. Calcd. for $C_{25}H_{21}O_4NS$: S, 7.42. Found: S, 7.00.

p-Methoxy-α-cumenesulfonyl-β-(2-quinolyl)propiophenone.- The product was prepared from 2.0 g. (0.007 mole) of 1-(4-methoxyphenyl)-3-(2-quinolyl)-2-propen-1-one and 1.4 g. (0.007 mole) of cumenesulfinic acid in 60 ml. of glacial acetic acid. After several recrystallizations from ethyl acetate the yield of the pure product was 2.5 g. (73%); m.p. 156-158° (decomp.).

Anal. Calcd. for $C_{28}H_{27}O_4NS$: S, 6.76. Found: S, 6.57.

3-Nitro-4'-acetamidochalcone.- The condensation between 15.1 g. (0.1 mole) of m-nitrobenzenzaldehyde and 16.5 g. (0.10 mole) of p-acetamidoacetophenone was carried out in the usual manner in 100 ml. of absolute ethanol. The yield was 25.5 g. (80%); m.p. 210°. Recrystallization of the product from a mixture of ethanol and ethyl acetate did not increase the melting point.

Anal. Calcd. for $C_{17}H_{14}O_4N_2$: N, 9.03. Found: N, 9.16.

3,4'-Diaminochalcone.- Twenty grams (0.065 mole) of 3-nitro-4'-acetamidochalcone was stirred with a solution of 60 g. (0.27 mole) of stannous chloride dihydrate in 100 ml. of concentrated hydrochloric acid. The reaction was stirred for one hour at room temperature and then heated on the water bath for two hours. The bright orange cake was triturated with water and the resulting suspension poured into a cold 40 percent sodium hydroxide solution. The yellow solid was filtered, washed with water, and recrystallized from ethanol. The yield was 10.5 g. (68%); m.p. 168-169°.

Anal. Calcd. for $C_{15}H_{14}ON_2$: N, 11.77. Found: N, 11.94.

Lithium p-Dimethylaminobenzenesulfinate.- p-Dimethylaminophenyllithium[118] was prepared from 16 g. (0.08 mole)

of p-bromodimethylaniline and 1.12 g. (0.16 g. atom) of lithium in ether. After filtering anhydrous sulfur dioxide was passed into the solution until Color Test No. I[111] for the organometallic compound was negative. The light green precipitate obtained was filtered, washed with fresh ether and dried at 100°. The yield of the crude sulfinate was 11.6 g. (76%).

β-(4-Dimethylaminobenzenesulfonyl)-α-phenylpropiophenone.- Five grams (0.024 mole) of benzalacetophenone and 5 g. (0.026 mole) of the crude sulfinate (described above) was dissolved in 50 ml. of absolute ethanol containing 2 ml. of glacial acetic acid. After standing at room temperature for two weeks, 2 g. (20%) of the addition product was obtained. The product sintered at 177° but melted sharply with decomposition at 191-192°.

Anal. Calcd. for $C_{23}H_{23}O_3NS$: S, 8.14. Found: S, 7.99 and 8.24.

2-Bromopyridine.- The procedure of Craig[119] was followed in the preparation of this compound. Into a three-liter, three-necked round-bottomed flask equipped with a

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118. Stuckwisch, C. G., Doctoral Dissertation, Iowa State College, 1943.

119. Craig, J. Am. Chem. Soc., 56, 231 (1934).

stirrer, a dropping funnel and a thermometer there was placed 500 ml. of 48 percent hydrobromic acid. The flask was cooled by means of an ice-salt mixture while 90 g. (0.94 mole) of 2-aminopyridine was cautiously added. To the resulting hydrobromide there was added dropwise and with stirring 144 ml. (432 g., 2.7 moles) of bromine.

A solution of 165 g. (2.4 mole) of sodium nitrite in 240 ml. of water was added at such a rate that the reaction temperature did not exceed 0°. Stirring was continued and after fifteen minutes a solution of 360 g. of sodium hydroxide in 1080 ml. of water was added keeping the temperature of the reaction below 25°.

The mixture was extracted with ether and the extract was dried over anhydrous calcium chloride. One hundred and twenty-six and five-tenths grams (85%) of the product was collected at 94-95° (25 mm.).

Lithium 2-Pyridinesulfinate (Attempted).- n-Butyllithium[120] was prepared in a 50 percent yield[121] from 27.4 g. (0.2 mole) of n-butyl bromide and 3 g. (0.43 g. atom) of lithium.

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120. Gilman, Langham, and Moore, J. Am. Chem. Soc., 62, 2327 (1940).

121. The yield of n-butyllithium was determined by the double titration method of Gilman and Haubein, J. Am. Chem. Soc., 66, 1515 (1944).

The halogen-metal interconversion between 2-bromopyridine and n-butyllithium was carried out according to the procedure of Spatz[122]. The filtered solution of n-butyllithium was cooled to 30° while 16 g. (0.11 mole) of 2-bromopyridine in 50 ml. of ether was added over a period of three minutes.

After the addition of the 2-bromopyridine had been completed, Color Test No. I[111] for the organometallic compound was positive. Upon applying Color Test No. III[123] to the reaction mixture a transitory deep purple color appeared with the subsequent formation of a deep orange precipitate.

Anhydrous sulfur dioxide was passed into the deep red solution until Color Test No. I[111] was negative. The red color was then replaced by a light tan precipitate which was filtered and washed with ether. The crude product was granular when first filtered but became amorphous on further exposure to the atmosphere. The crude yield was 27 g. (180%) (the calculation was based on the original amount of 2-bromopyridine).

The presence of sulfur and nitrogen in the compound was shown by qualitative tests (sodium fusion). The product was

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122. Spatz, S. M., Doctoral Dissertation, Iowa State College, 1941; Gilman and Spatz, J. Am. Chem. Soc., 62, 466 (1940).

123. Gilman and Yablunky, J. Am. Chem. Soc., 63, 839 (1941), obtained an immediate deep purple color on application of Color Test No. III in interconversion reactions between aryl halides and n-butyllithium.

partially soluble in water and sulfur dioxide was liberated from the aqueous solution upon acidification with hydrochloric acid.

Eight grams of this crude material and 8.3 g. (0.04 mole) of benzalacetophenone in 50 ml. of ethanol acidified with 4.8 ml. of glacial acetic acid was allowed to stand at room temperature for several days. From the reaction there was recovered 6 g. (75%) of benzalacetophenone (mixed m.p.).

p-Amino-β-(p-toluenesulfonyl)-β-(3-aminophenyl)propiophenone.- One gram (0.0042 mole) of 3,4'-diaminochalcone and 1 g. (0.005 mole) of sodium p-toluenesulfinate was dissolved in 20 ml. of glacial acetic acid. The solid product which crystallized from the solution after standing at room temperature was filtered and recrystallized from ethyl acetate. The yield was 1.2 g. (70%); m.p. 184-185° (decomp.).

Anal. Calcd. for $C_{22}H_{22}O_3N_2S$: S, 8.38. Found: S, 8.12.

p-Amino-β-(4-acetamidobenzenesulfonyl)-β-(3-aminophenyl)-propiophenone.- The reaction was run according to the above method using 1 g. (0.0042 mole) of 3,4'-diaminochalcone and 1 g. (0.0045 mole) of sodium p-acetamidobenzenesulfinate in 20 ml. of glacial acetic acid. The product could not be isolated from the acidic solution. However, after dilution with water and careful neutralization with ammonium hydroxide, a light tan precipitate was obtained. This product was filtered, washed first with water, then with ethanol, and finally puri-

fied by digesting with boiling ethyl acetate. The yield was 1.5 g. (77%); the product decomposed over a range of 186-200°.

Anal. Calcd. for $C_{23}H_{23}O_4N_3S$: S, 7.32. Found: S, 7.39.

β-Cumenesulfonyl-β-phenylpropiophenone.- Four grams (0.02 mole) of benzalacetophenone and 3.7 g. (0.02 mole) of cumenesulfinic acid was dissolved in 60 ml. of absolute ethanol. The ketosulfone crystallized from the solution after standing at room temperature for a short period of time. The yield of the crude product was 7.0 g. (91%); m.p. 154-156° (decomp.). After recrystallization from ethyl acetate, the yield was 5 g. (65%); m.p. 157-158° (decomp.).

Anal. Calcd. for $C_{24}H_{24}O_3S$: S, 8.2. Found: S, 8.57.

p-Methoxy-β-cumenesulfonyl-β-(2-chlorophenyl)propiophenone.- This compound was prepared by the addition of 3 g. (0.016 mole) of cumenesulfinic acid to 3.0 g. (0.015 mole) of 2-chloro-4'-methoxychalcone in 50 ml. of glacial acetic acid. The product was isolated by diluting the reaction mixture with several volumes of water. The crude material was purified by recrystallization from ethyl acetate. The yield was one gram (17%); m.p. 150° (decomp.).

Anal. Calcd. for $C_{25}H_{25}O_4ClS$: S, 7.02. Found: S, 7.14.

1-(2-Pyridyl)-3-(3-nitrophenyl)-2-propen-1-one.- The condensation between 12.6 g. (0.1 mole) of m-nitrobenzaldehyde and 12.1 g. (0.1 mole) of methyl α-pyridyl ketone was carried out in the usual manner. The crude product which crystallized from the solution was filtered and washed with 80 percent methanol. The yield was 22 g. (96%); m.p. 175° (decomp.).

Anal. Calcd. for $C_{14}H_{10}O_3N_2$: N, 11.03. Found: N, 11.3.

1-(2-Pyridyl)-3-cumenesulfonyl-3-(3-nitrophenyl)propen-one-1 Acetate.- Five and one-tenth grams (0.02 mole) of 1-(2-pyridyl)-3-(3-nitrophenyl)-2-propen-1-one and 3.7 g. (0.02 mole) of cumenesulfinic acid was dissolved in 50 ml. of warm glacial acetic acid. The product was formed immediately and was purified by recrystallization from ethyl acetate. The yield was 5 g. (57%); m.p. 170-172° (decomp.).

Anal. Calcd. for $C_{23}H_{21}O_5N_2S$: S, 7.14. Found: S, 6.20 and 6.21. Calcd. for $C_{23}H_{21}O_5N_2S \cdot CH_3COOH$: S, 6.45.

p-Chloro-β-(p-toluenesulfonyl)-β-phenylpropiophenone.- The compound was prepared from 2.4 g. (0.01 mole) of 4'-chlorochalcone[124] and 1.78 g. (0.01 mole) of sodium p-toluenesulfinate in 25 ml. of absolute ethanol containing 1 ml.

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124. Allen and Frame, Can. J. Research, 6, 605 (1933).

of glacial acetic acid. The product was recrystallized from ethyl acetate; the yield was 2.5 g. (60%); m.p. 188° (decomp.).

Anal. Calcd. for $C_{22}H_{19}O_3ClS$: S, 9.04. Found: S, 8.03.

1-(4-Quinolyl)-3-(2-quinolyl)-2-propen-1-one.* To a solution of 1.57 g. (0.01 mole) of 2-quinolinealdehyde and 1.71 g. (0.0.01 mole) of methyl 4-quinolyl ketone in 20 ml. of absolute ethanol was added ten drops of a 10 percent solution of sodium methoxide in methanol. The condensation took place after standing at room temperature for fifteen minutes. The product was filtered from the solution and purified by digesting with boiling ethyl acetate. The yield was 2 g. (65%); m.p. 188-189°.

Anal. Calcd. for $C_{21}H_{14}ON_2$: N, 9.03. Found: N, 9.25.

General Procedure for the Preparation of N-Substituted Amidosulfurous Acids and Their Addition to Chalcones. - The N-substituted aryl- or alkylamidosulfurous acids were prepared by passing anhydrous sulfur dioxide into a solution of the amine in anhydrous ether. After no further precipitate was formed, the product was filtered when possible, washed with fresh ether, and stored in vacuo over phosphorus pentoxide.

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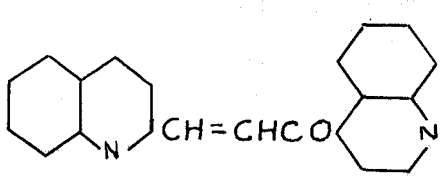
* 

The β-ketosulfonamides were prepared by two methods: (A). A slight excess of the amidosulfurous acid and the chalcone was dissolved in 50 ml. of absolute ethanol and the solution was allowed to stand at room temperature or in the ice box until the crystallization of the addition product was complete. In the event that the free acid could not be isolated, the ether was removed by distillation under reduced pressure, the residue taken up in ethanol and added to an ethanolic solution of the chalcone.

(B). A solution of the amine and the chalcone in absolute ethanol was saturated with anhydrous sulfur dioxide. In some cases, the addition product crystallized from the solution immediately whereas in other instances, it was necessary to concentrate the solution and allow it to stand in the ice box for several hours until the product had crystallized.

1-Piperidinesulfinic Acid.[125] Anhydrous sulfur dioxide was passed into a solution of 42.5 g. (0.5 mole) of piperidine in sodium-dried ether until no further precipitate was obtained. The white crystalline solid was filtered from the supernatant liquid and washed with fresh ether. The product was stored *in vacuo* over phosphorus pentoxide. The yield of

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125. (a) Michaelis, Ber., 24, 745 (1891); (b) ibid., 28, 1012 (1895).

the pure product was 63 g. (85%); m.p. 70°. This value corresponded to that reported in the literature cited[125]. The yield of the compound was not given by the authors.

β-Phenyl-*β*-(1-piperidinesulfonyl)propiophenone. Method (A).- In a solution of 5.2 g. (0.025 mole) of benzalacetophenone in 50 ml. of absolute ethanol there was dissolved 5 g. (0.03 mole) of 1-piperidinesulfinic acid. The crystalline addition product was obtained from the solution after standing at room temperature for twelve hours. The product was filtered and recrystallized from ethanol. The yield was 6 g. (66%); m.p. 176-178°.

Method (B).- A solution of 2.6 g. (0.0125 mole) of benzalacetophenone and 1.1 g. (0.013 mole) of piperidine in 25 ml. of absolute ethanol was saturated with anhydrous sulfur dioxide. The product which was formed almost immediately was filtered and recrystallized from ethanol. The yield was 3.8 g. (83%); m.p. 177-178°. The products obtained by both methods were identical (mixed m.p.).

Anal. Calcd. for $C_{20}H_{23}O_3NS$: S, 8.95; N, 3.92. Found: S, 8.5; N, 4.1.

Hydrolysis of *β*-Phenyl-*β*-(1-piperidinesulfonyl)propiophenone.- Two grams (0.0053 mole) of the sulfonamide was boiled for fifteen minutes with 30 ml. of 6N hydrochloric acid. The solution was cooled in an ice bath and the solid

product filtered off and recrystallized from water. One and six-tenths grams (quantitative) of a product which melted over a range of 70-75° was obtained. This compound analyzed for 1-phenyl-2-benzoylethanesulfonic acid tetrahydrate.

Anal. Calcd. for $C_{15}H_{14}O_4S \cdot 4H_2O$: S, 8.85. Found: S, 8.94 and 9.04.

The filtrate from the above hydrolysis was evaporated to dryness on the steam bath and the residue (m.p. 240-245°) identified as piperidine hydrochloride. The benzenesulfonyl derivative[126] melted at 90° and was identical with that prepared from an authentic sample of piperidine (mixed m.p.).

Oxidation of α-Phenyl-β-(1-piperidinesulfonyl)propiophenone.- Five-tenths of a gram (0.0016 mole) of the keto-sulfonamide was boiled for one half hour with 20 ml. of an aqueous solution containing 0.5 g. (0.0032 mole) of potassium permanganate. The manganese dioxide was filtered from the warm solution. From the cooled filtrate there was obtained a product which after acidification and recrystallization from water melted over the range of 70-75°. The mixed melting point of this product and that obtained from the acid hydrolysis of the compound showed no depression.

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126. Shriner and Fuson, "The Systematic Identification of Organic Compounds", John Wiley and Sons, Inc., New York, 1940, p. 193.

p-Chloro-β-phenyl-β-(1-piperidinesulfonyl)propiophenone (Attempted).- The compound was prepared according to Method (A) from 2 g. (0.0133 mole) of 1-piperidinesulfinic acid and 4'-chlorochalcone. The product was recrystallized from absolute ethanol yielding 3.1 g. (60%) of a white crystalline material; m.p. 180-182°. After several recrystallizations from ethanol without variation in the melting point, the compound analyzed low for sulfur.

Anal. Calcd. for $C_{20}H_{22}O_3NSCl$: S, 8.18. Found: S, 7.04, 7.12 and 7.12.

p-Methoxy-α-(2-chlorophenyl)-β-(1-piperidinesulfonyl)-propiophenone.- An attempt was made to carry out the addition reaction between 3 g. (0.02 mole) of 1-piperidinesulfinic acid and 5.4 g. (0.02 mole) of 2-chloro-4'-methoxychalcone in 50 ml. of ethanol according to Method (A). Five grams (93%) of the unsaturated ketone was recovered; m.p. 92° (mixed m.p.).

The compound was successfully prepared in the following manner. Three grams (0.02 mole) of the sulfinic acid was dissolved in a warm solution of 5.3 g. (0.02 mole) of the ketone in 100 ml. of absolute ethanol. After standing at room temperature for several days, a crystalline product which softened at 92° and melted over a range of 176-186° was obtained. The product was purified by extraction with

ethyl acetate and finally by recrystallization from absolute ethanol. The yield was 4.0 g. (48%); m.p. 190°.

Anal. Calcd. for $C_{21}H_{24}O_4NSCl$: S, 7.6. Found: S, 7.3 and 7.32.

The Reaction between 1-(p-Methoxyphenyl-3-(2-quinolyl)-2-propen-1-one and 1-Piperidinesulfinic Acid.- An attempt to prepare the corresponding β-ketosulfonamide from this unsaturated ketone led to the quantitative recovery of the starting material (mixed m.p.). The reaction was carried out according to the above procedure on 3 g. (0.01 mole) of the ketone and 1.5 g. (0.01 mole) of the sulfinic acid in 50 ml. of absolute ethanol.

1-Piperidineseleninic Acid.[127] A solution containing 11 g. (0.1 mole) of resublimed selenium dioxide and 8.5 g. (0.1 mole) of piperidine in 150 ml. of anhydrous benzene was stirred for twelve hours. The solid material was filtered from the solution, washed with benzene, and dried in vacuo over phosphorus pentoxide. The yield was 13 g. (65%); m.p. 65°. (Marino[127] et al. reported a melting point of 70° for the compound). The product readily absorbed moisture and

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127. Marino and Squintani, Atti. accad. Lincei, 20, II, 66 (1912) [C. A., 6, 625 (1912)]; Gazz. Chim. ital., 42, 419 (1912) [C. A., 6, 3271 (1912)]; Marino and Toninelli, ibid., 43, 409 (1913) [C. A., 7, 2936 (1913)].

selenium formed on the surface of the material on exposure to the atmosphere. Attempts to prepare an addition compound from 1-piperidineseleninic acid and benzalacetophenone were unsuccessful.

2-Benzoyl-N,N-diethyl-1-phenylethanesulfonamide (A).- A solution of 7.3 g. (0.1 mole) of diethylamine in 150 ml. of anhydrous ether was saturated with sulfur dioxide until no further precipitate was obtained. No attempt was made to isolate the free N,N-diethylamidosulfurous acid since this compound showed a great tendency to absorb atmospheric moisture. The excess ether was removed by distillation under reduced pressure and the oily residue dissolved in 80 ml. of absolute ethanol containing 10 g. (0.05 mole) of benzalacetophenone. The addition product crystallized from the solution after standing at room temperature for three days. After recrystallization from ethanol, the yield was 8.6 g. (49%); m.p. 150-152°.

(B).- A solution containing 3.6 g. (0.05 mole) of diethylamine and 5.2 g. (0.025 mole) of benzalacetophenone in 50 ml. of absolute ethanol was saturated with anhydrous sulfur dioxide. After standing in the ice box for two weeks, the solution was concentrated yielding 7.5 g. (87%) of the crude product. After recrystallization from absolute ethanol, the final yield of the product was 5.0 g. (58%); m.p.

150°. A mixed melting point determination on the two products showed no depression.

Anal. Calcd. for $C_{19}H_{23}O_3NS$: S, 9.26. Found: S, 8.8.

2-Benzoyl-N-butyl-1-phenylethanesulfonamide (A).- Into an ethereal solution of 3.7 g. (0.05 mole) of n-butylamine there was passed anhydrous sulfur dioxide until no further precipitation occurred. The solid N-butylamidosulfurous acid was not isolated but treated directly with 6 g. (0.03 mole) of benzalacetophenone in 50 ml. of absolute ethanol after removing the excess ether. The β-ketosulfonamide crystallized from the solution after standing at room temperature for twelve hours. The product was filtered and recrystallized from absolute ethanol. Five and seven-tenths grams (70%) was obtained; m.p. 130-131°.

(B).- The product was obtained directly by saturating a solution of 3.7 g. (0.05 mole) of the amine and 5.2 g. (0.025 mole) of benzalacetophenone with sulfur dioxide. The yield of the pure product was 5.6 g. (80%); m.p. 130-130.5°. A mixed melting point of the two products showed no depression.

Anal. Calcd. for $C_{19}H_{23}O_3NS$: S, 9.26. Found: S, 9.1 and 8.9.

N-Phenylamidosulfurous Acid.[125a,128,129] Anhydrous sulfur dioxide was passed into an ethereal solution containing 5 g. (0.052 mole) of aniline. The light yellow crystalline product which gradually precipitated from the solution was rapidly filtered and weighed. Five and five-tenths grams (69%) of the crude material was obtained. The product deliquesced too rapidly to obtain an accurate melting point. A value of "about 60°" has been reported[125a] in the literature. The yield of the compound was not given by the original investigators.

2-Benzoyl-1-phenylethanesulfonanilide (A).- The compound was prepared from 5.5 g. (0.034 mole) of N-phenylamidosulfurous acid and 6.2 g. (0.03 mole) of benzalacetophenone in 50 ml. of absolute ethanol. The yield was 6.5 g. (60%).

(B).- The yield from 5 g. (0.052 mole) of aniline, 5.2 g. (0.025 mole) of benzalacetophenone and sulfur dioxide was 8 g. (88%). Both products were difficultly soluble in boiling ethanol. Extraction of the crude products with this solvent gave a product which decomposed at 168-170°. After recrystallization from glacial acetic acid, a product which

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128. Boessneck, Ber., 21, 1906 (1888).

129. Schiff, Ann., 140, 126 (1866).

melted with decomposition at 181° was obtained. The keto-sulfonamide could be recrystallized from a large excess of absolute ethanol yielding a product which decomposed at 181°.

Anal. Calcd. for $C_{21}H_{19}O_3NS$: S, 8.76. Found: S, 8.48. (Found for compound recrystallized from acetic acid; S, 8.47 and 8.94). The products obtained from both methods of preparation were identical (mixed m.p.).

2-Benzoyl-N-methyl-1-phenylethanesulfonanilide (Attempted).- An ethereal solution of 5.4 g. (0.05 mole) of N-methylaniline was saturated with anhydrous sulfur dioxide. No insoluble solid product was formed during this reaction. The excess ether was removed by distillation, and the viscous red oil was dissolved in 25 ml. of absolute ethanol containing 5.2 g. (0.025 mole) of benzalacetophenone. Approximately 1 g. of a crystalline product which melted over a range of 175-179° was obtained. The compound analyzed high for nitrogen.

Anal. Calcd. for $C_{22}H_{21}O_3NS$: N, 3.69. Found: N, 5.11.

Attempt to Prepare 2-Benzoyl-N,N-dioctadecyl-1-phenylethanesulfonamide. - Attempts to prepare this compound from 2.2 g. (0.005 mole) of n-dioctadecylamine and 1.1 g. (0.005 mole) of benzalacetophenone by the methods (A) and (B) described above were unsuccessful. A sulfur-free product melt-

ing over a range of 65-70° was invariably obtained.

Attempt to Prepare 2-Benzoyl-N,N-didodecyl-1-phenylethanesulfonamide.- An ethereal solution containing 8 g. (0.023 mole) of di-n-dodecylamine was saturated with anhydrous sulfur dioxide. The solution became slightly turbid, and a white waxy solid which could not be filtered gradually precipitated. After removing the excess ether, 4.2 g. (0.02 mole) of benzalacetophenone was added and the mixture warmed on the water bath for two hours, then dissolved in 50 ml. of ethanol and allowed to stand at room temperature for twelve hours. A solid product (3.5 g.) which could not be identified was obtained and which after several recrystallizations from ethanol melted at 48°.

β-Phenyl-α-bromopropiophenone (Benzalacetophenone Hydrobromide).[91b] Twenty-one grams (0.1 mole) of benzalacetophenone was dissolved in 200 ml. of petroleum ether (b.p. 77-115°). To the resulting solution there was added dropwise and with stirring 50 g. (0.18 mole) of hydrogen bromide (30%) in glacial acetic acid. The bromoketone was filtered from the solution and recrystallized from a mixture of benzene and petroleum ether. The yield of the product was 26.2 g. (88.5%); m.p. 105°. Previous investigators[91b] reported a melting point of about 110° for the compound but gave no yield of the product.

Sodium 2-Benzoyl-1-phenylethanesulfonate (A).- To 100 ml. of 50 percent ethanol there was added 7.5 g. (0.025 mole) of β-phenyl-β-bromopropiophenone and 6.3 g. (0.05 mole) of sodium sulfite. The mixture was refluxed for twelve hours and the excess sodium sulfite filtered from the warm solution. The sodium sulfonate crystallized from the solution upon cooling to room temperature yielding 8 g. (quantitative) of the product.

(B).- A suspension of 5.2 g. (0.025 mole) of benzalacetophenone and 3 g. (0.03 mole) of sodium bisulfite in 50 ml. of water was boiled for seven hours. The resulting solution was filtered and cooled. Seven and three-tenths grams (94%) of the sodium sulfonate was obtained. Both of the above products melted with decomposition at 125°.

The preparation of sodium 2-benzoyl-1-phenylethanesulfonate by method (A) has not been described in the literature. Knoevenagel[20] prepared the corresponding potassium sulfonate by the addition of potassium bisulfite to benzalacetophenone. The compound decomposed when heated to 155°; no yield was reported in the literature cited[20].

The Reaction of Sulfur Dioxide with 1-Piperidylmagnesium Bromide.- 1-Piperidylmagnesium bromide was prepared by treating an ethereal solution of 8.4 g. (0.1 mole) of piperidine with a slight excess of methylmagnesium bromide in

ether. Anhydrous sulfur dioxide was passed into the solution until no further precipitate was obtained. The light tan solid which formed was filtered off and washed with fresh ether then dried in air. The yield of the crude sulfur-containing product was 50 g. (200%, based on the original amount of piperidine).

One gram of this material was dissolved in 15 ml. of ethanol containing 1 g. (0.0048 mole) of benzalacetophenone. The solution was acidified with 0.5 ml. of acetic acid and allowed to stand in the ice box several days. No definite product could be isolated from the reaction. Two and five-tenths grams (0.01 mole) of the product resulting from the action of sulfur dioxide on 1-piperidylmagnesium bromide (?) was refluxed for two hours with 2.9 g. (0.01 mole) of β-phenyl-β-bromopropiophenone in 30 ml. of absolute ethanol. No condensation product could be isolated from the reaction.

Lithium 1-Piperidinesulfinate.- To an ethereal solution of phenyllithium prepared from 16 g. (0.1 mole) of bromobenzene and 1.4 g. (0.2 g. atom) of lithium there was added 8.5 g. (0.1 mole) of piperidine 30 ml. of ether. Color Test No. I[111] for the organometallic compound was negative while the characteristic Color Test No. IV was obtained for the N-lithium derivative[130]. Anhydrous sulfur dioxide was passed

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130. Gilman and Woods, J. Am. Chem. Soc., 65, 33 (1943).

into the solution until no further precipitate was obtained and Color Test No. IV[130] was negative. The product was filtered, washed with ether, and dried *in vacuo* over phosphorus pentoxide. The yield of the crude material was 18.5 g. (quantitative).

Four grams (0.025 mole) of the sulfinate and 5.7 g. (0.02 mole) of the β-phenyl-β-bromopropiophenone was suspended in 50 ml. of absolute ethanol and the suspension refluxed for one hour. The inorganic material was removed by filtration and after concentrating and cooling the filtrate, 3 g. of a crude product melting over a range of 135-145° was obtained. Recrystallization of the material from absolute ethanol gave 2.2 g. (25%) of a pure product melting at 177-178°. This compound was identical (mixed m.p.) with the β-ketosulfonamide obtained by the addition of 1-piperidinesulfinic acid to benzalacetophenone.

The Synthesis of β-Phenyl-β-(1-piperidinesulfonyl)propiophenone from Sodium 2-Benzoyl-1-phenylethanesulfonate.- To a suspension of 3.1 g. (0.01 mole) of the sulfonate (prepared from benzalacetophenone and sodium bisulfite) in 50 ml. of anhydrous benzene was added 1.5 ml. (2.4 g., 0.02 mole) of thionyl chloride. The mixture was refluxed on the steam bath for twenty minutes then cooled under the tap. Without isolating the intermediate acid chloride, 1.7 g.

(0.02 mole) of piperidine was added to the mixture and refluxing was continued for thirty minutes. After cooling, the insoluble material was filtered from the solution and extracted with hot absolute ethanol. From the cooled extract was obtained 2 g. (56%) of the β-ketosulfonamide; m.p. 176-177°. The product was identical (mixed m.p.) with those obtained by other methods.

One gram (45%) of the product (mixed m.p.) was obtained by the above method from sodium 2-benzoyl-1-phenylethanesulfonate from β-phenyl-β-bromopropiophenone and sodium sulfite.

2-Benzoyl-1-phenylethanesulfonanilide from Sodium 2-Benzoyl-1-Phenylethanesulfonate.- The compound was prepared according to the above procedure from 3.1 g. (0.01 mole) of the sodium sulfonate, 1.2 g. (0.01 mole) of thionyl chloride and 1.9 g. (0.02 mole) of aniline. The inorganic products and aniline hydrochloride formed during the reaction were removed by extracting the solid material with hot water. The yield of the sulfonanilide was 2 g. (56%); the product melted at 181° after recrystallization from absolute ethanol or from glacial acetic acid. This product was identical with that obtained from the addition of N-phenylamidosulfurous acid to benzalacetophenone (mixed m.p.).

Sodium Benzylsulfonate.[131] A mixture of 50 g. (0.2 mole)

131. Johnson and Ambler, ibid., 36, 372 (1914).

of crystallized sodium sulfite and 25 g. (0.2 mole) of benzyl chloride in 100 ml. of water containing 50 ml. of a 10 percent sodium hydroxide solution was stirred and refluxed for three hours. After cooling, the crystalline product was filtered off and dried at 100°. The yield was 23.5 g. (65%). Johnson and Ambler[131] obtained an 80 percent yield of the product.

Benzylsulfonyl Chloride.[132] A cooled mixture of 25 g. (0.12 mole) of sodium benzylsulfonate and 35 g. (0.15 mole) of phosphorus pentachloride was triturated until liquefied. After warming at 70° for one hour, the mixture was rapidly poured into ice water. The heavy oil obtained solidified on stirring and the crude product was filtered, washed with water and recrystallized from a mixture of benzene and petroleum ether (b.p. 60-70°). The yield was 14.5 g. (63%). The product melted at 87-88° and was pure enough for most purposes. A second recrystallization raised this value to 91-92° as reported in the literature[132]. It was, however, necessary to work the product up as quickly as possible because of its ease of hydrolysis.

1-Piperidylbenzylsulfonamide.[133] To a solution of 14.5

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132. Limpricht and v. Pechmann, Ber., 6, 534 (1873).

133. Marvel and Gillespie, J. Am. Chem. Soc., 48, 2943 (1926).

g. (0.076 mole) of benzylsulfonyl chloride in 100 ml. of benzene was added 12.6 g. (0.15 mole) of piperidine. After warming the reaction on the water bath for one-half hour, the piperidine hydrochloride was filtered from the warm solution. The excess benzene was distilled off and the residue recrystallized from ethanol. The yield was 14 g. (70%); m.p. 135°. The reported melting point for the compound is 131.5[133].

Attempted Alkylation of 1-Piperidylbenzylsulfonamide with Phenacyl Bromide.- Two and four-tenths grams (0.01 mole) of the sulfonamide was dissolved in 50 ml. of warm ethanol containing 0.01 mole of sodium ethoxide. To the resulting solution was added 2 g. (0.01 mole) of phenacyl bromide in 20 ml. of ethanol. The reaction was stirred for two hours at room temperature, and the resulting solution was refluxed with Norite, filtered and cooled. Two grams (84%) of the original sulfonamide (mixed m.p.) was recovered. Refluxing the reaction for four hours did not effect alkylation.

To a stirred refluxing solution of 2.4 g. (0.01 mole) of the sulfonamide in 25 ml. of anhydrous toluene there was added 0.25 g. (0.011 g. atom) of finely cut sodium. Most of the metal dissolved producing a light orange gelatinous solution. To this was added 2.2 g. (0.011 mole) of phenacyl bromide in 20 ml. of toluene. Evidences of decomposition

and the evolution of sulfur dioxide were noted upon refluxing the solution. A low recovery of the original sulfonamide and some decomposition products which could not be characterized resulted from the reaction.

To a solution of sodium amide prepared from 0.25 g. (0.011 g. atom) of sodium in liquid ammonia there was added 2.4 g. (0.01 mole) of the pulverized sulfonamide. The reaction was stirred until the excess ammonia had evaporated, the residue dissolved in 50 ml. of anhydrous benzene, and 2.1 g. (0.01 mole) of phenacyl bromide was added to the solution. After refluxing this deep red solution for two hours, 1.7 g. (71%) of the original sulfonamide was recovered.

Attempted Bromination of 1-Piperidylbenzylsulfonamide.- To a mixture of 2.5 g. (0.011 mole) of 1-piperidylbenzylsulfonamide and 0.5 g. of anhydrous aluminum chloride in 50 ml. of carbon tetrachloride was added dropwise and with stirring 0.6 ml. (1.8 g., 0.011 mole) of bromine in 10 ml. of carbon tetrachloride.

Since the red color of the bromine persisted after stirring the mixture at room temperature for one hour, the reaction was refluxed on the steam bath for eight hours and then was allowed to stand at room temperature overnight.

After the removal of the bromine and the excess solvent by distillation under reduced pressure, the residue was re-

crystallized from ethanol. 1-Piperidylbenzylsulfonamide (mixed m.p.) was recovered quantitatively from the reaction.

Selenophenol.[134] To a solution of phenylmagnesium bromide prepared from 40 g. (0.25 mole) of bromobenzene and 6 g. (0.25 g. atom) of magnesium in 200 ml. of sodium-dried ether there was gradually added 20 g. (0.25 g. atom) of powdered selenium which had been previously dried *in vacuo* over sulfuric acid. The mixture was stirred and refluxed for two hours then poured into a mixture of ice and hydrochloric acid. The layers were separated and the aqueous layer extracted with ether; the combined ether extract was dried over anhydrous calcium chloride.

The product was distilled at 68-71° (15 mm.); 20.5 g. (52.3%) was obtained. Selenophenol has been prepared in yields of 57-71 percent; b.p. 57-59° (8 mm.) or 84-86° (25 mm.)[134].

p-Chloroselenophenol.[135] To a solution of p-chlorophenylmagnesium bromide prepared from 50 g. (0.25 mole) of p-chlorobromobenzene and 6.5 g. (0.27 g. atom) of magnesium in 200 ml. of sodium-dried ether was gradually added 20 g. (0.25 g. atom) of dried selenium. The reaction was stirred

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134. Foster, Org. Syn., 24, 89 (1944).

135. Foster, Rec. trav. chim., 53, 405 (1934).

at room temperature for one hour and then poured into a mixture of ice and hydrochloric acid. The procedure employed in working up the reaction was identical with that described above. The yield was 26 g. (55%); b.p. 100-103° (15 mm.), m.p. 54-55°. A melting point of 57° was obtained by the original investigator[135].

It was essential to use an efficient hood in the preparation of the selenophenols. They possess extremely obnoxious odors, and the highly toxic hydrogen selenide is often a by-product of the reaction. These reactions were worked up as rapidly as possible in order to avoid the oxidation of the selenol to the corresponding diphenyl diselenide. Considerable amounts of the diselenides were formed in the above reactions but were not purified.

Attempted Preparation of Thallous p-Chloroselenophenolate.- The procedure described by Abbott[136] for the preparation of thallous p-thiocresolate was employed. To a solution of 0.9 g. (0.0047 mole) of p-chloroselenophenol in 25 ml. of methanol there was added dropwise an aqueous solution of thallous hydroxide until no more of the bright orange precipitate formed. The product was filtered, washed with methanol, and dried. One and two-tenths grams (65%) of the

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136. Abbott, R. K., Doctoral Dissertation, Iowa State College, (1942).

solid which sintered between 157 and 160° and which melted completely at 170° was obtained. Digestion of the substance with methanol gave rise to a product which melted over a range of 160-170°.

β-Phenyl-β-benzeneselenopropiophenone.- To a solution of 4.2 g. (0.02 mole) of benzalacetophenone in 25 ml. of ethanol there was added 3.2 g. (0.02 mole) of selenophenol in 15 ml. of ethanol. Within nine minutes after mixing the two reactants, the addition product began to crystallize from the solution. A solid mass of crystals was formed within an additional ten minutes. The yield of the crude product was 5.5 g. (76%); m.p. 118-120°. Two recrystallizations from ethanol gave rise to 4.2 g. (58.5%) of the pure product which melted at 120-120.5°.

Anal. Calcd. for $C_{21}H_{18}OSe$: Se, 21.64. Found: Se, 21.88.

A qualitative comparison of the rate of addition of selenophenol and thiophenol, respectively, to benzalacetophenone was studied. The reaction described above was run simultaneously with a second reaction in which 2.2 g. (0.02 mole) of thiophenol[6,10] was substituted for the molar equivalent of selenophenol. No addition product was formed after five hours standing at room temperature. The addition of five drops of piperidine[10] effected the immediate precipitation of the corresponding ketosulfide. The yield was 6.3 g.

(quantitative); m.p. 118°. (The melting point value reported in the literature[6,10] is 121°).

The solubility of the sulfur-containing addition product in ethanol was much less than that of the corresponding selenium-containing compound. Although the addition of selenophenol to benzalacetophenone took place without the aid of a catalyst, the addition of a few drops of piperidine hastened the reaction with no appreciable increase in the yield of the product.

The Reaction of α-Phenyl-β-benzeneselenopropiophenone with Alkali.- Five-tenths of a gram (0.00125 mole) of the ketoselenide was dissolved in 15 ml. of ethanol to which 2.5 ml. of a 20 percent sodium hydroxide solution had been added. The resulting solution was allowed to stand at room temperature for one hour and was then diluted with water. Benzalacetophenone (mixed m.p.) was recovered from the reaction. The acidification of the mother liquor produced the characteristic odor of selenophenol.

Oxidation of α-Phenyl-β-benzeneselenopropiophenone.- Attempts to oxidize this compound to the corresponding ketoselenone were unsuccessful. In three successive trials, 30 percent hydrogen peroxide in glacial acetic acid, potassium permanganate in glacial acetic acid, and concentrated nitric acid, respectively, were used. In each case, the oxidation

products could not be characterized.

The Reaction of β-Phenyl-β-benzeneselenopropiophenone with Phenylhydrazine.- A solution of 0.5 g. (0.0045 mole) of phenylhydrazine and 0.5 g. (0.00125 mole) of the ketoselenide in 15 ml. of glacial acetic acid was refluxed for fifteen minutes. The white crystalline product obtained after cooling the solution was recrystallized from glacial acetic acid to a constant melting point of 140°.

The qualitative test for selenium in the compound was negative. The reported value for the melting point of the selenium-free 1,3,5-triphenylpyrazoline[137] is 135°. (1,3,5-triphenylpyrazoline has been reported to result from the action of phenylhydrazine on the corresponding ketosulfide in glacial acetic acid.) An attempt to prepare an authentic sample of this compound from benzalacetophenone and phenylhydrazine for a mixed melting point determination was unsuccessful.

n-Chloro-β-phenyl-β-benzeneselenopropiophenone.- To a solution of 6.1 g. (0.025 mole) of 4'-chlorochalcone in 50 ml. of ethanol there was added 4.0 g. (0.025 mole) of selenophenol in 15 ml. of ethanol. The flask was corked and allowed to stand at room temperature for twelve hours, after

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137. Knorr and Laubmann, Ber., 21, 1210 (1888); Fromm, Ann., 394, 305 (1913).

which time, the addition product was filtered from the solution and recrystallized from ethanol. The yield of the pure product was 5.8 g. (58%); m.p. 100-101°.

Anal. Calcd. for $C_{21}H_{17}OSeCl$: Cl, 8.77. Found: Cl, 8.9 and 9.0.

β-Anisyl-β-benzeneselenopropiophenone.- This compound was prepared from 5 g. (0.02 mole) of 4-methoxychalcone and 3.3 g. (0.021 mole) of selenophenol in 70 ml. of ethanol. The crystalline addition product was formed after allowing the reaction to stand at room temperature for twelve hours. The yield of the purified product (from ethanol) was 5.7 g. (69%); m.p. 87-88°.

Anal. Calcd. for $C_{22}H_{20}O_2Se$: Se, 20.00. Found: Se, 19.74 and 19.76.

β-Phenyl-β-(4-chlorobenzeneseleno)propiophenone.- The compound was obtained from the addition of 4.8 g. (0.025 mole) of p-chloroselenophenol to 5.2 g. (0.025 mole) of benzalacetophenone in 60 ml. of ethanol. The crystalline addition product was formed within fifteen minutes after mixing the reactants. Recrystallization of the crude product from ethanol produced 7 g. (80%) of the pure compound; m.p. 105°.

Anal. Calcd. for $C_{21}H_{17}OSeCl$: Cl, 8.77. Found: Cl, 8.68 and 8.66.

Refluxing (nitrogen atmosphere) a solution of sodium p-

chloroselenophenolate prepared from 2 g. (0.01 mole) of p-chloroselenophenol and 0.4 g. (0.01 mole) of sodium hydroxide in ethanol with 2.8 g. (0.01 mole) of β-bromo-β-phenylpropiophenone gave 3 g. (62%) of the ketoselenide which was identical with the product obtained from the addition of p-chloroselenophenol to benzalacetophenone; m.p. 105° (mixed m.p.).

β-Anisyl-β-(4-chlorobenzeneseleno)propiophenone.- A solution containing 5.5 g. (0.025 mole) of 4-methoxychalcone and 4.8 g. (0.025 mole) of p-chloroselenophenol in 60 ml. of ethanol was allowed to stand at room temperature until the crystallization of the addition product was complete. The crystalline substance was filtered from the supernatant solution and recrystallized from ethanol. The yield was 4.5 g. (44%); m.p. 97-98°.

Anal. Calcd. for $C_{22}H_{19}O_2SeCl$: Cl, 8.16. Found: Cl, 8.02.

p-Chloro-β-phenyl-β-(4-chlorobenzeneseleno)propiophenone.- This compound resulted from the addition of 3.4 g. (0.018 mole) of p-chloroselenophenol to 4.3 g. (0.018 mole) of 4'-chlorochalcone in 60 ml. of ethanol. The yield of the crude product was 6.2 g. (80%); m.p. 105-106°. Three recrystallizations from ethanol produced 4 g. (52%) of the pure product which melted at 110°.

Anal. Calcd. for $C_{21}H_{16}OSeCl_2$: Cl, 16.33. Found: Cl, 16.00 and 16.04.

p-Methoxy-β-(2-chlorophenyl)-β-benzeneselenopropiophenone (Attempted).- To 6.8 g. (0.025 mole) of 2-chloro-4'-methoxychalcone in 50 ml. of ethanol there was added a solution of 4.0 g. (0.025 mole) of selenophenol in 15 ml. of ethanol. After allowing the reaction to stand at room temperature for twelve hours none of the addition product had crystallized from the solution. The solution was then refluxed under nitrogen for two hours and set aside to cool. The crude material oiled out of solution and finally crystallized after standing at room temperature for several hours. Eight and two-tenths grams (76%) of a crude product melting over a range of 45-70° was obtained. Attempts to purify the material by recrystallization from ethyl acetate and from glacial acetic acid were unsuccessful.

The compound was not obtained when glacial acetic acid was used as the solvent for the reaction.

Benzeneseleninic Acid.[138] Selenophenol was prepared as previously described by means of the Grignard synthesis from 39.2 g. (0.25 mole) of bromobenzene, 6 g. (0.25 g. atom) of magnesium, and 19.7 g. (0.25 g. atom) of selenium.

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138. Pyman, J. Chem. Soc., 115, 166 (1919).

Subsequent to the hydrolysis of the magnesium complex, the crude ether extract which contained a mixture of selenophenol and diphenyl diselenide was separated and dried over anhydrous calcium chloride. The solution was then filtered and the solvent removed by distillation. The oily residue was oxidized directly by cautiously adding it dropwise into 160 ml. (4 ml. for each gram of the oil) of concentrated nitric acid (d. 1.4). Digesting the mixture on the water bath for two hours and then cooling produced 37 g. (58.7%) of the crude benzeneseleninic acid nitrate melting over the range of 105-115°. A product melting at 114-115° was obtained from the recrystallization of the crude nitrate from water. The melting point for the compound given in the literature[138] was 112°. A yield of 44 percent was reported.

Several attempts were made to obtain the free acid by the neutralization of benzeneseleninic acid nitrate. Following the procedure of Pyman[138], 10 g. of the nitrate was dissolved in 20 ml. of water and was neutralized with 6 ml. of 10 percent ammonium hydroxide. The resulting product melted at 118-120°.

A third method employed in securing benzeneseleninic acid from its nitrate was that described by Stoecker and Krafft[139]. To 5 g. (0.02 mole) of benzeneseleninic acid

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139. Stoecker and Krafft, Ber., 39, 2197 (1906).

nitrate dissolved in a slight excess of ammonium hydroxide there was added a solution of 3.4 g. (0.02 mole) of silver nitrate in 15 ml. of water. The neutralization of the resulting solution with dilute nitric acid produced a curdy, white precipitate which was filtered from the solution and washed with water. The addition of 2.2 ml. of 12N hydrochloric acid to an aqueous suspension of the silver salt of the acid produced a mixture of silver chloride and benzeneseleninic acid which could be separated by filtering the warm aqueous suspension. The product obtained from the cooled filtrate melted over a range of 110-118°.

Benzeneseleninic acid has been reported to melt at 121° and at 124-125°. The compound resolidified at 130°, forming the anhydride, which melted at 165-166°[138,139]. This behavior was observed in both of the products prepared above.

Attempted Addition of Benzeneseleninic Acid to Benzalacetophenone.- The experimental procedure employed was essentially the same as that described in the addition of sulfinic acids to chalcones. An equimolar amount of benzeneseleninic acid or its nitrate was added to a solution of benzalacetophenone in ethanol or glacial acetic acid and allowed to stand at room temperature. In all attempts made to bring about this addition, benzalacetophenone (mixed m.p.) was recovered from the reaction.

Quantitative Determination of Selenium.- The selenium analyses were run according to the method described by Banks and Hamilton[140]. Between 0.15 and 0.20 gram of the sample was digested with 5 ml. of concentrated sulfuric acid in a 250 ml. Erlenmeyer flask until completely charred. Fuming nitric acid was then added dropwise until the solution was clear, and after boiling off the excess nitric acid, the solution was transferred quantitatively to a 150 ml. beaker containing 50 ml. of water. About one gram of hydroxylamine sulfate was added, and the solution was then heated on the hot plate until the selenium had coagulated. The precipitate was collected on a sintered glass crucible, washed with water, then with alcohol and ether, and finally dried to constant weight at 110°.

In the above determination, it was found that the complete removal of nitric acid or any oxides of nitrogen was essential. The precipitation of the selenium was often more rapid when made from a weakly acidic solution obtained by neutralizing the sulfuric acid solution with ammonium hydroxide followed by reacidification with a few drops of concentrated sulfuric acid.

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140. Banks and Hamilton, J. Am. Chem. Soc., 61, 2306 (1939); see also Fredga, Uppsala Univ. Arsskrift, No. 5, 232 (1935) /C. A., 29, 7281 (1935)/.

2-Dodecylquinoline Hydrochloride. (A). Dodecyllithium.[141] To a suspension of 2.1 g. (0.3 g. atom) of finely cut lithium in 30 ml. of anhydrous ether contained in a 250 ml. three-necked, round-bottomed flask equipped with a mechanical stirrer, a dropping funnel, and a reflux condenser there was added over a period of one-half hour a solution of 24.9 g. (0.10 mole) of dodecyl bromide in 50 ml. of anhydrous ether. After the complete addition of the bromide, the reaction was refluxed on the water bath for fifteen minutes. Color Test No. I[111] for the organometallic compound was positive at this stage of the reaction.

The ethereal solution was filtered under nitrogen, and the yield (27%) of the organometallic compound was determined by the double titration method of Gilman and Haubein[121].

(B). 2-Dodecylquinoline Hydrochloride.- To the solution of dodecyllithium, cooled by means of an ice-salt mixture, there was added 5 g. (0.038 mole) of quinoline in 30 ml. of anhydrous ether. A considerable amount of tetracosane, a side product resulting from the coupling of the organometallic compound with the alkyl halide, crystallized from the solution. However, the characteristic yellow color[122] of the anil-addition product was present. The reaction was

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141. Meals, R. N., Doctoral Dissertation, Iowa State College, 1942; J. Org. Chem., 9, 211 (1944).

stirred for fifteen minutes and allowed to stand at room temperature for twelve hours after which time Color Test No. I[111] for the organometallic compound was negative. Hydrolysis was carried out by pouring the reaction mixture into a mixture of dilute (1:1) hydrochloric acid and ice. The ether layer was spearated, dried over anhydrous calcium chloride, and the filtered solution finally saturated with anhydrous hydrogen chloride. The yield of the hydrochloride was 2.5 g. (27.8%). The product melted over a range of 102-105° and could not be further purified.

Anal. Calcd. for $C_{21}H_{32}NCl$: N, 4.2. Found: N, 4.72 and 4.5.

N-Phenylanthranilic Acid.- This compound was prepared from 155 g. (1.66 moles) of aniline and 46.5 g. (0.3 mole) of o-chlorobenzoic acid according to the method of Allen and Kee[142]. The yield was 48 g. (74%); m.p. 180°. The yields reported in the literature ranged from 82-93%; the reported melting point for the compound is 179-181°[142].

9-Chloroacridine.-[143] From an attempt to prepare 9-chloroacridine from 48.1 g. (0.22 mole) of N-phenylanthranilic acid and 160 ml. (268 g., 1.75 moles) of phosphorus oxy-

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142. Allen and Kee, Org. Syn., Coll. Vol. II, 15 (1943).

143. Albert and Ritchie, ibid., 22, 5 (1942).

chloride by the method of Albert and Ritchie[143] there was obtained 36 g. (95%) of 9-acridone; m.p. above 300°.

The treatment of 20 g. (0.11 mole) of this product with 90 ml. (151 g., 0.99 mole) of phosphorus oxychloride yielded 20 g. (91%) of 9-chloroacridine; m.p. 120°. (This value agreed with that given in the literature[143]).

9-Dodecylaminoacridine Monohydrochloride.[144] Into a 250 ml. three-necked, round-bottomed flask equipped with a reflux condenser and a mechanical stirrer there was placed 10 g. of phenol, 4 g. (0.019 mole) of 9-chloroacridine, and 6.8 g. (0.037 mole) of dodecylamine. The reaction was stirred under nitrogen for three hours at 145-150°. After cooling, the dodecylamine hydrochloride was precipitated from the reaction mixture by the addition of ether. The filtered solution was washed with several portions of a 10 percent sodium hydroxide solution until free of phenol, then with water, and finally dried over anhydrous potassium carbonate. The product was isolated as the amine hydrochloride by passing anhydrous hydrogen chloride into the filtered solution, and was finally purified by recrystallization from a 50 percent mixture of ether and ethanol. The yield was 5.1 g.

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144. Since the completion of this investigation, the preparation of 9-dodecylaminoacridine hydrochloride in 85% yields (m.p. 92°) has been reported by Albert, Goldacre, and Heymann, J. Chem. Soc., 651 (1943).

(69%); m.p. 88-90°.

Anal. Calcd. for $C_{25}H_{35}N_2Cl$: N, 7.02. Found: N, 7.02.

9-Octadecylaminoacridine Hydrochloride.- This compound was prepared by the same procedure employed in the synthesis of 9-dodecylaminoacridine hydrochloride. A mixture of 4.0 g. (0.0187 mole) of 9-chloroacridine and 8.1 g. (0.03 mole) of octadecylamine in 10 g. of phenol was heated at 150-160° for three and one-half hours. After cooling, the crude product was extracted from the reaction mixture with 250 ml. of ether and the resulting ethereal solution washed free of phenol with three 100 ml. portions of a 10 percent sodium hydroxide solution then dried over anhydrous potassium carbonate.

The passage of anhydrous hydrogen chloride into the filtered solution yielded 7.1 g. (81%) of a yellow crystalline product which melted over a range of 97-100°. Four recrystallizations of this crude product from a 50 percent mixture of ethanol and ether raised the melting point to a constant value of 100-102°. The final yield of the product was 5.8 g. (67%).

Anal. Calcd. for $C_{31}H_{47}N_2Cl$: N, 5.79. Found: N, 5.91.

2-Methoxy-9-chloroacridine.[145]- Twenty-four and three-tenths grams (0.1 mole) of N-p-anisylanthranilic acid[145] and 135 ml. (217 g., 1.42 moles) of freshly distilled phosphorus oxychloride was placed in a 500 ml. round-bottomed flask. The flask was attached to a reflux condenser and then heated to 85-90° until the rather vigorous reaction which took place subsided. Heating was then continued at 135-140° for four hours and the excess phosphorus oxychloride removed by distillation under reduced pressure. The residue was cooled and rapidly introduced into a mixture containing 150 ml. of chloroform, 200 ml. of concentrated ammonium hydroxide, and 500 g. of ice. The organic layer was separated and dried over anhydrous calcium chloride. After removing the excess solvent, the residue was purified by recrystallization from a mixture of ethanol and chloroform. The yield was 21 g. (86%); m.p. 152°. The value reported in the literature[145] is 152-153°.

2-Methoxy-9-dodecylaminoacridine Monohydrochloride.- The compound was prepared according to the same procedure described under the preparation of 9-dodecylaminoacridine hydrochloride. From 6 g. (0.025 mole) of 2-methoxy-9-chloroacridine and 7.8 g. (0.043 mole) of dodecylamine there

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145. Magidson and Grigorowsky, Ber., 69, 405 (1936).

was obtained 5 g. of a product which melted at 107-108°. The product was purified by recrystallization from a 50 percent mixture of ether and ethanol.

Anal. Calcd. for $C_{26}H_{37}ON_2Cl$: N, 6.54. Found: N, 6.4.

2-Methoxy-9-dioctadecylaminoacridine (Attempted).- In an attempt to prepare this compound a mixture of 4.8 g. (0.02 mole) of 2-methoxy-9-chloroacridine and 7.3 g. (0.02 mole) of dioctadecylamine was heated for four hours (150°) in 10 g. of phenol. Eight grams (quantitative) of dioctadecylamine hydrochloride (mixed m.p.) was recovered from the reaction.

2-Methoxy-9-octadecylaminoacridine Monohydrochloride.- The procedure used in the preparation of this compound followed that previously described under the synthesis of 9-octadecylaminoacridine. The yield of the pure product from 4.4 g. (0.018 mole) of 2-methoxy-9-chloroacridine and 4.9 g. (0.018 mole) of octadecylamine was 5.1 g. (55%); m.p. 133-134° (from a 50 percent solution of ether and ethanol).

Anal. Calcd. for $C_{32}H_{49}ON_2Cl$: N, 5.47. Found: N, 5.64.

2,5-Dichlorobenzoic Acid.[146] To a stirred suspension of

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146. Hübner, Ann., 222, 201 (1884).

43 g. (0.25 mole) of 2-amino-5-chlorobenzoic acid in 110 ml. of concentrated hydrochloric acid cooled to 0° by means of an ice-salt mixture there was added a solution of 17.2 g. (0.25 mole) of sodium nitrite in 100 ml. of water. The resulting diazonium compound was rapidly added to a cooled solution of 50 g. (0.25 mole) of cuprous chloride in 110 ml. of concentrated hydrochloric acid. The reaction was stirred for approximately three hours and then heated on the water bath for one-half hour. The crude product was dissolved in a 10 percent solution of sodium bicarbonate, boiled with Norite, and filtered. Acidification of the filtrate yielded 40 g. (85%) of the free acid; m.p. 152°. The value reported in the literature is 153°[146].

2-Methoxy-7,9-dichloroacridine.[147]- The compound was prepared from 15 g. (0.054 mole) of N-p-anisyl-5-chloroanthranilic acid[147] and 100 ml. (167 g., 1.09 moles) of phosphorus oxychloride according to the procedure described under the preparation of 2-methoxy-9-chloroacridine. The yield was 10.3 g. (69%); m.p. 197°. The value found in the literature[147] is 203-204°.

2-Methoxy-7-chloro-9-dodecylaminoacridine Monohydrochloride.- The product was obtained from 4.5 g. (0.016 mole)

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147. Fel'dman and Kopeliovich, Arch. Pharm., 273, 488 (1935) /C. A. 30, 1378 (1936)/.

of 2-methoxy-7,9-dichloroacridine and 3 g. (0.016 mole) of dodecylamine. The yield was 4.2 g. (56%); m.p. 209-210° (recrystallized from an ether-ethanol mixture).

Anal. Calcd. for $C_{26}H_{36}ON_2Cl_2$: N, 6.05. Found: N, 6.21.

Dioctadecylaminomethyl n-Butyl Ether (Attempted).- The procedure of Robinson and Robinson[148] was followed in the attempted preparation of the above compound. To a warmed (80°) solution of 25 g. (0.05 mole) of dioctadecylamine in 150 ml. (121.5 g., 1.04 moles) of n-butyl alcohol there was gradually added 1.5 g. (0.05 mole) of paraformaldehyde. After stirring the solution for two hours, 7 g. (0.05 mole) of anhydrous potassium carbonate was added, and stirring at 80° was continued for four hours.

The inorganic material was filtered from the warm solution. From the filtrate there was recovered 21 g. (84%) of the original amine; m.p. 72-74° (mixed m.p.).

1-Dodecyl-2,5-dimethylpyrrole.[149] The general procedure used in the preparation of these 1-alkyl-2,5-dimethylpyrroles was that of Hazelwood, Hughes, Lions, and co-workers[150].

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148. Robinson and Robinson, J. Chem. Soc., 123, 532 (1923).

149. Hunter, B. A., Doctoral Dissertation, Iowa State College, 1941.

A mixture of 9.3 g. (0.05 mole) of dodecylamine and 5.7 g. (0.05 mole) of acetonylacetone was stirred at 125° for two and one-half hours. After cooling, the resulting solution was poured into ice-water, and the viscous oil was extracted with ether and dried over anhydrous sodium sulfate. The excess solvent was removed, and the product distilled at 173-175° (3 mm.). The yield was 11.7 g. (89%); d_{20}^{20} 0.8451; n_D^{20} 1.4795; MR calcd.: 87.68; Found: MR 88.37.

Anal. Calcd. for $C_{18}H_{33}N$: N, 5.32. Found: N, 5.63.

1-Octadecyl-2,5-dimethylpyrrole.[149] Eight and two-tenths grams (0.035 mole) of n-octadecylamine and 4.0 g. (0.035 mole) of acetonylacetone was stirred for two and one-half hours at 125°. A light tan solid was obtained upon pouring the reaction mixture over cracked ice. This crude product was filtered and recrystallized from absolute ethanol. The yield was 9.3 g. (76.5%); m.p. 39°.

Anal. Calcd. for $C_{24}H_{45}N$: N, 4.05. Found: N, 4.03.

Attempt to Prepare 9-(2,5-Dimethylpyrryl)acridine.- Into a 250 ml. three-necked, round-bottomed flask equipped with a stirrer and a reflux condenser there was placed 9.7 g. (0.05 mole) of 9-aminoacridine[143] and 5.7 g. (0.05 mole)

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150. Hazelwood, Hughes, Lions, and co-workers, J. Proc. Roy. Soc., N. S. Wales, 71, 92 (1937) /C.A., 32, 1695 (1938)/.

of acetonylacetone. No reaction took place after heating the mixture on the water bath for two hours.

The reaction was repeated using a mixture of 50 ml. of absolute ethanol and one milliliter of glacial acetic acid as a solvent. After refluxing the solution for six hours and cooling, 9-aminoacridine (mixed melting point) was recovered quantitatively from the reaction.

The original amine (mixed melting point) was recovered after refluxing 2.9 g. (0.025 mole) of acetonylacetone and 4.9 g. (0.025 mole) of 9-aminoacridine in isoamyl alcohol.

An attempt to prepare the compound using glacial acetic acid as the solvent led to the recovery of 9-aminoacridine. The addition of a small amount of hydrochloric acid failed to catalyze the reaction.

The Reaction of Phenylmagnesium Bromide with Ethylene Sulfide.[151a] In a 500 ml. three-necked, round-bottomed flask equipped with a reflux condenser, a mechanical stirrer and previously swept out with a stream of dry nitrogen there was placed 12.6 g. (0.52 g. atom) of magnesium and 50 ml. of sodium-dried ether. To the stirred suspension there was added

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151. (a) The general procedure described by Dreger for the preparation of n-hexyl alcohol from ethylene oxide and butylmagnesium bromide was followed. Org. Syn., Coll. Vol. I, 306 (1941); (b) The ethylene sulfide (b.p. 56°) was kindly supplied by S. P. Massie.

78.5 g. (0.5 mole) of bromobenzene in 150 ml. of ether at such a rate as to maintain a gentle refluxing of the solvent.

The reaction was stirred for 30 minutes after the addition of the bromobenzene then cooled to -10 to -5° by means of an ice-salt mixture while 30.8 g. (0.53 mole) of ethylene sulfide[151b] in 50 ml. of ether was gradually added. A white precipitate was formed with the addition of each drop of the solution to the Grignard reagent. After the complete addition of the ethylene sulfide, the ice bath was removed, and as the temperature of the mixture approached 25°, the solvent began to reflux gently. After this reaction had subsided, the flask was heated on the water bath for one hour.

The condenser was then arranged for downward distillation, and 70 ml. of the ether was removed. An equal volume (70 ml.) of anhydrous benzene was added to the flask by means of a dropping funnel and the distillation continued until the temperature of the vapors reached 65°. At this point in the procedure the reflux condenser was replaced and the mixture heated on the steam bath for one and one-half hours. The viscous, grey mass was poured into 250 ml. of ice water, and the resulting mixture acidified by the addition of 200 ml. of 30% sulfuric acid. An attempt was made to separate the product from the heavy emulsion by steam distillation. After separating the layers of the distillate and fractionally distilling the organic portion, there was

obtained at 135° (35 mm.) 2.7 g. of a product possessing a thiol-like odor. The corresponding 2,4-dinitrophenyl sulfide melted at 78°. (The melting point reported in the literature[152] for β-phenylethyl 2,4-dinitrophenyl sulfide is 89.5°.)

The Reaction between Phenyllithium and Ethylene Sulfide.- Phenyllithium was prepared from 78 g. (0.5 mole) of bromobenzene and 6.9 g. (1.0 g. atom) of lithium. The ether solution of the organometallic compound was filtered under nitrogen into a 500 ml. three-necked, round-bottomed flask equipped with a mechanical stirrer, a reflux condenser, and a dropping funnel. A solution of 30.8 g. (0.53 mole) of ethylene sulfide in 50 ml. of ether was introduced into the flask at such a rate as to maintain a steady refluxing of the solvent. The reaction was then heated on the water bath for one hour after which time Color Test No. I[111] for the presence of the organometallic compound was negative. The hydrolysis of the complex was effected by pouring the solution into a mixture of 250 g. of cracked ice and 100 ml. of dilute (1:1) hydrochloric acid. The organic layer was decanted off, the aqueous layer extracted with ether, and the combined ether extract was dried over anhydrous sodium sul-

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152. Bost, Turner, and Norton, J. Am. Chem. Soc., 54, 1985 (1932).

fate. After filtering the solution and removing the excess solvent, two products resulted from the fractional distillation of the residue: (a) b.p. 67-75° (3 mm.), 15.9 g. (23%) and (b) b.p. 110-120° (3 mm.), 18.8 g. (24.6% based on the assumption that this product was the disulfide).

β-Phenylethyl mercaptan was originally prepared by von Braun[153] by the alkaline hydrolysis of β-phenylethyl dithiocarbamate. The product boiled at 105° (23 mm.).

Repeated attempts to prepare the 2,4-dinitrophenyl sulfide from the product obtained above were unsuccessful.

Holmberg[154] has prepared di(β-phenylethyl) disulfide by the oxidation of β-phenylethyl mercaptan with iodine in ethanol. The physical properties of the compound were not reported. From the oxidation of fraction (b) by chlorine following the method of Lee and Dougherty[155] and by the subsequent treatment of the resulting sulfonyl chloride with ammonia there was obtained a small quantity of β-phenylethanesulfonamide (m.p. 120°). The reported melting point for this compound is 121.5-122.5°[156a].

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153. von Braun, Ber., 45, 1566 (1912).

154. Holmberg, Arkiv Kemi. Mineral. Geol., 12A, No. 14, 10 (1937) /C. A., 31, 4292 (1937)/.

155. Lee and Dougherty, J. Org. Chem., 5, 81 (1940).

156. (a) Johnson and Sprague, J. Am. Chem. Soc., 58, 1348 (1936); (b) Huston and Agett, J. Org. Chem., 6, 123 (1941); (c) Gilman and Kirby, J. Am. Chem. Soc., 54, 346 (1932).

The Reaction between Benzylmagnesium Chloride and Ethylene Sulfide.- Benzylmagnesium chloride was prepared from 63 g. (0.5 mole) of benzyl chloride and 12.6 g. (0.52 g. atom) of magnesium. The reaction with ethylene sulfide was carried out according to the procedure described under the preparation of β-phenylethyl mercaptan. Two products were isolated from the reaction: (a) b.p. 85-90° (3 mm.), 16.7 g. (22%); (b) b.p. 135-140°, 10.4 g. (14.7%).

γ-Phenylpropyl mercaptan has been prepared by the saponification of γ-phenylpropyl dithiocarbamate[153]. The product boiled at 109° (10 mm.).

Fraction (a) was identified as the mercaptan by conversion to 2,4-dinitrophenyl γ-phenylpropyl sulfide, m.p. 97-98°. The higher boiling fraction could not be identified.

Anal. Calcd. for $C_{15}H_{14}O_4N_2S$: S, 10.1. Found: S, 10.34.

Huston and Agett[156b] obtained a 73 percent yield of γ-phenylpropyl alcohol from a similar reaction with ethylene oxide and benzylmagnesium chloride. Gilman and Kirby[156c], however, have reported the rearrangement of benzylmagnesium chloride during the reaction with ethylene oxide. They obtained 41 percent of the oxidation product which represented p-rearrangement or the formation of β-(p-tolyl)ethanol. The possibility of p-rearrangement during the reaction between ethylene sulfide and benzylmagnesium chloride was not inves-

tigated in the present study.

Elaidic Acid.- To a well-stirred mixture of 28.2 g. (0.1 mole) of oleic acid and 45 ml. of 30 percent nitric acid there was added 1.5 g. of sodium nitrite. The reaction was stirred until most of the oil had solidified. Then after standing at room temperature for one hour, the solid acid was extracted with ether, washed with several portions of water, and dried over anhydrous sodium sulfate. The solvent was removed and the residue recrystallized from 95 percent ethanol. The yield of the pure elaidic acid was 16 g. (57%); m.p. 43-44°.

9,10-Chlorohydroxyelaidic Acid.[157] Into a two liter, three-necked, round-bottomed flask equipped with a mechanical stirrer and a gas-inlet tube and set up under the hood, there was placed a solution containing 23 g. (0.41 mole) of potassium hydroxide, 50 g. (0.36 mole) of potassium carbonate, and 56.4 g. (0.20 mole) of elaidic acid in 1.25 l. of water. The solution was cooled to 10° and stirred while chlorine was slowly bubbled into it for at least two hours. The reaction mixture gradually became acidic, and a light viscous oil floated to the surface of the supernatant liq-

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157. Nicolet and Poulter, J. Am. Chem. Soc., 52, 1186 (1930); see also Hilditch, J. Chem. Soc., 204 (1943).

uid. After destroying the excess chlorine and sodium hypochlorite by the addition of a 10 percent sodium thiosulfate solution, the organic material was extracted with ether and dried over anhydrous sodium sulfate. The excess solvent was removed, and the dark brown residue used without further purification in the preparation of 9,10-epoxyelaidic acid.

9,10-Epoxyelaidic Acid (9,10-Epoxystearic Acid).[157] The residue obtained from the preceding reaction was dissolved in a solution of 30 g. (0.53 mole) of potassium hydroxide in 200 ml. of ethanol. This solution was refluxed for six hours then poured into two liters of ice-water. Acidification of the resulting solution with dilute (1:1) hydrochloric acid gave rise to a light brown solid which was filtered off, washed with water and recrystallized from ethanol. The yield was 28.6 g. (48% based on the original amount of elaidic acid used). The product melted over a range of 49-52° and was further purified (m.p. 52-53°) by recrystallization from ether.

No definite product could be obtained when oleic acid was used in place of elaidic acid. Nicolet[157], however, reported that both oleic acid and the elaidic acid chlorohydrins were oils which could not be solidified but which could be converted into the corresponding epoxides by treatment with alcoholic sodium or potassium hydroxide. Oleic acid chlorohydrin formed 45 percent of the epoxide from

which only one-third of the product could be isolated whereas the elaidic acid chlorohydrin formed 75 percent of the epoxide from which two-thirds of the product was isolated. Both compounds melted at 53.8°[157].

9,10-Epithiolelaidic Acid.- The procedure used in the preparation of this compound was based on the general method employed in the synthesis of ethylene sulfide[158]. To 300 ml. of ethanol there was added 14.6 g. (0.15 mole) of potassium thiocyanate and 30 g. (0.10 mole) of 9,10-epoxyelaidic acid. The resulting solution was allowed to reflux for twenty-four hours, then cooled and poured with vigorous stirring into an equal volume of cold water. Dilute hydrochloric acid was added until the solution was neutral to Congo red. After cooling in the ice-box for twelve hours, the white crystalline product which formed was filtered from the solution and washed with water. The yield after recrystallization from ethanol was 21.5 g. (68%). The product melted over a range of 55-60°. Further purification by recrystallization from ether gave rise to 10.5 g. (32.4%) of the pure product which melted at 62°.

Anal. Calcd. for $C_{18}H_{34}O_2S$: Neut. Equiv., 314; S, 10.18. Found: Neut. Equiv., 308 and 310; S, 10.11.

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158. Unpublished studies by G. A. Martin from these laboratories. French Patent No. 797,621 (1934) [Chem. Zentr., 107, II, 1062 (1936)].

The Preparation of 9,10-Epithiolstearic Acid by the Thiocyanogenation of Oleic Acid.[159] To a solution of 38.8 g. (0.40 mole) of potassium thiocyanate and 28.2 g. (0.10 mole) of oleic acid in 200 ml. of glacial acetic acid there was slowly added with stirring 10.6 ml. (32 g., 0.2 mole) of bromine in 30 ml. of glacial acetic acid. Stirring was continued for one hour after which time the flask was corked and allowed to stand for twenty-four hours in the dark at room temperature. After removing the inorganic material by filtration, the solvent was removed by distillation under reduced pressure. The residue was washed with water, extracted with ether, and the extract washed free of acetic acid with water. After removing the ether, the residual oil was dissolved in 300 ml. of 5% sodium hydroxide and boiled for two and one-half hours, then allowed to cool, and was acidified with dilute hydrochloric acid. The crude product was extracted with ether and dried over anhydrous sodium sulfate. The residue obtained after removing the ether was dissolved in ethanol, boiled with Norite and filtered. Nine and two-tenths grams (29%) of the pure product (m.p. 62°) was obtained. A mixed melting point determination showed this compound to be identical with that obtained from 9,10-

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159. Salchow, Kautschuk, 13, 119 (1937) /C. A., 31, 8991 (1937)/; ibid., 14, 12 (1938) /C. A., 32, 4007 (1938)/.

epoxyelaidic acid.

Anal. Calcd. for $C_{18}H_{34}O_2S$: Neut. Equiv., 314; S, 10.18. Found: Neut. Equiv., 316.8; S, 10.53.

Cleavage of 9,10-Epoxyelaidic Acid with Diethylamine (Attempted).- A solution of 3 g. (0.01 mole) of 9,10-epoxyelaidic acid and 15 ml. (10.6 g., 0.145 mole) of diethylamine was refluxed for one hour. The reaction mixture was poured into 150 ml. of cold water whereupon a clear, soapy solution resulted. Neutralization with dilute (1:1) hydrochloric acid produced a white solid which after filtration and recrystallization from ethanol melted at 52-53°. This product was identified as the starting material by a mixed melting point determination.

Cleavage of 9,10-Epithiolelaidic Acid with Diethylamine (Attempted).- Three and one-tenth grams (0.01 mole) of 9,10-epithiolelaidic acid and 3.5 g. (0.05 mole) of diethylamine in 50 ml. of ethanol was refluxed for two hours. The resulting solution was diluted with an equal volume of water, cooled, and neutralized to Congo red with dilute (1:1) hydrochloric acid. The solid acid which formed was filtered from the solution and recrystallized from ethanol. Two and five-tenths grams (80%) of the starting material (m.p. 61-62°, mixed m.p.) was recovered.

n-Dodecyl Bromide.- The procedure used in the preparation of this compound was similar to that reported by Kamm and Marvel[160]. A mixture of 301.2 g. (1.8 moles) of 48 percent hydrobromic acid, 55 ml. of concentrated sulfuric acid, and 186 g. (1.0 mole) of dodecyl alcohol was refluxed for eight hours. An additional 100 ml. portion of hydrobromic acid was added and refluxing was continued for twelve hours. The organic layer was separated, washed first with cold concentrated sulfuric acid, then with water, and finally with a dilute sodium carbonate solution. The crude product was dried over anhydrous calcium chloride, filtered and distilled at 98-99° (0.8 mm.). The yield was 237.2 g. (94%).

n-Dodecyl Mercaptan.- The procedure used in this preparation was essentially that described by Urquhart, Gates, and Connor[161]. From 62.5 g. (0.25 mole) of dodecyl bromide and 19 g. (0.25 mole) of thiourea, there was obtained 45.5 g. (90%) of the product; b.p. 78-82° (0.2 mm.).

p-Nitrophenyl Dodecyl Sulfide.- To 50 ml. of an alcoholic solution of 3.7 g. (0.075 mole) of sodium hydroxide there was added 15.2 g. (0.075 mole) of dodecyl mercaptan. To the resulting solution of the sodium mercaptide there was added

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160. Kamm and Marvel, Org. Syn., Coll. Vol. I, 29 (1941).

161. Urquhart, Gates, and Connor, Org. Syn., 21, 36 (1941).

11.8 g. (0.075 mole) of p-nitrochlorobenzene in 100 ml. of absolute ethanol. After refluxing for four hours and cooling, the crystalline product was filtered from the solution and recrystallized from acetone. The product obtained from this reaction was identified as didodecyl disulfide by sulfur analysis and by a mixed melting point determination with an authentic sample prepared by the oxidation of dodecyl mercaptan.

Anal. Calcd. for $C_{24}H_{50}S_2$: S, 15.9. Found: S, 15.6.

The sulfide was obtained, however, by refluxing an ethanolic solution of sodium dodecyl mercaptide prepared from 10 g. (0.05 mole) of dodecyl mercaptan and 1.2 g. (0.05 g. atom) of sodium in ethanol and 6 g. (0.04 mole) of p-nitrochlorobenzene. The oxidation of the mercaptan to the disulfide was minimized by running the reaction in an inert atmosphere (nitrogen). There was obtained 3.1 g. (38%) of didodecyl disulfide (m.p. 33-34°) and 8 g. (61.5%) of the crude p-nitrophenyl dodecyl sulfide; m.p. 45-47°. After recrystallizing the product from glacial acetic acid, the yield was 6.4 g. (53%); m.p. 46-48°.

Anal. Calcd. for $C_{18}H_{29}O_2NS$: S, 9.9. Found: S, 10.01 and 10.13.

p-Nitrophenyl Dodecyl Sulfone.- To a stirred solution of 5.4 g. (0.017 mole) of p-nitrophenyl dodecyl sulfide in

100 ml. of glacial acetic acid warmed to 60° there was added dropwise and with stirring 10 ml. of 30 percent hydrogen peroxide in 15 ml. of glacial acetic acid. Stirring was continued for fifteen minutes, and an additional 10 ml. of hydrogen peroxide was added. The reaction was heated on the water bath for four hours and then allowed to cool. The crude product melted over a range of 58-62° and was purified by recrystallization from absolute ethanol. The yield was 4 g. (66%); m.p. 65°.

Anal. Calcd. for $C_{18}H_{29}O_4NS$: S, 9.01. Found: S, 9.02 and 9.05.

o-Nitrophenyl Dodecyl Sulfide.- To a solution of sodium ethoxide prepared by dissolving 1.7 g. (0.075 g. atom) of sodium in 100 ml. of ethanol there was added 16.5 g. (0.075 mole) of dodecyl mercaptan. The system was protected from the atmosphere by nitrogen, and 11.8 g. (0.075 mole) of o-nitrochlorobenzene in 100 ml. of ethanol was added. After heating the reaction on the steam bath for six hours, the sodium chloride was filtered from the warm solution and washed with ethanol. Twenty-four grams (99%) of the crude sulfide (m.p. 35-36.5°) was obtained from the cooled filtrate. The product was recrystallized from ethanol yielding 19.3 g. (80%) of the pure substance; m.p. 35-36.5°.

Anal. Calcd. for $C_{18}H_{29}O_2NS$: S, 9.9. Found: S, 10.08 and 9.64.

o-Nitrophenyl Dodecyl Sulfone.- Six and five-tenths grams (0.02 mole) of o-nitrophenyl dodecyl sulfide was oxidized to the corresponding sulfone with 25 ml. of 30 percent hydrogen peroxide using the same procedure described in the preparation of p-nitrophenyl dodecyl sulfone. The yield of the pure product after recrystallization from ethanol was 6.9 g. (97%); m.p. 46-48°.

Anal. Calcd. for $C_{18}H_{29}O_4NS$: S, 9.01. Found: S, 9.05 and 9.16.

o-Aminophenyl Dodecyl Sulfone Hydrochloride.- To a solution of 18.9 g. (0.10 mole) of stannous chloride dihydrate in 20 ml. of concentrated hydrochloric acid there was added 6.1 g. (0.017 mole) of o-nitrophenyl dodecyl sulfone. The suspension was stirred and warmed to 40° on the water bath for two hours after which time the waxy, white solid which formed was filtered and washed free of hydrochloric acid with cold water. The crude product was suspended in ether, and the amine liberated by shaking the suspension with a 40 percent sodium hydroxide solution. After separating the organic layer and drying over anhydrous potassium carbonate, the amine hydrochloride was precipitated from the ethereal solution by the addition of an equal volume of ethanolic hydrogen chloride. The yield was 5 g. (81%); m.p. 143-144°.

Anal. Calcd. for $C_{18}H_{32}O_2NSCl$: S, 8.86. Found: S,

8.59.

p-Acetamidophenyl Dodecyl Sulfone.- Forty grams (0.16 mole) of sodium p-acetamidobenzenesulfinate[106] was heated in 100 ml. of cellosolve until completely dissolved. To the resulting solution there was added 40 g. (0.16 mole) of dodecyl bromide and the mixture stirred and refluxed for ten hours and then poured into 500 ml. of ice-water. The crystalline precipitate was filtered, washed with cold water, and finally recrystallized from ethanol. The yield of the pure product was 46.5 g. (79%); m.p. 102-103°.

Anal. Calcd. for $C_{20}H_{33}O_3NS$: S, 8.72. Found: S, 8.45.

p-Aminophenyl Dodecyl Sulfone.- A solution of 7.3 g. (0.02 mole) of p-acetamidophenyl dodecyl sulfone in 150 ml. of 1.5 N alcoholic sodium hydroxide was refluxed for three hours. The solution was allowed to cool and then poured into 500 ml. of cold water. The white crystalline solid was filtered, washed free of base with cold water, and recrystallized from ethanol. The yield of the pure aminosulfone was 5.5 g. (85%); m.p. 113.5-114°.

Anal. Calcd. for $C_{18}H_{31}O_2NS$: S, 9.85. Found: S, 9.89.

p-(2,5-Dimethylpyrryl)phenyl Dodecyl Sulfone.- This

preparation followed the method of Hazelwood, Hughes, and Lions[150]. A mixture of 3.5 g. (0.01 mole) of p-aminophenyl dodecyl sulfone and 2.5 g. (0.02 mole) of acetonylacetone was heated at 120-125° for one hour. The product was extracted with hot ethanol, boiled with Norite, and filtered. Approximately 2.5 g. (72%) of the aminosulfone (m.p. 112°, mixed m.p.) was recovered from the reaction. A small amount of material melting over a range of 45-49° was also obtained.

The compound was successfully prepared according to the following procedure. A solution of 5 g. (0.015 mole) of p-aminophenyl dodecyl sulfone and 2.5 g. (0.02 mole) of acetonylacetone in 50 ml. of absolute ethanol containing five drops of concentrated hydrochloric acid was refluxed for two hours. The crude product was obtained by cooling the concentrated alcoholic solution. Recrystallization from absolute ethanol gave rise to 4 g. (66%) of the pure product which melted at 49-50°.

Anal. Calcd. for $C_{24}H_{37}O_2NS$: S, 7.93. Found: S, 7.95 and 7.62.

Cetyl Mercaptan.- The method of Urquhart, Gates, and Connor[161] was used in the preparation of this compound. From 76.5 g. (0.25 mole) of cetyl bromide and 19 g. (0.25 mole) of thiourea there was obtained 51 g. (78%) of the product; b.p. 135-140° (0.5 mm.).

o-Nitrophenyl Hexadecyl Sulfide.- To a solution of sodium hexadecyl mercaptide prepared from 10.3 g. (0.04 mole) of hexadecyl mercaptan and 1 g. (0.043 g. atom) of sodium in 200 ml. of absolute ethanol there was added 8 g. (0.04 mole) of o-nitrochlorobenzene. The mixture was refluxed under nitrogen for four hours then filtered while warm. From the filtrate there was obtained 14 g. (92%) of the product; m.p. 49-50°. Recrystallization from absolute ethanol gave rise to a yellow crystalline product which melted at the same temperature.

Anal. Calcd. for $C_{22}H_{37}O_2NS$: S, 8.45. Found: S, 8.38.

o-Nitrophenyl Hexadecyl Sulfone.- Twelve grams (0.10 mole) of 30 percent hydrogen peroxide in 20 ml. of glacial acetic acid was added dropwise to a solution of 7.6 g. (0.02 mole) of o-nitrophenyl hexadecyl sulfide in 30 ml. of glacial acetic acid warmed to 60°. The solution was stirred for one-half hour, then a second 12 g. (0.10 mole) portion of hydrogen peroxide in 20 ml. of glacial acetic acid was added; after stirring at 60-70° for one hour, the solution was cooled, diluted with water and filtered. Recrystallization of this product from ethanol yielded 7 g. (85%) of the pure sulfone; m.p. 64°.

Anal. Calcd. for $C_{22}H_{37}O_4NS$: S, 7.73. Found: S, 7.73.

Dodecyl Sulfate.[162] n-Dodecanechlorosulfonate was prepared by gradually adding with stirring 33.2 g. (0.20 mole) of dodecyl alcohol (Eastman Kodak Co. technical grade) to 16.3 ml. (27 g., 0.2 mole) of sulfuryl chloride contained in a 500 ml. three-necked, round-bottomed flask equipped with a mechanical stirrer, a thermometer, and a dropping funnel, and cooled by means of an ice bath.

While removing the hydrogen chloride from the above reaction by drawing a current of dry air through the mixture, dodecyl sulfite was prepared by the following procedure. To 66 g. (0.40 mole) of dodecyl alcohol there was gradually added with stirring 14.5 ml. (23 g., 0.2 mole) of thionyl chloride. The addition was accompanied by the evolution of heat and the elimination of hydrogen chloride which was removed from the reaction by a current of dry air. During the addition of the first seven milliliters of the thionyl chloride, a reaction temperature of 40-45° was maintained. The flask was then warmed by means of a water bath, and after the complete addition of the thionyl chloride, the reaction was heated at 80° for two hours.

The crude chlorosulfonate was then added to the sulfite and the mixture heated by means of an oil bath maintained at

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162. Barkenbus and Owens, J. Am. Chem. Soc., 56, 1204 (1934).

150-160° until the frothing had ceased. The tarry black mass was cooled, extracted with 500 ml. of ether, and the extract boiled with Norite and filtered. The yield of the pure, colorless crystalline compound was 55 g. (63.4%); m.p. 48-49°. The melting point reported in the literature[162] is 48.5°; 58 percent of the product was obtained.

2,4,6-Tribromophenyl Dodecyl Ether. Alkylation Reaction with Dodecyl Sulfate.- To a solution of sodium 2,4,6-tribromophenolate prepared from 5 g. (0.015 mole) of 2,4,6-tribromophenol and 0.7 g. (0.017 mole) of sodium hydroxide in 75 ml. of ethanol there was added 6.5 g. (0.016 mole) of dodecyl sulfate. The solution was refluxed for six hours and the excess ethanol removed by distillation. The residue was taken up in ether, washed with a 10 percent sodium hydroxide solution, then dried over anhydrous sodium sulfate. After filtering and removing the solvent, the residue was recrystallized from ethanol to a constant melting point of 43-44°. The yield was 4.6 g. (61%).

Anal. Calcd. for $C_{18}H_{27}OBr_3$: Br, 48.09. Found: Br, 47.98 and 47.73.

1-Hexadecanesulfonyl Chloride.[163]- Into a solution of 10

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163. Sprague and Johnson, J. Am. Chem. Soc., 59, 1837 (1937).

g. (0.028 mole) of S-cetylisothiuronium bromide in one liter of water cooled to 15° there was bubbled chlorine for approximately one hour. The curdy white solid which formed was filtered, dissolved in ether, washed with a 5 percent sodium bisulfite solution, then dried over anhydrous sodium sulfate. After removing the excess solvent, the residue was recrystallized from petroleum ether (b.p. 60-68°). The yield of the product melting over a range of 49-53° was 6.5 g. (72%). Sprague and Johnson[163] obtained from 70-80 percent of the product melting at 52-53°.

The Reaction between 1-Hexadecanesulfonyl Chloride and Benzene in the Presence of Anhydrous Aluminum Chloride.- To a well-stirred suspension of 3.5 g. (0.025 mole) of anhydrous aluminum chloride in 50 ml. of anhydrous thiophene-free benzene cooled to 10° there was slowly added 6.5 g. (0.02 mole) of 1-hexadecanesulfonyl chloride dissolved in 25 ml. of benzene. The reaction was stirred at 50° for four hours and finally refluxed on the steam bath for two hours. After decomposing the complex by pouring the reaction mixture into an ice-hydrochloric acid mixture, the benzene layer was separated, washed with water, then with a 5 percent solution of sodium carbonate, and finally dried over anhydrous calcium chloride. The product was obtained by recrystallization of the residue from acetone after removing the solvent by distillation under reduced pressure. The yield

was 1.4 g. (19.2%); m.p. 58-60°.

Anal. Calcd. for $C_{22}H_{38}O_2S$: S, 8.75. Found: S, 8.4.

o-Chlorophenyl Dodecyl Ether.- Sodium o-chlorophenolate was prepared by the addition of 64 g. (0.5 mole) of o-chlorophenol to 300 ml. of anhydrous ethanol in which 11.5 g. (0.5 g. atom) of sodium had been previously dissolved. To the resulting solution there was added 125 g. (0.5 mole) of dodecyl bromide and the mixture allowed to reflux on the steam bath for ten hours. The sodium bromide formed during the reaction was removed by filtration and washed with one portion of hot ethanol. After concentrating the combined filtrates, the residue was taken up in ether, washed with three 100 ml. portions of a 5 percent sodium hydroxide solution, then with distilled water, and finally dried over anhydrous calcium chloride.

The product was collected at 153-155° (0.4 mm.); the yield was 115.4 g. (78%); n_D^{20} 1.4970, d_{20}^{20} 0.97308, MR calcd.: 88.27. Found: MR 88.08.

Anal. Calcd. for $C_{18}H_{29}OCl$: Cl, 11.81. Found: Cl, 11.78 and 11.62.

m-Nitrophenyl Dodecyl Ether.[164] To a solution of sodium

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164. French Patent 788,429 (1935) [Chem. Zentr., 107, I, 4367 (1936); C. A., 30, 1520 (1936)].

m-nitrophenolate prepared from 14 g. (0.1 mole) of m-nitrophenol and 2.3 g. (0.1 g. atom) of sodium dissolved in 150 ml. of ethanol there was added 25 g. (0.1 mole) of dodecyl bromide. The resulting mixture was refluxed on the steam bath for eight hours, filtered, and the filtrate allowed to stand in the ice-box for several hours. From the cooled solution there was obtained 29.8 g. (97%) of the pure compound which melted at 43°. (This value agreed with that reported in the literature[164].)

m-Aminophenyl Dodecyl Ether.- To a solution of 22.5 g. (0.10 mole) of stannous chloride dihydrate in 150 ml. of concentrated hydrochloric acid there was added 6 g. (0.02 mole) of m-nitrophenyl dodecyl ether. The mixture was stirred at 50° for two hours, then cooled and the waxy, white solid filtered off and washed free of residual hydrochloric acid with cold water. The treatment of an ethanolic solution of the product with an excess of a 10 percent sodium hydroxide solution produced the free amine which was extracted with ether and dried over potassium hydroxide.

After filtering the solution and distilling off the excess solvent, the residue was recrystallized from ethanol. The yield was 4.5 g. (85%); m.p. 59°. The amine hydrochloride melted at 114-115°. These values corresponded to those reported in the literature cited[164].

The Reaction between o-Chlorophenyl Dodecyl Ether and Sodium Amide in Liquid Ammonia.- An attempt was made to prepare m-aminophenyl dodecyl ether by the amination and rearrangement of o-chlorophenyl dodecyl ether. The general procedure of Gilman and Avakian[165] was followed.

To 250 ml. of liquid ammonia containing 0.3 g. of ferric chloride there was gradually added with stirring 9.2 g. (0.4 g. atom) of finely cut metallic sodium. Stirring was continued while 60 g. (0.2 mole) of o-chlorophenyl dodecyl ether was added to the reaction over a period of one-half hour. No evidences of a reaction were observed; however, the high-molecular weight ether was insoluble in the reagent.

The mixture was stirred for an additional hour, and the excess sodium amide decomposed by the cautious addition of ammonium chloride to the flask. After allowing the ammonia to evaporate, the residue was extracted with ether, and the extract filtered free of inorganic material, washed with water and finally dried over anhydrous potassium carbonate.

The passage of anhydrous hydrogen chloride into the dried ethereal solution failed to produce an insoluble amine hydrochloride. The fractional distillation of the crude reaction product gave rise to 45.7 g. (76%) of the starting material (b.p. 159-160° (0.4 mm.); n_D^{20} 1.4970) and a viscous

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165. Gilman and Avakian, J. Am. Chem. Soc., 67, 349 (1945).

tarry residue from which no definite product could be isolated.

The reaction was repeated according to the above procedure with 30 g. (0.10 mole) of o-chlorophenyl dodecyl ether in 150 ml. of toluene as a solvent. Twenty and eight-tenths grams (70%) of the original ether was recovered (b.p. 153-156° (0.4 mm.); n_D^{20} 1.4970).

A third attempt to prepare m-aminophenyl dodecyl ether by way of molecular rearrangement was made in which 15 g. (0.05 mole) of o-chlorophenyl dodecyl ether dissolved in 150 ml. of diethyl ether was used. The high molecular-weight compound was soluble in this mixture, however, none of the amino compound could be isolated from the reaction. Ten grams (67%) of the pure starting material (b.p. 152-153° (0.3 mm.); n_D^{20} 1.4965) was recovered from the reaction.

A low yield of the rearrangement product was obtained when the ammonolysis of 23 g. (0.078 mole) of o-chlorophenyl dodecyl ether was carried out under high pressure conditions. From 16.3 g. of the crude material recovered from the reaction there was obtained 3.5 g. (20.4%) of m-aminophenyl dodecyl ether hydrochloride. The product melted at 114-115° and showed no depression of melting point when mixed with a sample of the amine hydrochloride prepared by the reduction of m-nitrophenyl dodecyl ether. The identity of the amination-rearrangement product was further established by mixed

melting point determinations on the free amines (m.p. 58-59°) and their acetyl derivatives (m.p. 86°). No depression of the melting point was observed in either case.

Approximately 11 g. (48%) of the initial 23 g. of o-chlorophenyl dodecyl ether was recovered (n_D^{20} 1.4971). The yield of m-aminophenyl dodecyl ether hydrochloride based on the original 23 g. of the starting material was 15%.

Attempted Preparation of Triphenylthiosilanol from Triphenylsilanol.- Anhydrous hydrogen sulfide was passed into a solution of 7.0 g. (0.025 mole) of triphenylsilanol in 150 ml. of ether over a period of four hours. After removing the excess solvent, the original silanol was recovered quantitatively (mixed m.p.).

Attempted Preparation of Triphenylthiosilanol from Triphenylchlorosilane and Potassium Hydrosulfide.- Triphenylchlorosilane was prepared by saturating a solution of 27.6 g. (0.1 mole) of triphenylsilanol in 150 ml. of ether with anhydrous hydrogen chloride[166b].

After the removal of the excess ether, the product was dissolved in 150 ml. of benzene and the resulting solution

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166. (a) Bloxam, J. Chem. Soc., 77, 785 (1900); (b) Kraus and Rosen, J. Am. Chem. Soc., 47, 2739 (1925). This procedure for preparing triphenylchlorosilane has been recently modified by Nobis. Unpublished studies.

was added to a suspension of potassium hydrosulfide prepared in benzene from 4 g. (0.1 g. atom) of potassium and hydrogen sulfide according to the procedure of Bloxam[166a]. The mixture was refluxed with stirring for twelve hours and then filtered. After removing the excess solvent by distillation, the residue was recrystallized from petroleum ether (b.p. 77-115°) yielding 21 g. (78%) of the impure starting material (m.p. 84-89°). The qualitative test for sulfur was negative while that for chlorine was positive.

The Reaction of Triphenylchlorosilane with Thiourea.- (1) A solution of 7.3 g. (0.025 mole) of triphenylchlorosilane and 2 g. (0.025 mole) of thiourea in 100 ml. of ethanol was refluxed for four hours.

From the cooled solution there was obtained 6.5 g. of an unidentified sulfur-free solid melting over a range of 55 to 60° and approximately 2 g. of a product which melted between 175 and 180°. This high melting material was identified as thiourea by a mixed melting point with an authentic sample.

(2) A suspension of 3 g. (0.01 mole) of triphenylchlorosilane and 1 g. (0.012 mole) of thiourea in 50 ml. of dioxane was refluxed for four hours. The reaction mixture was then made alkaline by a 10 percent solution of sodium hydroxide, stirred for one-half hour, and then filtered. Ac-

idification of the resulting filtrate gave rise to a small amount of material which after recrystallization from ethanol melted at 113°. A positive test for sulfur was obtained, but further characterization of the compound was prevented by the insufficient amount of material.

The Reaction of Triphenylsilane with Sodium Hydrosulfide.- In view of the peculiar reactions exhibited by triphenylsilane toward organoalkali compounds and certain inorganic salts of the alkali metals, an attempt was made to prepare triphenylthiosilanol from triphenylsilane and sodium hydrosulfide.

Sodium hydrosulfide was prepared by saturating a solution of sodium ethoxide, prepared from 0.25 g. (0.011 g. atom) of sodium and 25 ml. of ethanol, with hydrogen sulfide. To the resulting solution there was added 2.6 g. (0.01 mole) of triphenylsilane and the solution refluxed for two hours.

A crude product melting at 55° was obtained after diluting the solution with 100 ml. of water. From the recrystallization of this material from ethanol, there was obtained 1.7 g. (55%) of a product melting at 65° and a small quantity of material which melted at 220°. The higher melting product was identified as hexaphenyldisiloxane by a mixed-melting with an authentic sample[167] whereas the lower melting compound was identified as triphenylethoxysilane by

an analysis for silicon.

Anal. Calcd. for $C_{20}H_{20}OSi$: Si, 9.21. Found: Si, 9.36 and 9.37*.

Triphenylethoxysilane was prepared by Polis[168] from triphenylchlorosilane and ethanol. However, no constants for the compound were reported. The compound has been recently prepared from tetraethoxysilane and phenyllithium[169]. This product was identical (mixed m.p.) with the analytical sample obtained by the above procedure.

The Reaction of Triphenylchlorosilane and Hydrogen Sulfide in Ethanol.- In a further attempt to prepare triphenylthiosilanol, hydrogen sulfide was passed into a solution of 5 g. (0.017 mole) of triphenylchlorosilane in 100 ml. of ethanol for four hours.

After concentrating the resulting solution and cooling, 3 g. (60%) of a product melting at 64-65° was obtained. The product melted at 63° after one recrystallization from eth-

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167. Unpublished work from these laboratories by H. W. Melvin.

168. Polis, Ber., 19, 1012 (1886).

169. Clark, R. N., Doctoral Dissertation, Iowa State College, 1946.

* The analyses for silicon were run according to the method of Gilman, Clark, Wiley, and Diehl, J. Am. Chem. Soc., 68, 2728 (1946).

anol, and a depression of 3° in the melting point was observed when this material was mixed with the authentic sample of triphenylethoxysilane. Subsequent attempts to recrystallize the material gave rise to an insoluble crystalline material melting over a range of 192 to 197°.

The Reaction between Triphenylchlorosilane and Sodium Hydrosulfide in Ethanol.- Sodium hydrosulfide was obtained by saturating a solution of sodium ethoxide prepared from 0.3 g. (0.013 g. atom) of sodium and 50 ml. of ethanol with anhydrous hydrogen sulfide. Three grams (0.01 mole) of triphenylchlorosilane was added and the mixture refluxed for three hours while hydrogen sulfide was continuously passed into it.

After removing the insoluble inorganic material by filtration, the solution was concentrated and cooled. There was obtained 2.5 g. of a sulfur-free product which melted between 58 and 62°. Recrystallization of this material gave rise to a small amount of triphenylethoxysilane (m.p. 63-65°, mixed m.p.).

The Reaction between Triphenylsilane and Potassium Hydrosulfide in Ether.- Potassium hydrosulfide was prepared by passing anhydrous hydrogen sulfide into a suspension of 0.4 g. (0.01 g. atom) of potassium in 100 ml. of ether. To the resulting suspension there was added 2.6 g. (0.01 mole) of

triphenylsilane, and the mixture was stirred at room temperature for twenty hours. There was recovered from the reaction 2.2 g. (84%) of triphenylsilane (m.p. and mixed m.p. 46°).

The silane was recovered quantitatively after heating directly with potassium hydrosulfide at 100° for four hours.

Attempted Reduction of Triphenylsilanol.- An attempt was made to prepare triphenylsilane by the reduction of triphenylsilanol according to the procedure described by Dolgov and Volnov[170a].

A mixture of 5 g. (0.018 mole) of triphenylsilanol, 60 g. (0.44 mole) of anhydrous zinc chloride, and 30 ml. of ethanol was heated for three hours. The mixture was then poured into 100 ml. of water whereupon a sticky, semi-solid mass was obtained. No definite product could be isolated from this crude mixture.

A second reaction was run according to the above procedure except that the reaction mixture was extracted with ether and dried over anhydrous sodium sulfate. After remov-

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170. (a) Dolgov and Volnov, Zhur. Obshchei Khim., I, 91 (1931) /C.A., 25, 4535 (1931)/; (b) When small amounts of zinc chloride were used, triphenylethoxysilane was isolated from the reaction. Inseparable oils were obtained when a large excess of zinc chloride was employed. (Unpublished studies by G. E. Dunn and G. N. R. Smart.)

ing the excess solvent, an attempt was made to isolate the product by fractional distillation. None of the silane was obtained.

Attempted Preparation of Triphenylsilyl p-Toluenesulfonate.- The general method of synthesis of p-toluenesulfonic acid esters described by Marvel and Sekera[171] was followed in this reaction. To a solution of 13.8 g. (0.05 mole) of triphenylsilanol in 15.8 g. (0.2 mole) of anhydrous pyridine cooled to 10° there was gradually added 10.5 g. (0.055 mole) of p-toluenesulfonyl chloride. After the addition was completed, the reaction was stirred at room temperature for three hours and then poured into ice water. The crude, gummy mass obtained was recrystallized from a mixture of benzene and petroleum ether (b.p. 75-115°). Twelve and five-tenths grams (91%) of the original triphenylsilanol (m.p. 150-152°, mixed m.p.) was recovered.

The ester was not obtained after running the reaction in refluxing benzene.

The Reaction between Triphenylsilane and Sodium p-Toluenesulfinate.- A suspension of 2.6 g. (0.01 mole) of triphenylsilane and 1.8 g. (0.01 mole) of sodium p-toluenesul-

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171. Marvel and Sekera, Org. Syn., 20, 50 (1940); J. Am. Chem. Soc., 55, 345 (1933).

finate in 50 ml. of benzene was refluxed with stirring for six hours. The insoluble material was removed by filtration and identified (addition product with benzalacetophenone, mixed m.p.) as sodium p-toluenesulfinate. There was also recovered from the reaction 2 g. (77%) of triphenylsilane (m. p. 46°, mixed m.p.).

A similar reaction was attempted in which sodium p-thiocresolate was used in place of the corresponding sulfinate. Triphenylsilane was recovered from the reaction.

The Reaction between Silicon Tetrachloride and Sodium p-Toluenesulfinate.- A suspension of 31 g. (0.17 mole) of pulverized sodium p-toluenesulfinate and 7 g. (0.042 mole) of silicon tetrachloride in 150 ml. of benzene was stirred at room temperature for twenty-four hours. From this reaction, there was recovered 29.2 g. (94%) of the original sodium p-toluenesulfinate. The recovered salt formed an addition product with benzalacetophenone which was identical (mixed m.p.) to that obtained from the ketone and an authentic sample of the sulfinate.

In a further attempt to prepare triphenyl-p-tolylsulfonylsilane, 2.2 g. (0.01 mole) of triphenylchlorosilane and 1.8 g. (0.01 mole) of sodium p-toluenesulfinate in 50 ml. of toluene was refluxed for six hours. The unchanged sodium sulfinate was recovered quantitatively from the reaction.

Attempted Preparation of Triphenylsilyl p-Bromobenzenesulfonate.- A suspension of 2.9 g. (0.01 mole) of triphenylchlorosilane and 2.5 g. (0.01 mole) of sodium p-bromobenzenesulfonate in 60 ml. of benzene was refluxed for six hours. The original sodium sulfonate was recovered quantitatively from the reaction.

Attempted Preparation of Triphenyl-p-tolylmercaptosilane.- Sodium p-thiocresolate was prepared in 50 ml. of benzene from 1.3 g. (0.01 mole) of p-thiocresol and 0.25 g. (0.011 g. atom) of sodium. To the resulting suspension there was added 2.9 g. (0.01 mole) of triphenylchlorosilane and the mixture refluxed for twenty-four hours. After removing the inorganic materials from the reaction, there was obtained the unreacted triphenylchlorosilane (mixed m.p.).

Triphenylchlorosilane was recovered after refluxing 5.8 g. (0.02 mole) of the material with 3.1 g. (0.025 mole) of p-thiocresol in benzene for three hours.

Attempted Preparation of Tetra-n-dodecylsilane.- The procedure for this reaction followed that described by Post and Hofricher[172] for the preparation of tetra-n-butylsilane from phenylmagnesium bromide and tetraethoxysilane.

n-Dodecylmagnesium bromide was prepared from 25 g.

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172. Post and Hofricher, J. Org. Chem., 5, 572 (1940).

(0.10 mole) of n-dodecyl bromide and 3 g. (0.125 g. atom) of magnesium in 150 ml. of ether. The yield of the organometallic compound determined by acid titration was 79%.

To the resulting solution there was slowly added 4.2 g. (0.02 mole) of tetraethoxysilane in 25 ml. of ether. The reaction was refluxed for six hours after which time Color Test No. I^{III} for the organometallic compound was negative. Subsequent to hydrolysis, the ether layer was separated and dried over anhydrous sodium sulfate.

There was obtained from the reaction 2 g. of a waxy solid which melted between 47 and 50° and a viscous oil which could not be distilled.

Attempted Preparation of Tri-n-dodecylphenylsilane.- To a solution of 0.093 mole of n-dodecylmangesium bromide in 150 ml. of ether prepared from 25 g. (0.01 mole) of n-dodecyl bromide and 3 g. (0.125 g. atom) of magnesium there was gradually added 3.6 ml., (5.3 g., 0.031 mole) of silicon tetrachloride in 50 ml. of ether. The addition was accompanied by a slight refluxing of the solvent and the formation of a white precipitate. Color Test No. I^{III} for the organometallic compound was negative after the complete addition of the silicon tetrachloride.

Three-hundredths of a mole of phenyllithium was then added, and the reaction was stirred at room temperature for

twelve hours. After hydrolysis by the usual method, the ether layer was separated and dried over anhydrous sodium sulfate. The fractional distillation of the residue after removing the excess solvent gave rise to three products: (1) 6.7 g. of an oil boiling at 58° (0.1 mm.) and 214-215° (760 mm.); n_D^{20} 1.4235; (2) 4 g. of a semisolid material, b.p. 170 to 174° (0.05 mm.); and (3) 7.5 g. of a residual oil which could not be distilled. The physical constants for fraction (1) corresponded to those given in the literature[173] for n-dodecane. Recrystallization of the second fraction from ethanol gave rise to 1.5 g. of a silicon-free product which melted between 47 and 50° and which was identical (mixed m.p.) with that obtained from the reaction of n-dodecylmangesium bromide with tetraethoxysilane.

Attempted Preparation of Tri-n-hexadecylphenylsilane.- To 0.097 mole of n-hexadecylmagnesium bromide prepared from 30.5 g. (0.1 mole) of hexadecyl bromide and 3 g. (0.125 g. atom) of magnesium in 150 ml. of ether there was gradually added with stirring 3.9 ml. (5.7 g., 0.03 mole) of silicon tetrachloride in 100 ml. of ether. During the addition the solvent refluxed slightly and a white crystalline precipi-

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173. "Beilstein's Handbuch der Organischen Chemie" Vierte Auflage, Band I, Verlag von Julius Springer, Berlin, 1918, p. 171.

tate was formed. After the complete addition of the chloride, Color Test No. I^{111} was negative.

After stirring the mixture for five hours at room temperature, 0.03 of a mole of phenyllithium was added and stirring was continued at room temperature for twelve hours after which time hydrolysis was carried out in the usual manner. There was obtained from this reaction an ether insoluble, silicon-free solid melting at 67° and an oil which solidified at a temperature slightly below room temperature. Neither product was characterized.

IV. DISCUSSION

A. Method of Testing

The physiological testing of most of the compounds prepared during the course of this investigation was conducted by Dr. Guy P. Youmans of the Northwestern Medical School, Chicago, Illinois. Pharmacological reports on many of these products are presently unavailable; however, significant results will be indicated wherever possible.

Methods of testing synthetic agents on avian malaria have been thoroughly reviewed by Tolman[174] and by Fullhart[8]. A summary of *in vivo* and *in vitro* methods of testing potential antituberculous compounds has been presented by Massie[175].

B. Chalcones

The use of chalcones as chemotherapeutic agents has been relatively uninvestigated. Geiger and Conn[4] have re-

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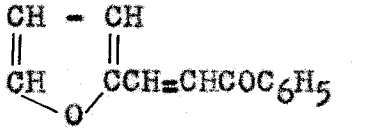
174. Tolman, L. L., Doctoral Dissertation, Iowa State College, 1945.

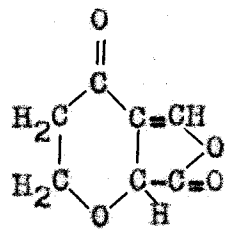
175. Massie, S. P., Doctoral Dissertation, Iowa State College, 1946.

cently reported that chalcone (I) and the structurally related α,β-unsaturated ketones, acrylophenone (XLIX) and furfuralacetophenone (L), exhibit bactericidic and fungicidic activities comparable in many instances to those shown by the antibiotic substances clavacin (LI) and penicillic acid (LII).

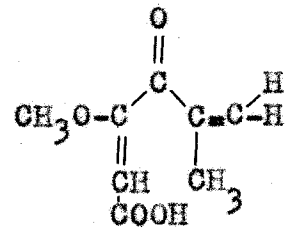
$CH_2 = CHCOC_6H_5$ (XLIX)



(L)



(LI)



(LII)

These naturally occurring and synthetic agents possess the common unsaturated grouping -CH=C-C=O, a structural unit which is highly reactive toward the sulfhydryl group (see pp. 3 to 8). Since the significance of sulfhydryl compounds in the living system has been amply demonstrated, it can be logically assumed that these α,β-unsaturated ketones produce antibacterial effects by combining with certain sulfhydryl systems of the living organism.

These speculations are to some measure supported by results of the *in vitro* antituberculous testing of certain intermediate chalcones prepared during this study and in earlier investigations in these laboratories[8]. 4-Dimethylamino-4'-methoxychalcone and 3,4-methylenedioxychalcone were

found to be one-half as active as the reference compound, p,p'-diaminodiphenyl sulfone, while 4-methoxy-4'-acetamidochalcone[8] was of equal activity. 2-Chloro-4'-acetamidochalcone was twice as active as the reference compound[8].

The relative ease of preparation and the great reactivity of the chalcones and certain of their heterocyclic analogues suggested their use as intermediates in the syntheses of compounds of possible medicinal value. The method of Claisen[176] was conveniently employed in the preparation of the α,β-unsaturated ketones. From 0.10 to 0.15 mole of the appropriate aldehyde and methyl aryl ketone dissolved in 50 to 60 ml. of ethanol was condensed in the presence of catalytic amounts of sodium methoxide. Products of high purity resulted from this procedure in yields ranging from 80 to 96 percent (Table IV). In these small runs the method of Kohler and Chadwell[177] in which aqueous 10 percent sodium hydroxide is used as the condensation agent was found to be slightly inferior to the above procedure. A low yield (44 percent) of the unsaturated ketone was obtained from the condensation of methyl 2-pyridyl ketone in the presence of aqueous 10 percent sodium hydroxide. The condensation of 2-acetyldibenzothiophene with benzaldehyde and with p-di-

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176. Claisen, Ber., 20, 657 (1887).

177. Kohler and Chadwell, Org. Syn., Coll. Vol., I, 78 (1941).

Table IV

α,β-Unsaturated Ketones

RCH=CHCOR'

R	R'	% Yield	m.p. °C	Anal. or Calcd.	Ref. Found
p-$CH_3OC_6H_4$-	p-ClC_6H_4-	93	122		103
p-$(CH_3)_2NC_6H_4$-	p-ClC_6H_4-	94	140-1		104
p-$(CH_3)_2NC_6H_4$-	p-$CH_3OC_6H_4$-	37	127		104
C_6H_5-	α-C_5H_4N-	44[a]	73[b]		110
o-C_6H_4Cl-	p-$CH_3OC_6H_4$-	96	91-2		112
2-C_9H_6N-	p-$CH_3OC_6H_4$-	88	133-4	N, 4.84	4.61
2-C_9H_6N-	p-ClC_6H_4-	30[c]	165	Cl, 11.94	11.77, 11.91
2-C_9H_6N-[d]	4-C_9H_6N-	65	188	N, 9.03	9.25
C_6H_5-	2-Dibenzothienyl-	62[e]	154.5-155.5	S, 10.19	10.04, 9.97
p-$(CH_3)_2NC_6H_4$-	2-Dibenzothienyl-	57[e]	163-4	S, 8.96	9.02
m-$NO_2C_6H_4$-	$C_6H_4NHCOCH_3$-p	80	210	N, 9.03	9.16
m-$NO_2C_6H_4$-	α-C_5H_4N	96	178	N, 11.03	11.3
m-$NH_2C_6H_4$-	p-$NH_2C_6H_4$-	68	168-9	N, 11.77	11.94

(a) 10% aqueous sodium hydroxide was used as the condensing agent. In all other cases 10% sodium methoxide in methanol was employed.
(b) Reported m.p. 75°.
(c) Secondary condensation products were formed.
(d) The product was purified by digesting with hot ethyl acetate.
(e) These reactions were run at 40° and the products were separated from oils.

methylaminobenzaldehyde resulted in comparatively low yields (62 and 57 percent, respectively) of the corresponding α,β-unsaturated ketones. Because of the limited solubility of 2-acetyldibenzothiophene in ethanol, these reactions were run at 40°, a condition favoring the formation of secondary products.

Certain difficulties were encountered in the preparation of chalcone types derived from 2-quinolylaldehyde. Although the condensation between p-methoxyacetophenone and 2-quinolylaldehyde proceeded smoothly (88 percent), only 30 percent of the unsaturated ketone and a considerable amount of insoluble material was obtained from this aldehyde and p-chloroacetophenone. Methyl 4-quinolyl ketone and 2-quinolylaldehyde reacted to yield 65 percent of the desired condensation product which was sparingly soluble in most of the common organic solvents.

C. The Sulfinic Acids

The sulfinic acids and alkali arylsulfinates used in this study were in general prepared by known procedures[106,117]. However, lithium benzenesulfinate and lithium p-dimethylaminobenzenesulfinate were prepared in 76 and 74 percent yields, respectively, by the action of anhydrous sulfur dioxide on ethereal solutions of phenyllithium and p-dimethylaminophenyllithium.

$$(CH_3)_2NC_6H_4Br \xrightarrow{Li} (CH_3)_2NC_6H_4Li \xrightarrow{SO_2} (CH_3)_2NC_6H_4SO_2Li$$

Although the syntheses of magnesium aryl- or alkylsulfinates from sulfur dioxide and Grignard reagents is well known[178,179], the present synthetic application of aryllithium compounds has not been heretofore reported. By an analogous procedure, however, Fullhart[8] obtained a 60 percent yield of lithium p-dimethylaminothiophenolate from the addition of sulfur to p-dimethylaminophenyllithium.

D. Chalcone Addition Products

1. β-Ketosulfones

Within recent years the antibacterial activity of certain sulfur-containing compounds--in particular the arylaminosulfones and sulfides and certain sulfonamides--has received considerable attention. The unusual ability of chalcones to add mercaptans and sulfinic acids provided an elegant and expedient method of introducing these potentially active groups into the molecule. In this connection a number of β-ketosulfones was prepared and submitted for physiological testing. Currently available results of *in vitro* testing for the tuberculocidal activity of these compounds

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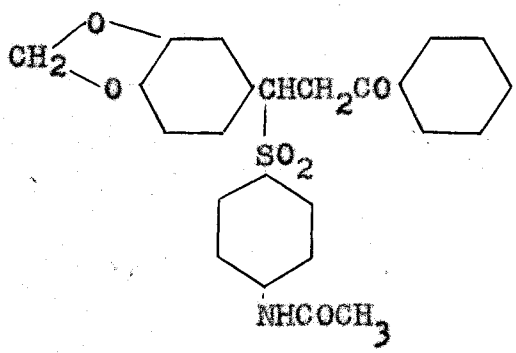
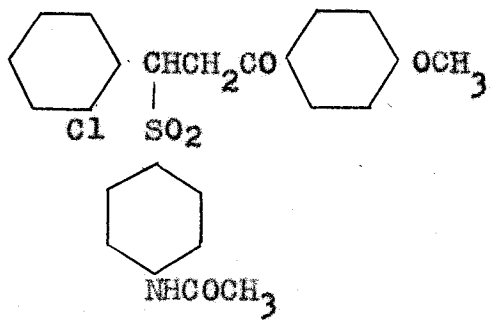
178. Reference 32 a. Chapter X.

179. Allen, J. Org. Chem., 7, 23 (1942).

have shown that β-(3,4-methylenedioxyphenyl)-β-(4-acetamidobenzenesulfonyl)propiophenone (LIII) was as active as the base compound, p,p'-diaminodiphenylsulfone, whereas p-methoxy-β-(2-chlorophenyl)-β-(4-acetamidobenzenesulfonyl)propiophenone (LIV) possessed one-half of the activity of the reference compound. The compounds were inactive against avian



(LIII)



(LIV)

malaria, and reports on their analgesic activity are unavailable.

Of the three methods employed in the syntheses of the β-ketosulfones (see p. 51) procedures (B) and (C) apparently offered two distinct advantages over the first method. The use of acetic acid in the liberation of the sulfinic acid from its alkali salt required only a one-step operation since the small quantity of sodium acetate formed was soluble in the excess solvent. Furthermore, the danger of oxidation and rearrangement[178,180] of the relatively unstable sulfinic

180. Gilman and Fothergill, J. Am. Chem. Soc., 51, 3501 (1929).

acid was minimized by its liberation directly in the presence of the chalcone. The use of glacial acetic acid as the solvent was often advantageous when chalcones which were sparingly soluble in ethanol were employed. These reactions generally proceeded smoothly and rapidly yielding from 68 to 94 percent of the addition product. The resulting sulfones (see Table V) were difficultly soluble in ethanol but could be recrystallized from ethyl acetate or from a 50 percent mixture of ethyl acetate and acetic acid, and, without exception, decomposed at their melting points.

Irregularities were observed on the attempted addition of the sulfinic acids to the basically substituted 4-dimethylaminochalcones and to those α,β-unsaturated ketones derived from 2-quinolylaldehyde. The original ketone was recovered when procedure (B) was employed. Yields of 30 to 42 percent and 53 to 64 percent of the respective addition product resulted from the use of method (C), and a longer period of reaction was usually required. p-Thiocresol added to 4-dimethylamino-4'-methoxychalcone (70 percent) only after refluxing the reactants for twelve hours in ethanol containing a trace of piperidine. 2-Quinolyl mercaptan did not add to chalcone under these conditions. In few cases the reaction between the sulfinic acids and 2-chloro-4'-methoxychalcone proceeded with difficulty.

In attempting to explain these inconsistencies, four

Table V

β-Ketosulfones--$RCH(SO_2R'')CH_2COR'$

R	R'	R''	% Yield	m.p. °C[a]	%S Calcd.	%S Found
p-$CH_3OC_6H_4$-	p-C_6H_4Cl-	p-C_7H_7-	72	158	7.5	7.4, 7.5
p-$(CH_3)_2NC_6H_4$-	p-C_6H_4Cl-	p-C_7H_7-	53	153-6	7.02	7.36, 7.24
p-$(CH_3)_2NC_6H_4$-	p-$CH_3OC_6H_4$-	p-C_7H_7-	30	149	7.32	7.34
p-$(CH_3)_2NC_6H_4$-	p-ClC_6H_4-	p-C_7H_7-[b]	70	148-9	7.83	7.82
C_6H_5-	C_6H_5-	p-$CH_3CONHC_6H_4$-	80	176-8	7.85[c]	7.85
p-$CH_3OC_6H_4$-	p-ClC_6H_4-	p-$CH_3CONHC_6H_4$-	71	159-160	6.79[b]	6.72, 6.77
C_6H_5-	α-C_5H_4N-	p-C_7H_7-	86	172-4	8.75[c]	8.4
o-ClC_6H_4-	p-$CH_3OC_6H_4$-	p-$CH_3CONHC_6H_4$-	81	160-1	6.78	6.46
3,4-$CH_2O_2C_6H_3$-	C_6H_5-	p-$CH_3CONHC_6H_4$-	69	150-3	7.1	7.32
2-Dibenzothienyl-	C_6H_5-	p-C_7H_7-	68	180-2	13.66	12.86, 12.75[f]
p-$(CH_3)_2NC_6H_4$-	p-$CH_3CC_6H_4$-	p-$CH_3CONHC_6H_4$-	42	155-156	6.67	6.65
p-$(CH_3)_2NC_6H_4$-	p-ClC_6H_4-	p-$CH_3CONHC_6H_4$-	32	158	6.61	6.66

Table V (continued)

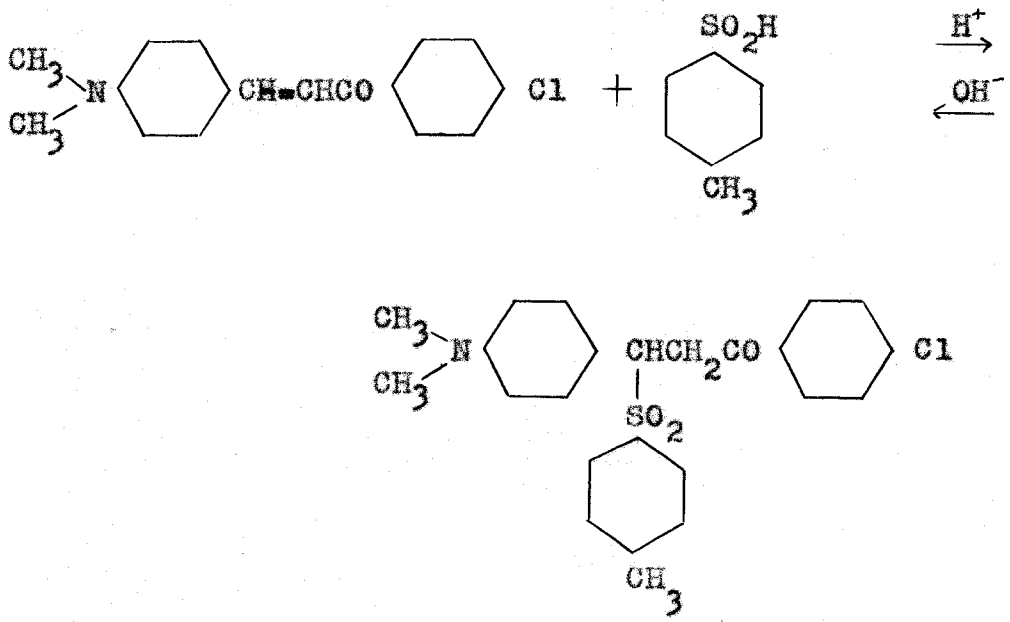
R	R'	R"	% Yield	m.p. °C[a]	%S Calcd.	%S Found
3,4-$CH_2O_2C_6H_3$-	C_6H_5-	p-C_7H_7-	41	145-8	7.84	7.73
o-ClC_6H_4-	p-$CH_3OC_6H_4$-	p-C_7H_7-	83	149-50	7.47	7.2
C_6H_5-	C_6H_5-	p-C_6H_4Cl-	89	175-6	8.31	8.26
C_6H_5-	C_6H_5-	-$C_6H_3(Cl)(OCH_3)$-3,4	94	172-4	7.72	7.75
C_6H_5-	C_6H_5-	-C_6H_3(3-$NHCOCH_3$, 4-OCH_3)	39	155-6	7.32	7.38
p-$(CH_3)_2NC_6H_4$-	p-$CH_3OC_6H_4$-	p-ClC_6H_4-	45	149-50	7.00	7.06
p-$(CH_3)_2NC_6H_4$-	p-ClC_6H_4-	-C_6H_3(3-$NHCOCH_3$, 4-OCH_3)	39	176	6.24	6.33
2-C_9H_6N-	p-$CH_3OC_6H_4$-	p-$C_6H_4NHCOCH_3$-	53	170.2	6.56	6.81
2-C_9H_6N-	p-$CH_3OC_6H_4$-	p-ClC_6H_4-	64	158-60	6.88	6.83
2-C_9H_6N-	p-$CH_3OC_6H_4$-	C_6H_5-	59	150-2	7.42	7.00
2-C_9H_6N-	p-$CH_3OC_6H_4$-	-$C_6H_4C_3H_7$-iso(p)	73	156-8	6.76	6.57
C_6H_5-	C_6H_5-	p-$(CH_3)_2NC_6H_4$-	20[g]	191.2	8.14	7.99, 8.24
m-$NH_2C_6H_4$-	p-$NH_2C_6H_4$-	p-C_7H_7-	70	184-5	8.38	8.12

Table V (continued)

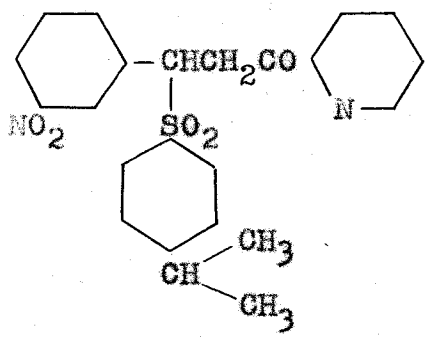
R	R'	R"	% Yield	m.p.,°C[a]	%S Calcd.	%S Found
m-$NH_2C_6H_4$-	p-$NH_2C_6H_4$-	p-$CH_3CONHC_6H_4$-	77	186-200	7.32	7.39
C_6H_5-	C_6H_5-	-$C_6H_4C_3H_7$-iso(p)	65	157-8	8.2	8.57
o-ClC_6H_4-	p-$CH_3OC_6H_4$-	-$C_6H_4C_3H_7$-iso(p)	17	150	7.02	7.14
-$C_6H_4NO_2$-m	α-C_5H_4N-	-$C_6H_4C_3H_7$-iso(p)	57	170-2	7.16	6.2, 6.21[h]
C_6H_5-	p-ClC_6H_4-	p-C_7H_7-	60	188	8.04	8.03

(a) All of the products decomposed at their melting points.
(b) A mixture of the chalcone and p-thiocresol in ethanol containing a trace of piperidine was refluxed for 12 hours.
(c) Calcd. for $C_{23}H_{21}O_4NS$: N, 3.44. Found: N, 3.59.
(d) Calcd. for $C_{24}H_{22}O_5NClS$: N, 2.97; Cl, 7.5. Found: N, 3.16; Cl, 7.2 and 7.3.
(e) Calcd. for $C_{21}H_{19}O_3NS$: N, 4.06. Found: N, 4.02.
(f) Several recrystallizations from acetic acid did not alter the purity of the compound.
(g) The product formed after the reaction was allowed to stand at room temperature for two weeks. The material sintered at 177°.
(h) The product analyzed for amine acetate: Calcd. for $C_{23}H_{21}O_5N_2S \cdot CH_3COOH$: S, 6.45. Found: S, 6.2 and 6.21.

possible contributing factors have been considered: (1) the limited solubility of the chalcone, (2) the instability of the addition product, (3) the basic nature of the reactants, and (4) steric hindrance. The last idea can be readily eliminated except in the case of 2-chloro-4'-methoxychalcone and is rather doubtful in this instance since the addition of p-acetamidobenzenesulfinic acid to this ketone took place to the extent of 81 percent. The limited solubility of these unsaturated ketones in ethanol seemed to be of prime importance. Nevertheless, on the basis of previous information concerning other addition reactions of chalcones, the remaining factors cannot be rejected. For example, Stewart and Pollard[27,28] explained the failure of morpholine and piperazine to add to certain chalcones on the basis that the addition products were formed but might have been too unstable to permit isolation. The fact that these addition reactions are reversible in the presence of a base[11,14] cannot be overlooked (pp. 7-8). It is, therefore possible that, in addition to the solubility factor the basic nature of these substituents--the p-dimethylamino- and quinolyl groups--may cause a reversal of the reaction. The use of an excess of acetic acid as the solvent /procedure (C)/ not only increases the solubility of the starting material but should be effective in bringing about a more rapid and more



complete reaction. However, the formation of an easily hydrolyzed amine acetate might account for the low yields obtained in this series. Only in the case of 1-(2-pyridyl)-3-(p-cumenesulfonyl)-3-(3-nitrophenyl)propanone-1 (LV) was the acetate isolated.



(LV)

Incidental to the negative results obtained from the attempted addition of 2-quinolyl mercaptan to chalcone re-

cent work[8] has indicated that the failure of β-diethylaminoethyl mercaptan to add to chalcone was due to the basic nature of this addendum. The addition was readily effected, however, when the corresponding amine hydrochloride was used. The conversion of the resulting β-ketosulfide amine hydrochloride to the free base was complicated by the reversible nature of the reaction.

2. β-Ketosulfonamides

During the course of this study a series of β-ketosulfonamides was prepared through the addition of N-substituted aryl- and alkylamidosulfurous acids to chalcones.

$$R_2NH + SO_2 \longrightarrow R_2NSO_2H$$

$$C_6H_5CH{=}CHCOC_6H_5 + R_2NSO_2H \longrightarrow C_6H_5\underset{\displaystyle SO_2NR_2}{\underset{|}{C}}HCH_2COC_6H_5$$

This type of an addition has not been previously investigated and represents a rather simple and relatively useful method of introducing a sulfonamido group into molecules containing 1,4-conjugated systems.

The substituted amidosulfurous acids were prepared by passing anhydrous sulfur dioxide directly into an ethereal solution of the appropriate primary or secondary amine. The insoluble crystalline product was filtered, washed with

ether and stored in vacuo over phosphorus pentoxide. Products which were too deliquescent to isolate were reacted directly after removing the excess ether with the appropriate chalcone in absolute ethanol. 1-Piperidinesulfinic acid[125] (LVI) and N-phenylamidosulfurous acid[125a,128,129] (LVII) were isolated in yields of 85 and 70 percent, respectively.

$C_5H_{10}NSO_2H$ (LVI) $C_6H_5NHSO_2H$ (LVII)

Two procedures were employed in the syntheses of the β-ketosulfonamides (see p. 86). The yields of the addition products obtained from method (A) ranged from 48 to 70 percent while those obtained from procedure (B) varied from 58 to 88 percent (Table VI). The products obtained by both methods were identical (mixed m.p.). In addition to the superior yields, the more direct procedure

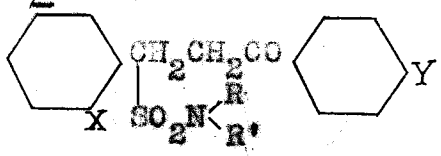
$$C_6H_5CH{=}CHCOC_6H_5 + R_2NH + SO_2 \longrightarrow C_6H_5\underset{\displaystyle SO_2NR_2}{\underset{|}{CH}}\text{-}CH_2COC_6H_5$$

was advantageous from the standpoint of expediency as well as eliminating the rather difficult isolation of the deliquescent, intermediate substituted amidosulfurous acid.

These reactions generally proceeded rapidly and smoothly. However, the unsaturated ketone was recovered when 1-piperidinesulfinic acid (LVI) was added to 1-(p-methoxy-

Table VI

β-Ketosulfonamides



X	Y	R	R'	Yield % Method (A)	(B)	m.p. °C	Anal. %S Calcd.	Found
H	H	C_5H_{10}	--	66	83	176-8	8.95	8.5[a]
Cl	OCH_3	C_5H_{10}	--	48[b]	--	190	7.6	7.3 7.32
H	H	C_2H_5	C_2H_5	49[c]	58[d]	150-2	9.26	8.8
H	H	C_4H_9	C_4H_9	70	80	130-1	9.26	9.0
H	H	C_6H_5	H	60	88	181[e]	8.76	8.48
H	H	C_6H_5	CH_3	--[f]	--	175-9	--	--
H	Cl	C_5H_{10}	--	60	--	180-2	8.18	7.12[h] 7.12[h]
H	H	$C_{12}H_{25}$	$C_{12}H_{25}$	--[g]	--	--	--	--
H	H	$C_{18}H_{37}$	$C_{18}H_{37}$	--[g]	--	--	--	--

(a) Calcd. for $C_{20}H_{23}O_3NS$: N, 3.92. Found: N, 4.1.

(b) The crude β-Ketosulfonamide crystallized from the reaction mixture after standing at room temperature for several days. The product was purified by extraction with ethyl acetate and finally by recrystallization from ethanol.

(c) The addition product was obtained after allowing the reaction mixture to stand at room temperature for three days.

(d) This reaction required two weeks' standing in the icebox. The crude yield was 87 percent.

(e) The product decomposes at its melting point and is sparingly soluble in ethanol.

(f) The compound analyzed high for nitrogen. Calcd. for $C_{22}H_{21}O_3NS$: N, 3.69. Found: N, 5.11.

(g) No addition product could be obtained from these secondary high-molecular weight aliphatic amines.

(h) Repeated recrystallization from ethanol did not yield a product of higher analytical purity.

phenyl)-3-(2-quinolyl)-2-propen-1-one. Also, the addition of the acid to 2-chloro-4'-methoxychalcone proceeded with difficulty. Indefinite products were obtained when the reaction was attempted with di-n-octadecylamine, di-n-dodecylamine, and with N-methylaniline.

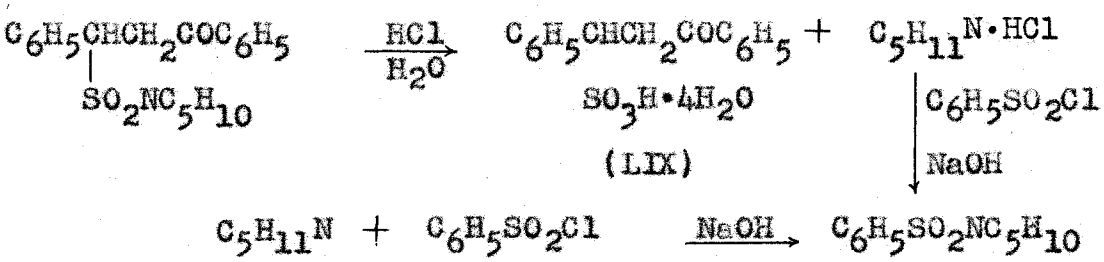
In addition to the previously discussed factors influencing the ease of addition of sulfinic acids to α,β-unsaturated ketones it may be pointed out here that the possibility of steric effects is not unlikely--keeping in mind the negative results obtained by Tambor and Wildi[23] in attempts to add mixed aliphatic-aromatic secondary amines to chalcone.

The β-ketosulfonamides were in general well-defined crystalline products which with the exception of 2-benzoyl-1-phenylethanesulfonanilide (LVIII) melted sharply without

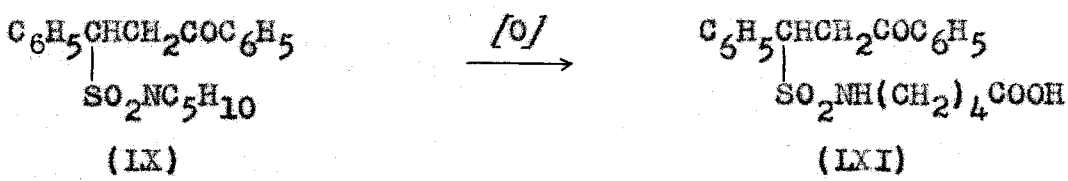
$$\begin{array}{l} C_6H_5CHCH_2COC_6H_5 \\ \quad\quad | \\ \quad SO_2NHC_6H_5 \end{array} \qquad \text{(LVIII)}$$

decomposition. These compounds exhibited relatively polar properties being sparingly soluble in benzene and in ether but easily recrystallizable from boiling ethanol and often from hot water. Refluxing with dilute hydrochloric acid gave rise to the corresponding amine hydrochloride and a compound which analyzed for the corresponding β-ketosulfonic acid tetrahydrate (LIX). The amine was identified by conversion into its benzenesulfonyl derivative which was com-

pared with that obtained from an authentic sample.



On further examination of the properties and reactions of these addition products, the oxidation of β-phenyl-β-(1-piperidinesulfonyl)propiophenone (LX) by aqueous potassium permanganate was attempted. From this reaction there was expected the β-(δ-sulfonamidovaleric) acid derivative (LXI) of benzylacetophenone. However, the resulting product was 2-benzoyl-1-phenylethanesulfonic acid (LIX). δ-Aminovaleric acid was not isolated from the reaction.



From the similar oxidation of 1-piperidinebenzenesulfonamide Schotten and Schöemann[181] obtained δ-benzenesulfonamidovaleric acid.

Previous to this investigation the structure of the substituted amidosulfurous acids was a subject of controver-

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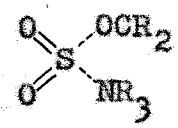
181. Schotten and Schöemann, Ber., 24, 3687 (1891).

sy. These types of compounds had been prepared and long recognized as derivatives of the unstable amidosulfurous acid, NH_2SO_2H[125,128,129]. Michaelis[182], however, was unable to decide whether the SO_2 group in these molecules was of the symmetrical, -SOO-, or of the unsymmetrical, $=SO_2$, configuration. Marino and his coworkers[127] investigated the physical and chemical properties of 1-piperidinesulfinic acid and its selenium analogue. They were of the opinion that a change of position of the imino hydrogen to produce the corresponding amidosulfurous or the amidoselenious acid was impossible. These products were therefore thought to be simple addition compounds of the type $R_2NH \cdot SO_2$ or $R_2NH \cdot SeO_2$.

Incidently, ternary compounds of the type (LXII) have been reported[128,183] to result from the action of sulfur di-



(LXII)

oxide on mixtures of amines and ketones in ethanol.

In view of the previously presented discussion concerning the addition reactions of chalcones, there can be little

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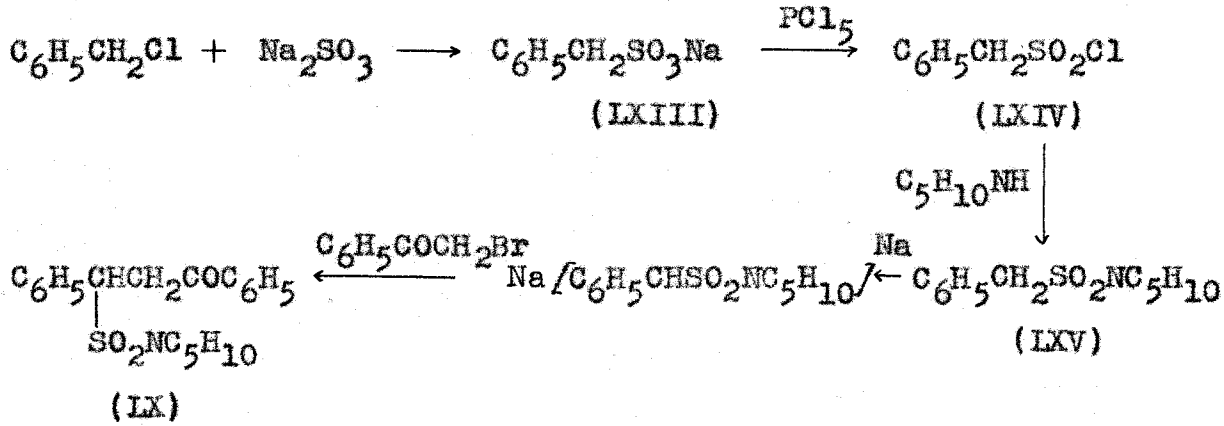
182. Michaelis, Ann., 274, 173 (1893).

183. Feigl and Feigl, Zeit. anorg. allgem. Chem., 203, 57 (1931).

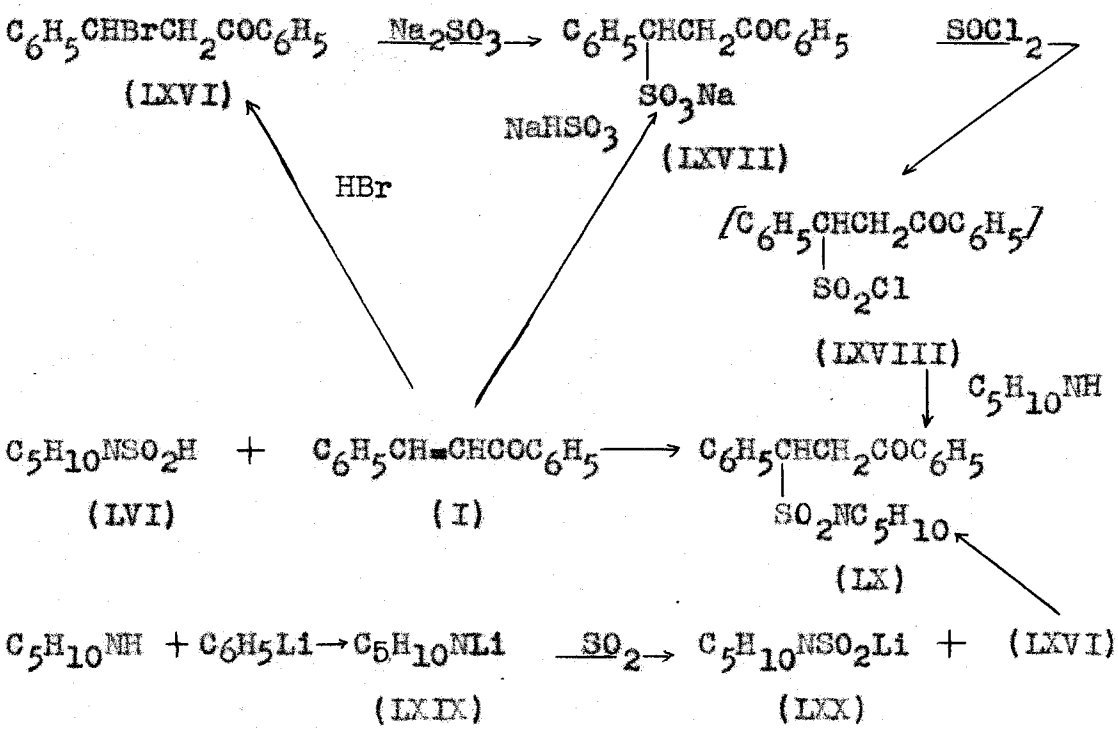
doubt that the addition of these substituted amidosulfurous acids to the α,β-unsaturated ketones is 1,4- and that the resulting products are constituted like the one formed from 1-piperidinesulfinic acid and chalcone (LX). However, the existence of the previously mentioned controversial issues made it imperative to secure unequivocal evidence for the structure assigned to these β-ketosulfonamides. To this end the following independent synthesis of β-phenyl-β-(1-piperidinesulfonyl)propiophenone was proposed.



Sodium benzylsulfonate (LXIII) was obtained in 65 percent yields by the method of Johnson and Ambler[131]. The treatment of the sodium sulfonate with a slight excess of phosphorus pentachloride yielded 65 percent of benzylsulfonyl chloride[132] (LXIV). This product readily condensed with an excess of piperidine to produce 70 percent of 1-piperidinebenzylsulfonamide[133] (LXV). Although the monosodio derivative of this compound was apparently formed, its alkyl-

ation with phenacyl bromide did not take place. These results were parallel to those obtained by Shriner and his coworkers[184]. They observed that a methylene hydrogen atom on benzyl phenyl sulfone could be replaced by sodium, but no alkylation of the compound took place with methyl iodide.

An alternate method of synthesis was successfully carried out according to the following series of reactions.

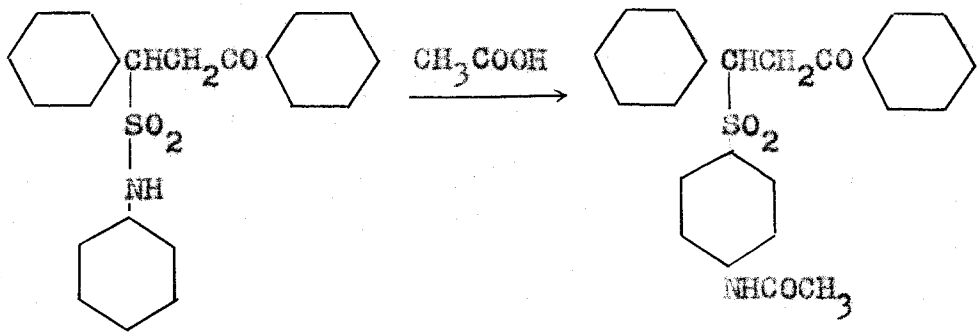


Sodium 2-benzoyl-1-phenylethanesulfonate (LXVII) was obtained quantitatively from the condensation of β-phenyl-β-bromopropiophenone (LXVI) with sodium sulfite and more di-

184. Shriner, Struck, and Jorison, J. Am. Chem. Soc., 52, 2060 (1930); see also reference 18.

rectly in 94 percent yields by the known addition of sodium bisulfite to chalcone[20,21]. Refluxing a suspension of the sulfonate (prepared by either method) with thionyl chloride in benzene gave rise to the corresponding β-ketosulfonyl chloride (LXVIII). This product when treated directly, without isolation, with an excess of piperidine yielded 56 percent of the β-ketosulfonamide (LX). Lithium 1-piperidinesulfinate (LXX) was obtained directly by passing anhydrous sulfur dioxide into an ethereal solution of 1-piperidyllithium (LXIX). This product condensed with the β-bromoketone (LXVI) yielding 25 percent of β-phenyl-β-(1-piperidinesulfonyl)propiophenone (LX). The products obtained from these three procedures were identical (mixed m.p.).

2-Benzoyl-1-phenylethanesulfonanilide (LVIII) was sparingly soluble in ethanol. This product melted with decomposition at 168 to 170° after digesting with ethanol but decomposed sharply at 181° after recrystallization from glacial acetic acid. This unusual behavior suggested the possibility of a molecular rearrangement of the sulfonamide to the structurally similar sulfone (LXXI) prepared earlier in this study by the addition of p-acetamidobenzenesulfinic acid to chalcone. Moreover, the fact that the rearrangements of certain sulfonamides to aminosulfones have been re-



(LVIII) (LXXI)

ported[185] to take place under the catalytic influence of heat or acids gave further support to this postulation. Results of mixed melting point determinations were unreliable. After further investigation, however, a product melting with decomposition sharply at 181° was obtained when the sulfonanilide was recrystallized from a large excess of ethanol. No rearrangement to the sulfone had occurred. The product was identical (mixed m.p.) to that prepared from aniline and 2-benzoyl-1-phenylethanesulfonyl chloride (LXVIII).

In summary, the experimental results obtained from these studies seem to indicate that sulfur dioxide reacts with certain primary and secondary amines to produce the

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185. For general information concerning this subject consult Suter, C. M., "The Organic Chemistry of Sulfur", John Wiley and Sons, Inc., New York, 1944, pp. 582 and 704. Also Bambas has reported the rearrangement of 2-(4-nitrophenyl-sulfen)aminothiazole to 4-nitrophenyl-2'-acetamidothiazolyl-5-sulfide after heating to 85° with acetic anhydride. J. Am. Chem. Soc., 67, 671 (1945).

corresponding N-substituted aryl- or alkylamidosulfurous acid, R_2NSO_2H, as originally proposed by Michaelis[125,182] and earlier by Schiff[129]. In contrast to the view of Marino and his co-workers[127] a displacement of the imino hydrogen from the nitrogen to the sulfur atom is possible. Moreover, the 1,4-addition of these acids to chalcones suggests that the SO_2 group in the molecule is unsymmetrical, $=SO_2$. However, the possible existence of an equilibrium mixture of the two forms

$$R_2N-\underset{\underset{O}{|}}{\overset{H}{S}}\rightarrow O \rightleftharpoons R_2N-\underset{OH}{S}=O \quad \text{or} \quad R_2N-\underset{\underset{O}{|}}{\overset{Li}{S}}\rightarrow O \rightleftharpoons R_2N-\underset{OLi}{S}=O$$

in which the chalcone reacts preferentially with the unsymmetrical form cannot be excluded.

In addition to the ability of lithium 1-piperidinesulfinate to undergo alkylation further evidence supporting the existence of the unsymmetrical SO_2 group in this molecule may be deduced from the work of Gilman and his co-workers[180,186a,b]. They were able to obtain arylsulfonylmagnesium chloride-etherates from the direct reaction of magnesium with arylsulfonyl chlorides--compounds of undebatable structure.

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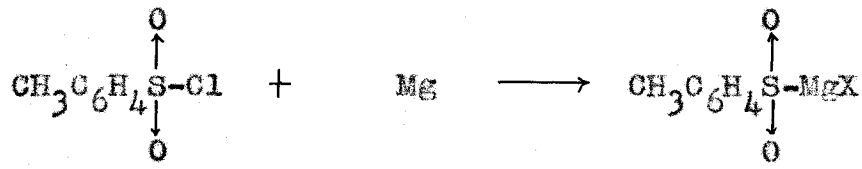
186. (a) Gilman and Fothergill, J. Am. Chem. Soc., 50, 802 (1929); (b) Gilman, Smith, and Parker, ibid., 47, 851 (1925).



These investigators concluded that the -MgX group was directly attached to the sulfur atom. However, the corresponding sulfones were not obtained on the attempted alkylation of these products with diethyl sulfate.

3. β-Ketoselenides

By reason of the location of sulfur and selenium in the same periodic family, the extension of these addition reactions of chalcones to selenophenols and to arylseleninic acids seemed logical. In addition, it was of interest to determine the effectiveness of the chalcone molecule in altering the highly toxic properties of the selenium atom.

The selenophenols readily added to chalcones in the absence of a catalyst producing well-defined crystalline products in yields varying from 44 to 80 percent (Table VII). No addition to 2-chloro-4'-methoxychalcone was observed, however. These β-ketoselenides were easily recrystallized from ethanol and were similar in reaction to their sulfur analogues (p. 7). They decomposed into the chalcone and the selenol after standing at room temperature in the presence of a base. Refluxing the compounds with phenylhydrazine in

Table VII

β-Ketoselenides - $RCHCH_2COR'$ (SeR")

R	R'	R"	Yield %	°C m.p.	Anal. Calcd.	Found
C_6H_5-	C_6H_5-	C_6H_5-	76	120	Se, 21.64	21.88
C_6H_5-	p-ClC_6H_4-	C_6H_5-	58	100-1	Cl, 8.77	9.0 8.9
C_6H_5-	C_6H_5-	p-ClC_6H_4-	80	105	Cl, 8.77	8.66 8.68
p-$CH_3OC_6H_4$-	C_6H_5-	p-ClC_6H_4-	44	97-8	Cl, 8.16	8.02
C_6H_5-	p-ClC_6H_4-	p-ClC_6H_4-	52	110	Cl, 16.33	16.00
p-$CH_3OC_6H_4$-	C_6H_5-	C_6H_5-	69	87-8	Se, 20.0	19.74 19.76

glacial acetic acid gave rise to the selenium-free 1,3,5-triphenylpyrazoline. However, the attempted oxidation yielded indefinite products.

As a matter of establishing the structure of these compounds β-phenyl-β-(4-chlorobenzeneseleno)propiophenone (LXXII) was prepared by the alkylation of the sodium salt of p-chlorobenzeneselenophenol with β-phenyl-β-bromopropiophenone. The product obtained was identical (mixed m.p.) with that prepared by the addition of p-chloroselenophenol to chalcone.

$$C_6H_5CH{=}CHCOC_6H_5 + p\text{-}ClC_6H_4SeH \longrightarrow C_6H_5CHCH_2COC_6H_5$$
$$\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\quad |$$
$$\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad SeC_6H_4Cl\text{-}p$$
$$\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\quad (LXXII)$$
$$C_6H_5CHBrCH_2COC_6H_5 + p\text{-}ClC_6H_4SeNa \nearrow$$

It is interesting to note that the formation of an addition product from 0.02 of a mole of selenophenol and an equivalent amount of chalcone in ethanol required only nine minutes. Under identical conditions thiophenol did not add to the ketone after allowing the reaction mixture to stand for five hours. The introduction of a few drops of piperidine brought about the immediate formation of the β-ketosulfide.

In contrast to the smooth addition of the selenophenols to chalcones, no reaction was observed to take place between these ketones and benzeneseleninic acid or the structurally

related l-piperidineseleninic acid. These negative results are not surprising in view of some distinct differences in reactions existing between certain sulfur-containing compounds and their selenium analogues. One of the most pronounced differences between aromatic selenides and their corresponding sulfides is the increasing basic properties of oxidized selenium as shown by the tendency to remain in the tetravalent state[187a]. The organic sulfides, on the other hand, undergo oxidation to the corresponding sulfone under relatively mild conditions. Only one arylselenone has been reported in the literature[187b,c], and this product showed the characteristics of a peroxide rather than those of the relatively inert analogous sulfone[187c]. Benzeneseleninic acid crystallizes as its nitrate, $C_6H_5SeO_2H.HNO_3$, from concentrated nitric acid[187b], conditions under which the corresponding sulfinic acid would be extremely unstable. Kenyon and others[187c] have further pointed out that the unsymmetrical ethyl ethanesulfonate is obtained from ethyl iodide and silver sulfite while under the same conditions silver selenite yields the symmetrical diethyl selenite.

In the older literature the structure of the sulfinic

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187. (a) Foster and Brown, ibid., 50, 1182 (1928); (b) Krafft and Vorster, Ber., 26, 2895 (1893); (c) Gaythwaite, Kenyon, and Phillips, J. Chem. Soc., 2280 (1928).

acids was a subject of controversy[180a,186a]. Some reactions indicate the presence of an -OH group while others can be best explained by assuming that the hydrogen is attached to sulfur. There is little doubt that the addition of the sulfinic acids to chalcones is made possible by the latter arrangement. On these grounds and in the light of the previous discussion it is entirely possible that the seleninic acids do not exist with the configuration, $R-\overset{H}{\underset{O}{Se}}\rightarrow O$, which undergoes 1,4-addition to chalcones.

E. High-Molecular Weight Aliphatic Compounds

During the course of this investigation a number of high-molecular weight aliphatic compounds was prepared. This particular study was carried out with two objects in mind. First, to determine the therapeutic effects of the introduction of lipoid-solublizing groups into molecules or nuclei of known physiological activity, and second, to extend certain known reactions of aliphatic compounds within the homologous series. For more general and more detailed information on these subjects the reader is referred to a recent thesis by S. P. Massie[175].

The bactericidal and antimalarial activity of certain amino derivatives of quinoline and acridine are well known. With this in mind, 2-dodecylquinoline and a series of 9-do-

decyl- and 9-octadecylaminoacridine derivatives[188] were synthesized and tested as possible antimalarial agents. These compounds, however, were ineffective against avian malaria. Concurrent with these investigations, 9-dodecylaminoacridine and its hydrochloride were prepared by Albert, Goldacre, and Heymann[144] as possible antiseptic agents. No report of their activity was given, however.

A significant development in the field of chemotherapy has been the discovery of the antibacterial action of certain amino substituted phenyl sulfones and sulfoxides. Recent reports have indicated that like properties are exhibited by various amino substituted phenyl sulfides[189]. The syntheses of similarly constructed molecules containing the lipoid-solublizing dodecyl ($C_{12}H_{25}$-) and hexadecyl ($C_{16}H_{33}$-) radicals was therefore desirable. None of the high-molecular weight aliphatic aminophenyl sulfones and sulfides or their derivatives prepared during this investi-

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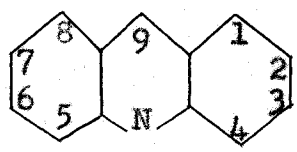
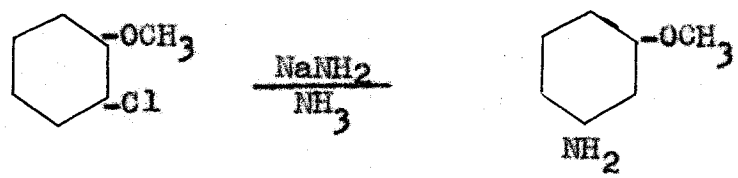
188. The Chemical Abstracts system of numbering the acridine derivatives was used. C. A., 39, 5889 (1945).



189. Broadbent, H. S., Doctoral Dissertation, Iowa State College, 1946.

gation exhibited significant pharmacological activity.

Gilman and Avakian[165] have recently shown that in the amination of o-halogenaryl alkyl ethers with sodium amide in liquid ammonia an interesting rearrangement takes place from which the m-aminophenyl alkyl ether results.



In order to test the generality of this reaction, the amination-rearrangement of o-chlorophenyl n-dodecyl ether was attempted. No rearrangement was found to occur under the conditions employed in the analogous reaction with o-chloroanisole. Rearrangement did occur to a small extent, however, when the reaction was run at elevated temperatures and under high pressure conditions. These results were similar to those reported by Kyle[190]. He was able to obtain 38 percent of the meta-amine from the reaction of o-chlorophenetole with lithium diethylamide as compared with 35 percent of the meta-amine from o-chloroanisole under the same conditions. The similar amination and subsequent rearrangement did not take place between o-chlorophenyl dodecyl ether and lithium

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190. Kyle, R., Masters Thesis, Iowa State College, 1945; unpublished studies.

diethylamide after allowing the reaction to proceed for 24 hours.

F. Organosilicon Compounds

In recent years the interest in the chemistry of organic-silicon compounds has been rather active. One particular phase of this line of research has been devoted to the syntheses of organosilanes containing functional groups. In these laboratories comparative studies concerning the chemical and biological activities of similar silicon and carbon molecules have been of great interest. Therefore, as a part of the present study the possible preparation of triphenylthiosilanol and certain related arylmercapto- and arylsulfonylsilanes was investigated.

In attempting to synthesize triphenylthiosilanol, the known procedure for the preparation of triphenylthiocarbinol[191a,b] was followed. Triphenylchlorosilane was refluxed with a suspension of sodium hydrosulfide in benzene over a

$$(C_6H_5)_3SiCl + NaHS \longrightarrow (C_6H_5)_3SiSH + NaCl$$

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191. (a) Blicke, J. Am. Chem. Soc., 45, 1965 (1923); (b) Vorländer and Mittag, Ber., 46, 3453 (1913). These investigators used ethanol as the solvent for the reaction but obtained low yields of the product because of the interaction of triphenylmethyl chloride with the solvent.

period of 24 hours after which time the original silane was recovered. In this connection, it may be pointed out that while triphenylmethyl chloride reacted with sodium hydrosulfide under these conditions, a low yield of the mercaptan was obtained, and the product showed a marked tendency to lose the thiol group.[191]

The extreme ease of hydrolysis of triphenylchlorosilane in semi-polar solvents limited the use of this compound in other well established mercaptan syntheses. However, the unique chemical reactions of the triaryl- or trialkylsilanes suggested an alternate method of obtaining the thiosilanol.

$$(C_6H_5)_3SiH + NaHS \longrightarrow (C_6H_5)_3SiSH + NaH$$

For example, from the reaction between triethylsilane[192a,193] or triphenylsilane[192b] and an organolithium compound there was obtained the tetraalkyl- or tetraarylsilane and lithium hydride. Refluxing a mixture of triethylsilane, lithium ethoxide, and ethanol gave rise to a 74 percent yield of triethylethoxysilane[193]. Very recently triphenylphenoxysilane was obtained in yields of 84 percent by heating triphenylsilane with sodium phenoxide in refluxing phenol[194].

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192. (a) Gilman and Massie, J. Am. Chem. Soc., 68, 1128 (1946); (b) Unpublished studies.

193. Meals, ibid., 1880 (1946).

194. Smart, unpublished studies.

In general, these types of reactions involving the triaryl- or the trialkylsilanes can be expressed by the following equations

$$R_3SiH + MX \longrightarrow R_3SiX + MH$$
$$MH + HX \longrightarrow MX + H_2$$

in which X can be -OH, $-OC_2H_5$, $-NH_2$, or $-NHC_2H_5$[193].

The treatment of triphenylsilane with sodium hydrosulfide in ether led to the quantitative recovery of the silane. A 55 percent yield of triphenylethoxysilane was obtained on refluxing a solution of triphenylsilane with sodium hydrosulfide in ethanol.

Attempts to prepare triphenyl-p-toluenesulfonylsilane or triphenyl-p-toluenemercaptosilane from triphenylsilane and sodium p-toluenesulfinate or sodium p-thiocresolate in ether or in refluxing benzene led to the recovery of the starting materials. No reactions took place between these alkali salts and triphenylchlorosilane. Identical results have been obtained by Melvin[195]. In a similar reaction[196] a low yield of phenylmercaptotrichlorosilane resulted from heating four moles of thiophenol with one mole of silicon

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195. Unpublished studies.

196. (a) Jorg and Stetter, J. prakt. Chem., 117, 305 (1927); (b) Backer and Stienstra, Rec. trav. chim., 52, 912 (1933).

tetrachloride[196a]. Backer and Stienstra[196b] obtained phenyl tetrathioorthosilicate in 8% yields and p-tolyl tetrathioorthosilicate in 25% yields by refluxing a mixture of the sodium mercaptide and silicon tetrachloride in benzene.

V. SUMMARY

1. A general review of some addition reactions of chalcones has been presented.

2. Several new chalcones and related heterocyclic α,β-unsaturated ketones have been synthesized. Some previously reported chalcones prepared as intermediates in this study were submitted to physiological testing. Two of these compounds possessed tuberculocidal activity.

3. The syntheses of certain arylsulfinic acids was carried out by a new procedure in which sulfur dioxide was interacted with an aryllithium compound.

4. A series of β-ketosulfones was prepared by means of the 1,4-addition of sulfinic acids to chalcones. These compounds have been submitted for pharmacological testing.

5. Two new 1,4-addition reactions of chalcones were carried out. β-Ketoselenides were prepared by the addition of selenophenols to chalcones. Substituted aryl- and alkylamidosulfurous acids of the type R_2NSO_2H added to chalcones yielding β-ketosulfonamides. The structural configuration of these 1,4-addition products were established by independent syntheses.

6. Several high-molecular weight aliphatic 9-aminoacridine derivatives were prepared and tested as possible anti-

malarial agents. The results of these tests were not significant.

7. A few miscellaneous n-dodecyl and n-hexadecyl aminophenyl sulfides and sulfones or their derivatives were prepared and submitted for pharmacological testing.
8. The amination-rearrangement of o-chlorophenyl dodecyl ether took place to a small extent only under high temperature and pressure conditions.
9. Attempts to prepare triphenylthiosilanol and certain arylmercapto- and arylsulfonylsilanes were unsuccessful.

VI. APPENDIX

The following communications from members of the Editorial Board of Chemical Abstracts, were received in reply to inquiries regarding the proper method of naming certain α,β-unsaturated ketones and their 1,4-addition products.

COPY

March 5, 1946

Mr. Louis F. Cason,
Iowa State College,
Ames, Iowa.

Dear Mr. Cason:

I am writing in answer to your letter of February 26. Before doing so I have consulted with Dr. Mary Magill of this office. She specializes in the organic side of our work and I often turn to her for advice on nomenclature problems.

If compound I is named as a ketone, the name according to the C.A. system is 1-(2-dibenzothienyl)-3-(p-dimethylaminophenyl)-2-propen-1-one. If it is named as a derivative of dibenzothiophene, the name is 2-(p-dimethylaminocinnamoyl)dibenzothiophene. In the C.A. indexes, preference is given to the ketone name; the second name would appear as a daggered (extra) entry.

Compound II may be named as a derivative of acetanilide: 5-[α-(2-dibenzothienylcarbonylmethyl)benzylsulfonyl]-o-acetaniside; as a ketone: 3-(3-acetamido-4-methoxyphenylsulfonyl)-1-(2-dibenzothienyl)-3-phenyl-1-propanone; or as a derivative of dibenzothiophene: 2-[β-(3-acetamido-4-methoxyphenylsulfonyl)hydrocinnamoyl]dibenzothiophene. In the C.A. index, the first name would be pre-

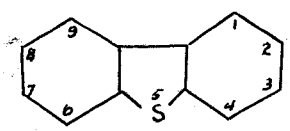
ferred; the third name would be entered as an extra entry.

C.A. would name compound III: 1-(2-quinolyl)-3-(4-quinolyl)-2-propen-1-one.

The name for compound IV is: 1-piperidinesulfinic acid.

Compound V may be named as a ketone derivative: β-phenyl-β-(1-piperidylsulfonyl)propiophenone; or as a piperidine derivative: 1-(2-benzoyl-1-phenylethylsulfonyl)piperidine. In the C.A. index, the first name would be preferred; the second would be entered with a dagger.

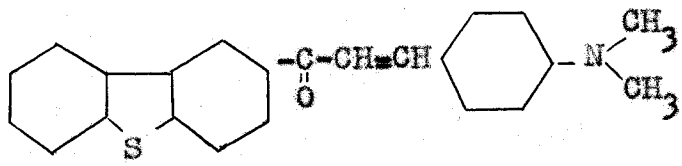
In these names, the C.A. numbering for dibenzothiophene has been used:



Sincerely yours,

EJC:MW (Signed) E. J. Crane

(I)



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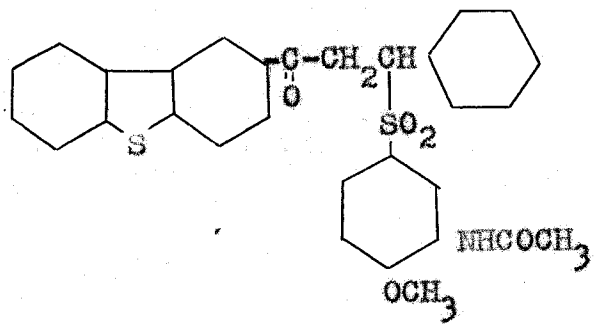

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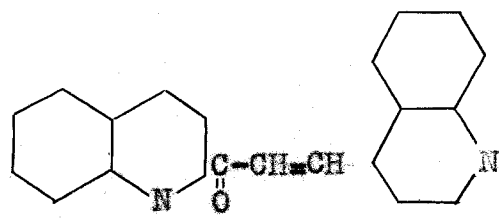
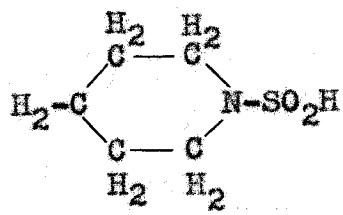
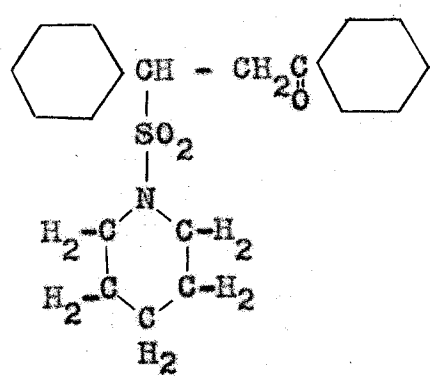


(IV)



(V)



COPY

Aug. 13, 1946

Mr. Louis F. Cason
Department of Chemistry
Iowa State College
Ames, Iowa

Dear Mr. Cason:

Dr. Crane gave me your letter of July 29 and asked me to suggest names for the compounds listed.

H_2NSO_2H has been called amidosulfurous acid, amidosulfinic acid, and aminosulfinic acid. These names correspond to amidosulfuric, amidosulfonic and aminosulfonic for H_2NSO_3H, which, however, has the common name sulfamic acid. In the absence of an accepted common name, we feel that the name given to H_2NSO_2H should be formed in accordance with the general method of naming inorganic acids (see § 32 of Introduction to 1945 Chemical Abstracts Subject Index), and that it should be called amidosulfurous acid.

We would name compounds I, II, and III, which are derivatives of amidosulfurous acid, as follows, giving the uninverted name and the inverted name as it would appear in the C. A. index.

I	$C_6H_5NHSO_2H$	N-Phenylamidosulfurous acid Amidosulfurous acid, N-phenyl-
II	$C_4H_9NHSO_2H$	N-Butylamidosulfurous acid Amidosulfurous acid, N-butyl-
III	$(C_2H_5)_2NSO_2H$	N,N-Diethylamidosulfurous acid Amidosulfurous acid, N,N-diethyl-

In the above names the use of N- to designate the position of the substituent is probably unnecessary.

Compounds IV, V, and VI, which are derivatives of the amide of ethanesulfonic acid, would be named as follows:

IV	$C_6H_5CH(SO_2NHC_6H_5)CH_2COC_6H_5$	2-Benzoyl-1-phenylethanesulfonanilide Ethanesulfonanilide, 2-benzoyl-1-phenyl-

COPY

2---Cason

V $C_6H_5CH(SO_2NHC_4H_9\text{-}n)CH_2COC_6H_5$

2-Benzoyl-N-butyl-1-phenylethanesulfonamide

Ethanesulfonamide, 2-benzoyl-N-butyl-1-phenyl-

VI $C_6H_5CH(SO_2N(C_2H_5)_2)CH_2COC_6H_5$

2-Benzoyl-N-N-diethyl-1-phenylethanesulfonamide

Ethanesulfonamide, 2-benzoyl-N,N-diethyl-1-phenyl-

Sincerely yours,

(Signed) Leonard T. Capell

LTC:mh