TABLE II

| Molar proportion of Diphenoxypropane | Chlorosulfonic acid | % excess of chlorosulfonic acid | % yield of disulfonamide |
|---|---|---|---|
| 1 | 4 | 0 | 26 |
| 1 | 5 | 25 | 85 |
| 1 | 6 | 50 | 83 |
| 1 | 8.5 | 112 | 64 |

The disulfonamide, after recrystallization from an ethanol–methyl ethyl ketone mixture, was in the form of feather-like clusters, m. p. 194.5–195°[7] (see Table I for analysis). The structure of the material prepared in these Laboratories has been unequivocally proved, as will be shown in the following paragraph.

**N,N,N',N'-Tetramethyl-α,γ-diphenoxypropane-4,4'-disulfonamide (IV). A.**—A portion of the same chloroform solution of α,γ-diphenoxypropane-4,4'-disulfonyl chloride, of which part had been used to prepare the amide III, m. p. 194.5–195°, was treated with an excess of aqueous dimethylamine. The resultant solid, after two recrystallizations from ethanol, was in the form of flaky crystals, m. p. 191° (see Table I for analysis).

**B.**—A mixture of 4-hydroxybenzenesulfondimethylamide[1] (620 mg., 3.1 millimoles), potassium hydroxide (175 mg., 3.1 millimoles), and trimethylene bromide (300 mg., 1.5 millimoles) in ethanol (10 cc.) was refluxed one hour. The mixture was poured into water and the white solid formed was recrystallized once from ethanol then once from methanol; m. p. 187–189°. When this substance (m. p. 187–189°) was mixed with a sample of the same material (m. p. 191°) prepared by procedure A, the mixture melted at 188–190°.

**N,N'-Diethyl-α,γ-diphenoxypropane-4,4'-disulfonamide (V).**—α,γ-Diphenoxypropane-4,4'-disulfonyl chloride (42.5 g., 0.10 mole, crude, m. p. 116–117°) dissolved in chloroform (200 cc.) was stirred at room temperature for forty five minutes with aqueous ethylamine (100 g. of 33% solution, 0.73 mole), the chloroform was separated and the solvent was removed to leave the crude product (33.0 g.), m. p. 138–142°. After recrystallization from ethanol it weighed 30.7 g. (69% yield) and melted at 143.5–144° (see Table I for analysis).

**N,N'-Diacetyl-α,γ-diphenoxypropane-4,4'-disulfonamide (VI).**—A mixture of α,γ-diphenoxypropane-4,4'-disulfonamide (31.5 g., 0.0815 mole) and acetic anhydride (250 cc.) was refluxed one hour then poured onto ice and allowed to stand overnight. The solid product (m. p. 163–168°) was recrystallized from aqueous acetic acid to give the pure diacetyl derivative (25.6 g., 67% yield), m. p. 169–170° (see Table I for analysis).

The material crystallizes as a monohydrate and if the sample is dried in a vacuum at not over 80° it analyzes for a monohydrate.

*Anal.* Calcd. for $C_{19}H_{22}N_2O_8S_2 \cdot H_2O$: C, 46.71; H, 4.92; N, 5.73. Found: C, 46.73; H, 4.72; N, 5.92.

The diacetyl derivative VI (25.0 g., 0.0512 mole of monohydrate) was dissolved in 106 cc. of 0.962 *N* sodium hydroxide (the theoretical amount), the solution was evaporated to a thick paste and the residue was triturated with ethanol to give the white solid disodium salt VII (see Table I for analysis).

(7) A compound of m. p. 245–255° prepared in 44% yield from α,γ-diphenoxypropane with chlorosulfonic acid, and giving satisfactory analyses, was reported by Huntress and Carten.[4] In the light of results reported in the present paper, however, their product could not have been α,γ-diphenoxypropane-4,4'-disulfonamide.

## Summary

1. α,γ-Diphenoxypropane has been converted by chlorosulfonic acid followed by ammonia into the 4,4'-disulfonamide.

2. The orientation of the two chlorosulfonyl groups entering the molecule has been proved by showing that an amide prepared from the disulfonyl chloride is identical with that synthesized directly from the corresponding 4-hydroxybenzenesulfonamide and trimethylene bromide.

3. The following four other N-substituted disulfonamides were prepared: dimethyl, ethyl acetyl, and sodio-acetyl.

4. None of these compounds have trypanocidal activity.

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# NOTES

## Mechanism of the Reaction between Hindered Allyl Esters and Grignard Reagents

BY RICHARD T. ARNOLD AND R. WINSTON LIGGETT[1]

In two previous publications from this Laboratory[2,3] it was shown that allylic esters of hindered carboxylic acids react with Grignard reagents to give hydrocarbons and halomagnesium salts according to the following equation.

$$R{-}C(=O){-}OCH_2CH{=}CH_2 + R'MgX \longrightarrow R{-}C(=O){-}OMgX + R'CH_2CH{=}CH_2$$

An experimental result obtained over a year ago has forced us to make some drastic alterations in the mechanism proposed earlier.[2] It has been found that the olefin produced when phenylmagnesium bromide is allowed to react with *n*-crotyl mesitoate is pure *n*-crotylbenzene (I) and apparently contains none of the isomeric isocrotylbenzene.

$$2,4,6\text{-}(CH_3)_3C_6H_2COCH_2CH{=}CHCH_3 + C_6H_5MgBr \longrightarrow 2,4,6\text{-}(CH_3)_3C_6H_2CO_2MgBr + \underset{\text{I}}{C_6H_5CH_2CH{=}CHCH_3}$$

This seems of especial interest since it is well known that either of the pure isomeric crotyl halides gives a mixture of isomeric hydrocarbons when treated with the Grignard reagent.

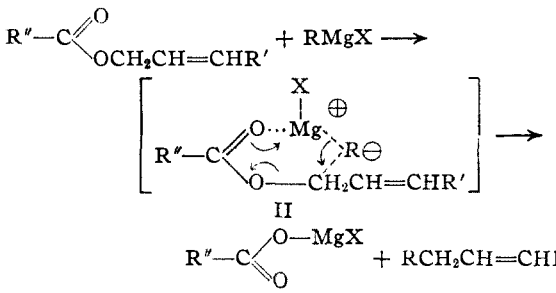
We believe that the new mechanism outlined

(1) Dupont Post Doctorate Fellow 1941–1942.

(2) Arnold, Bank and Liggett, THIS JOURNAL, **63**, 3444 (1941).

(3) Arnold and Liggett, *ibid.*, **64**, 2875 (1942).

below offers an accurate description of the reaction which is under investigation in these Laboratories.



By inspection of II it can be seen that group R (from RMgX) is one element of a quasi six-membered ring and because of this fact it is geometrically in a position such that it must attack only the $\alpha$-carbon atom of the allylic system $\left(\overset{\alpha}{-CH_2}-\overset{\beta}{CH}=\overset{\gamma}{CH}-R'\right)$ when the redistribution of electrons (as indicated by the arrows) is completed. We regard the breaking and formation of bonds in the decomposition of II as occurring simultaneously.

When conditions permit, a systematic investigation to prove or disprove this newly proposed mechanism will be undertaken.

### Experimental

***n*-Crotyl Mesitoate.**—This ester was prepared from pure *n*-crotyl alcohol, mesitoyl chloride and pyridine in cold chloroform solution as described earlier in other examples; yield 58%; b. p. 160–165° (17 mm.).

*Anal.* Calcd. for $C_{14}H_{18}O_2$: C, 77.0; H, 8.3. Found: C, 76.8; H, 8.7.

The ester on ozonolysis gave acetaldehyde as the sole volatile aldehyde.

***n*-Crotylbenzene.**—Cleavage of *n*-crotyl mesitoate with phenylmagnesium bromide as described earlier[2] for other examples gave a hydrocarbon; yield 75.5%; b. p. 81–83° (22 mm.). (Reported 81–82° (18 mm.).[4])

*Anal.* Calcd. for $C_{10}H_{12}$: C, 90.9; H, 9.1. Found: C, 91.0; H, 9.15.

This hydrocarbon gave acetaldehyde as the only identifiable volatile aldehyde. Catalytic hydrogenation gave a non-olefinic hydrocarbon whose vapor pressure curve was identical with pure *n*-butylbenzene and quite different from that of *s*-butylbenzene.

(4) Auwers, Roth and Eisenlohr, *Ann.*, **385**, 108 (1911).

SCHOOL OF CHEMISTRY
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## 1,2,5,6-Diacetone *d*-Mannitol and 1,2,5,6-Diacetone *l*-Mannitol

BY ERICH BAER

The chemical synthesis of pure enantiomorphs of optically active compounds of biological interest often involves the use of difficultly accessible intermediates. The recently described syntheses of the enantiomorphs of a number of unsymmetrically substituted glycerols have been laborious because of the commercial unavailability and the lack of an efficient synthesis of the 1,2,5,6-diacetone derivatives of *d*- and *l*-mannitol. The key position of these two compounds is illustrated by the fact that they have become essential intermediates in the synthesis of $d(+)\alpha$-glycerophosphate,[1] $l(-)\alpha$-glycerophosphate,[2] the normal aliphatic $\alpha$-monoglycerides,[3,4] $\alpha,\beta$-diglycerides,[5] triglycerides,[3] batyl alcohol,[6] chimyl alcohol,[6] and selachyl alcohol.[7] Since the number of applications can be expected to increase, the importance of finding an improved method of preparing these mannitol derivatives is obvious when one considers the labor involved in the older methods.

The first synthesis and description of 1,2,5,6-diacetone *d*-mannitol was given by E. Fischer and Rund in 1916.[8] They obtained the substance on acetonation of *d*-mannitol with acetone and hydrochloric acid, but in a yield of 2% only. By changing the solvent used for extracting the product from the reaction mixture Fischer and Baer in 1934[9] succeeded in raising the yield of this process to approximately 6%. An entirely different procedure was reported by von Vargha,[10] who conducted the acetonation with concd. sulfuric acid in the presence of boric acid. The resulting boric acid ester (4.5) of 1,2-acetone *d*-mannitol was freed from boric acid by alcoholysis and the second acetone introduced by acetonation with copper sulfate. The yield was still very low (14%); moreover, the outcome of the synthesis was unpredictable. With the chemicals then (1934) available in Basel (Switzerland) we succeeded only twice out of many trials in obtaining any yield of diacetone *d*-mannitol. It is possible that some reactant in the successful preparations contained a contaminant which acted as a catalyst for the condensation.

The successful application of zinc chloride as catalyst in other acetonation reactions [Fischer and Taube,[11] Fischer and Baer[12]] prompted a study of its use for the preparation of the diacetone mannitols. These studies resulted in 1939 in the development of a quite satisfactory method (Baer and Fischer[13a,13b]), the yields being raised to 56%, but owing to the labor involved in the removal of large amounts of zinc chloride and solvents the method as described then was still cumbersome and only applicable to small scale preparation. The consequent necessity of repeating the synthesis at fre-

(1) E. Baer and H. O. L. Fischer, *J. Biol. Chem.*, **135**, 321 (1940).
(2) E. Baer and H. O. L. Fischer, *ibid.*, **128**, 491 (1939).
(3) E. Baer and H. O. L. Fischer, *ibid.*, **128**, 475 (1939).
(4) E. Baer and H. O. L. Fischer, communication in preparation for THIS JOURNAL.
(5) J. C. Sowden and H. O. L. Fischer, THIS JOURNAL, **63**, 3244 (1941).
(6) E. Baer and H. O. L. Fischer, *J. Biol. Chem.*, **140**, 397 (1941).
(7) E. Baer, L. Rubin and H. O. L. Fischer, *ibid.*, **155**, 447 (1944).
(8) E. Fischer and C. Rund, *Ber.*, **49**, 91 (1916).
(9) H. O. L. Fischer and E. Baer, *Helv. Chim. Acta*, **17**, 622 (1934).
(10) L. von Vargha, *Ber.*, **66**, 1394 (1933).
(11) H. O. L. Fischer and C. Taube, *ibid.*, **60**, 485 (1927).
(12) H. O. L. Fischer and E. Baer, *ibid.*, **63**, 1749 (1930).
(13) (a) E. Baer and H. O. L. Fischer, *J. Biol. Chem.*, **128**, 463 (1939). (b) E. Baer and H. O. L. Fischer, THIS JOURNAL, **61**, 761 (1939).