centrated and desiccated yielding 0.0645 g. of crude phenyl-(acetic-1-C^{14}) acid (IX) melting 69–73°; yield 100%. Several preparations gave similar results. When the reaction temperature was allowed to rise above 200°, the yield was considerably decreased. Recrystallization from water yielded white crystals melting 73–74.5°.

Anal. 0.0249 microcurie carbon-14 per 4.32-mg. sample.

Benzoic Acid and Carbon-14 Dioxide.—A 0.030-g. sample of phenyl-(acetic-1-C^{14}) acid was treated with 0.050 g. of chromic anhydride and 0.01 g. of sulfuric acid at 100° for one-half hour. The evolved carbon dioxide was passed into half-saturated barium hydroxide solution. The carefully washed and dried barium carbonate weighed 0.031 g. or 71% of the theoretical amount.

Anal. 0.1185 microcurie carbon-14 per 30-mg. sample.

The oxidation solution was diluted with water and extracted with ether; the ether was evaporated. The residue which contained traces of phenyl-(acetic-1-C^{14}) acid and benzaldehyde was oxidized at 100° in a 1-ml. aqueous solution containing 0.01 g. of potassium hydroxide and 0.020 g. of potassium permanganate. After being heated under reflux for 1 hour, the solution was acidified and extracted with ether. The recovered benzoic acid weighed 0.022 g. or 82% of theory; m.p. 121°.

Anal. A 3.425-mg. sample contained activity indistinguishable from background.

OAK RIDGE, TENNESSEE RECEIVED OCTOBER 14, 1950

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, SWARTHMORE COLLEGE]

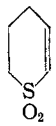
Thiapyran Derivatives. II. The Preparation, Properties, and Reactions of Δ^3-Dihydrothiapyran 1,1-Dioxide[1]

BY EDWARD A. FEHNEL AND PATRICIA A. LACKEY

An unsaturated, six-membered heterocyclic sulfone, Δ^3-dihydrothiapyran 1,1-dioxide, has been prepared by the abnormal Clemmensen reduction of tetrahydro-1,4-thiapyrone 1,1-dioxide. The addition reactions of the unsaturated sulfone with hydrogen, bromine, hydrogen iodide, hydrogen bromide and methanol are described, and the hydrogen halide addition products are characterized as 4-halotetrahydrothiapyran dioxides. Dehydrohalogenation of 3,4-dibromotetrahydrothiapyran 1,1-dioxide yields an unsaturated bromosulfone from which Δ^3-dihydrothiapyran 1,1-dioxide may be obtained by hydrogenolysis. The base-catalyzed addition of methanol to the unsaturated sulfone to give 3-methoxytetrahydrothiapyran 1,1-dioxide is considered to proceed *via* the tautomeric rearrangement of the Δ^3-dihydrosulfone to the Δ^2-isomer, but all attempts to prepare the latter compound by isomerization of the Δ^3-form have been unsuccessful. 2,2,6,6-Tetramethyl-Δ^3-dihydrothiapyran 1,1-dioxide and several of its derivatives have been prepared and their properties compared with those of the unmethylated analogs in the parent series.

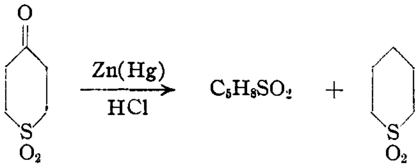
The ability of the sulfone function to promote prototropic rearrangement in an adjacent allylic system has been demonstrated in studies of several unsaturated heterocyclic and acyclic sulfones.[2,3] Thus the facile interconversion of the Δ^α- and Δ^β-forms of the so-called butadiene sulfones in the presence of dilute aqueous alkali has been known for some time, and recently it has been found possible to bring about the isomerization of allyl benzyl sulfone to propenyl benzyl sulfone by refluxing with anhydrous tertiary amines.[3b] Since earlier studies with heterocyclic sulfones have been limited to the more or less readily available five-membered rings, little is known about the effects that structural variations might have upon the tautomeric mobility and position of equilibrium in systems of this type, and it would be of interest to have information on the properties of the unsaturated six-membered heterocyclic sulfones. The preparation, properties and reactions of one of the simplest representatives of this previously unexplored class of compounds is described in the present paper.

I



II

An unsaturated sulfone having the empirical formula $C_5H_8SO_2$ and presumably corresponding, therefore, either to structure I or II or to a tautomeric mixture of these was unexpectedly obtained as the major product (*ca.* 85%) of an attempted Clemmensen reduction of tetrahydro-1,4-thiapyrone 1,1-dioxide (III), along with a small amount (*ca.* 15%) of the expected tetrahydrothiapyran 1,1-dioxide (IV).



III IV

Variations in the conditions under which the reduction was carried out, such as changes in time, acid concentration, physical form of the zinc, etc., failed to alter the results significantly, and, in view of the rather similar results obtained in the reduction of 2,2,6,6-tetramethyltetrahydro-1,4-thiapyrone 1,1-dioxide (see below), it appears that this mode of reduction is the usual course of the reaction in this series of ketosulfones. Attempts to effect a separation of the mixture of saturated and unsaturated sulfones obtained in the reduction of III by repeated recrystallization from ligroin or cyclohexane proved to be impractical. The purification of the product was therefore carried out by treating the crude reduction product with an excess of bromine in glacial acetic acid, collecting and recrystallizing the precipitated dibromide and regenerating the unsaturated sulfone by treatment of the dibromide with zinc dust in ethanol. The unchanged saturated sul-

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(1) For the preceding paper in this series, see E. A. Fehnel and M. Carmack, THIS JOURNAL, **70**, 1813 (1948).

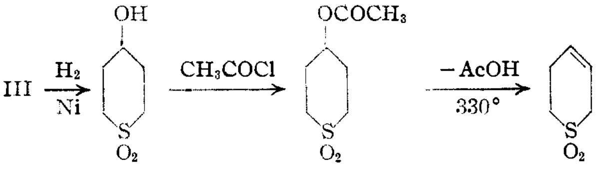
(2) (a) H. J. Backer and J. Strating, *Rec. trav. chim.*, **54**, 170, 618 (1935); (b) J. Böeseken and E. de Roy van Zuydewijn, *Proc. Acad. Sci.* (Amsterdam), **40**, 23 (1937) [*C. A.*, **31**, 4953 (1937)]; (c) E. de Roy van Zuydewijn, *Rec. trav. chim.*, **56**, 1047 (1937).

(3) (a) E. Rothstein, *J. Chem. Soc.*, **309**, 317 (1937); (b) H. J. Backer and G. J. de Jong, *Rec. trav. chim.*, **67**, 884 (1948); (c) C. C. J. Culvenor, W. Davies and W. E. Savige, *J. Chem. Soc.*, 2198 (1949).

fone IV was recovered from the acetic acid filtrate after removal of the dibromide and was identified by comparison with an authentic sample of tetrahydrothiapyran 1,1-dioxide prepared by oxidation of the corresponding sulfide.

That no rearrangement of the carbon skeleton had occurred in the course of the reduction of the ketone III to the unsaturated sulfone was proved by hydrogenation of the latter compound to tetrahydrothiapyran 1,1-dioxide (IV) in the presence of Adams platinum oxide catalyst. Attempts to establish the position of the double bond in the six-membered ring by permanganate oxidation were uniformly unsuccessful, the only isolable organic substance from these reactions (with the crude Clemmensen reduction product) being the unattacked saturated sulfone IV which was originally present in the mixture. The method of preparation of the dihydrothiapyran dioxide from a ketone under the conditions of a Clemmensen reduction does indeed suggest that the β-unsaturated structure I is the correct one, since conversion of a carbonyl carbon to an ethylenic carbon is known to occur under these conditions.[4] The reported formation of ethyl 3-pentenoate, along with the expected ethyl valerate, in the Clemmensen reduction of ethyl levulinate[4b] is particularly interesting in this connection, since, if the carboxyl and sulfonyl groups may be considered to exhibit rather similar electronic effects,[5] the γ-ketoesters would be expected to resemble the γ-ketosulfones in their chemical behavior.[6]

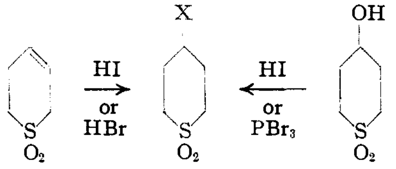
The observation that the same unsaturated sulfone is formed when 4-acetoxytetrahydrothiapyran 1,1-dioxide (V) is heated for some time at its boiling point may also be offered in support of structure I. Since the acetate is obtained from the corresponding hydroxysulfone VI, which may in turn be prepared from the ketosulfone III by catalytic reduction over Raney nickel, this series of reactions offers an alternative, though less convenient, method of synthesis for the dihydrosulfone. The failure of the dihydrosulfone to undergo the Diels–Alder reaction with butadiene under conditions which are known to give successful results with Δ^2-unsaturated sulfones[7] likewise favors the Δ^3 structure.



VI V I

Although the ultraviolet absorption spectra of the simpler sulfones are not very satisfactory for drawing conclusions regarding structure because the absorption is weak and no maxima are found in the region accessible with the usual instruments, nevertheless, the observable portions of the first absorption bands of several typical Δ^2- and Δ^3-unsaturated sulfones (Fig. 1) appear to be sufficiently characteristic of the respective structures for purposes of identification. As would be anticipated on the basis of a certain amount of conjugation between the ethylenic double bond and the sulfone function in the Δ^2-compounds,[5] the absorption curves for these compounds are shifted toward longer wave lengths as compared with the Δ^3-compounds, in which the observed absorption is that of the isolated ethylenic grouping.[8] The fact that the ultraviolet absorption spectrum of the dihydrothiapyran dioxide under discussion resembles the spectra of the Δ^3-sulfones rather than those of the Δ^2-sulfones is thus in agreement with the chemical evidence supporting the Δ^3-formulation.

The addition reactions of Δ^3-dihydrothiapyran 1,1-dioxide with the electrophilic reagents, hydrogen iodide and hydrogen bromide, are interesting in that they apparently lead to the 4-halogen substituted tetrahydro derivatives, rather than to 3-halogen compounds such as are obtained as the major products when simple allyl sulfones are treated with these reagents.[9] Several lines of evidence support the assignment of the halogen atom to the 4-position in these halosulfones. (1) The same iodotetrahydrothiapyran dioxide is obtained when either Δ^3-dihydrothiapyran 1,1-dioxide (I) or 4-hydroxytetrahydrothiapyran 1,1-dioxide (VI) is refluxed with 47% hydriodic acid; similarly, the same bromotetrahydrothiapyran dioxide is obtained when I is refluxed with 48% hydrobromic acid and when VI is treated with phosphorus tribromide.[10] (2) The bromosulfone prepared by the action of hydrobromic acid on I or of phosphorus tribromide on VI is identical with the bromosulfone prepared by the oxidation of 4-bromotetrahydrothiapyran. (3) The reactivity of the halogen atoms in these halosulfones toward alkali is of a relatively low order, as is shown by their failure to react with cold dilute aqueous sodium hydroxide under conditions which readily lead to the loss of



I VII (X = I) VI
VIII (X = Br)

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[4] (a) E. Clemmenson, *Ber.*, **46**, 1837 (1913); (b) W. Steinkopf and A. Wolfram, *Ann.*, **430**, 113 (1923); (c) E. Müller, *Z. Elektrochem.*, **33**, 253 (1927).

[5] E. A. Fehnel and M. Carmack, THIS JOURNAL, **71**, 231 (1949); *ibid.*, **72**, 1292 (1950).

[6] However, it is reported [G. Komppa, *Ann. Acad. Sci. Fennicae*, **A51**, No. 3 (1938); *C. A.*, **34**, 2335 (1940)] that neither γ-ketopimelic acid nor its dimethyl ester is reduced in the Clemmensen reaction.

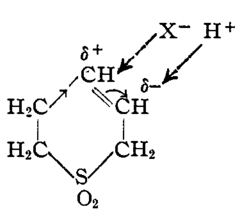
[7] K. Alder, H. F. Rickert and E. Windemuth, *Ber.*, **71B**, 2451 (1938).

[8] The isolated sulfone function shows no absorption above 200 mμ; see ref. 5.

[9] Compare, for example, the addition reactions of allyl benzyl sulfone described by E. Rothstein, *J. Chem. Soc.*, 684 (1934); H. J. Backer and G. J. de Jong, ref. 3b.

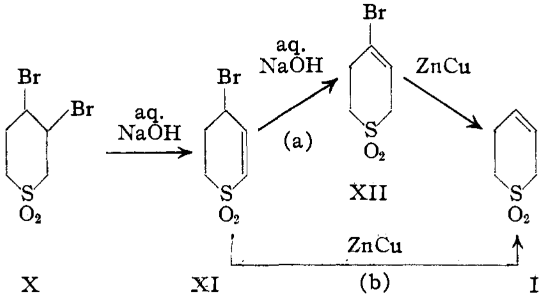
[10] It might be suggested that in the action of these reagents on the hydroxysulfone VI this secondary carbinol first undergoes dehydration to the dihydro compound I, which then adds the hydrogen halide (formed, in the case of PBr_3, during the reaction), so that the same products would be obtained from I and VI regardless of the mode of addition to the double bond. This mechanism seems unlikely, however, in view of the large number of similar reactions in the literature in which the hydroxyl group is known to be replaced directly by the halogen atom. For some especially pertinent examples, see A. Skita, *Ann.*, **431**, 1 (1923); A. Lipp, *Ber.*, **22**, 1196 (1889); *Ann.*, **289**, 173 (1896); N. Zelinsky and A. Moser, *Ber.*, **35**, 2684 (1902); L. Henry, *Bull. soc. chim.*, [2] **46**, 65 (1886).

one molecule of hydrogen bromide from 3,4-dibromotetrahydrothiapyran 1,1-dioxide. It is significant to note that 2,2,6,6-tetramethyl-3,4-dibromotetrahydrothiapyran 1,1-dioxide, which lacks the α-hydrogen necessary to labilize the β-bromine, also fails to react under these conditions. (4) An analogous situation with regard to mode of addition is encountered among the higher homologs of vinylacetic acid, *e. g.*, Δ³-hexenoic acid,[11] Δ³-heptenoic acid[12] and 2,2-dimethyl-Δ³-pentenoic acid,[13] all of which yield the 4-halogen adducts on treatment with the hydrogen halides. Presumably the electron-releasing effects of the alkyl groups attached to the 4-carbon atoms in this series of unsaturated acids predominate over any electron-releasing tendencies possessed by the negatively-substituted carbon atoms attached at the 3-positions. A similar interpretation would account for 4-halogen addition in Δ³-dihydrothiapyran 1,1-dioxide, in which the $-CH_2CH_2-$ group interposed between the vinyl and sulfonyl functions would be expected to exhibit a greater electron-releasing effect than a single methylene group between these same functions (IX).



IX

Dehydrohalogenation of the 4-halosulfones may be accomplished by refluxing with anhydrous pyridine, the only product being Δ³-dihydrothiapyran 1,1-dioxide. In the much more facile removal of one molecule of hydrogen bromide from 3,4-dibromotetrahydrothiapyran 1,1-dioxide (X) with cold dilute aqueous sodium hydroxide, a bromodihydrothiapyran dioxide is obtained which yields Δ³-dihydrothiapyran 1,1-dioxide on reduction with the zinc–copper couple in ethanol. Since it is very probable that the initial product of dehydrobromination of X is 4-bromo-Δ²-dihydrothiapyran 1,1-dioxide (XI), the formation of the Δ³-dihydro compound on reduction indicates that a prototropic rearrangement must have occurred either in the course of the dehydrohalogenation (route a) or in the subsequent reduction (route b).



Culvenor, Davies and Savige[3c] have recently reported examples of both types of rearrangement in

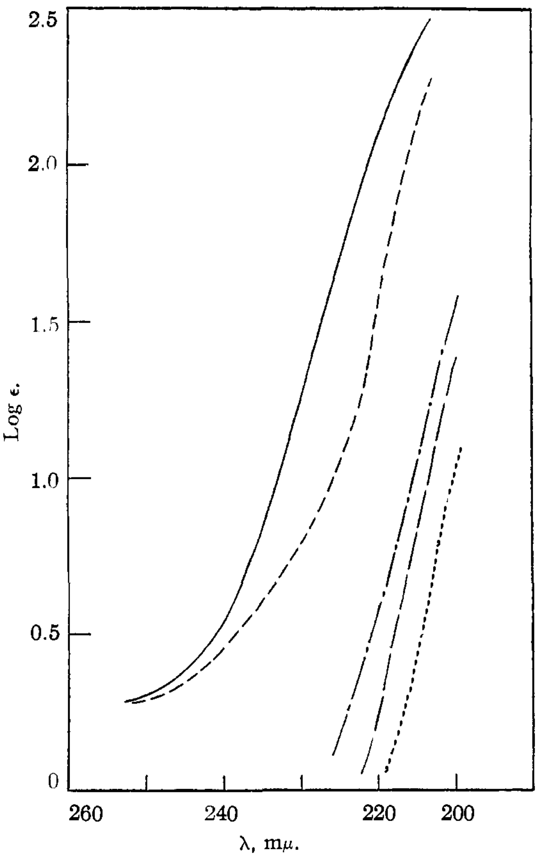


Fig. 1.—Absorption spectra: vinyl ethyl sulfone, —; α-butadiene sulfone, - - - - -; β-butadiene sulfone, —·—·—; Δ³-dihydrothiapyran 1,1-dioxide (I), — — —; 2,2,6,6-tetramethyl-Δ³-dihydrothiapyran 1,1-dioxide (XIV), · · · · · ·.

connection with an investigation of certain arylsulfonylpropane derivatives. Both routes are thus rendered feasible, but the available data on the properties of the unsaturated bromosulfone do not permit a decision between the alternative structures XI and XII. The failure of this unsaturated sulfone to add butadiene under conditions applicable to β-unsaturated sulfones suggests that XII is the correct structure and that route a represents the sequence of reactions leading to the Δ³-dihydrosulfone (I).

When Δ³-dihydrothiapyran 1,1-dioxide is refluxed with methanolic sodium methoxide, a methoxytetrahydrothiapyran dioxide is obtained which is not identical with the methyl ether of 4-hydroxytetrahydrothiapyran 1,1-dioxide (VI) and which is therefore doubtless 3-methoxytetrahydrothiapyran 1,1-dioxide (XIII). This result is in accord with the observations of Rothstein,[9] who prepared a β-methoxysulfone by the addition of methanol to allyl benzyl sulfone under similar conditions. Since the mechanism of this base-catalyzed nucleophilic addition is considered to involve the preliminary rearrangement of the Δ³- to the Δ²-unsaturated tautomer,[3b] the reaction provides further evidence for the tautomeric mobility of the three-carbon system in these six-membered rings. The observation that 2,2,6,6-tetramethyl-Δ³-dihydrothiapyran 1,1-dioxide (XIV), in which there is no possibility of rearrangement to a Δ²-dihydro structure, fails to react

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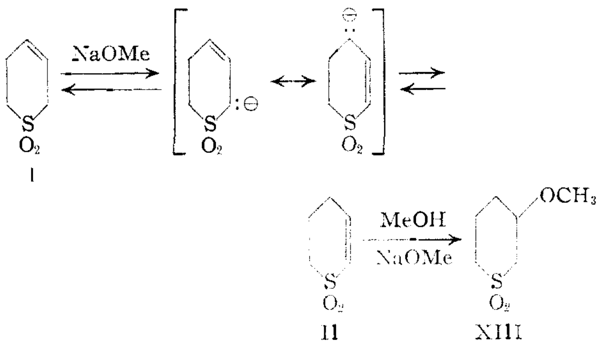
[11] R. Fittig, *Ann.*, **200**, 21 (1880); **208**, 111 (1881).

[12] R. Fittig and A. Schmidt, *ibid.*, **255**, 68 (1889).

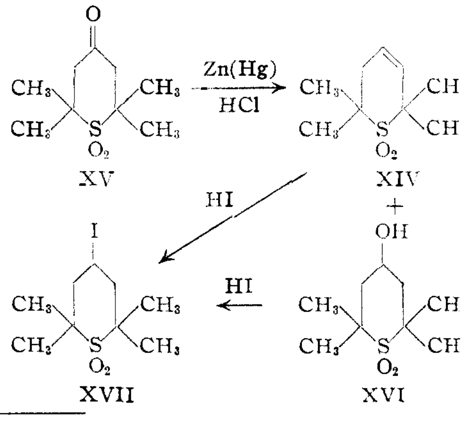
[13] E. E. Blaise and A. Courtot, *Bull. soc. chim.*, [3] **35**, 580 (1906).



with methanolic sodium methoxide may be offered in support of this mechanism.

In spite of the above evidence for tautomerism in this series of unsaturated heterocyclic sulfones, all attempts to prepare Δ^2-dihydrothiapyran 1,1-dioxide (II) by isomerization of the Δ^3-dihydro compound I have thus far been unsuccessful.[14] Among other methods, we have employed those reported to effect the isomerization of β-butadiene sulfone to α-butadiene sulfone (ultraviolet irradiation in aqueous alkali)[2] and of allyl benzyl sulfone to propenyl benzyl sulfone (refluxing with tertiary aliphatic amines),[3b] but in every attempt the only isolable material proved to be unchanged starting material, usually recoverable in almost quantitative amounts. The identity of the recovered material has been checked by means of melting points, mixed melting points, ultraviolet absorption spectra and conversion to the dibromide; in no case has there been any evidence for the presence of the tautomer. This raises the interesting question of whether the Δ^2-dihydro isomer is capable of independent existence or whether the position of tautomeric equilibrium is so far displaced toward the Δ^3-isomer that it alone can be isolated. This aspect of the problem is being investigated further.

The preparation of 2,2,6,6-tetramethyl-Δ^3-dihydrothiapyran 1,1-dioxide (XIV) and its derivatives was undertaken in order to provide comparison compounds which lacked α-hydrogen atoms and which would therefore afford data useful in the elucidation of structures and reactions in the parent series. Some of the reactions of these tetramethyl derivatives have been described above in connection with the discussion of their unmethylated analogs. A few further points of interest may be mentioned here. In the Clemmensen reduction of 2,2,-6,6-tetramethyltetrahydro-1,4-thiapyrone 1,1-dioxide (XV), although the major product is the dihydrosulfone XIV, an appreciable amount of the carbinol XVI is also obtained, instead of a completely saturated tetrahydrosulfone such as is found in the analogous reaction in the parent series. On refluxing with 47% hydriodic acid, this carbinol affords the same iodo compound as is obtained by the addition of hydrogen iodide to the dihydrosulfone, and structure XVII is therefore assigned to the product. The ultraviolet absorption spectrum of XIV (Fig. 1) is similar to that of the unmethylated dihydrosulfone I.



Acknowledgment.—The authors are happy to acknowledge the support of a portion of this work by a Frederick Gardner Cottrell grant from the Research Corporation.

Experimental[15]

Abnormal Clemmensen Reduction of Tetrahydro-1,4-thiapyrone 1,1-Dioxide (III).—A mixture of 28.0 g. of III,[16] 60 g. of amalgamated zinc dust and 200 ml. of 6 *N* hydrochloric acid was refluxed for seven hours with the addition of 8 ml. of concd. hydrochloric acid down the condenser every hour. The mixture was then cooled and filtered, and the filtrate was extracted repeatedly with small portions of chloroform (total volume, *ca.* 500 ml.). The combined extracts were dried over anhydrous magnesium sulfate and evaporated to dryness on the steam-bath. The residual oil crystallized on cooling, yielding 22.1 g. of a colorless solid, m.p. 68–72°. Two recrystallizations from ligroin followed by one from cyclohexane raised the m.p. to 75–76°.

Anal. Calcd. for $C_5H_8O_2S$: C, 45.42; H, 6.10; calcd. for $C_5H_{10}O_2S$: C, 44.75; H, 7.51. Found: C, 45.62, 45.58; H, 6.58, 6.41.

In an experiment in which 2.96 g. of III was refluxed for seven hours with 7 g. of amalgamated *mossy* zinc and 10 ml. of *concd.* hydrochloric acid, 1 ml. of concd. acid being added every hour, there was obtained from the chloroform extract 2.05 g. of colorless crystalline material melting at 73–75°.

Permanganate oxidation of the crude Clemmensen reduction product was carried out under various conditions of temperature and *p*H, but in every case the only isolable substance was tetrahydrothiapyran 1,1-dioxide. In a typical experiment involving 1.00 g. of the reduction product, extraction of the reaction mixture with chloroform afforded 0.15 g. of colorless crystals, m.p. 94–97°, which showed no depression when mixed with authentic tetrahydrothiapyran 1,1-dioxide (m.p. 98–99°) prepared by oxidation of the sulfide with hydrogen peroxide in acetic acid.[17] Attempts to isolate any other organic material from the aqueous reaction mixture were unsuccessful.

When 2.00 g. of the Clemmensen reduction product was heated in an autoclave at 175–185° for 10 hours with 25 ml. of purified dioxane containing *ca.* 3.8 g. of butadiene, there was recovered from the reaction mixture 1.94 g. (97%) of unchanged starting material, m.p. 74–76°, after recrystallization from cyclohexane.

3,4-Dibromotetrahydrothiapyran 1,1-Dioxide (X).—Treatment of a cold solution of 12.8 g. (0.097 mole, calculated as the unsaturated sulfone) of the crude reduction product in 15 ml. of glacial acetic acid with 17.7 g. (0.11 mole) of bromine provided 23.2 g. (82%) of colorless crystals, m.p. 168–173°. Recrystallization from glacial acetic acid raised the melting point to 178–179°.

Anal. Calcd. for $C_5H_8Br_2O_2S$: C, 20.57; H, 2.76. Found: C, 20.64, 20.73; H, 2.79, 2.78.

When the acetic acid filtrate from the bromination reaction was evaporated to dryness, a pale yellow waxy solid

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[14] *Cf.* E. Rothstein, ref. 9.

[15] Microanalyses were performed by the Clark Microanalytical Laboratory, Urbana, Illinois, and by Mrs. Sarah M. Woods, University of Pennsylvania. All melting points are corrected.

[16] E. A. Fehnel and M. Carmack, THIS JOURNAL, **70**, 1813 (1948).

[17] *Cf.* E. Grischkewitsch-Trochimowski, *J. Russ. Phys.-Chem. Soc.*, **48**, 928 (1916); *Chem. Zentr.* **94**, I, 1503 (1923).

remained, from which 1.9 g. of a colorless crystalline solid, m.p. 85–90°, was extracted with boiling cyclohexane. Recrystallization from cyclohexane raised the melting point to 95–97°; no depression was observed on admixture with tetrahydrothiapyran 1,1-dioxide.

The same dibromide (X) was obtained when 2.00 g. (0.013 mole) of 4-hydroxytetrahydrothiapyran 1,1-dioxide (VI) was ground together with 6.9 g. (0.016 mole) of freshly prepared phosphorus pentabromide and the pasty mixture allowed to stand for 15 minutes. Dilution with 30 ml. of ice-water caused the precipitation of 1.4 g. of a colorless solid melting at 167–172°. Recrystallization from water afforded colorless crystals which melted at 176–178° and showed no depression when mixed with the dibromide described above.

Δ^3-Dihydrothiapyran 1,1-Dioxide (I).—Six and one-half grams (0.10 g.-atom) of zinc dust was added in small portions to a hot suspension of 14.6 g. (0.050 mole) of the dibromide X in 275 ml. of 90% ethanol, and after the initial exothermic reaction had subsided the mixture was refluxed for an additional 15 minutes. The excess zinc was then filtered off and most of the solvent was removed by distillation. The residue was taken up in 250 ml. of water and extracted repeatedly with small portions of chloroform (total volume, *ca.* 250 ml.). The combined extracts were dried over anhydrous magnesium sulfate and evaporated on the steam-bath. The oily residue crystallized on cooling to give 6.4 g. (97%) of pale yellow crystals, m.p. 67–70°. This product is soluble in water, methanol, ethanol, acetic acid, chloroform and acetone, moderately soluble in benzene and insoluble in ether and cold saturated hydrocarbons. Purification of the crude product was accomplished by recrystallization from rather large volumes of cyclohexane. The pure compound melted at 71–72° and showed a slight *elevation* of the melting point when mixed with a small amount of tetrahydrothiapyran 1,1-dioxide.

Anal. Calcd. for $C_5H_8O_2S$: C, 45.42; H, 6.10. Found: C, 45.51; H, 6.20.

Reduction of 1.5 g. of I with hydrogen at three atmospheres pressure over 0.1 g. of Adams platinum oxide catalyst in ethanol for 90 minutes gave 1.4 g. (92%) of colorless crystals which melted at 97.5–98.5° after recrystallization from ligroin and which failed to depress the melting point of authentic tetrahydrothiapyran 1,1-dioxide.

When 2.00 g. of I was dissolved in 25 ml. of 0.5 *N* aqueous potassium hydroxide and exposed in an open dish to intense ultraviolet radiation ("Mineralite," model V41, at 3 inches) for two hours, there was recovered from the solution by chloroform extraction 1.92 g. (96%) of crystalline material melting at 69–71° and exhibiting the same absorption spectrum as the original compound. Similar results were obtained after 8 hours of irradiation in 0.5 *N* aqueous sodium hydroxide, after refluxing a suspension in triethylamine for 19 hours, and after refluxing a homogeneous solution in a mixture of xylene and triethylamine for 29 hours.

4-Hydroxytetrahydrothiapyran 1,1-Dioxide (VI).—A solution of 12.1 g. (0.080 mole) of tetrahydro-1,4-thiapyrone 1,1-dioxide (III) in 200 ml. of water was hydrogenated in the presence of *ca.* 1 g. of Raney nickel catalyst at 100 atmospheres and 110–120° for 90 minutes. After removal of the catalyst, the mixture was evaporated to dryness on the steam-bath and the waxy orange-colored residue was extracted repeatedly with boiling benzene until no further solid precipitated from the extracts on cooling. The colorless crystalline product thus obtained melted sharply at 137.5–138°; yield 11.2 g. (91%). Recrystallization from benzene raised the melting point to 138–138.5°.

Anal. Calcd. for $C_5H_{10}O_3S$: C, 39.98; H, 6.71. Found: C, 39.96; H, 6.61.

4-Acetoxytetrahydrothiapyran 1,1-dioxide (V) was obtained as a colorless solid, m.p. 123–124°, on treatment of the carbinol VI with excess acetyl chloride under reflux; yield 92%. Recrystallization of the product from a benzene–ligroin mixture afforded colorless crystals melting at 124–125°.

Anal. Calcd. for $C_7H_{12}O_4S$: C, 43.74; H, 6.30. Found: C, 44.05; H, 6.14.

Pyrolysis of V was accomplished by heating 1.26 g. of the compound at its boiling point (*ca.* 330°) for one hour in an open test-tube. At the end of this time no further acetic acid appeared to be escaping and the dark-colored melt was allowed to cool. Extraction with boiling cyclohexane yielded 0.57 g. (68%) of tan crystalline material which melted over a wide range (55–68°) and which was characterized by conversion to the dibromide by treatment with bromine in acetic acid. The crude dibromide thus obtained melted at 166–173° and showed no depression in melting point when mixed with a small amount of the 3,4-dibromotetrahydrothiapyran 1,1-dioxide (X) previously described.

4-Bromo-$\Delta^{3(\text{or }2)}$-dihydrothiapyran 1,1-Dioxide (XII or XI).—A suspension of 14.6 g. (0.050 mole) of 3,4-dibromotetrahydrothiapyran 1,1-dioxide (X) in 130 ml. of 3% sodium hydroxide solution (0.10 mole) was allowed to stand at room temperature with occasional agitation during a period of 24 hours. The crystalline product was collected, washed thoroughly with water and dried; yield 9.0 g. (86%) of almost colorless needles, m.p. 130–138°. After several recrystallizations from water (Norit), the pure compound was obtained as colorless leaflets melting at 144–145°.

Anal. Calcd. for $C_5H_7BrO_2S$: C, 28.45; H, 3.34; Br, 37.86. Found: C, 28.45; H, 3.16; Br, 37.73.

When 3.0 g. of the unsaturated bromosulfone was heated in an autoclave at 170–180° for 10 hours with 25 ml. of purified dioxane containing *ca.* 3.8 g. of butadiene, there was recovered from the reaction mixture 2.4 g. (80%) of unchanged starting material, m.p. 144–145°, after recrystallization from water.

Reduction of XII (or XI) with the Zinc–Copper Couple.—Ten grams of zinc dust was shaken with 250 ml. of 4% copper sulfate solution, washed thoroughly with water, and with ethanol and suspended in 50 ml. of ethanol. The unsaturated bromosulfone (3.37 g.) was added and the mixture was refluxed for two hours. After removal of the unreacted zinc, the clear liquid was evaporated to dryness on the steam-bath and the residual oil was taken up in 50 ml. of water. Extraction of the aqueous solution with numerous small portions of chloroform, followed by drying and removal of the solvent on the steam-bath, afforded 2.11 g. (100%) of a colorless crystalline solid, m.p. 66–70°, which showed no depression when mixed with Δ^3-dihydrothiapyran 1,1-dioxide (I). The product was further characterized by conversion to the dibromide as previously described; m.p. 174–177°, no depression when mixed with 3,4-dibromotetrahydrothiapyran 1,1-dioxide (X).

4-Iodotetrahydrothiapyran 1,1-Dioxide (VII).—A solution of 7.8 g. of I in 35 ml. of 47% hydriodic acid was refluxed for one hour and was then evaporated to dryness on the steam-bath. The solid residue was triturated with a little water, collected on a filter, washed with water, and dried; yield 12.3 g. (80%) of almost colorless crystals, m.p. 121–124°. This product was treated with charcoal and recrystallized several times from benzene and finally from water to give colorless needles melting at 125–126°.

Anal. Calcd. for $C_5H_9IO_2S$: C, 23.09; H, 3.49; I, 48.80. Found: C, 23.23; H, 3.55; I, 48.63.

The same compound was obtained when 2.00 g. of the carbinol VI was refluxed with 10 ml. of 47% hydriodic acid for three hours. On dilution of the cold reaction mixture with water, a crystalline precipitate appeared and was collected, washed with water and dried. A further small amount of crude product was extracted from the solution with chloroform and was added to the original precipitate; total yield 0.86 g. (25%), m.p. 124–126°. No melting point depression was observed on admixture with the iodo compound described above.

No test for iodide ion was obtained when a suspension of VII in cold aqueous 5% sodium hydroxide was shaken for several minutes and was then filtered, acidified with dilute nitric acid, and treated with silver nitrate solution. Under these conditions the dibromide X gives a positive silver halide test.

4-Bromotetrahydrothiapyran 1,1-Dioxide (VIII).—A solution of 1.00 g. of I in 5 ml. of 48% hydrobromic acid was refluxed for one hour and was then cooled and diluted with water to precipitate 0.50 g. (32%) of almost colorless crystals, m.p. 122–125°. Recrystallization from a mixture of benzene and petroleum ether (b.p. 35–60°) provided colorless crystals melting at 127–128°.

Anal. Calcd. for $C_5H_9BrO_2S$: C, 28.18; H, 4.26; Br, 37.50. Found: C, 28.35; H, 4.19; Br, 37.36.

The same compound was obtained when a mixture of 1.00 g. of VI and 5.4 g. of freshly distilled phosphorus tribromide was heated under reflux for 20 minutes. The excess phosphorus tribromide was decanted from the mixture and the residue was drowned with water. The crystalline precipitate was collected and combined with an additional small quantity of crude product obtained by extraction of the filtrate with chloroform; total yield 0.46 g. (33%) of colorless crystals, m.p. 119–123°, which showed no depression when mixed with the bromosulfone described above.

4-Bromotetrahydrothiapyran 1,1-dioxide was also prepared by oxidation of the corresponding sulfide derived from 4-hydroxytetrahydrothiapyran as follows: 4-Hydroxytetrahydrothiapyran[18] (9.5 g.) was treated with 9.0 g. of freshly distilled phosphorus tribromide at 80° for several hours, and the reaction mixture was then diluted with water and extracted with ether. The combined ether extracts were washed with aqueous sodium bicarbonate, dried over anhydrous magnesium sulfate, and evaporated on the steam-bath to provide 8.3 g. of crude **4-bromotetrahydrothiapyran** as a yellow oil, which was oxidized directly to the sulfone without further purification. Eight grams (0.044 mole) of the crude product was treated with 10.2 ml. (0.090 mole) of 30% hydrogen peroxide in acetic acid solution in the usual way,[16] and the oil remaining after removal of most of the solvent was diluted with water to precipitate 5.0 g. (30% over-all yield based on 4-hydroxytetrahydrothiapyran) of colorless crystals which melted at 123.5–125° and showed no depression when mixed with the bromosulfone described above.

No test for bromide ion was observed when a suspension of VIII in cold aqueous 5% sodium hydroxide was shaken for several minutes and was then filtered and the filtrate tested in the usual way.

Dehydrohalogenation of VII and VIII was accomplished by refluxing the halosulfone for one hour in dry pyridine, diluting the cooled mixture with an excess of 2 *N* hydrochloric acid and extracting the product with chloroform. Removal of the solvent on the steam-bath left an oil which solidified on cooling; yield 89–95% of crude product melting *ca.* 63–67°. Recrystallization from cyclohexane gave colorless needles which melted at 70.5–71.5° and failed to depress the melting point of the dihydrothiapyran dioxide obtained by debromination of the dibromide X. Treatment of the product with bromine in acetic acid yielded the dibromide, m.p. 173–176°, which showed no depression when mixed with X.

3-Methoxytetrahydrothiapyran 1,1-Dioxide (XIII).—A solution of 2.00 g. of I in 25 ml. of 1 *N* methanolic sodium methoxide was refluxed for one hour and was then cooled, poured into 50 ml. of water, and acidified with a few ml. of concd. hydrochloric acid. The aqueous solution was extracted with chloroform and the combined extracts were dried over anhydrous magnesium sulfate and evaporated to dryness on the steam-bath. The residual oil crystallized on cooling to give 2.25 g. (91%) of a colorless solid, m.p. 58–62°. Recrystallization from benzene–petroleum ether raised the m.p. to 66–66.5°.

Anal. Calcd for $C_6H_{12}O_3S$: C, 43.89; H, 7.37. Found: C, 43.86; H, 7.39.

4-Methoxytetrahydrothiapyran 1,1-dioxide was prepared by methylation of the carbinol VI (1.50 g.) with dimethyl sulfate (1.9 g.) in an aqueous solution kept slightly alkaline by the gradual addition of 30% sodium hydroxide solution.[19] The product was extracted from the solution with chloroform and was obtained as a waxy solid (0.71 g., 43%), m.p. 50–60°, on evaporation of the chloroform. Several recrystallizations from rather large volumes of cyclohexane afforded colorless needles melting at 61–62°. The melting point of this material was greatly depressed on admixture with the 3-isomer (XIII) described above.

Anal. Calcd. for $C_6H_{12}O_3S$: C, 43.89; H, 7.37. Found: C, 43.83; H, 7.24.

Abnormal Clemmensen Reduction of 2,2,6,6-Tetramethyltetrahydro-1,4-thiapyrone 1,1-Dioxide (XV).—Fourteen grams of the hemihydrate of 2,2,6,6-tetramethyltetrahydro-1,4-thiapyrone 1,1-dioxide[20] was refluxed with 20 g. of amalgamated zinc dust and 80 ml. of 6 *N* hydrochloric acid for eight hours with the hourly addition of 3 ml. of concd. hydrochloric acid. The mixture was cooled and filtered, and the residue on the filter was washed with several portions of chloroform to dissolve a small amount of crystalline material which separated when the mixture was cooled. The filtrate was extracted with chloroform, and the combined extracts and washings were dried over anhydrous magnesium sulfate. After removal of the solvent on the steam-bath, there remained a viscous yellow oil, which was taken up in several times its volume of boiling cyclohexane. On cooling, the cyclohexane solution deposited 1.8 g. of colorless microcrystalline powder, m.p. 99–101°, which was soluble in water and alcohol, and insoluble in petroleum ether, benzene and carbon tetrachloride. Recrystallization of this material from a large volume of cyclohexane afforded colorless silky needles of **4-hydroxy-2,2,6,6-tetramethyltetrahydrothiapyran 1,1-dioxide (XVI)** melting at 103–104°.

Anal. Calcd. for $C_9H_{18}O_3S$: C, 52.40; H, 8.79. Found: C, 52.80; H, 8.67.

When 0.72 g. of XVI was refluxed for several minutes with 2 ml. of acetyl chloride, a quantitative yield (0.87 g.) of **4-acetoxy-2,2,6,6-tetramethyltetrahydrothiapyran 1,1-dioxide** was obtained; m.p. 83.5–84° after recrystallization from cyclohexane.

Anal. Calcd. for $C_{11}H_{20}O_4S$: C, 53.21; H, 8.12. Found: C, 53.46; H, 8.21.

The cyclohexane solution remaining after removal of the crude hydroxysulfone XVI was evaporated down to a small volume to precipitate the unsaturated sulfone as colorless crystals, m.p. *ca.* 55–65°; yield 7.8 g. Since recrystallization of this crude product from cyclohexane failed to improve the melting point, purification was effected by bromination and subsequent debromination of the purified dibromide.

3,4-Dibromo-2,2,6,6-tetramethyltetrahydrothiapyran 1,1-Dioxide.—A solution of 3.00 g. (0.016 mole) of the crude unsaturated sulfone (XIV) in 3 ml. of acetic acid was treated with 3.2 g. (0.018 mole) of bromine, and after several minutes the crystalline precipitate was collected, washed with acetic acid and dried; yield 3.47 g. (63%), m.p. 161–163°. Recrystallization from glacial acetic acid afforded colorless crystals melting at 164–165°.

Anal. Calcd. for $C_9H_{16}Br_2O_2S$: C, 31.05; H, 4.63. Found: C, 31.34; H, 4.63.

In another experiment, in which 20 g. of the tetramethylketosulfone (XV) hemihydrate was reduced with amalgamated zinc in the usual way and the semi-crystalline residue from the evaporated chloroform extracts was dissolved in 12 ml. of acetic acid and brominated directly with 14 g. of bromine, there was obtained 13.3 g. (41% over-all yield based on the ketone) of crude dibromide melting at 158–162°.

When a suspension of 0.50 g. of the dibromide in 5 ml. of aqueous 5% sodium hydroxide was allowed to stand with occasional agitation over a period of 20 hours and was then filtered, 0.48 g. (96%) of unchanged starting material was recovered (m.p. 164–165°, no depression when mixed with starting material) and the aqueous filtrate gave no precipitate with silver nitrate after acidification with nitric acid. Similar results were obtained when a suspension of 1.00 g. of the dibromide in 10 ml. of aqueous 5% sodium hydroxide was refluxed for 10 minutes; recovery, 0.98 g. (98%), m.p. 162–164°.

2,2,6,6-Tetramethyl-Δ^3-dihydrothiapyran 1,1-Dioxide (XIV).—A suspension of 10.1 g. (0.029 mole) of the dibromide and 3.8 g. (0.058 g.-atom) of zinc dust in 150 ml. of 95% ethanol was refluxed for 30 minutes, after which the mixture was cooled and filtered. The filtrate was distilled down to a small volume and the residue was diluted with 200 ml. of water to precipitate a portion of the product as an oil which quickly crystallized to a colorless solid, m.p. 68–70°; yield 2.2 g. The major portion (3.1 g.) of the product was extracted from the aqueous filtrate with chloroform and was obtained as colorless crystals melting at 72–74° by evaporation of the dried chloroform extracts on the steam-bath; total crude yield 5.3 g. (98%). Recrystallization from a mixture of petroleum ether and cyclohexane raised the melting point to 76–77°.

Anal. Calcd. for $C_9H_{16}O_2S$: C, 57.40; H, 8.57. Found: C, 57.48; H, 8.52.

When a solution of 1.00 g. of this compound in 15 ml. of 1 *N* methanolic sodium methoxide was refluxed for one hour and was then cooled and poured into dilute hydrochloric

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(18) R. F. Naylor, *J. Chem. Soc.*, 2749 (1949).

(19) Procedure of W. N. Haworth, *ibid.*, **107**, 11 (1915).

(20) F. Arndt, R. Schwarz, C. Martius and E. Aron, *Rev. faculté sci. univ. Istanbul*, **A13**, 57 (1948); *C. A.*, **42**, 4176 (1948).

acid, only unchanged starting material was obtained on chloroform extraction; recovery, 0.91 g. (91%), m.p. 72–75°; no depression when mixed with starting material.

4-Iodo-2,2,6,6-tetramethyltetrahydrothiapyran 1,1-Dioxide (XVII).—A solution of 1.30 g. of XIV in 13 ml. of 47% hydriodic acid was refluxed for four hours and was then evaporated almost to dryness on the steam-bath. The semi-crystalline residue was washed with dilute sodium bisulfite solution and with water, filtered, and dried to afford 1.11 g. (51%) of colorless crystals, m.p. 146–149° with previous sintering. On recrystallization from dilute aqueous acetic acid the pure product was obtained in the form of silky needles melting at 150–151°.

Anal. Calcd. for $C_9H_{17}IO_2S$: C, 34.18; H, 5.42. Found: C, 34.32; H, 5.30.

The same compound was obtained when a solution of 0.20 g. of XVI in 1.0 ml. of 47% hydriodic acid was refluxed for three hours. The crystalline precipitate which appeared on dilution with water was collected, washed with water and dried to yield 0.08 g. (52%) of crude product; m.p. 149–151° after recrystallization from aqueous acetic acid, no depression when mixed with the iodosulfone described above.

Ultraviolet Absorption Spectra.—The spectra were determined with a Beckman quartz spectrophotometer, model DU, using an approximately constant spectral band width of 1–2 mμ down to wave lengths in the neighborhood of 220 mμ. Readings at shorter wave lengths were obtained by using the 0.1 switch position and balancing the galvanometer for 100% transmission with the solvent in position before the phototube. Absolute ethanol was used as the solvent.

SWARTHMORE, PENNA. RECEIVED SEPTEMBER 22, 1950

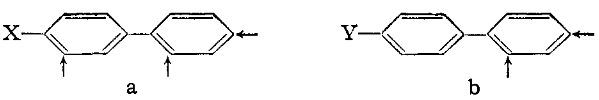
[CONTRIBUTION FROM THE MARION EDWARDS PARK LABORATORY OF BRYN MAWR COLLEGE]

The Dissociation Constants of Substituted 4-Biphenylcarboxylic Acids[1]

BY ERNST BERLINER AND ELIZABETH A. BLOMMERS

The dissociation constants of ten substituted 4-biphenylcarboxylic acids have been determined potentiometrically and compared with the dissociation constants of substituted benzoic acids. The dissociation constants fall on a line when plotted against Hammett's sigma values. The rho value is +0.37 (benzoic acids +1). These results show that the effect of substituents is transmitted through the biphenyl system, but that it is quantitatively less than in benzoic acids.

The problem of the conjugation of the two benzene rings in biphenyl in chemical reactions was last summarized in 1928 by Le Fevre and Turner who concluded that the two rings in biphenyl act independently.[2] This conclusion was drawn almost exclusively from the orientation characteristics of substituted biphenyls in electrophilic substitution. An activating group in one of the rings directs an electrophilic reagent into the ortho–para positions of the second ring (Fig. 1a),[3] but a meta directing substituent also directs the entering group into the ortho and para positions of the other ring (Fig. Ib). 4′-Nitrobiphenyl on nitration produces 37% of 2,4′- and 63% of 4,4′-dinitrobiphenyl.[4] Similar results are obtained if the nitro group is in position 2′ or 3′, or if two nitro groups, or other meta directing groups, are present in one of the rings.[5] The supposition that the two rings act independently in substitution reactions is therefore amply documented experimentally as far as the *direction* of electrophilic substitution is concerned, and the rule that one phenyl group is ortho–para directing irrespective of its substituent appears to be a valid one. This rule has also been invoked in one case of nucleophilic displacement, where a 4′-nitro group was found not to activate a bromine atom in the 4-position.[6] It would appear then that the resonance structures which are responsible for meta substitution in nitrobenzene cannot be extended across the bond joining the two benzene rings and into the second ring.



(X, ortho–para directing) (Y, meta directing)

Fig. 1.

There is, on the other hand, a wealth of data on physical and physico–chemical measurements which can best be explained on the basis of resonance interaction of the two benzene rings in biphenyl. Indeed, on the basis of dipole measurements Le Fevre concluded in 1936 that "the lack of conjugation is not as complete as previously stated."[7] Thermochemical data (and from them the derived resonance energies).[8] X-ray measurements,[9] quantum-mechanical calculations,[10] the inferences drawn from the existence of diradicals[11] and particularly the measurements of absorption spectra[12] indicate

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(1) Taken from a dissertation submitted by Miss E. A. Blommers to the Graduate School of Bryn Mawr College in partial fulfillment of the requirements for the Ph.D. degree.

(2) (a) R. J. W. Le Fevre and E. E. Turner, *J. Chem. Soc.*, 245 (1928); (b) D. Vorländer, *Ber.*, **58**, 1893 (1925). For a discussion of the problem see also: (c) G. N. Burckhardt, C. Horrex and D. I. Jenkins, *J. Chem. Soc.*, 1654 (1936); (d) A. E. Gillem and D. A. Hey, *ibid.*, 1170 (1939).

(3) For instance: (a) F. Bell and J. Kenyon, *ibid.*, 3044 (1926); F. Bell, J. Kenyon and P. H. Robinson, *ibid.*, 1242 (1926); 1127 (1927); J. Kenyon and P. H. Robinson, *ibid.*, 3050 (1926); (b) H. A. Scarborough and W. A. Waters, *ibid.*, 557 (1926); 89, 1133 (1927); (c) W. S. M. Grieve and D. H. Hey, *ibid.*, 2245 (1932).

(4) H. C. Gull and E. E. Turner, *ibid.*, 491 (1929).

(5) Ref. 2b; F. Bell and J. Kenyon, *J. Chem. Soc.*, 2705 (1926); W. Blakely and H. A. Scarborough, *ibid.*, 3000 (1927); W. S. M. Grieve and D. A. Hey, *ibid.*, 970 (1933); A. H. Popkin and G. B. McVea, THIS JOURNAL, **66**, 796 (1944).

(6) N. Campbell, W. Anderson and J. Gilmore, *J. Chem. Soc.*, 446 (1940). See also H. Burton and J. Kenner, *ibid.*, **121**, 489 (1922). A case where such activation does occur has now been observed. Unpublished results with Miss T. Riaboff.

(7) R. J. W. Le Fevre and C. G. Le Fevre, *ibid.*, 1130 (1936).

(8) (a) G. W. Wheland, "The Theory of Resonance and Its Application to Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1944, p. 69 ff.; (b) L. Pauling and J. Sherman, *J. Chem. Phys.*, **1**, 606, 676 (1933); (c) M. Szwarc, *Nature*, **161**, 890 (1948).

(9) J. Dhar, *Indian J. Phys.*, **7**, 43 (1932); *Proc. Natl. Inst. Sci. India*, **15**, 11 (1949) (*C. A.*, **43**, 4655 (1949)); ref. 8a, p. 108.

(10) Ref. 8a, p. 81; ref. 8b; J. E. Lennard-Jones and J. Turkevich, *Proc. Roy. Soc. (London)*, **A158**, 297 (1937); Y. K. Syrkin and M. Dyatkina, *Acta Physicochem. U. R. S. S.*, **21**, 641 (1946); C. A. Coulson and J. Jacobs, *J. Chem. Soc.*, 2805 (1949); E. Hückel, *Z. Elektrochem.*, **43**, 752 (1937).

(11) Ref. 8a, p. 203.

(12) L. W. Pickett, G. F. Walter and H. France, THIS JOURNAL, **58**, 2296 (1936); R. N. Jones, *ibid.*, **63**, 1658 (1941); B. Williamson and W. H. Rodebush, *ibid.*, **63**, 3018 (1941). Also ref. 2d.