

sym - Bis(2 - methylaminoethyl)oxaldiimidate, $\text{(CH}_3\text{NHC}_2\text{H}_4\text{OC}-\text{)}_2$ gave no such reaction with hydrogen sulfide.

The hydrogen sulfide reaction resembles the partial hydrolysis of oxamidines which can be accomplished by allowing a cold aqueous solution to stand in the presence of amine.⁵



EXPERIMENTAL

Oxamidines were prepared by the reaction of cyanogen with amines.⁶ Dithiooxamide was a gift from the Malinkrodt Chemical Works.

N,N'-Di-*n*-butyldithiooxamide. (a) A cold solution of *sym*-di-*n*-butyloxamidine, prepared by dissolving 2 g. of the compound in the smallest possible amount of ethanol and adding water as long as the solution remained clear, was saturated with hydrogen sulfide. The solution gradually acquired a reddish-brown color and a few orange crystals appeared. After standing overnight the mixture was filtered and the orange solid recrystallized as follows: 2 ml. of water was added to remove any ammonium sulfide and the solid residue dissolved in ethanol at 40°. After filtration to remove sulfur, water was added until a cloudiness persisted, then a few drops of ethanol. The mixture was finally cooled in an ice bath. After three recrystallizations the melting point of the orange needles was 41.5–43.0°. The yield of crude material was 70%.

Anal. Calcd. for $\text{C}_{10}\text{H}_{20}\text{N}_2\text{S}_2$: N, 12.1; S, 27.6. Found: N, 12.1; S, 27.2.

(b) Di-*n*-butyldithiooxamide was also prepared by the method of Wallach.⁴ To a suspension of 12.0 g. (0.1 mole) of dithiooxamide in 48 g. of ethanol was added 15.6 g. (2.1 moles) of *n*-butylamine. Hydrogen sulfide and ammonia were evolved and some of the dithiooxamide went into solution. The mixture was heated until clear, after which a few drops of dilute sulfuric acid were added. Orange crystals formed on standing overnight. These were recrystallized as above and melted at 41.5–42.5°.

A mixed melting point with the product from (a) showed no depression. Infrared curves (10% solution in CHCl_3) of the two products were identical.

N,N'-Diethylthiooxamide. (a) Saturation with hydrogen sulfide of a concentrated ethanolic solution of diethyl-oxamidine produced orange needles melting at 57.5–59.0°. Recrystallization from ethanol-water was carried out below 55°. The yield of crude product was 45%.

This compound had previously been prepared by Wallach.⁴ A sample prepared by his method mixed with the product from above showed no depression of melting point. Infrared curves of the two products were identical.

(b) Oxamidines are often best isolated as dihydrochlorides. Saturation with hydrogen sulfide of either an aqueous or ethanolic solution of diethyl-oxamidine dihydrochloride failed to yield the dithiooxamide. Consequently a solution of 0.5 g. of diethyl-oxamidine dihydrochloride in the minimum amount of water was made basic to litmus with dilute sodium hydroxide and then treated with hydrogen sulfide until it became pale yellow and a few crystals appeared. More crystals formed overnight. Recrystallization gave orange needles which showed no melting point depression when mixed with the product from (a). The yield was 50%.

N,N'-Bis(3-methoxypropyl)-dithiooxamide. (a) One gram of *sym*-bis(3-methoxypropyl)oxamidine² was dissolved in 95% ethanol and saturated with hydrogen sulfide. The solu-

(5) H. M. Woodburn, B. Morehead, and M. C. Chen, *J. Org. Chem.*, **15**, 535 (1950).

tion turned orange-red and a few reddish crystals appeared on standing. These were filtered off and proved to be dithiooxamide. Water was added to the filtrate until it became cloudy and crystallization was completed by cooling in the ice chest. The product was obtained after one recrystallization from ethanol-water (below 40°) as orange-yellow needles melting at 44.0–45.5°. The yield of crude product was 60%.

Anal. Calcd. for $\text{C}_{10}\text{H}_{20}\text{N}_2\text{O}_2\text{S}_2$: N, 10.6; S, 24.2. Found: N, 10.5; S, 23.7.

(b) Following the method of Wallach,⁴ dithiooxamide and 3-methoxypropylamine gave crystals which showed no melting point depression when mixed with the product from (a). Infrared curves (10% solution in CHCl_3) of the two products were identical.

N,N'-Bis(2-ethoxyethyl)dithiooxamide was prepared from *sym*-bis(2-ethoxyethyl)oxamidine² and hydrogen sulfide as described above. After recrystallization from ethanol-water, the yellow needles melted at 51–52°. Because of the small amount of starting material available, the yield of purified product was not sufficient for analysis.

N,N'-Bis(2-hydroxyethyl)dithiooxamide. (a) Hydrogen sulfide was passed into a solution of 1.0 g. of *sym*-bis(2-hydroxyethyl)oxamidine² in 20 ml. of water until an orange precipitate began to form. After standing for 4 hr. the mixture was filtered. The solid proved to be dithiooxamide.

The filtrate was extracted with 25-ml. portions of ether. Evaporation of the extracts produced 0.1 g. of yellow-orange crystals melting at 83–85°. The yield was 8.5%.

(b) To 12 g. (0.2 mole) of ethanolamine was added 6 g. (0.06 mole) of dithiooxamide. An immediate reaction produced much heat and hydrogen sulfide. After the initial reaction had subsided, the flask was heated gently with constant stirring for 0.5 hr.

After cooling, the mixture was diluted with 20 ml. of water and crystallization induced by scratching the inner surface of the flask. The yield of crude product was 29%. Recrystallization was accomplished from ethyl acetate-carbon tetrachloride. The yellow solid melted at 89–91° and gave no depression of melting point when mixed with the product from (a).

Anal. Calcd. for $\text{C}_6\text{H}_{12}\text{N}_2\text{O}_2\text{S}_2$: N, 13.4; S, 30.7. Found: N, 13.2; S, 30.3.

Attempted reaction of *sym*-bis(2-methylaminoethyl)-oxaldiimidate² with hydrogen sulfide: One gram of the hydrochloride of *sym*-bis(2-methylaminoethyl)oxaldiimidate was dissolved in the minimum amount of water. The solution was made basic with dilute sodium hydroxide. Hydrogen sulfide was passed in until the solution was pale green in color. No crystals formed. The aqueous solution was extracted with ether and the extracts evaporated to dryness. No residue was obtained.

DEPARTMENT OF CHEMISTRY
THE UNIVERSITY OF BUFFALO
BUFFALO 14, N. Y.

A New Synthesis of 3-Indolesuccinic Acid

WAYLAND E. NOLAND¹ AND CHARLES F. HAMMER²

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Maleyldiindole,³ an addition product of indole and

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(2) Research Corporation Research Assistant, 1956–1957. We are indebted to the Research Corporation for a Frederick Gardner Cottrell grant in support of this research.

(3) O. Diels, F. Alder, and W. Lübbert, *Ann.*, **490**, 277 (1931).

maleic anhydride, is formulated⁴ as I, based on the now established⁵ structure for diindole. It has been reported previously that malelydiindole is hydrolyzed by refluxing with 30% potassium hydroxide solution to indole (in 71% yield of one mole) and a dibasic acid (in 71–86% yield), m.p. 197°, having the composition of a molecule of indole plus a molecule of maleic acid. This dibasic acid yielded a dimethyl ester, m.p. 74°; neither the diacid nor the diester absorbed hydrogen in the presence of platinum oxide.³

We have found that the diacid has a molecular weight consistent with the formula $C_{12}H_{11}NO_4$. It has an intact indole nucleus, as shown by the ultraviolet spectrum. Alkylation on nitrogen has not occurred, as shown by the presence of NH stretching absorption in the infrared spectrum. An unsubstituted 2- or 3-position is indicated by a positive Ehrlich⁶ test. Pyrolysis of the diacid gave carbon dioxide and 3-indolepropionic acid, as shown by comparison with an authentic sample. Anhydride exchange between the diacid and acetic anhydride gave an anhydride (III, in 84% yield), m.p. 102.5–103.5°. Finally, the diacid was found to be identical with a sample of 3-indolesuccinic acid⁷ (II) prepared by coupling indole with diethyl diazosuccinate, as shown by no depression in mixed melting point and identity of the infrared spectra. The melting point of the diethyl ester of the diacid was also in agreement with that reported.⁷ Thus, alkaline hydrolysis of malelydiindole (I) appears to represent a

most convenient synthesis of 3-indolesuccinic acid (II).

Indole and maleic or fumaric acids do not react under the same alkaline hydrolysis conditions as those under which II was formed. It appears, therefore, that II is formed from I prior to the formation of free indole and maleate dianion. The results of our study of the mechanism of this interesting rearrangement will be reported later.

EXPERIMENTAL

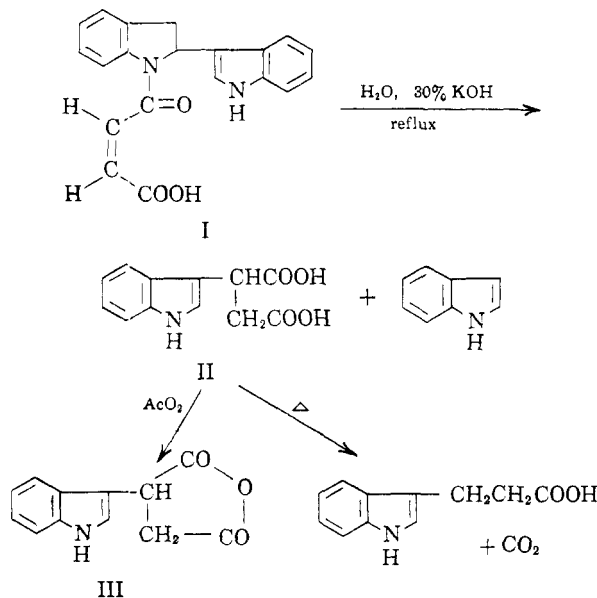
Melting points were determined on a calibrated hot stage.

Alkaline hydrolysis of malelydiindole (I): preparation of 3-indolesuccinic acid (II). The procedure is that described previously,³ except for modifications in the workup procedure.

Malelydiindole^{3,4} (10.0 g., 0.0301 mole) was refluxed for 3 hr. with 30% aqueous potassium hydroxide solution (100 cc.). The reaction mixture was cooled and extracted with ether, and the ether was evaporated, yielding crude indole (3.41 g., 0.0291 mole, 97%), m.p. 41–45°. The alkaline solution was acidified to Congo Red with dilute sulfuric acid and extracted with ether for 1–2 days in a liquid-liquid extractor. Evaporation of the ether left a pink solid (5.12 g., 0.0220 mole, 73%). Recrystallization, with charcoal, from ethanol-water yielded very pale pinkish white platelets (4.08 g.), m.p. 197–198° d. (with gas evolution). Mol. wt. Calcd. for $C_{12}H_{11}NO_4$: 233.22. Found (Rast): 274, 251, 272, average 266.⁸ λ_{max} in 95% EtOH: 221 m μ (log ϵ 4.98), 273 (4.04), 280 (4.06), 290 (4.00).⁸ ν_{NH} 3390, ν_{OH} ~2630, $\nu_{C=O}$ 1686 cm^{-1} in Nujol. Mixed m.p. with 3-indolesuccinic acid^{7,9} of m.p. 195–197°, 195–197° d.; reported m.p. 199° d.⁷ The infrared spectra of the two samples in Nujol were identical.

The diethyl ester of the diacid had m.p. 77–78.5°, in agreement with that reported for diethyl 3-indolesuccinate, m.p. 79–80°.⁷ Heating of the diacid for 30 min. in an oil bath maintained at 201–204° caused evolution of a gas which formed a white precipitate when passed into barium hydroxide solution. Recrystallization of the pyrolysis residue, with charcoal, from ethanol-water gave white platelets in 44% yield, m.p. 131.5–132.5°, mixed m.p. with 3-indolepropionic acid,¹⁰ 131.5–132.5°. The infrared spectra of the two samples in KBr disks were identical.

3-Indolesuccinic anhydride (III). 3-Indolesuccinic acid (2.00 g., 0.00858 mole), derived from the alkaline hydrolysis of malelydiindole, was dissolved in freshly distilled acetic anhydride (50 cc.) and set aside at room temperature for 2 days. The acetic acid and acetic anhydride were removed at 0.3 mm. during 5 hr. while the temperature was kept below 70°. After standing for 2 days at room temperature the light brown residue crystallized in long needles (1.56 g., 0.00726 mole, 85%), m.p. 96.5–99.5°. Three recrystallizations from methylene chloride-light petroleum (b.p. 60–68°) and one recrystallization from methylene chloride at dry ice temperature yielded white crystals, m.p. 102.5–103.5°. ν_{NH} 3440 in Nujol, 3420 in KBr, 3510 in $CHCl_3$; $\nu_{C=O}$ 1861, 1781 in Nujol, 1863, 1776 in KBr, 1866, 1788 cm^{-1} in $CHCl_3$.



(4) W. E. Noland, R. K. Lange, F. B. Stocker, and G. L. Sauer, Paper 10 presented before the Organic Division at the 132nd National American Chemical Society Meeting, New York, N. Y., Sept. 9, 1957, Abstracts, p. 6P.

(5) (a) G. F. Smith, *Chemistry & Industry*, 1451 (1954).
(b) H. F. Hodson and G. F. Smith, *J. Chem. Soc.*, 3544 (1957).

(6) A. Treibs and E. Herrmann, *Hoppe-Seyler's Z. physiol. Chem.*, 299, 168 (1955).

(7) R. W. Jackson and R. H. Manske, *Can. J. Research*, 13B, 170 (1935).

(8) Gerald L. Sauer, M. S. thesis, University of Minnesota, 1955.

(9) We are grateful to Dr. Léo Marion, Director, Division of Pure Chemistry, National Research Council, Ottawa, Ont., and to Dr. R. H. Manske for sending us a sample of 3-indolesuccinic acid prepared by Dr. Manske.

(10) We are indebted to Mr. L. A. Crisorio, Carbide and Carbon Chemicals Company, Chicago, Ill., for a generous sample of 3-indolepropionic acid.

Anal. Calcd. for $C_{12}H_9NO_2$ (215.20): C, 66.97; H, 4.22; N, 6.51. Found: C, 66.92; H, 4.20; N, 6.28.

Attempted reaction of indole and maleic and fumaric acids under alkaline hydrolysis conditions. Indole (7.06 g., 0.0602 mole) and maleic acid (3.49 g., 0.0301 mole) were refluxed for 3 hr. with 30% aqueous potassium hydroxide solution (100 cc.). The reaction mixture was cooled, extracted with ether (3–50 cc. portions), and the ether evaporated, yielding crude indole (6.88 g., 97%), m.p. 39–43°.

In an identical experiment, with fumaric acid in place of maleic acid, the recovery of crude indole was 7.05 g., 100%, m.p. 39–43°.

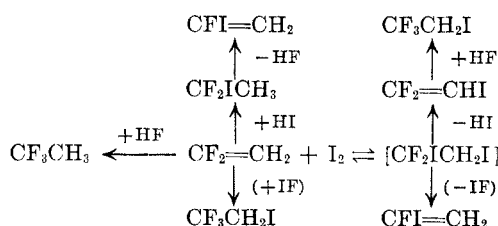
SCHOOL OF CHEMISTRY
UNIVERSITY OF MINNESOTA
MINNEAPOLIS 14, MINN.

Thermal Reaction of 1,1-Difluoroethylene with Iodine¹

MURRAY HAUPTSCHNEIN, ARNOLD H. FAINBERG, AND MILTON BRAID

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1,1-Difluoroethylene has been found to react thermally with iodine to form quite unexpectedly, 1,1,1-trifluoro-2-iodoethane as the major product. Another principal product of the reaction was an olefin boiling at *ca.* 40°, for which the structure 1-fluoro-1-iodoethylene is proposed. Two minor products were also identified in the reaction mixture, 1,1-difluoro-1-iodoethane and 1,1-difluoro-2-iodoethylene, as well as some polymeric material. In the presence of the very large excess of 1,1-difluoroethylene used in the present work, 1,1,1-trifluoroethane was a major by-product.²



It is obvious that the conditions employed in the single experiment reported herein were not designed to produce the iodine-containing products in optimum yields, which, of course, would be greatly improved by use of an excess of iodine.

(1) The work herein reported was carried out under contract between the Office of Naval Research and the Pennsalt Chemicals Corp. Reproduction in whole or in part is permitted for any purpose of the United States Government.

(2) All of the products isolated can be related schematically through the iodine adduct of 1,1-difluoroethylene (not isolated) as shown below:

EXPERIMENTAL

Thermal reaction of 1,1-difluoroethylene with iodine. Into a 170-ml. monel autoclave were placed 63.5 g. (0.25 mole) of crystalline iodine. The autoclave was cooled in liquid nitrogen, and 80 g. (1.25 moles) of 1,1-difluoroethylene were condensed in it by means of gaseous transfer *in vacuo*. After heating at 185° with shaking for 160 hr., during which the pressure dropped from 3200 to 1300 p.s.i., the autoclave was cooled to room temperature and vented at atmospheric pressure into a liquid nitrogen-cooled receiver.

The recovered product consisted of 53 g. of material, gaseous at room temperature, shown by infrared analysis to consist only of unreacted $\text{CH}_2=\text{CF}_2$ (mostly) and CF_3CH_3 ,³ 53 g. of liquid product, and 37 g. of solids, containing some polymeric material and unreacted iodine. Distillation of the liquid product gave 38 g. of liquid boiling below 55°, and 14 g. of polymer boiling above 145°.

Fractional distillation of a 25-g. portion⁴ of the liquid product through a 2 ft. \times 8 mm. Mini-Cal Podbielniak column gave several fractions totalling 8 g., b.p. 40–46°, n_D^{20} 1.39–1.41 and 16 g. of $\text{CF}_3\text{CH}_2\text{I}$, b.p. 54–55°, center cut: b.p. 55.0° (756 mm.), n_D^{20} 1.3962, reported⁵ b.p. 55.0°, n_D^{25} 1.3981. Its infrared spectrum was identical with that of an authentic sample prepared by iodide displacement on 2,2,2-trifluoroethyl *p*-toluenesulfonate. Principal infrared bands for $\text{CF}_3\text{CH}_2\text{I}$: 3.36, 6.81, 7.01, 7.43, 7.78, 8.19, 8.90, 9.44, 11.9, 14.9 μ .

The infrared spectrum of the fractions b.p. 40–46° showed that the mixture consisted principally of an olefin A, b.p. *ca.* 40°, with a double bond stretching band at 6.09, 6.14 μ (doublet). Also indicated were minor amounts of a second olefin B, boiling virtually at the same temperature as A (perhaps slightly higher), having a double bond stretching band at 5.79 μ , and a saturated compound boiling several degrees higher than the olefins, and exhibiting remarkably intense C—H stretching bands at 3.33 and 3.40 μ .

The saturated compound was identified as $\text{CH}_3\text{CF}_2\text{I}$, reported⁶ b.p. 45°, n_D^{19} 1.4183 on the basis that the infrared spectrum of the mixture contained the nine major peaks found⁷ for an authentic sample. Olefin B was similarly identified spectroscopically as $\text{CF}_2=\text{CHI}$, reported⁸ b.p. 35.5° at 622 mm.

Olefin A has principal peaks in the infrared at 6.09, 6.14, *ca.* 8.3, 8.68, 8.95, 9.55, 9.60, 10.20, 11.03, 11.82, and 12.26 μ . Its double bond stretching frequency is consistent with a $\text{CH}_2=\text{CFX}$ type of structure,⁹ and the structure $\text{CH}_2=\text{CFI}$, is proposed.

PHILADELPHIA, PA.

(3) A.P.I. Research Project 44, Catalog of Infrared Spectral Data, No. 979.

(4) This portion was not an entirely representative sample of the 38 g. of liquid boiling below 55°, but was richer in the least volatile component.

(5) G.V.D. Tiers, H. A. Brown, and T. S. Reid, *J. Am. Chem. Soc.*, **75**, 5978 (1953).

(6) R. N. Haszeldine, *J. Chem. Soc.*, 61 (1956).

(7) R. N. Haszeldine, private communication: 3.34, 3.40, 7.20, 8.47, 9.03, 9.07, 10.40, 11.27, 11.35 μ .

(8) Private communication of J. D. Park; M. Hein, Ph.D. Thesis, University of Colorado (1954): 5.80, 7.62, 7.68, 8.77, 8.85, 10.52, 10.63, 13.58 μ .

(9) *E.g.*, the double-bond stretching frequency of $\text{CH}_2=\text{CClF}$ is 6.08 μ . See I. P. Torkington and H. W. Thompson, *Trans. Faraday Soc.*, **41**, 236 (1945).