Anal. Calcd. for $C_{11}H_{17}O_6NS$: C, 45.3; H, 5.88; N, 4.80. Found: C, 44.8; H, 6.04; N, 4.34.

On chromatograms III migrated as a single component, R_f = 0.42, and reacted immediately with ninhydrin.

L-Threonine *p*-Toluenesulfonate Benzyl Ester (IV).—L-Threonine, 0.30 g. (2.5 mmoles) and 0.53 g. of *p*-toluenesulfonic acid monohydrate (2.8 mmoles) were dissolved in 5 ml. of benzyl alcohol by heating on the steam bath. Carbon tetrachloride (25 ml.) was added and the mixture heated under reflux for 20 hr., the carbon tetrachloride being distilled from the mixture very slowly. Addition of dry ether precipitated an oil which was partially soluble in ethyl acetate. The material which was insoluble in ethyl acetate was identified as III, m.p. 136–137°. After 5 ml. of fresh benzyl alcohol and 25 ml. of carbon tetrachloride had been added, distillation of the carbon tetrachloride was resumed for an additional 19 hr. Addition of dry ether (100 ml.) precipitated 0.33 g. of a colorless oil after drying *in vacuo* over calcium chloride. Attempts to crystallize the oil from benzene–ether, benzene–petroleum ether, methanol–ether, and/or acetone–ether either at 0° or at $-70°$ were unsuccessful.

Anal. Calcd. for $C_{18}H_{23}O_6NS$: NH_2—N, 3.67. Found: NH_2 —N, 3.80.

Chromatography disclosed contamination of IV, R_f = 0.83, with III, R_f = 0.40. The material was dissolved in 40 ml. of benzene and purified by extraction with a dilute solution of sodium bicarbonate as described above for II. Following addition of one equivalent of *p*-toluenesulfonic acid monohydrate and evaporation of the solvent at reduced pressure, chromatographically pure IV, R_f = 0.82, was obtained as an oil, which could not be induced to crystallize. Although pure IV was obtained by this procedure in several runs, attempts to crystallize the resulting oil were unsuccessful.

***N*-Carbobenzoxy-L-threonine Benzyl Ester (V).**—L-Threonine, 0.40 g. (3.4 mmoles), and 0.71 g. of *p*-toluenesulfonic acid monohydrate (3.8 mmoles) were dissolved in 5 ml. of benzyl alcohol and 30 ml. of dry benzene. Esterification was carried out for 25 hr. as described for IV. The remaining benzene was removed by distillation at reduced pressure and IV precipitated by addition of 100 ml. of dry ether. After the ether had been decanted and the oil dried for 12 hr. *in vacuo* over calcium chloride, it was dissolved in 10 ml. of water and cooled in an ice bath. Carbobenzoxy chloride (0.60 ml.) and 1.4 g. of potassium carbonate in 25 ml. of water were added. After a few minutes of shaking, V precipitated from the reaction mixture. Following addition of a few drops of pyridine the reaction mixture was extracted with ethyl acetate. The organic phase was washed with 5% sodium bicarbonate and water in succession and dried over anhydrous sodium sulfate. After the solvent had been evaporated at reduced pressure, the oily residue solidified upon addition of petroleum ether to yield 0.80 g. of crystalline V; m.p. 79–80°, 68% yield. One recrystallization from ethyl acetate–petroleum ether afforded needles, m.p. 79–80°, $[\alpha]^{25}_D$ $-10.5°$ (*c* 2.0, 95% ethanol).

Anal. Calcd. for $C_{19}H_{21}O_5N$: C, 66.5; H, 6.17; N, 4.10. Found: C, 66.7; H, 6.23; N, 4.36.

Conversion of V to L-Threonine.—V, 0.71 g. (2.1 mmoles), was dissolved in 25 ml. of methanol. Following addition of three drops of glacial acetic acid, hydrogenolysis was carried out with palladium oxide[11] as catalyst. The product which had precipitated partially during the reaction was brought back into solution by addition of water. After the reaction mixture had been filtered, the solvent was removed at reduced pressure and the residue recrystallized from methanol–ether to yield 0.18 g. of L-threonine, $[\alpha]^{23}_D$ $-28.2°$ (*c* 1.5, water); 74% yield.

New Synthetic Route to 6-Nitroisatin *via* Nitration of 3-Indolealdehyde

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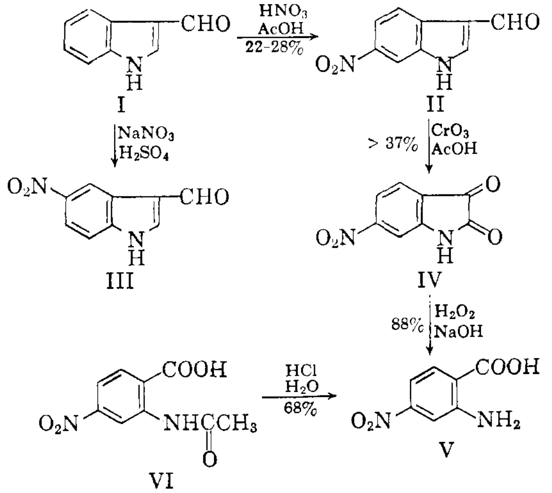
Nitration of 3-indolealdehyde (I) in acetic acid was first reported, by Majima and Kotake,[2] to give in unstated yield a mononitro derivative, having a melting point of 290° with decomposition, in which the position of nitration was not determined. Recently, and subsequent to the completion of our work, Berti and da Settimo[3] have reported that they have repeated the nitration of 3-indolealdehyde in acetic acid, and have obtained in 16% yield a mononitro derivative, having a melting point of 302–304° with decomposition. The mononitro derivative was proved to be 6-nitro-3-indolealdehyde (II), by oxidation to the corresponding acid and decarboxylation to authentic 6-nitroindole.[2] Berti and da Settimo[3] also reported that nitration of 3-indolealdehyde with potassium nitrate in concentrated sulfuric acid gave in 85% yield a mixture of mononitro derivatives, having a melting point of 260–270° with decomposition, shown by ultraviolet analysis to contain 66% 5-nitro-3-indolealdehyde and 34% 6-nitro-3-indolealdehyde. The structure of 5-nitro-3-indolealdehyde (III), isolated in small amount by fractional crystallization, was proved by oxidation to the corresponding acid and decarboxylation to a compound having a melting point and ultraviolet spectrum in good agreement with those reported for 5-nitroindole.[4]



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[11] R. L. Shriner and R. Adams, *J. Am. Chem. Soc.*, **46**, 1683 (1924).

[1] From the senior thesis research of Reuben D. Rieke, 1960–1961.

[2] R. Majima and M. Kotake, *Ber.*, **63**, 2237 (1930).

[3] G. Berti and A. da Settimo, *Gazz. chim. ital.*, **91**, 728 (1961).

[4] S. M. Parmerter, A. G. Cook, and W. B. Dixon, *J. Am. Chem. Soc.*, **80**, 4621 (1958).

We also repeated the nitration of 3-indolealdehyde in acetic acid, and obtained in 22–28% yield a mononitro derivative, having a melting point of 301.5–302° with decomposition, corresponding to the mononitro derivative previously described.[2,3] We have proved the mononitro derivative to be 6-nitro-3-indolealdehyde (III), but by a different degradative method, and our results confirm the structure proved by Berti and da Settimo.[3] We have also carried out the nitration of 3-indolealdehyde, with sodium nitrate instead of potassium nitrate, in concentrated sulfuric acid, and have obtained in 93% yield a nitration product, from which was isolated the major product, a yellow, crystalline mononitro derivative, having a melting point of 312–314° with decomposition, different from 6-nitro-3-indolealdehyde, and assumed to be 5-nitro-3-indolealdehyde (III). Our crystalline product has a higher melting point than the microcrystalline powder of melting point 301.5–302° with decomposition, described for 5-nitro-3-indolealdehyde,[3] but the infrared and ultraviolet spectra appear to agree with those reported.

Our proof of the structure of 6-nitro-3-indolealdehyde is by chromic acid oxidation in better than 37% yield to 6-nitroisatin (IV), having a melting point in agreement with that reported,[5] followed by alkaline hydrogen peroxide oxidation[6] of the 6-nitroisatin in 88% yield to 4-nitroanthranilic acid[7] (V), identical with a sample prepared by acid hydrolysis of *N*-acetyl-4-nitroanthranilic acid[8] (VI). Our synthesis of 6-nitroisatin by chromic acid oxidation of 6-nitro-3-indolealdehyde appears to be the most convenient method; the previously reported method is by oxidation of 6,6′-dinitroindigo in 26% yield with a mixture of chromic, nitric, and sulfuric acids.[5] Similar chromic acid oxidations of 3-indolecarbonyl derivatives to the corresponding isatins have been described by Majima and Kotake,[2] involving oxidation of 6-bromo- and 5,6-dibromo-3-indolecarboxylic acids to the corresponding 6-bromo- and 5,6-dibromoisatins.

Ethyl 6-nitro-3-indolecarboxylate was prepared in 6% yield, for the purpose of ultraviolet comparison, by nitration of ethyl 3-indolecarboxylate in acetic acid according to the procedure of Majima and Kotake,[2] who did not state the yield. The ultraviolet spectrum was found to be quite similar to that of 6-nitro-3-indolealdehyde and different from that of 5-nitro-3-indolealdehyde (see data in Experimental).

Experimental

Melting points were determined on a calibrated Kofler micro hot stage.

3-Indolealdehyde (I) was prepared through a Vilsmeier reaction from indole and *N,N*-dimethylformamide in the presence of phosphorus oxychloride[9]; λ_{max} mμ (log ϵ) in 95% C_2H_5OH: 242 (4.14), 260 (4.07), 296 (4.12); ν_{NH} 3440 m in $CHCl_3$, 3140 ms in Nujol, $\nu_{C=O}$ 1655 s in $CHCl_3$, 1625 s cm.$^{-1}$ in Nujol.

6-Nitro-3-indolealdehyde (II).—The procedure is essentially that of Majima and Kotake,[2] who did not, however, state the relative quantities of reactants or the yield. Concentrated nitric acid (*d* 1.42, 50 cc.) was added, with rapid stirring, to a solution of 3-indolealdehyde (10.0 g., 0.0692 mole) in acetic acid (100 cc.). The first few cubic centimeters of nitric acid were added dropwise, causing a large amount of the yellow 1:1 addition product[2] of 3-indolealdehyde and nitric acid to precipitate. The remainder of the nitric acid was then added rapidly. The resulting suspension was heated to 65° on a water bath, whereupon a violent reaction took place. The reaction flask was immediately cooled in an ice bath and the solid which precipitated (2.86 g., 0.0150 mole, 22%), m.p. 285–290°, washed with water, dried, and recrystallized three times from acetone–benzene (acetic acid,[2] acetone–ethanol,[3] or ethanol–water may also be used), yielding light yellow needles, m.p. (turns brown at 292°) 301.5–302° dec.; reported: m.p. 290° dec.,[2] 16%, m.p. 302.5–304° dec.;[3] λ_{max} mμ (log ϵ) in 95% C_2H_5OH: 278 (4.23), 316 infl. (3.72); ν_{NH} 3180 m, $\nu_{C=O}$ 1647 s, ν_{NO_2} 1512 ms, 1340 s cm.$^{-1}$ in Nujol.

Anal. Calcd. for $C_9H_6N_2O_3$ (190.15): C, 56.84; H, 3.18; N, 14.73. Found: C, 57.09; H, 3.22; N, 14.67.

In other experiments, under similar conditions, yields of 23–28% were obtained.

5-Nitro-3-indolealdehyde (III).—A solution of sodium nitrate (2.93 g., 0.0345 mole) in concd. sulfuric acid (50 cc.) was added dropwise, with stirring, to a solution of 3-indolealdehyde (5.00 g., 0.0345 mole) in concd. sulfuric acid (60 cc.) cooled to 0° in an ice bath over a period of 1 hr. and 20 min. The solution was then poured onto ice (400 cc.). The cream-colored precipitate (6.1 g., 0.032 mole, 93%) was filtered, washed with water, and dried under vacuum for 2 days. The resulting reddish pink solid was extracted with large amounts of 95% ethanol, leaving a light blue solid residue, m.p. 280–290°. Four or five recrystallizations, once with charcoal, from *N,N*-dimethylformamide-water yielded the major product as light yellow needles, m.p. 312–314° dec.; λ_{max} mμ (log ϵ) in 95% C_2H_5OH: 257 (4.41), 263 infl. (4.40), 312 (3.96); ν_{NH} 3140 m and 3090 m (broad), $\nu_{C=O}$ 1650 s, ν_{NO_2} 1511 m and 1345 s or 1326 ms cm.$^{-1}$ in Nujol.

Anal. Calcd. for $C_9H_6N_2O_3$ (190.15): C, 56.84; H, 3.18; N, 14.73. Found: C, 57.22; H, 3.40; N, 14.32, 14.62.

Treatment of the ethanol extracts with charcoal, and subsequent evaporation, left a bright orange-red residue. Two crystallizations from *N,N*-dimethylformamide (DMF)–water gave a yellow solid, m.p. 270–280°, which was dissolved in DMF and chromatographed on an alumina column (2.0 × 30 cm.). Elution with 1:1 DMF–benzene removed a light yellow solid. Two crystallizations from DMF–water gave a light yellow solid, m.p. 265–267°, which still did not appear to be a pure compound and was not further characterized.

6-Nitroisatin (IV).—A solution of chromium trioxide (1.93 g., 0.0193 mole) in acetic acid (10 cc.) and water (2 cc.)

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(5) E. Giovannini and P. Portmann, *Hev. Chim. Acta*, **31**, 1375 (1948).

(6) W. C. Sumpter and W. F. Jones, *J. Am. Chem. Soc.*, **65**, 1802 (1943).

(7) (a) A. M. Berkenheim and R. S. Livshits, *J. Gen. Chem. U. S. S. R.*, **6**, 1025 (1936); *Chem. Abstr.*, **31**, 1779 (1937). (b) H. Rupe and L. Kersten, *Helv. Chim. Acta*, **9**, 578 (1926). (c) E. Chapman and H. Stephen, *J. Chem. Soc.*, **127**, 1791 (1925).

(8) Kindly provided by Dr. Lowell R. Smith; prepared by acetylation of Eastman Kodak Co. white label 2-methyl-5-nitroaniline: (a) Lowell R. Smith, Ph.D. thesis, Univ. of Minnesota, May, 1960, pp. 56–57, 70; followed by oxidation. (b) H. L. Wheeler and B. Barnes, *Am. Chem. Soc. J.*, **20**, 217 (1898).

(9) P. N. James and H. R. Snyder, *Org. Syntheses*, **39**, 30 (1959).

was added dropwise over a period of 15 min. to a mixture of 6-nitro-3-indolealdehyde (1.00 g., 0.00520 mole) and acetic acid (200 cc.). The light yellow solution turned dark brown and all of the 6-nitro-3-indolealdehyde dissolved. The solution was stirred at room temperature for 30 hr., during which time a bright orange solid precipitated. The solid (0.37 g., 0.00193 mole, 37%), m.p. 287–290°, was filtered, washed with water, dried, and recrystallized three times from 95% ethanol, yielding 6-nitroisatin as a mixture of dark orange needles and light yellow fluffy solid, m.p. 288–290° dec.; reported[5] m.p. 288–290° dec.; λ_{max} mμ (log ϵ) in 95% C_2H_5OH: 239 (4.37), 272 infl. (3.85), 339 infl. (3.20), 395 diffuse infl. (3.06); ν_{NH} 3150 m, $\nu_{C=O}$ 1750 s infl., 1741 s, 1711 ms, 1624 s, ν_{NO_2} 1550 s, and 1360 ms or 1335 s cm.$^{-1}$ in Nujol.

Anal. Calcd. for $C_8H_4N_2O_4$ (192.13): C, 50.01; H, 2.10; N, 14.58; C, 50.04; H, 2.29; N, 14.77.

The acetic acid mother liquor was diluted with water (600 cc.) and extracted with ether (6 × 100 cc.). Evaporation of the ether extracts left an orange-brown solid (0.2 g., 0.00104 mole, 20%). One recrystallization from 95% ethanol gave a sample, m.p. 263–273°, shown by its infrared spectrum in Nujol to be 6-nitroisatin contaminated by 6-nitro-3-indolealdehyde starting material.

4-Nitroanthranilic Acid (V). A. By Hydrolysis of *N*-Acetyl-4-nitroanthranilic Acid.—A solution of *N*-acetyl-4-nitroanthranilic acid[8] (1.00 g., 0.00446 mole) and 6 *N* hydrochloric acid (50 cc.) was refluxed for 1.5 hr. The cooled solution was extracted with ether (3 × 125 cc.), and the ether extracts were dried over anhydrous magnesium sulfate and evaporated, leaving a bright orange solid. Recrystallization from 95% ethanol yielded bright orange needles (0.55 g., 0.00302 mole, 68%), m.p. 266–268° dec.; reported: m.p. 263–264°[7a], 264°,[7b] 269°[7c]; ν_{NH} 3460 m, 3360 m, $\nu_{C=O}$ 1683 s, ν_{NO_2} 1528 s, 1362 ms cm.$^{-1}$ in Nujol.

B. By Oxidation of 6-Nitroisatin.—The procedure is essentially that used previously for oxidation of 5-nitroisatin to 5-nitroanthranilic acid.[6] 6-Nitroisatin (0.13 g., 0.00068 mole) was dissolved in aqueous 10% sodium hydroxide solution (5 cc.), 3% hydrogen peroxide solution (4.3 cc.) was added, and the solution was kept at room temperature for 30 min. The solution was filtered through a sintered glass funnel and acidified to *p*H 1 with concd. hydrochloric acid, causing precipitation of a heavy yellow solid (0.11 g., 0.00060 mole, 88%), m.p. 263–266° dec. A mixed melting point with the sample prepared by acid hydrolysis of *N*-acetyl-4-nitroanthranilic acid (see part A, above) was undepressed, and the infrared spectra in Nujol were identical.

Ethyl 3-Indolecarboxylate was prepared by a Grignard coupling reaction from indolemagnesium iodide and ethyl chloroformate.[2,10,11] After elution from alumina with ethyl acetate and three recrystallizations from ethanol–water, our sample had a melting point, 126–127°,[12] higher than the 118–119° reported;[10] λ_{max} mμ (log ϵ) in 95% C_2H_5OH: 213 (4.56), 242 infl. (3.97), 281 (4.06), 286 (4.04); ν_{NH} 3450 m, 3300 m in $CHCl_3$, 3240 ms in Nujol, $\nu_{C=O}$ 1678 s in $CHCl_3$, 1685 m, 1661 s cm.$^{-1}$ in Nujol.[12]

Ethyl 6-nitro-3-indolecarboxylate was prepared in 6% yield by nitration of ethyl 3-indolecarboxylate in acetic acid by the method of Majima and Kotake,[2] who did not state the yield. The product, obtained by elution from alumina and recrystallization from ethanol-water, had a melting point of 200–201°; reported m.p. 198–199°;[2] λ_{max} mμ (log ϵ) in 95% C_2H_5OH: 270 (4.16), 320 (3.72), 329 infl. (3.68); ν_{NH} 3230 m, $\nu_{C=O}$ 1692 s infl., 1679 s, ν_{NO_2} 1521 s, 1349 s cm.$^{-1}$ in Nujol.

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[10] R. Majima and M. Kotake, *Ber.*, **55**, 3865 (1922).

[11] We are indebted to Daryl L. Ostercamp for this preparation.

[12] Donald N. Robinson, Ph.D. thesis, Univ. of Minnesota, March, 1959, p. 129.

Sodium Triphenylgermanethiol. Synthesis of Some New Organothiogermanes

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Only a few organogermanium compounds have been synthesized which contain germanium directly linked to sulfur. Of this type the following have been prepared: R_3GeSR,[2a] R_2GeS,[2b] $(RS)_4Ge$,[3a] $(RS)_3GeX$,[3b] $R_3GeSSGeR_3$,[4] $(R_3Ge)_2S$,[4] and $(R\text{-}GeS)_2S$.[5]

Gilman and Lichtenwalter[6] have reported the synthesis of lithium triphenylsilanethiol in tetrahydrofuran solution by treating triphenylsilyllithium with elemental sulfur. Proof of its existence was established by reaction with several RX type compounds. Solutions of triphenylgermyllithium[7] do not react as smoothly with elemental sulphur as the corresponding silyllithium compound.

The sodium salt of triphenylgermanethiol, on the other hand, may be prepared and isolated in good yields after dropwise addition of a benzene solution of triphenylbromogermane to a freshly prepared suspension of sodium sulfide in ethanol:

$$(C_6H_5)_3GeBr + Na_2S \longrightarrow (C_6H_5)_3GeSNa(I) + NaBr$$

The pure salt (I), although hygroscopic, has been stored in a dessicator containing Drierite for over a month without change. It is soluble in benzene, alcohol, and water. An aqueous solution, alkaline to *p*H paper, becomes turbid after several minutes with the liberation of a hydrogen sulfide-like odor. Refluxing in commercial anhydrous alcohol produces bis(triphenylgermanium) sulfide and sodium sulfide. The reaction is reversible since bis(triphenylgermanium) sulphide when refluxed with excess sodium sulfide produces starting material (I):

$$(C_6H_5)_3GeSNa \underset{XS.Na_2S}{\overset{C_2H_5OH}{\rightleftarrows}} (C_6H_5)_3GeSGe(C_6H_5)_3 + Na_2S$$

The reaction of I with RX type compounds presents a convenient method for the synthesis of sulfur containing organogermanium compounds, Table I:

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[1] Research Fellow sponsored by the Germanium Research Committee.

[2] (a) H. H. Anderson, *J. Org. Chem.*, **21**, 869 (1956). (b) *J. Am. Chem. Soc.*, **78**, 1692 (1956).

[3] (a) H. J. Backer and F. Stienstra, *Rec. trav. chim.*, **52**, 1033 (1933), **54**, 607 (1935). (b) **54**, 38 (1935).

[4] R. Burschkies, *Ber.*, **69**, 143 (1936).

[5] H. Bauer and R. Burschkies, *Ber.*, **65**, 956 (1932).

[6] H. Gilman and G. Lichtenwalter, *J. Org. Chem.*, **25**, 1064 (1960).

[7] H. Gilman and C. W. Gerow, *J. Am. Chem. Soc.*, **77**, 4675 (1955).