II. Since Auwers[3] did not take into consideration the relative position of the triple bond in non-terminal acetylenes, these results explain in part the wide deviations found by him.

The group refraction of the triple bond was calculated from some of the older data, also.[7,8] In many cases the values found did not agree with those reported above, but in a few cases there was good agreement. The values so found are indicated in Fig. 2 by dark circles; they were not used in computing the averages.

TABLE II

NON-TERMINAL, STRAIGHT-CHAIN ACETYLENES

| Compound | $n^{20}D$ | $d^{20}_4$ | Triple bond value | Average | Ref. |
|---|---|---|---|---|---|
| 2-Pentyne | 1.4040 | 0.7115 | 2.521 | | a |
| | 1.4039 | .7104 | 2.553 | | 4 |
| 2-Hexyne | 1.4135 | .7317 | 2.511 | | 5 |
| 2-Octyne | 1.4278 | .7596 | 2.562 | | 4 |
| | 1.4270 | .7592 | 2.522 | | 5 |
| | | | | 2.534 | |
| 3-Hexyne | 1.4110 | .7231 | 2.696 | | 5 |
| 3-Heptyne[b] | 1.415 | .7335 | 2.698 | | 7 |
| 3-Octyne | 1.4250 | .7522 | 2.714 | | 4 |
| | 1.4250 | .7529 | 2.679 | | 5 |
| 3-Nonyne[b] | 1.4295 | .7616 | 2.729 | | c |
| | | | | 2.696 | |
| 4-Octyne | 1.4248 | .7509 | 2.763 | | 4 |
| | 1.4243 | .7512 | 2.708 | | 5 |
| | | | | 2.735 | |
| 5-Decyne | 1.4332 | .7688 | 2.767 | 2.767 | 5 |
| 6-Dodecyne[b] | 1.4425 | .787 | 2.748 | | 8 |
| 9-Octadecyne[b] | 1.4488 | .8022 | 2.786 | | 7 |

[a] Sherrill, THIS JOURNAL, **60**, 2563 (1938). [b] These data were not used in determining the averages. [c] Unpublished work, Campbell and Campbell.

Huggins has shown that the molecular refraction of saturated hydrocarbons and olefins is not strictly an additive function, but is influenced to some extent by the type and amount of branching.[9] In this connection it seemed of interest to ascertain whether the group refraction of the triple bond was affected by branching of the chain. Unfortunately, there are but few branched chain acetylenes known which have been made in large enough amounts for satisfactory purification, so any conclusions are tentative.

Where the branching is not adjacent to the triple bond, there seems to be little effect, judging from the value calculated from 5-methyl-1-hexyne (2.342)[4] and 7-methyl-3-octyne (2.695)[10] which are the only members of this class conforming to the requirements.

Where the branching is adjacent to the triple bond, calculations made from literature data[7,8] indicated a large increase in the group refraction. In the course of other work, however, we have had occasion to prepare 3,3-dimethyl-4-nonyne in large amounts, by the method of Campbell and Eby.[11] Careful fractionation of this material through a very good column showed that it contained a small amount of a hydrocarbon (probably an enyne) with almost the same boiling point, but with a much higher index of refraction. This impurity could only be removed by repeated distillations. From the physical constants of the purified material ($n^{20}D$ 1.43168, $d^{20}_4$ 0.76666) the group refraction is 2.882; this shows a slight increase over the value for the straight-chain 4-acetylenes. The group refraction calculated from the data on *t*-butylacetylene[8] (2.57) likewise shows only a slight increase over the straight-chain acetylenes. The large increase found for other branched-chain acetylenes reported in the literature may well be due to small amounts of impurities, as most of these acetylenes have not been made in large enough amounts for efficient fractionation.

(7) M. P. Doss, "Physical Constants of the Principal Hydrocarbons," The Texas Co., New York, N. Y., 1942.

(8) Egloff, "Physical Constants of Hydrocarbons," A. C. S. Monograph, Vol. I, Reinhold Publishing Corp., New York, N. Y., 1939.

(9) Huggins, THIS JOURNAL, **63**, 116, 916 (1941).

(10) Campbell and O'Connor, *ibid.*, **61**, 2897 (1939).

(11) Campbell and Eby, *ibid.*, **62**, 1798 (1940).

DEPARTMENT OF CHEMISTRY
UNIVERSITY OF NOTRE DAME
NOTRE DAME, INDIANA

RECEIVED AUGUST 6, 1945

## $N^1$-Alkoxysulfanilamide Derivatives

BY A. ROBERT GOLDFARB

Among the large number of sulfanilamide derivatives reported, the greatest emphasis has been placed on $N^1$-substituted derivatives in which the substituent is an organic residue. Kharasch and Reinmuth[1] and Moore, Miller and Miller[2] have reported the preparation of $N^1$-hydroxysulfanilamide and the $N^4$-acylated derivatives. These compounds are relatively unstable[3] and it was thought desirable to prepare the more stable O alkyl ethers of sulfanilhydroxamide.

The acetyl derivatives of $N^1$-methoxysulfanilamide and $N^1$-benzyloxysulfanilamide were prepared from the corresponding hydroxylamine derivative and acetylsulfanilyl chloride. The hydrolysis of the acetyl derivatives was readily accomplished with aqueous hydrogen chloride.

The $pK_a$ and $pK_b$ of both compounds were determined potentiometrically. For $N^1$ methoxysulfanilamide $pK_a$ is 4.27 and $pK_b$ is 12.03. For $N^1$-benzyloxysulfanilamide $pK_a$ is 3.86 and $pK_b$ is 11.77. The bacteriostatic activity[4] lies generally between that of sulfanilamide and sulfathiazole, which is the approximate activity to be ex-

(1) Kharasch and Reinmuth, U. S. Patent 2,097,415.

(2) Moore, Miller and Miller, THIS JOURNAL, **62**, 2097 (1940).

(3) Moore, Miller and Miller, ref. 2, have reported that $N^4$-hexanoylsulfanilhydroxamide hydrolyzed readily in cold aqueous alkali to give the corresponding sulfinic acid. See also Gilman "Organic Chemistry," Vol. 1, 1938, pp. 631, 632.

(4) The author is indebted to Dr. H. J. White of the American Cyanamid Laboratories, Stamford, Conn., for the bacteriological studies.

pected on the basis of the $pK_a$-activity curve reported by Bell and Roblin.[5]

### Experimental

**Methoxyamine.**[6]—This compound (b. p. 49–50°, hydrochloride m. p. 149°) was prepared by the methylation of hydroxylaminedisulfonic acid[7] with methyl sulfate. It was found necessary to use freshly prepared hydroxylamine disulfonic acid to obtain maximum yields.

**Benzyloxyamine.**[8]—This compound (b. p. 118° at 30 mm.) was prepared by the hydrolysis of O-benzyl acetoxime.

**$N^4$-Acetyl-$N^1$-methoxysulfanilamide.**—To a solution of 6.1 g. of methoxyamine hydrochloride in 40 ml. of pyridine was added 17.1 g. of acetylsulfanilyl chloride, in portions with stirring and cooling. The mixture was stirred overnight at room temperature, poured into water, filtered and dried at 100°. The yield of crude is quantitative. One crystallization from a benzene–, alcohol mixture gave colorless waxy crystals, m. p. 205–206°.

*Anal.* Calcd. for $C_9H_{12}O_4N_2S$: N, 11.5. Found: N, 11.4.

**$N^1$-Methoxysulfanilamide.**—Fifteen grams of the acetyl derivative was refluxed in 150 ml. of 2 *N* hydrochloric acid for one hour. On cooling and neutralization with excess sodium acetate a white solid was obtained which on crystallization from water gave 66% of a product, m. p. 134.5–135.0°.

*Anal.* Calcd. for $C_7H_{10}O_3N_2S$: N, 13.9. Found: N, 14.0.

**$N^4$-Acetyl-$N^1$-benzyloxysulfanilamide.**—The acetyl derivative was prepared in a manner similar to that given for the $N^1$-methoxy derivative. On crystallization from aqueous alcohol a 50% yield of a product, m. p. 181–182°, was obtained.

*Anal.* Calcd. for $C_{15}H_{16}O_4N_2S$: N, 8.76. Found: N, 8.65.

**$N^1$-Benzyloxysulfanilamide.**—Nine and four-tenths grams of the acetyl derivative was hydrolyzed by refluxing for one hour in 100 ml. of 6 *N* hydrochloric acid. The mixture was placed in a refrigerator overnight and filtered. The crystalline precipitate was triturated with excess aqueous sodium acetate, filtered and finally crystallized from alcohol. Eighty-three per cent. of a white crystalline product was obtained, m. p. 130°.

*Anal.* Calcd. for $C_{13}H_{14}O_3N_2S$: N, 10.1. Found: N, 10.1.

(5) Bell and Roblin, THIS JOURNAL, **64**, 2908 (1942).
(6) Traube, Ollendorf and Zander, *Ber.*, **53**, 1477 (1920).
(7) Raschig, *Ber.*, **40**, 4581 (1907); Traube, *ibid.*, **53**, 1477 (1920).
(8) Behrend and Leuchs, *Ann.*, **257**, 206 (1890).

3600 FIELDSTON ROAD
NEW YORK 63, N. Y.

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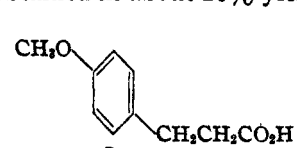
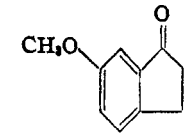
## The Cyclization of β-*p*-Methoxyphenylpropionic Acid

BY WILLIAM S. JOHNSON AND WESLEY E. SHELBERG

In connection with some studies on the formation of cyclic ketones by intramolecular acylation,[1] we have found that the cyclization of β-*p*-methoxyphenylpropionic acid, I, affords a particularly interesting case. Chakravarti and Swaminathan[2] have noted that this acid is especially resistant to cyclization. Using the Friedel–Crafts reaction of the acid chloride with aluminum chloride in nitrobenzene they found conditions whereby 6-methoxyhydrindone-1, II, could be obtained in about 20% yield.




I




II

Since hydrogen fluoride has been shown to have a unique cyclizing power in the case of γ-(4-methoxy-3-biphenyl)-butyric acid[3] (which resists cyclization by the Friedel–Crafts method[4]), it seemed worthwhile to investigate the action of this reagent in the present case. When the acid I was treated by the customary procedure,[3] only a 3% yield of the cyclic ketone was realized, 94% of unchanged acid being recovered. When the reaction was conducted in a closed bomb a 36% yield of the ketone was obtained after five days at room temperature. The low susceptibility of the acid to cyclization is attributable largely to the deactivating influence of the *p*-methoxyl group toward the meta position involved in the acylation. This effect has been noted before. For example, while γ-phenylbutyric acid is cyclized to tetralone-1 in 92% yield by hydrogen fluoride,[3] the *p*-methoxy derivative is converted by the same treatment to 7-methoxytetralone-1 in only 61.5% yield.[5] The even greater resistance of the lower homolog I to cyclization observed in the present work would, therefore, seem to be due to the size of the ring formed, and is consistent with the premise that six-membered rings are formed more readily than five-membered ones.[1]

The Friedel–Crafts method of cyclization has also been investigated. Using a modified procedure of Newman[6] we have been able to obtain yields of II as high as 85%. The acid chloride of I was prepared with phosphorus pentachloride, the phosphorus oxychloride being removed under reduced pressure, and the cyclization was conducted in benzene with aluminum chloride at room temperature for three and one-half hours. Three interesting observations result from this work: (1) In spite of the intrinsic resistance of I to cyclization it is unnecessary to heat the reaction mixture as advocated in previous general procedures.[1,6] (2) As observed by Newman, it is important to remove the phosphorus oxychloride. When this was not done the yield of II dropped to 69%. (3) Even though the reaction was carried out in benzene solution, little, if any, intermolecular acylation occurred. Thus, in spite of the low cyclization susceptibility of I, the intramolecular reaction is preferred.

### Experimental[7]

β-*p*-Methoxyphenylpropionic acid, I, has been prepared in excellent yield by Howard J. Glenn from anisaldehyde.

(1) Adams, "Organic Reactions," Vol. II, 1944, p. 114.
(2) Chakravarti and Swaminathan, *J. Ind. Chem. Soc.*, **11**, 101 (1934).
(3) Fieser and Hershberg, THIS JOURNAL, **61**, 1272 (1939).
(4) Fieser and Bradsher, *ibid.*, **58**, 1738 (1936).
(5) Campbell and Todd, *ibid.*, **64**, 928 (1942).
(6) Newman, *ibid.*, **60**, 2947 (1938); **62**, 870 (1940).
(7) All melting points are corrected.