Anal. Calcd. $C_{21}H_{27}NO_5S$: C, 62.20; H, 6.71; N, 3.45; S, 7.91. Found: C, 62.38; H, 6.69; N, 3.53; S, 7.78.

Nicotinic Acid Methochloride.—The synthesis was performed in the same manner as that reported above for isonicotinic acid methochloride. A 92% yield of product, m.p. 258–259° dec., was obtained (lit.[8] m.p. 245–250° dec.)

Anal. Calcd. for $C_7H_7NO_2 \cdot HCl$: C, 48.53; H, 4.65; N, 8.07; Cl, 20.42. Found: C, 48.72; H, 4.47; N, 7.80; Cl, 19.95.

***dl*-1-Methyl-3-carboxypiperidine Hydrochloride.**—The reduction of nicotinic acid methochloride by the procedure reported above for the reduction of isonicotinic acid methochloride gave a quantitative yield of a product, m.p. 201.5–202.5° dec.

Anal. Calcd. $C_7H_{13}NO_2 \cdot HCl$: C, 46.81; H, 7.86; N, 7.80; Cl, 19.74. Found: C, 46.81; H, 735; N, 7.70; Cl, 19.69.

***dl*-1-Methyl-3-benzoylpiperidine.**—The acyl chloride of *dl*-1-methyl-3-carboxypiperidine hydrochloride was allowed to react under the Friedel–Crafts conditions described above for the 4-isomer to give an 89% yield of the desired product, b.p. 119–120° (0.2 mm.). The material was crystallized from Skelly A, m.p. 34–35°. The hydrochloride salt was recrystallized from acetone, m.p. 176–177° dec.

Anal. Calcd. for $C_{13}H_{17}NO \cdot HCl$: C, 65.13; H, 7.57; N, 5.84; Cl, 14.79. Found: C, 65.67; H, 7.68; N, 6.04; Cl, 14.50.

The methyl *p*-toluenesulfonate was recrystallized from ethanol–ethyl acetate, m.p. 225–226° dec.

Anal. Calcd. $C_{21}H_{27}NO_4S$: C, 64.75; H, 6.99; N, 3.60; S, 8.23. Found: C, 64.63; H, 6.94; N, 3.52; S, 8.20.

***dl*-1-Methyl-3-benzoyl-3-chloropiperidine.**—The chlorination procedure used for the preparation of the 4-isomer gave a 93% yield of the 3-isomer, m.p. 169.5–170.5° dec. when recrystallized from chloroform.

Anal. Calcd. for $C_{13}H_{16}NOCl$; C, 56.94; H, 6.25; N, 5.11; Cl, 25.86. Found: C, 57.16; H, 6.37; N, 5.40; Cl, 26.00.

The free amine had m.p. 25–25.5° when recrystallized from Skelly A.

Rearrangement of *dl*-1-Methyl-3-chloro-3-benzoylpiperidine.—The conditions described above for the rearrangement of 1-methyl-4-chloro-4-benzoylpiperidine (VI) were modified in the following manner. To a refluxing mixture of 4.80 g. (0.120 mole) of finely powdered, dry sodium hydroxide in 200 ml. of dry xylene was added 50 ml. of a xylene solution containing 5.94 g. (0.025 mole) of *dl*-1-methyl-3-chloro-3-benzoylpiperidine. The mixture was cooled and the volume reduced to 50 ml.; 100 ml. of ether was added and the organic phase was extracted with 10-ml. portions of water until the aqueous washings were nearly neutral. The combined aqueous extract was acidified to *p*H 2.0 with hydrochloric acid and extracted with ether. The aqueous acidic solution was concentrated under vacuum and the dried residue extracted in a Soxhlet extractor with glacial acetic acid. The extract was concentrated to 15 ml. and 100 ml. of ether was added. A buff powder precipitated, m.p. 267–270° dec. This material was dissolved in 4 ml. of 2% sodium hydroxide. After adding 1 ml. of acetic acid, the solution was evaporated to dryness. The residue was sublimed under reduced pressure at 210° and the sublimate recrystallized from chloroform to give 420 mg. (7.7%) of 1-methyl-3-phenyl-3-carboxypiperidine, m.p. 250–250.5° dec.

Anal. Calcd. for $C_{13}H_{17}NO_2$: C, 71.20; H, 7.81; N, 6.39. Found: C, 71.19; H, 7.79; N, 6.37.

***dl*-1-Methyl-3-hydroxy-3-benzoylpiperidine.**—The organic phase from the above rearrangement was treated as previously outlined for the 4-isomer. The resulting viscous oil was crystallized from Skelly A to give 4.16 g. (0.19 mole, 76%) of a white crystalline product, m.p. 53–53.5°.

Anal. Calcd. for $C_{13}H_{17}NO_2$: C, 71.20; H, 7.81; N, 6.39. Found: C, 71.19; H, 8.33; N, 6.26.

The methyl *p*-toluenesulfonate was prepared and crystallized from ethanol–ethyl acetate, m.p. 192–193° dec.

Anal. Calcd. for $C_{21}H_{27}NO_5S$: C, 62.20; H, 6.71; N, 3.45; S, 7.91. Found: C, 62.54; H, 6.60; N, 3.87; S, 8.23.

The hydrochloride, m.p. 162–163° dec., was crystallized from ethanol–ethyl acetate.

Anal. Calcd. for $C_{13}H_{17}NO_2 \cdot HCl$: C, 61.05; H, 7.09; N, 5.48; Cl, 13.86. Found: C, 60.51; H, 6.99; N, 5.78; Cl, 14.12.

(8) R. Turneau, *Monatsh.*, **26**, 552 (1905).

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[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY, UNIVERSITY OF MINNESOTA]

The Nitroethylation of Indoles. III.[1-3] A Synthetic Route to Substituted Tryptamines

BY WAYLAND E. NOLAND AND RONALD F. LANGE[4]

RECEIVED JULY 28, 1958

The previously described nitroethylation of indole has been extended successfully to four readily available substituted indoles: 2-methylindole, 1,2-dimethylindole, 1-methylindole and 2-phenylindole. As had been the case with indole, the best yields of adducts were obtained with β-nitrostyrene, with good yields of adducts also often obtainable from β-methyl-β-nitrostyrene, and lesser yields from the other nitroölefins tried. Catalytic hydrogenation of the adducts yielded the corresponding tryptamines, which were converted to phthalimide derivatives. Indole–nitroölefin addition appears to be a quite general synthetic route to tryptamines from substituted indoles, as well as from indole itself.

The addition of unsubstituted indole to the nitroolefins, nitroethylene, 1-nitropropene, β-nitrostyrene and β-methyl-β-nitrostyrene, forming the adducts Ia–Id, has been described previously.[1,2] The nitroethylene adduct Ia also has been prepared by other methods[5-7] and has been proposed

(1) Paper I, W. E. Noland and P. J. Hartman, THIS JOURNAL, **76**, 3227 (1954).

(2) Paper II, W. E. Noland, G. M. Christensen, G. L. Sauer and G. G. S. Dutton, *ibid.*, **77**, 456 (1955).

(3) Presented in part as Paper 10 before the Organic Division at the 132nd National Meeting of the Am. Chem. Soc., New York, N. Y., Sept. 9, 1957, Abstracts p. 6P.

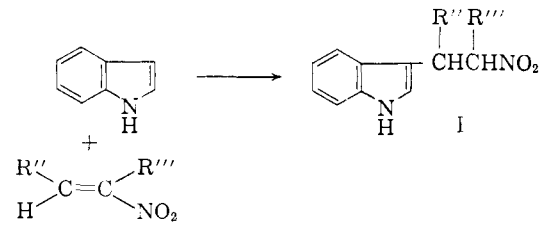
(4) Taken in part from the Ph.D. thesis of Ronald F. Lange, University of Minnesota, June, 1958. We gratefully acknowledge the financial support provided R. F. L. through academic year fellowships by the Ethyl Corporation and the Monsanto Chemical Co., and through summer fellowships provided by the Procter and Gamble Co. and the Hercules Powder Co. A part of the work described here was carried out by students in the advanced organic chemistry laboratory course at the University of Minnesota. Particular credit is due to: (a) Richard E. Duvall, (b) Kenneth J. Krost, (c) Kathleen E. Jongedyk, (d) Arnold A. Liebman, (e) Donald C. Johnson, (f) Elmer W. Lippmann, Jr., (g) Lois E. Kelley. We are also indebted to Donald N. Robinson and James A. Elberling for carrying out several reactions.

(5) D. I. Weisblat and D. A. Lyttle (to the Upjohn Co.), U. S. Patent 2,616,896, Nov. 4, 1952.

(6) D. A. Lyttle and D. I. Weisblat, THIS JOURNAL, **77**, 5747 (1955).

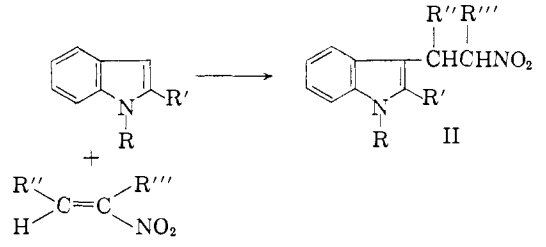
(7) D. W. Henry and E. Leete, *ibid.*, **79**, 5254 (1957).

as an intermediate in another reaction.[8] The hypothetical adducts of 2-nitro-1-propene (Ie) and 2-nitro-1-butene (If) have been prepared by another method.[9]



	R″	R‴		R″	R‴
Ia	H	H	Id	C_6H_5	Me
Ib	Me	H	Ie	H	Me
Ic	C_6H_5	H	If	H	Et

The purpose of the present work was to develop a general synthetic route to substituted 3-(2-nitroethyl)-indoles and the corresponding tryptamines by extending the indole reaction to substituted indoles. For this purpose we have studied the addition to nitroölefins of four readily available indoles having substituents in the 1- and 2-positions. The resulting adducts (IIa–IIj) are summarized in Table I, and their more important spectral properties are given in Table Ia.



	R	R′	R″	R‴
IIa	H	Me	H	H
IIb	H	Me	C_6H_5	H
IIc	H	Me	C_6H_5	Me
Id	H	Me	C_6H_5	Et
IIe	Me	Me	H	H
IIf	Me	Me	C_6H_5	H
IIg	Me	Me	C_6H_5	Me
IIh	Me	H	C_6H_5	H
IIi	H	C_6H_5	C_6H_5	H
IIj	H	C_6H_5	C_6H_5	Me

Equimolar portions of the indole and the nitroolefin were allowed to react without solvent, except that with the most reactive nitroölefin, nitroethylene, benzene was used as a solvent to moderate the otherwise too violent reaction with 2-methylindole. Room temperature was used in this case, as well as in the reactions of nitroethylene with 1,2-dimethylindole and 1-methylindole, which were carried out similarly in benzene solution. The yields diminished in going from 2-methylindole (58%) to 1,2-dimethylindole (9%), and with 1-methylindole no crystalline adduct was obtained. The trend of decreasing melting points (with the exception of IIb) in going down the series of adducts from 2-methylindole, 1,2-dimethylindole, indole[1,2] and 1-methylindole suggests that, if it was formed, the adduct from 1-methylindole and nitroethylene may have been an oil.

The great reactivity of most of the aliphatic nitroölefins, such as nitroethylene, is an adverse factor in the yields and purity of the adducts. Polymerization of the nitroölefin is an important competing reaction, as well as, possibly, reaction of the nitroölefin with an addition intermediate or with the adduct itself. The dark brown, tarry reaction mixtures were treated with charcoal, filtered, and concentrated. Treatment of these residues with methanol gave brownish crystalline solids having melting points considerably below those of the analytical samples. It was felt, however, that the weight of product at this point, before further purification, gives the best comparative indication of the total amount of adduct actually formed in the reactions; the yields (reported in Table I) were determined only at this point. Further purification was effected by repeated recrystallization, with charcoal, from methanol or light petroleum (b.p. 60–68°).

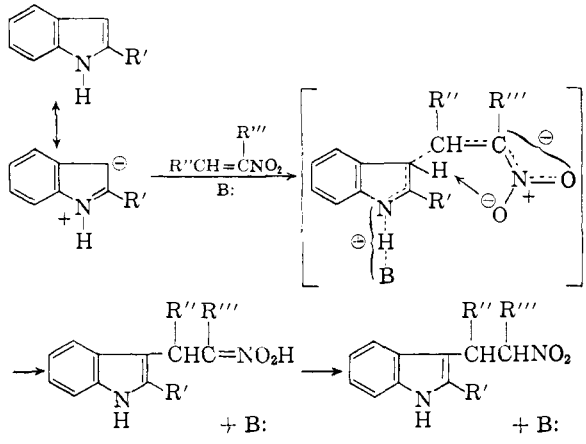
The reactions of β nitrostyrene with 2-methylindole and 1,2-dimethylindole proceed in the best yields (93–95%), with few side reactions Undoubtedly, the reduced tendency of the nitroölefin to polymerize, combined with a still satisfactory level of reactivity toward indole addition, are favorable factors here. Homogeneity was effected by warming an intimate mixture of the reactants for 2–5 min. on the steam-bath. The reddish oils were then kept at room temperature for several (2–12) hr. until they had set to a reddish glass, or had crystallized. Recrystallization from methanol–water gave light brown crystalline solids, on which the yields were determined. Further purification was effected by recrystallization, with charcoal, from methanol–water, ethanol or methylene chloride–light petroleum (b.p. 60–68°). A similarly good yield (73%) was obtained by warming a mixture of 2-phenylindole and β-nitrostyrene for 20 min. on a steam-bath, with subsequent standing overnight at room temperature.

β-Methyl-β-nitrostyrene is considerably less reactive toward indoles than β-nitrostyrene. Nevertheless, satisfactory yields (48–69%) of adducts can be obtained by increasing the severity of the reaction conditions, a factor which is possible because β-methyl-β-nitrostyrene showed no tendency to polymerize. Warming with 2-methylindole and 1,2-dimethylindole was carried out at 85–100° for 5 hr. Even then, additional adduct could sometimes be recovered by concentrating and rewarming unreacted material obtained from the ethanol filtrate and washes from crystallization of the first product. Purification was accomplished by recrystallization, with charcoal, from methanol or ethanol. An adduct was obtained in low yield (18%) from 2-phenylindole and β-methyl-β-nitrostyrene by heating at 130° for 8 hr. In keeping with the lower reactivity of 1-methylindole, however, an attempt to form an adduct by heating with β-methyl-β-nitrostyrene gave no crystalline product. That other β-alkyl-β-nitrostyrenes will also form adducts with sufficiently reactive indoles is shown by the formation of an adduct in satisfactory yield (51%) from β-ethyl-β-nitrostyrene[10]

(8) H. Hellman and D. Starck, *Angew. Chem.*, **70**, 271 (1958).
(9) H. R. Snyder and L. Katz, THIS JOURNAL, **69**, 3140 (1947).
(10) H. B. Hass, A. G. Susie and R. L. Heider, *J. Org. Chem.*, **15**, 8 (1950).

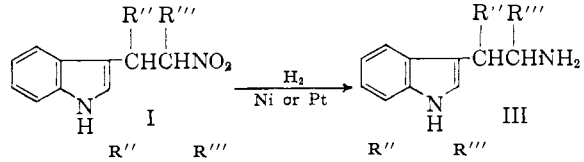
and 2-methylindole after warming the reactants on a steam-bath just long enough to form a homogeneous solution, then standing 5 days at room temperature.

1-Methylindole is markedly less reactive than the 2-substituted indoles. The best yield (51%) of adduct from 1-methylindole and β-nitrostyrene was obtained after the reaction mixture, which had initially been warmed on the steam-bath for 15 min., had been allowed to stand for 281 days at room temperature. The reaction can be accelerated when desired, however, by heating: a fair yield (28%) was obtained after warming 1-methylindole and β-nitrostyrene on a steam-bath for 3 days. Our qualitative observations in this and earlier[1,2] work indicate this reactivity series for the indoles studied: 2-methylindole ≥ 1,2-dimethylindole > 2-phenylindole > indole > 1-methylindole. Skatole, having an already occupied 3-position, appeared to be unreactive, at least toward β-nitrostyrene. The enhanced reactivity of the 2-substituted indoles, particularly with a 2-methyl substituent, may be attr.buted to the favorable electronic effect of the 2-substituent in stabilizing the build-up of negative charge at the 3-position in the transition state. What appears to be an attractive formulation involving a 6-membered ring transition state for indole-nitroölefin addition is



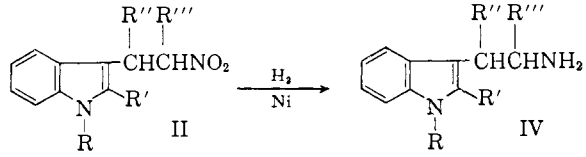
The relatively low reactivity of 1-methylindole may be accounted for on the basis that it has no proton at the 1-position which can be lost at least partially to a base in the transition state. Consequently, all of the developing positive charge (resulting from donation of electrons to the 3-position) must be centered on nitrogen in the 1-position. In this case the solvation requirements of the transition state may well be higher than in cases where a proton can be at least partially lost from the nitrogen.

A number of 3-(2-nitroethyl)-indole derivatives (Ia, c, e, f) have been catalytically hydrogenated to the corresponding tryptamines (III),[1,2,5,6,9] showing that they are suitable intermediates for a general synthesis of tryptamines. We have now similarly hydrogenated the 1-nitro-1-propene adduct (Ib)[2] to the corresponding tryptamine (IIIb), previously prepared by another method. The melting point of the picrate, 224–226°, is in agreement with that previously reported,[11] 224°.



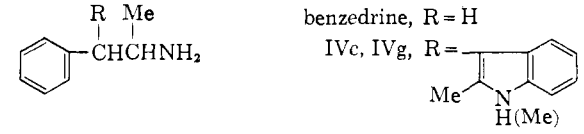
	R″	R‴		R″	R‴
IIIa	H	H	IIIc	C_6H_5	H
IIIb	Me	H	IIIe	H	Me
			IIIf	H	Et

The substituted indole-nitroölefin adducts (II) were hydrogenated at 2 atm. pressure over Raney nickel catalyst in absolute ethanol (IIa, b, g, h, i), ethyl acetate (IIc) or dioxane (IIf) solutions. The corresponding tryptamines (IV), obtained in fair to good yields, are described in Tables II and IIa. The solid tryptamines were purified by recrystallization from ethanol.



	R	R′	R″	R‴
IVa	H	Me	H	H
IVb	H	Me	C_6H_5	H
IVc	H	Me	C_6H_5	Me
IVf	Me	Me	C_6H_5	H
IVg	Me	Me	C_6H_5	Me
IVh	Me	H	C_6H_5	H
IVi	H	C_6H_5	C_6H_5	H

The melting point of the picrate of the tryptamine (IVa) derived from the 2-methylindole–nitroethylene adduct (IIa) was in complete agreement with the melting point of the picrate from the same tryptamine, previously prepared by other methods.[12,13] The 1,2-dimethylindole adducts (IIf, IIg) took up hydrogen very slowly and several days were required for complete reduction. Reduction of the β-methyl-β-nitrostyrene adduct (IIg) took place only when a large excess of catalyst was used. Two attempts to hydrogenate the adduct of 2-phenylindole and β-methyl-β-nitrostyrene (IIj) gave neither unreacted adduct nor the corresponding tryptamine. It is interesting to note the structural similarity between the tryptamines (IVc, IVg) derived from β-methyl-β-nitrostyrene adducts and the sympathomimetic amine, benzedrine.

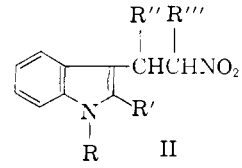


All of the new tryptamines were converted to phthalimide derivatives (V), described in Tables III and IIIa. The phthalimides are desirable derivatives because they specifically characterize the primary amino group, and have conveniently high melting points and low solubilities.

(11) K. Eiter and O. Svierak, *Monatsh.*, **83**, 1453 (1952).
(12) T. Hoshino and K. Tamura, *Ann.*, **500**, 42 (1933).
(13) T. Hoshino and K. Shimodaira, *ibid.*, **520**, 19 (1935).

TABLE I

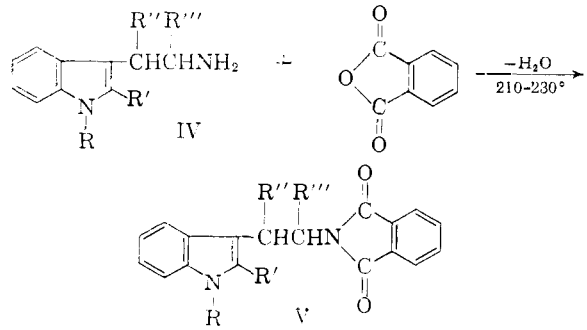
3-(2-NITROETHYL)-INDOLES



II

	R	R′	R″	R‴	Mol. formula, weight	M.p., °C.	Best yield, %	C, % Calcd. Found	H, % Calcd. Found	N, % Calcd. Found
	-Indole									
IIa	H	Me	H	H	$C_{11}H_{12}N_2O_2$	89–90	58	64.69	5.92	13.72
	2-Methyl-3-(2-nitroethyl)-				204.22			64.65	5.80	13.48
IIb	H	Me	C_6H_5	H	$C_{17}H_{16}N_2O_2$	104–105	95	72.84	5.75	9.99
	2-Methyl-3-(1-phenyl-2-nitroethyl)-				280.31			72.60	5.63	9.74
IIc	H	Me	C_6H_5	Me	$C_{18}H_{18}N_2O_2$	198–199	69	73.47	6.12	9.52
	2-Methyl-3-(1-phenyl-2-nitropropyl)-				294.34			73.48	6.20	9.35
IId	H	Me	C_6H_5	Et	$C_{19}N_{20}N_2O_2$	177.5–179.5	51	74.00	6.54	9.09
	2-Methyl-3-(1-phenyl-2-nitrobutyl)-				308.37	170.5–172.5[a]		74.18	6.27	9.13
IIe	Me	Me	H	H	$C_{12}H_{14}N_2O_2$	71–72	9	66.03	6.47	12.84
	1,2-Dimethyl-3-(2-nitroethyl)-				218.25			66.40	6.59	12.66
IIf	Me	Me	C_6H_5	H	$C_{18}H_{18}N_2O_2$	139–140	93	73.45	6.16	9.52
	1,2-Dimethyl-3-(1-phenyl-2-nitroethyl)-				294.34			73.41	6.31	9.67
IIg	Me	Me	C_6H_5	Me	$C_{19}H_{20}N_2O_2$	177–178	48	74.00	6.54	9.09
	1,2-Dimethyl-3-(1-phenyl-2-nitropropyl)-				308.37			74.19	6.65	8.99
IIh	Me	H	C_6H_5	H	$C_{17}H_{16}N_2O_2$	94–95	51	72.84	5.75	9.99
	1-Methyl-3-(1-phenyl-2-nitroethyl)-				280.31			72.54	5.79	9.76
IIi	H	C_6H_5	C_6H_5	H	$C_{22}H_{18}N_2O_2$	144–147	73	77.17	5.30	8.18
	2-Phenyl-3-(1-phenyl-2-nitroethyl)-				342.38			77.57	5.34	7.99
IIj	H	C_6H_5	C_6H_5	Me	$C_{23}H_{20}N_2O_2$	226–228	18	77.50	5.66	7.86
	2-Phenyl-3-(1-phenyl-2-nitropropyl)-				356.41			77.09	5.63	8.04

[a] Dual m.p.



IV V

Experimental

Melting points were determined on calibrated hot-stages.

2-Methylindole was prepared from acetyl-*o*-toluidine by the Madelung synthesis.[14]

1,2-Dimethylindole was prepared from 2-methylindole by methylation with dimethyl sulfate or methyl iodide[15] and sodamide in liquid ammonia.

1-Methylindole was prepared from indole by methylation with dimethyl sulfate[16] or methyl iodide[15] and sodamide in liquid ammonia.

2-Phenylindole was prepared from acetophenone phenylhydrazone by the Fischer indole synthesis.[17]

3-(2-Nitroethyl)-indoles (II).—Five examples illustrating the preparation of substituted indole-nitroölefin adducts are described below:

2-Methyl-3-(2-nitroethyl)-indole (IIa).—A solution of nitroethylene[18,19] (36.5 g., 0.500 mole) in benzene (150 cc.) was added, with vigorous stirring, over a period of 40 min. to a solution of 2-methylindole (65.5 g., 0.500 mole) in benzene (150 cc.) at room temperature. The solution became brown and darkened throughout the addition period. Stirring was continued for one hour at room temperature; the lachrymatory odor of nitroethylene was not detectable at the end of this time. Charcoal (several teaspoonsful) was added to the dark brown solution and then the solution was boiled to one-half its volume and filtered. Further concentration of the filtrate by distillation left a brown oily residue. Trituration of the residue with cold methanol (75 cc.) resulted in crystallization of a brown solid (25.9 g.), m.p. 84–85°. Repetition of the work-up procedure gave two additional fractions of adduct: 20.4 g., m.p. 78–82°, and 12.7 g., m.p. 60–85°. The total yield was 59.0 g., 0.289 mole, 58%. Three recrystallizations of the combined fractions from methanol, with charcoal, gave pale yellow crystals, m.p. 89–90°. Two additional recrystallizations from light petroleum (b.p. 60–68°) yielded the analytical sample of 2-methyl-3-(2-nitroethyl)-indole as fluffy white needles, m.p. 89–90°.

2-Methyl-3-(1-phenyl-2-nitroethyl)-indole (IIb).—2-Methylindole (6.55 g., 0.0500 mole) and β-nitrostyrene[20] (7.45 g., 0.0500 mole) were mixed, causing the immediate appearance of a reddish-orange color and the formation of a red oil after a short time. The oily mixture was warmed gently on the steam-bath for 5 min. and then set aside for 2 hr. at room temperature. The resulting reddish glass was dissolved in hot methanol (120 cc.) and diluted with hot water (80 cc.). Cooling caused crystallization of a light brown solid (10.97 g.), m.p. 90–100°. Further dilution of the filtrate with water gave more light brown solid (2.29 g.), m.p. 78–85°. The total yield was 13.26 g., 0.0474

(14) C. F. H. Allen and J. Van Allan, in E. C. Horning, "Organic Syntheses." Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1955, p. 597; *Org. Syntheses*, **22**, 94 (1942).

(15) K. T. Potts and J. E. Saxton, *J. Chem. Soc.*, 2641 (1954).

(16) H. Plieninger, *Chem. Ber.*, **87**, 127 (1954).

(17) R. L. Shriner, W. C. Ashley and E. Welch, in "Organic Syntheses," Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1955, p. 725; *Org. Syntheses*, **22**, 98 (1942).

(18) G. D. Buckley and C. W. Scaife, *J. Chem. Soc.*, 1471 (1947).

(19) W. E. Noland, H. I. Freeman and M. S. Baker, THIS JOURNAL, **78**, 188 (1956).

(20) D. E. Worrall, in H. Gilman and A. H. Blatt, "Organic Syntheses," Coll. Vol. I, 2nd ed., John Wiley and Sons, Inc., New York, N. Y., 1941, p. 413; 1st ed., 1932, p. 405; *Org. Syntheses*, **9**, 66 (1929).

TABLE Ia

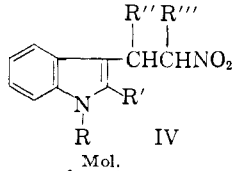
SPECTRAL DATA ON 3-(2-NITROETHYL)-INDOLES

	Ultraviolet[c]					Infrared frequencies, cm.$^{-1}$ NH		NO_2	
						Nujol	$CHCl_3$	Nujol	$CHCl_3$
IIa	223			282	289	3370	3460	1556	1552
	(4.58)			(3.86)	(3.79)			1381	1383
IIb	222	274[a]	279	282	290	3370	3440	1547	1551
	(4.57)	(3.86)	(3.88)	(3.89)	(3.82)			1373	1379
IIc	223	274[a]	279		289	3360	3420	1547	1547
	(4.46)	(3.83)	(3.84)		(3.77)			1386 or 1360	1388 or 1368
IId	223		279		289	3390	3440	1544	1548
	(4.54)		(3.85)		(3.79)			1375	1372
IIe	225		279	285	292[a]	None	None	1544	1553
	(4.56)		(3.83)	(3.87)	(3.82)			1382	1382
IIf	225		278[a]	285	292[a]	None	None	1548	1553
	(4.56)		(3.81)	(3.85)	(3.81)			1379	1377
IIg	226		278[a]	285	292[a]	None	None	1546	1553
	(4.51)		(3.81)	(3.85)	(3.82)			1387 or 1359	1391 or 1362
IIh	223		277[a]	287	296[a]	None	None	1548	1548
	(4.57)		(3.76)	(3.81)	(3.73)			1375	1375
IIi[b]	220	234[a]			300	3420	...	1555	..
	(4.51)	(4.40)			(4.23)			1385	
IIj[b]	221	235[a]			299	3420	...	1561	..
	(4.53)	(4.40)			(4.17)			1393 or 1365	

[a] Inflection. [b] Compare with 2-phenyl-3-methylindole: 228.5 (4.37), 237.5[a] (4.35), 307.5 (4.32); C. E. Blades and A. L. Wilds, *J. Org. Chem.*, **21**, 1013 (1956). [c] Wave lengths of maxima in 95% ethanol are given in mμ with intensities in log ε beneath them in parentheses.

TABLE II

TRYPTAMINES



IV

	Indole R	R'	R''	R'''	Mol. formula, weight	M.p., °C.	C, % Calcd.	C, % Found	H, % Calcd.	H, % Found	N, % Calcd.	N, % Found
IVa	H	Me	H	H	$C_{11}H_{14}N_2 \cdot C_6H_3N_3O_7$	Picrate,	50.62		4.25		17.36	
	2-Methyl-3-(2-aminoethyl)-picrate				403.35	218–219 d.[a]	50.88		4.44		17.42	
IVb	H	Me	C_6H_5	H	$C_{17}H_{18}N_2$	158–160	81.56		7.25		11.19	
	2-Methyl-3-(1-phenyl-2-aminoethyl)-				250.33	150–152[b]	81.57		7.26		11.22	
IVc	H	Me	C_6H_5	Me	$C_{18}N_{20}N_2$	183–184	81.78		7.63		10.60	
	2-Methyl-3-(1-phenyl-2-aminopropyl)-				264.36		81.84		7.46		10.50	
IVf	Me	Me	C_6H_5	H	$C_{18}H_{20}N_2 \cdot HCl$	Oil, HCl	71.86		7.04		9.31	
	1,2-Dimethyl-3-(1-phenyl-2-aminoethyl)-HCl				300.82	259–261	71.85		6.94		9.03	
IVg	Me	Me	C_6H_5	Me	$C_{19}H_{22}N_2$	123–126	81.97		7.97		10.06	
	1,2-Dimethyl-3-(1-phenyl-2-aminopropyl)-				278.38		81.81		7.51		9.78	
IVh	Me	H	C_6H_5	H	$C_{17}H_{18}N_2$	Oil	...		..		...	
	1-Methyl-3-(1-phenyl-2-aminoethyl)-				250.33							
IVi	H	C_6H_5	C_6H_5	H	$C_{22}H_{20}N_2$	180–182	84.58		6.45		8.97	
	2-Phenyl-3-(1-phenyl-2-aminoethyl)-				312.40		84.57		6.65		8.80	

[a] Reported m.p. 218–219° d. (ref. 12), but no C and H analysis given. [b] Dual m.p., probably due to a mixture of dimorphic forms.

mole, 95%. Three recrystallizations of the combined solids from methanol–water, with charcoal, yielded the analytical sample of 2-methyl-3-(1-phenyl-2-nitroethyl)-indole as white needles, m.p. 104–105°.

2-Methyl-3-(1-phenyl-2-nitropropyl)-indole (IIc).—2-Methylindole (13.1 g., 0.100 mole) and β-methyl-β-nitrostyrene[10,21] (16.3 g., 0.100 mole) were fused on a boiling water-bath for 4.5 hr. The resulting dark reddish viscous oil was washed with hot ethanol, leaving a crystalline solid residue (15.8 g.). Concentration of the ethanol washings and heating on the steam-bath for 5 hr., followed by cooling and washing with ethanol yielded additional product (4.5 g.). The product was in the form of pale yellow crystals (20.3 g., 0.0689 mole, 69%), m.p. 194–195°. Several recrystallizations from methanol, with charcoal, yielded the analytical sample of 2-methyl-3-(1-phenyl-2-nitropropyl)-indole as pale yellow crystals, m.p. 198–199°.

1-Methyl-3-(1-phenyl-2-nitroethyl)-indole (IIh).—1-Methylindole (26.2 g., 0.200 mole) and β-nitrostyrene[20] (29.8 g., 0.200 mole) were heated on a steam-bath for 3 days. The highly viscous brown mass was dissolved in 95% ethanol (450 cc.) and treated twice with charcoal. Concentration

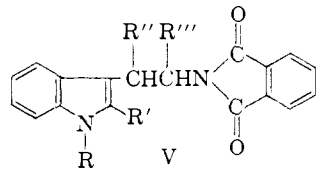
(21) E. Knoevenagel and L. Walter, *Ber.*, **37**, 4502 (1904).

TABLE IIa
SPECTRAL DATA ON TRYPTAMINES

	Ultraviolet[b]						Infrared frequencies cm.$^{-1}$ NH	
							Nujol	$CHCl_3$
IVa	223		279	283	290	358	3390	..
picrate	(4.69)		(3.93)	(3.93)	(3.89)	(4.19)	3180	
IVb	224	274[a]	280[a]	283	290		3330	3440
	(4.54)	(3.83)	(3.85)	(3.85)	(3.80)		3110	
IVc	225	274[a]	280[a]	283	290		3340	3430
	(4.51)	(3.82)	(3.84)	(3.85)	(3.81)		3280	
							3120	
IVf·HCl	226	278[a]		285	293		3090	..
	(4.56)	(3.82)		(3.88)	(3.85)		2020	
IVg	229			286	293		..	..
	(4.48)			(3.83)	(3.82)			
IVi	219[a]	235[a]			302		3340	3440
	(4.47)	(4.39)			(4.23)		3110	3170

[a] Inflection. [b] Wave lengths of maxima in 95% ethanol are given in mμ with intensities in log ε beneath them in parentheses.

TABLE III
PHTHALIMIDE DERIVATIVES OF TRYPTAMINES



V

	R	R′	R″	R‴	Mol. formula, weight	M.p., °C.	C, % Calcd. Found	H, % Calcd. Found	N, % Calcd. Found
Vb	H	Me	C_6H_5	H	$C_{25}H_{20}N_2O_2$	175–177	78.92	5.30	7.36
					380.43		79.03	5.04	7.20
Vc	H	Me	C_6H_5	Me	$C_{26}H_{22}N_2O_2$	202–203	79.16	5.62	7.10
					394.45		79.11	5.46	7.03
Vf	Me	Me	C_6H_5	H	$C_{26}H_{22}N_2O_2$	163–164	79.16	5.62	7.10
					394.45		79.02	5.66	7.32
Vg	Me	Me	C_6H_5	Me	$C_{27}H_{24}N_2O_2$	244–245	79.38	5.92	6.86
					408.48		79.12	5.93	6.72
Vh	Me	H	C_6H_5	H	$C_{25}H_{20}N_2O_2$	139–141	78.92	5.30	7.36
					380.43		79.13	5.24	7.12
Vi	H	C_6H_5	C_6H_5	H	$C_{30}H_{22}N_2O_2$	232–233	81.43	5.01	6.33
					442.49		80.94	5.03	6.51

TABLE IIIa
SPECTRAL DATA ON PHTHALIMIDE DERIVATIVES OF TRYPTAMINES

	Ultraviolet[b]					Infrared[c]	
						NH	C=O
Vb	220	240[a]	275[a]	283	290	3420	1760, 1704
	(4.88)	(4.17)	(3.90)	(3.92)	(3.89)		
Vc	221	241[a]	274[a]	282	289	3390	1757, 1697
	(4.87)	(4.12)	(3.85)	(3.88)	(3.84)		
Vf	221	241[a]	280[a]	286	292[a]	None	1757, 1703
	(4.90)	(4.24)	(3.88)	(3.93)	(3.92)		
Vg	221				289	None	1765, 1706
	(4.82)				(3.88)		
Vh	222	240[a]		290	298[a]	None	1764, 1709
	(4.87)	(4.17)		(3.88)	(3.84)		
Vi	221	236[a]			301	3410	1768, 1712
	(4.84)	(4.52)			(4.24)		

[a] Inflection. [b] Wave lengths of maxima in 95% ethanol are given in mμ with intensities in log ε beneath them in parentheses. [c] Frequencies in cm.$^{-1}$ in Nujol mulls.

of the filtrate and extraction of the charcoal with 95% ethanol, and then three recrystallizations from 95% ethanol gave white platelets (15.5 g., 0.0552 mole, 28%), m.p. 93–94°. Recrystallization from methanol yielded the analytical sample of 1-methyl-3-(1-phenyl-2-nitroethyl)-indole as small white platelets, m.p. 94–95°.

2-Phenyl-3-(1-phenyl-2-nitroethyl)-indole (IIi).—A mixture of 2-phenylindole (14.1 g., 0.0729 mole) and β-nitrostyrene[20] (11.0 g., 0.0737 mole) was warmed on the steam-bath for 20 min. and then set aside overnight at room temperature. The resulting very dark, glassy product was dissolved in methylene chloride and treated three times with

charcoal. Addition of light petroleum (b.p. 60–68°) to the filtrate produced a white precipitate (18.1 g., 0.0529 mole, 73%), m.p. 143–144°. Three recrystallizations from methylene chloride–light petroleum (b.p. 60–68°) and three from 95% ethanol yielded the analytical sample of 2-phenyl-3-(1-phenyl-2-nitroethyl)-indole as white crystals, m.p. 144–147°.

3-(1-Amino-2-propyl)-indole (IIIb) Picrate.—A solution of 3-(1-nitro-2-propyl)-indole[2] (1.35 g., 0.00664 mole) in absolute ethanol (100 cc.) was hydrogenated at 2 atm. over Raney nickel (1 teaspoonful), with shaking, for 20 hr. The catalyst was removed by filtration through diatomaceous earth and the solvent was distilled under aspirator pressure. The resulting oily residue was taken up in ether and extracted with 10% hydrochloric acid solution (3 × 67 cc.). The acid extracts were basified with 10% sodium hydroxide solution, extracted with ether, and the ether extract dried over anhydrous sodium sulfate. One-half of the dried ether solution was evaporated and redissolved in benzene (20 cc.) to which picric acid (0.76 g., 0.00332 mole) was added. The precipitate, which formed immediately, was refluxed for an hour and then the orange yellow crystals (0.78 g., 0.00194 mole, 59%), m.p. 223–227°, were filtered off. Five recrystallizations from ethanol, once with a little picric acid, yielded the analytical sample of 3-(1-amino-2-propyl)-indole picrate as orange crystals, m.p. 224–226°, reported m.p. 224°.[11]

Anal. Calcd. for $C_{17}H_{17}N_5O_7$ (403.35): C, 50.62; H, 4.25; N, 17.36. Found: C, 51.18; H, 4.37; N, 17.57.

Tryptamines (IB).—In addition to the hydrogenation of 3-(1-nitro-2-propyl)-indole (IIb) described above, two examples illustrating the hydrogenation of substituted 3-(2-nitroethyl)-indoles are described below:

2-Methyl-3-(1-phenyl-2-aminopropyl)-indole (IVc).—A solution of 2-methyl-3-(1-phenyl-2-nitropropyl)-indole (14.7 g., 0.050 mole) in ethyl acetate (300 cc.) was hydrogenated at 2 atm. over Raney nickel, with shaking, for 15 hr. Filtration of the catalyst and evaporation of the solvent left a residue, which was recrystallized from methylene chloride–light petroleum (b.p. 60–68°), yielding a light tan solid (8.0 g., 0.030 mole, 60%), m.p. 179°. Three recrystallizations from ethanol, with charcoal, yielded the analytical sample of 2-methyl-3-(1-phenyl-2-aminopropyl)-indole as white crystals, m.p. 183–184°.

2-Phenyl-3-(1-phenyl-2-aminoethyl)-indole (IVi).—A solution of 2-phenyl-3-(1-phenyl-2-nitroethyl)-indole (7.8 g., 0.0228 mole) in absolute ethanol (200 cc.) was hydrogenated at 2 atm. over Raney nickel, with shaking, for 24 hr. After filtration of the catalyst, water was added to the filtrate, forming a colloidal suspension. To precipitate the product with an electrolyte, a dilute solution of potassium hydroxide was added and the mixture was set aside in the refrigerator overnight. The resulting curdy precipitate (6.25 g., 0.0200 mole, 88%), m.p. 177–178°, was recrystallized several times from 95% ethanol, yielding the analytical sample of 2-phenyl-3-(1-phenyl-2-aminoethyl)-indole as white needles, m.p. 180–182°.

Phthalimide Derivatives (V) of Tryptamines.—A modification of the method of Manske[22] for 1-methyltryptamine phthalimide was used for preparation of the phthalimide derivatives. Phthalic anhydride (in 20–100% molar excess) was used in place of phthalic acid. The reactants were heated slowly in a Woods metal-bath and held at 210–230° for 1–15 min. The cooled residue was taken up in ether, washed with sodium bicarbonate solution and refluxed with ethanol for an hour. The precipitate which formed on cooling was recrystallized several times from ethanol or methylene chloride–light petroleum (b.p. 60–68°), yielding white to yellow crystals of the phthalimide derivatives.

(22) R. H. F. Manske, *Can. J. Research*, **5B**, 592 (1931).

MINNEAPOLIS 14, MINN.

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY, UNIVERSITY OF MINNESOTA]

A Novel Rearrangement in the 5-Nitronorbornene Series[1]

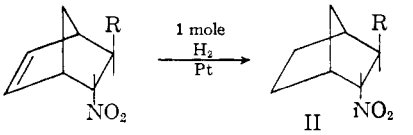
BY WAYLAND E. NOLAND, JAMES H. COOLEY[2] AND PATRICIA A. MCVEIGH[2]

RECEIVED AUGUST 26, 1958

5-Nitronorbornene undergoes a novel rearrangement under acid solvolysis conditions to *cis*-6-cyclopentena[e]tetrahydro-1,2-oxazin-3-one (VII). Reduction of VII yields a dihydro derivative, *cis*-cyclopentana[e]tetrahydro-1,2-oxazin-3-one (XII), and a tetrahydro derivative, *cis*-2-hydroxycyclopentaneacetamide (XIII). Hydrolysis of XIII yielded the known lactone, *cis*-cyclopentana[b]tetrahydrofuran-2-one (XI). Compound VII yielded an unstable nitroso derivative VIII. Compounds VII and XII appear to be the first examples of alicyclic hydroxamic esters and VIII appears to be the first nitroso derivative of a hydroxamic ester. Compound VIII decomposes to an unsaturated lactone, *cis*-5-cyclopentena[b]tetrahydrofuran-2-one (IX), which undergoes hydrogenolysis to cyclopentaneacetic acid. Probable mechanisms involved in the formation of VII and IX are discussed.

Introduction

The failure of salts of the 5-nitronorbornenes (I) to undergo the Nef reaction[3,4] has been noted previously. The action of cold dilute sulfuric acid on the sodium salt of 5-nitro-6-phenylnorbornene (Ic) resulted in a non-ketonic oil, which appeared to be principally unchanged nitro compound.[5,6] Addition of an aqueous solution of the sodium salt of 5-nitro-6-methylnorbornene (Ib) to dilute sulfuric acid did not give nitrous oxide, but an oily material which could not be separated into pure components by crystallization or chromatography.[7] Similarly, when a solution of the sodium salt of 5-nitrobornene (Ia) was added to cold dilute hydrochloric acid no ketonic material could be isolated from the reaction mixture.[8]



II

Ia, R = H
b, R = CH_3
c, R = C_6H_5

(1) Preliminary communication: W. E. Noland, J. H. Cooley and P. A. McVeigh, THIS JOURNAL, **79**, 2976 (1957).

(2) Taken in part from the theses of James H. Cooley, Ph.D., August, 1958, and Patricia A. McVeigh, M.S., October, 1954, both at the University of Minnesota. We are indebted to the Procter and Gamble Co. for financial support provided J. H. C. through a 1955 summer fellowship.

(3) W. E. Noland, *Chem. Revs.*, **55**, 137 (1955).

(4) M. F. Hawthorne, THIS JOURNAL, **79**, 2510 (1957).

(5) W. E. Parham, W. T. Hunter and R. Hanson, *ibid.*, **73**, 5068 (1951).

(6) W. C. Wildman and R. B. Wildman, *J. Org. Chem.*, **17**, 581 (1952).

(7) E. E. van Tamelen and R. J. Thiede, THIS JOURNAL, **74**, 2615 (1952).

(8) W. C. Wildman and C. H. Hemminger, *J. Org. Chem.*, **17**, 1641 (1952).