was concentrated and a few ml. of water added to the concentrate. On cooling, white needles of 3,4-dimethoxy-2,5-dicarbethoxythiophene were obtained. A further yield of crystals was obtained from the mother liquor by additional concentration. Crystallization from an alcohol–water mixture gave white needles, m.p. 52–53°, 9.5 g. (95.4%).

Anal. Calcd. for $C_{12}H_{16}O_6S$: C, 49.99; H, 5.59. Found: C, 50.13; H, 5.47.

(B) 3,4-Dimethoxy-2,5-dicarbethoxythiophene was also prepared by methylation of the sodium salt, obtained by the reaction between ethyl thiodiacetate and ethyl oxalate, with methyl sulfate. Finely powdered sodium salt (30 g.) was placed in a 500-ml. flask and 80 g. of freshly distilled methyl sulfate was added quickly. The flask was fitted with a reflux condenser having a calcium chloride drying-tube and the contents of the flask were refluxed gently for one-half hour. Excess of methyl sulfate was removed by distillation under reduced pressure. The residue in the flask was treated with 5 per cent. sodium carbonate solution and stirred thoroughly for about 15 minutes to decompose excess methyl sulfate. The contents were cooled in an ice-bath and the solid removed by filtration. The residue was washed with ice-water and the sticky mass was dissolved in a methanol–water mixture and crystallized using Norite. The product could be further purified by recrystallization from petroleum ether or a methanol–water mixture as a solvent to give white needles, m.p. 52–53°, 14.6 g. (50.7%) based on the weight of ethyl thiodiacetate used, mixed m.p. 52–53°.

The ultraviolet absorption spectra in 95% alcohol (Fig. 1) of the dimethoxy compounds were identical.

3,4-Dimethoxy-2,5-dicarboxythiophene.—To a solution of 3 g. (0.0104 mole) of 3,4-dimethoxy-2,5-dicarbethoxythiophene in 100 ml. of methanol in a 250-ml. flask fitted with a reflux condenser was added 2 g. (0.036 mole) of potassium hydroxide in 100 ml. of water and the contents were refluxed for 2 to 4 hours. On cooling, the crystalline mass separated out and was removed by filtration. It was dissolved in a small amount of water, cooled and acidified with dilute hydrochloric acid solution. A further amount of the compound was obtained by concentrating the methanol mother liquor and acidifying with dilute hydrochloric acid as described above. The combined product was crystallized twice from methanol to give white material decomposing at 260° without melting, 2.21 g. (91.5%). Fager[2] reported a decomposition at 250° and a yield of 58.8% based on the weight of methyl thiodiacetate. Fager[2] did not isolate a dimethoxy methyl ester but saponified the reaction mixture from the condensation to obtain the diacid directly.

Anal. Calcd. for $C_8H_8O_6S$: neut. equiv., 116.1; $-OCH_3$, 26.73. Found: neut. equiv., 116; $-OCH_3$, 26.65.

The Fager[2] procedure was repeated to give an identical acid; dec. point, 258°. Ethyl thiodiacetate was used instead of the methyl ester employed by Fager.

3,4-Dimethoxythiophene.—An intimate mixture of 15 g. (0.0647 mole) of 3,4-dimethoxy-2,5-dicarboxythiophene and 2 g. of copper powder was placed in a 150-ml. flask. The latter was connected to a condenser, a receiver and two Dry Ice traps. The flask was heated to 180–190° under a vacuum of about 20–40 mm. The distillate from the receiver and the traps was taken up in ether and the ethereal layer concentrated. The concentrate was then distilled through a small center tube column. The 3,4-dimethoxythiophene distilled at 110° (17 mm.), $n^{25}D$ 1.5386, d^{25}_4 1.2081, 8.15 g. (87.5%). Turnbull[3] reported a b.p. of 100–101.5° (10–11 mm.) and a yield of 70% by reaction of 3,4-dihydroxythiophene with diazomethane. Fager[2] reported a b.p. 108–115° (12 mm.) and a yield of 58% by decarboxylation of 3,4-dimethoxy-2,5-decarboxythiophene with copper chromite in quinoline, but no analysis is given.

Anal. Calcd. for $C_6H_8O_2S$: C, 50.00; H, 5.55. Found: C, 50.34; H, 5.69.

The 3,4-dimethoxythiophene was also prepared according to the procedure described by Fager except that copper powder was used instead of copper chromite. However, the product obtained by this procedure could not be purified and characterized.

3,4-Dimethoxy-2,5-dinitrothiophene.—The nitration of 3,4-dimethoxythiophene was carried out in a similar manner to that described for 2-nitrothiophene in reference 8. From 4 g. (0.0274 mole) of dimethoxythiophene dissolved in 25 ml. of acetic anhydride and 8 g. (0.12 mole) of fuming nitric acid in 50 ml. of glacial acetic acid, crude yellow crystals were obtained. The crystals were washed with ice-water, pressed and dried in a vacuum desiccator. The dry mass was crystallized from petroleum ether (b.p. 60–68°), using Norite to give 4 g. of yellow, needle-like crystals, m.p. 110–115°. Recrystallization twice from petroleum ether (b.p. 60–68°), gave bright yellow needles, m.p. 116.5–117.2°, 3 g. (46.2%).

Anal. Calcd. for $C_6H_6O_6SN_2$: C, 30.80; H, 2.54. Found: C, 30.79; H, 2.58.

Ultraviolet Absorption Spectrum.—The ultraviolet absorption spectrum of 3,4-dimethoxy-2,5-dicarbethoxythiophene was determined with a Beckman quartz ultraviolet spectrophotometer with 95% ethanol as the solvent. The spectrum is shown in Fig. 1 in which the molar extinction coefficients are plotted against the wave lengths in ångström units.

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RECEIVED FEBRUARY 27, 1951

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[8] V. S. Babasinian, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., second edition, p. 466.

The Characterization of Indole-3-acetic Acid and its Esters[1]

BY CARL T. REDEMANN, SYLVAN H. WITTWER AND HAROLD M. SELL

Although several of the esters of indole-3-acetic acid have been described previously[2,3,4] the only means of characterizing these compounds besides saponification and identification of the resulting hydrolysis products has been conversion to the picrates. Hydrolysis followed by identification of the liberated alcohol is a very difficult process when only minute quantities of material, such as might be isolated from plant tissues, are available. Unfortunately, the picrates of many of the esters are so readily soluble that identification of an ester by conversion to the picrate is also unsatisfactory for use with milligram quantities of the esters.

The reaction of 1,3,5-trinitrobenzene with indole-3-acetic acid, as well as with the indole-3-acetates which we have prepared, leads to the formation of addition products which crystallize well, have distinct melting points, and are sufficiently insoluble in cold ethanol to permit ready purification of small quantities of derivative by recrystallization from this solvent.

Experimental

Preparation of the Esters.—The esters of indole-3-acetic acid were prepared from the free acid and the appropriate alcohol, with hydrogen chloride catalyst, as described by Jackson for the ethyl ester.[3] The yields ranged from 60 to 90%.

Inasmuch as neither the *n*-butyl nor the *n*-amyl esters of indole-3-acetic acid have thus far been described, they were recrystallized from petroleum ether (b.p. 30–60°) and analyzed. Their properties are summarized in Table I.

TABLE I

PROPERTIES OF ESTERS OF INDOLE-3-ACETIC ACID .

				Analysis, %					
				Calcd.			Found		
Ester	M.p., °C.	B.p., °C.	Mm.	C	H	N	C	H	N
n-Butyl	29–30	155	0.1	72.7	7.4	6.1	72.7	7.2	6.3
n-Amyl	34–35	156	0.02	73.4	7.8	5.7	73.6	7.7	5.8

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[1] Journal Article No. 1208 from the Michigan Agricultural Experiment Station, East Lansing. This research was supported by the Horace H. Rackham Research Endowment of Michigan State College.

[2] T. Hoshino and K. Shimodaira, *Ann.*, **520**, 19 (1935).

[3] R. W. Jackson, *J. Biol. Chem.*, **88**, 659 (1930).

[4] F. Kögl and D. G. F. R. Kostermans, *Z. physiol. Chem.*, **235**, 201 (1935).

TABLE II

PROPERTIES OF 1,3,5-TRINITROBENZENE ADDUCTS OF INDOLE-3-ACETIC ACID AND OF SEVERAL ESTERS OF INDOLE-3-ACETIC ACID

Trinitrobenzene derivative of	M.p., °C.	Color	Formula	Analyses, % Calcd. C	H	N	Found C	H	N
Indole-3-acetic acid	199 dec.	Orange	$C_{16}H_{12}N_4O_8$	49.5	3.1	14.4	49.7	2.9	14.4
Methyl ester	135	Yellow	$C_{17}H_{14}N_4O_8$	50.8	3.6	13.9	50.8	3.6	13.6
Ethyl ester	88	Yellow	$C_{18}H_{16}N_4O_8$	51.9	3.9	13.5	51.9	3.8	13.4
n-Propyl ester	111	Yellow	$C_{19}H_{18}N_4O_8$	53.0	4.2	13.0	53.2	4.4	13.2
n-Butyl ester	101	Yellow	$C_{26}H_{20}N_4O_8$	54.1	4.5	12.6	54.4	4.4	12.8
n-Amyl ester	96	Yellow	$C_{21}H_{22}N_4O_8$	55.0	4.8	12.2	54.9	5.0	12.1

Preparation of the Addition Products.[5]—One millimole of the indole-3-acetic acid derivative and one millimole of 1,3,5-trinitrobenzene were dissolved in 10 ml. of hot absolute ethanol and placed in the refrigerator to cool. The crystals which formed were recrystallized once from absolute ethanol and dried at room temperature *in vacuo* over phosphorus pentoxide prior to analysis. The properties of these derivatives are shown in Table II.

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[5] J. J. Sudborough, *J. Chem. Soc.*, **109**, 1339 (1916).

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RECEIVED JANUARY 9, 1951

A Preparative Method for Thiosemicarbazones of Aromatic Aldehydes[1]

BY BRUNO PUETZER, WILLIAM E. HAMLIN[2] AND LEON KATZ

In the course of experiments designed to prepare chemotherapeutically active thiosemicarbazones a new method was sought which would eliminate the use of thiosemicarbazide. It has been found that an aqueous solution of hydrazinium thiocyanate will react with aromatic aldehydes in the presence of acetic acid to give the respective thiosemicarbazones directly. The products listed in Table I were prepared this way and compared with products made from the aromatic aldehyde and thiosemicarbazide.

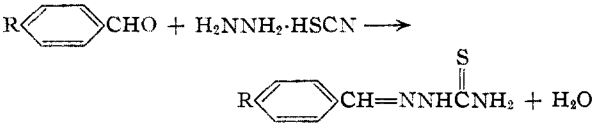

TABLE I

BENZALDEHYDE THIOSEMICARBAZONES

Benzaldehyde	Yield, %	M. p., °C., dec. [a]	[b]
$4-CH_3CONH$	86	234–236	235–236
$4-(CH_3)_2N$	97	211–214	214–215
4-OH	88	229–231	231–232
2-OH	81	220–223	228–229
$4-NO_2$	86	247–249	257–259

[a] Material isolated directly from reaction mixture, not recrystallized. [b] Recrystallized material prepared by condensation of thiosemicarbazide and the respective benzaldehyde. All melting points were uncorrected.

Experimental

Preparation of Hydrazinium Thiocyanate Solution.—Into a 4-l. beaker were charged 485 g. (5.0 moles) potassium thiocyanate, 425 g. (95% real, 2.50 moles real) dihydrazine sulfate, and 1 l. of water. The mixture was stirred and heated to 95° in 20 minutes, held at 95° five minutes, and cooled to 10° in three-quarter hour. The white slurry of potassium sulfate was collected on a Büchner funnel containing a thin bed of filter-cel, sucked well and the cake washed with 50 ml. of water. The volume of the filtrate was 1335 ml., equivalent to 0.00375 mole of hydrazinium thiocyanate per ml. This solution was used without further analysis.

4-Dimethylaminobenzaldehyde Thiosemicarbazone.—Into a 500-ml. three-necked flask equipped with a glas-col mantle, sealed stirrer, reflux condenser and thermometer were charged 28.5 g. (0.191 mole) of dimethylaminobenzaldehyde and 150 ml. of glacial acetic acid. This mixture was stirred and heated to 100°. Ninety-five ml. of the hydrazinium thiocyanate solution described above (0.356 mole) was heated to 100° and added to the acetic acid solution. After five minutes a red precipitate began to appear. The slurry was held at 95–100° for one hour longer, cooled to 10°, and filtered through a Büchner funnel. The cake was washed with 500 ml. of water and dried *in vacuo* at 65° for 15 hours. The weight of solid, m.p. 211–214° dec., was 40.7 g. An additional 0.5 g. of material was obtained from the filtrate.

As a solvent for the aromatic aldehydes ethanolic acetic acid of varying composition can be employed. A series of experiments were run with 4-acetylaminobenzaldehyde to determine the optimum usage of hydrazinium thiocyanate. An excess of 25–50% appeared to give the optimum yields.

Fractional crystallization from glacial acetic acid of the thiosemicarbazone formed from 4-nitrobenzaldehyde led to the isolation of a small quantity of azine; m.p. 307–309°. *Anal.* Calcd. for $C_{14}H_{10}O_4N_4$: C, 56.38; H, 3.36; N, 18.78. Found: C, 56.50; H, 3.30; N, 18.97.

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RECEIVED FEBRUARY 1, 1951

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[1] After the completion of this work a report by Stig Sunner (*C. A.*, **45**, 548b (1951)) appeared which described the reaction of hydrazinium thiocyanate with acetone to yield acetone thiosemicarbazone. At least two products were formed in this reaction whereas we obtained only the respective thiosemicarbazone under the conditions described in the experimental section with the exception of 4-nitrobenzaldehyde. In this case less than 5% of azine was isolated.

[2] The Upjohn Co., Kalamazoo, Mich.

The Double Sulfates of Zirconium and the Bivalent Metals

BY S. R. PATEL

A series of compounds of the type $RSO_4 \cdot Zr(SO_4)_2$ (where R = a bivalent metal) has been prepared (Table I). The compound $MgSO_4 \cdot Zr(SO_4)_2$ a typical example, was obtained by heating together 0.1 g. of zirconium nitrate (=0.04 g. zirconia) and 0.025 g. to 0.4 g. of $MgSO_4 \cdot 7H_2O$ in 40 cc. of sulfuric acid (sp. gr. 1.79). A clear solution was first obtained from which on further concentration a precipitate separated which after washing free from adhering sulfuric acid with absolute alcohol and then drying at 230° agreed with the formula $MgSO_4 \cdot Zr(SO_4)_2$.

TABLE I

R	Calcd., % R	Zr	SO_4	Found, % R	Zr	SO_4
Mg	6.024	22.59	71.39	5.58	22.73	71.60
Zn	14.70	20.50	64.79	15.11	20.18	65.05
Cd	22.85	18.55	58.60	22.63	18.51	58.54
Co	13.45	20.81	65.75	13.82	20.71	66.05
Mn	12.65	21.00	66.36	12.48	21.19	66.52