Anal. Calcd. for $C_6H_{12}O_2$: C, 62.04; H, 10.41. Found: C, 62.17; H, 10.62.

The carbamates tested gave negative results in the Sarcoma 180 tests.

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LITERATURE CITED

(1) Campbell, A.W., Tyron, P.F., *Ind. Eng. Chem.* **45**, 125–30 (1953).
(2) D'Alelio, G.F., U.S. Patent **2,694,690** (November 16, 1954).
(3) Erdmann, E., *Ber. Deut. Chem. Ges.* **34**, 2281 (1901).
(4) Herzog, J., *Ber. Deut. Chem. Ges.* **40**, 1833 (1907).
(5) Pinchas, S., Ben-Ishai, O., *Bull. Research Council Israel* **6A**, 166 (1957); *CA* **51**, 17455 (1957).
(6) Valega, T.M., Ingangi, J.C., J. CHEM. ENG. DATA **12**, 457 (1967).
(7) von Meyer, E., *J. Prakt. Chem.* **82**, 521–38 (1911); *CA* **5**, 1595 (1911).

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Synthesis in Indole Series

Chloromethylation and Chlorosulfonation of 1-Acetyl-5-bromoindoline

RAPHAEL IKAN[1] and YEHUDA FATAL
Department of Organic Chemistry, Hebrew University, Jerusalem, Israel

Chloromethylation and chlorosulfonation of 1-acetyl-5-bromoindoline yielded 1-acetyl-5-bromo-7-chloromethyl- and 7-chlorosulfonyl indolines, which were transformed to the corresponding indole derivatives. Percent yields, melting points, and infrared data are given for the reported compounds.

In a recent paper (*4*), we described the preparation of the 5-, 6-, and 7-carboxy- and cyanoindolines and indoles. The present communication describes the preparation of 7-substituted indolines and indoles, mainly the chloromethyl and chlorosulfonyl derivatives.

The easily available 1-acetyl-5-bromoindoline (*2*) gave with dichlorodimethyl ether, 1-acetyl-5-bromo-7-chloromethylindoline. This product tended to polymerize and was immediately treated with aniline to give the 7-anilinomethyl compound. The structure of the 1-acetyl-5-bromo-7-chloromethylindoline was proved by its transformation to 7-methylindole.

Also, chlorosulfonic acid replaced 1-acetyl-5-bromoindoline at the 7-position. The product, 5-bromo-7-chlorosulfonylindoline, was deacetylated with concentrated hydrochloric acid and then treated either with ammonium carbonate or diethylamine, yielding the sulfonamide and the *N,N*-diethylsulfonamide, respectively. The latter was dehydrogenated with chloranil to form the corresponding indole.

5-Sulfonamides derived from indoline and indole had been prepared before by Terent'ev and co-workers (*6*), but no analogs substituted in the 7-position have been known.

EXPERIMENTAL

1-Acetyl-5-bromo-7-chloromethylindoline. 1-Acetyl-5-bromoindoline (5 grams) was stirred into a cooled solution of dichlorodimethyl ether (8 ml) (*1*), in concentrated sulfuric acid (50 ml). The temperature was then raised to 10° C and the stirring continued for 2 hr. The crude product was poured onto ice, and the solid phase filtered off. It was then recrystallized from ethanol yielding 4.2 grams (70%) of material of mp 169–170° C. $\nu_{\max}^{\mathrm{KBr}}$ 1675 cm^{-1}.

1-Acetyl-5-bromo-7-anilinomethylindoline. A mixture of 1-acetyl-5-bromo-7-chloromethylindoline (3 grams), aniline (5 ml), and a saturated solution of sodium carbonate (50 ml) was heated on the water bath for 2 hr. After it was cooled, the mixture was extracted with benzene (50 ml); most of the benzene was removed under reduced pressure. Then hexane was added. The product was obtained in 70% yield (2.45 grams); mp 151–153°.

1-Acetyl-5-bromo-7-diethylaminomethylindoline. This compound was prepared similarly to the previous one, using diethylamine. It melted at 133–135°. $\nu_{\max}^{\mathrm{KBr}}$ 1660 cm^{-1} (C=O).

1-Acetyl-7-methylindoline. 1-Acetyl-5-bromo-7-chloromethylindoline (3 grams) in 100 ml of absolute ethanol was dehalogenated by treating it with hydrogen at 3.5 atm in the presence of 2 grams of Pd/C (10%). After 30 min, the catalyst was filtered off and the filtrate concentrated under reduced pressure. The residue was recrystallized from methanol, mp 98–100°. Yield, 1.35 g (75%).

7-Methylindole. 1-Acetyl-7-methylindoline (1.2 grams) and concentrated hydrochloric acid (10 ml) were refluxed for 30 min. The cooled mixture was neutralized with solid sodium carbonate, and the oily product extracted with xylene and dried over magnesium sulfate. To the filtered solution, chloranil (1 gram) was added and the mixture refluxed for 3 hr and filtered. The filtrate was concentrated under reduced pressure. Recrystallization of the residue from benzene-hexane yielded crystals (200 mg) of 7-methylindole of mp 79–81°. The product was further purified by preparative thin-layer chromatography on silica gel G plates (7-methylindole serving as a reference) and

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[1] To whom correspondence should be addressed.

developed with chloroform. The compound was detected by spraying the edge of the plate with Ehrlich reagent; it appeared as a blue band, R_f 0.84. The band was scraped off the plate and extracted with chloroform. Evaporation of the solvent and recrystallization from benzene-hexane yielded crystals of mp 83° [lit: 82°, (*3*); 85°, (*5*)].

1-Acetyl-5-bromoindoline-7-sulfochloride. 1-Acetyl-5-bromoindoline (10 grams) was added to chlorosulfonic acid (150 ml) in small portions with intensive stirring and cooling (ice). The mixture was heated at 60°, stirred for 3 hr. and poured onto ice. The white precipitate was filtered off and recrystallized from methyl ethyl ketone. Yield: 9 g, 50%; mp 212°. $\nu_{\max}^{\mathrm{KBr}}$ 1670 cm^{-1}.

5-Bromoindoline-7-sulfonamide. 1-Acetyl-5-bromoindoline-7-sulfochloride (5 grams) and a saturated solution of ammonium carbonate (50 ml) were heated for 2 hr in a water bath. The solid product was filtered off and recrystallized from methyl ethyl ketone. It melted at 189–190°. Yield, 2.3 grams (50%). This product and 50 ml of concentrated hydrochloric acid were refluxed for 1 hr. The reaction mixture was neutralized with sodium carbonate and the precipitate filtered off and recrystallized from methanol. Yield: 1.6 g, 45%; mp 163–165°.

5-Bromoindoline-7-(*N,N*-diethylsulfonamide). The compound was prepared from 1-acetyl-5-bromoindoline-*N,N*-diethyl-7-sulfonamide, mp 193–195°, which was deacetylated with concentrated hydrochloric acid. The mp of the product was 133–134°.

5-Bromoindole-7-(*N,N*-diethylsulfonamide). 5-Bromoindoline-7-(*N,N*-diethylsulfonamide) was dehydrogenated with chloranil to yield 5-bromoindole-7-(*N,N*-diethylsulfonamide); mp 145–146°.

Elemental analyses (for C, H, and some N compounds) were in agreement with the theoretical values obtained and were submitted for review. Infrared absorption measurements were made in KBr pellets with a Perkin-Elmer 337 infrared spectrophotometer.

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LITERATURE CITED

(1) Buc, S. R., *Org. Syn.*, **4**, 101 (1963).

(2) Gall, W. G., Astill, B. A., Boekelheide, V., *J. Org. Chem.*, **20**, 1538 (1955).

(3) Hoffmann, E., Ikan, R., Galun, A. B., *J. Heterocycl. Chem.*, **2**, 298 (1965).

(4) Ikan, R., Rapaport, E., *Tetrahedron*, **23**, 3823 (1967).

(5) Kruber, O., *Ber.*, **2753** (1926).

(6) Terent'ev A. P., Ban-lun, Ge, Preobrazhenskaya, M. N., *J. Gen. Chem.* (USSR), **32**, 173 (1962).

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