Tetrahedron, 1963, Vol. 19, pp. 681 to 690. Pergamon Press Ltd. Printed in Northern Ireland

SOME ALKYLATION REACTIONS OF MANNICH BASES IN AQUEOUS MEDIUM

SYNTHESES OF SOME MONO- AND POLYINDOLYL COMPOUNDS

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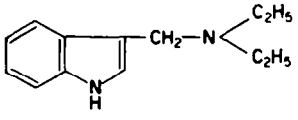
(*Received* 13 *September* 1962)

Abstract—Alkylation reactions of the Mannich bases Viz: 3-diethylaminomethylindole and 3-(diethylaminomethyl)-2-methylindole with nitromethane, ammonium carbonate, levulinic acid, methylcyanide and acetamide in aqueous medium have been described.

BETHELL and Maitland[1] have reported a number of condensations *vis-a-vis* effects on them of varying pH at room temperature in aqueous medium. In all these condensations the reactants employed by them were soluble in water. In the present paper we have studied alkylations of some representative types of compounds like nitromethane, ammonium carbonate, levulinic acid, methylcyanide and acetamide with the Mannich bases I and II of indole and 2-methylindole, respectively in water. The yields obtained are very high although the Mannich bases are insoluble and the other reactants either soluble or partly soluble in boiling water.

Mannich bases[2] have considerable application in organic syntheses. They gained importance when Snyder[3] in the synthesis of tryptophane, reacted gramine methiodide with diethylacetylaminomalonate, obtaining skatylacetylaminomalonate, but this paper reports the first investigation into alkylation reactions of Mannich bases in water.



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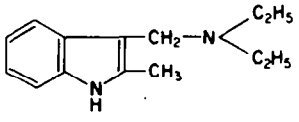

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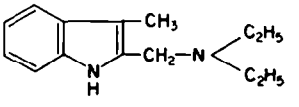


III

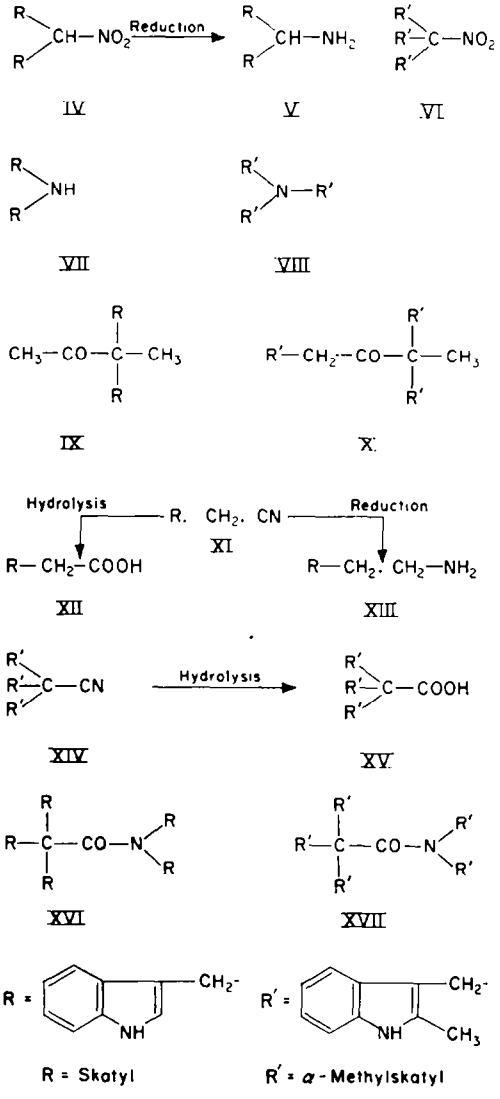
The three Mannich bases selected are, 3-diethylaminomethylindole[4] (I), 3-(diethylaminomethyl)-2-methylindole[5] (II) and 2-(diethylaminomethyl)-3-methylindole (III). Compound III, not reported in literature, was prepared in accordance with the method of Kuhn and Stein.[4] It was, however, observed that, the yield of III increased from 18 to 64%, when the quantity of acetic acid used was increased from 1 to 1·5 moles, but a further increase did not improve the yield. This Mannich base (III) is unstable (shown later) and being a liquid like 1,3-dimethylindole and not a solid like 2,3-dimethylindole, suggests that the substitutent may be in the 2-position and not in the 1-position. The presence of an I.R. absorption band at 3400 cm^{-1} (>NH) indicates the absence of a tertiary nitrogen and suggests 2-(diethylaminomethyl)-3-methylindole (III)

[1] I. R. Bethell and P. Maitland, *J.C.S.*, 5211 (1961).
[2] A. C. Mannich and G. Ball, *Arch. Pharm.*, **264**, 64, 164 (1926).
[3] H. R. Snyder and W. S. Curtis, *J.A.C.S.*, **66**, 350 (1944).
[4] H. Kuhn and O. Stein, *Ber.*, **70**, 567 (1937).
[5] Richard Dahlhom and Alfons Misiorny, *Acta. Chem. Scand.*, **9**, 1074 (1955).

as the structure. Further, the U.V. absorption bands (in ethanol) at λ_{max} 283 mμ (log ϵ 3·99), 226 mμ (log ϵ 4·63) and λ_{min} 248 mμ (log ϵ 3·46) with shoulder at 290 mμ (log ϵ 3·95) were in conformity with the bands for 2,3-dimethylindole[6] viz λ_{max} 227 mμ (log ϵ 4·49), 283 mμ (log ϵ 3·83); 290 mμ (log ϵ 3·78) and also with the bands for 3-diethylaminomethylindole (I) and 3-(diethylaminomethyl)-2-methylindole (II).

Snyder and Katz[7] have reported syntheses of derivatives of tryptamine by alkylation of nitromethane or nitroethane with gramine in sodium hydroxide solution. The product obtained from nitromethane melted at 206°, the yield being 20%.

Alkylation of nitromethane with 3-diethylaminomethylindole in boiling water yields diskatylnitromethane (IV), in 74% yield; m.p. 206°, undepressed with sample



[6] W. E. Noland and D. N. Robinson, *Tetrahedron*, **3**, 68 (1958).
[7] H. R. Snyder and L. Katz, *J.A.C.S.*, **69**, 3140 (1947).

prepared in accordance with the method of Snyder and Katz. This product on catalytic reduction with Raney nickel[8] yields diskatylmethylamine (V), m.p. 195°, in 70% yield.

The nitro product (IV) may also be obtained by leaving the reactants at room temperature for 20 days, the yield being 60%. Reaction in boiling ethyl alcohol (95%) yields 57% of the same product.

Alkylation of nitromethane with the Mannich base of 2-methylindole gives the *tri*-(α-methylskatyl)-nitromethane (VI); m.p. 222°, (dec) not hitherto reported in literature.

Alkylation of ammonium carbonate in aqueous solution with 3-diethylaminomethylindole yields diskatylamine (VII), m.p. 88°, in 83% yield.

In the case of 3-(diethylaminomethyl)-2-methylindole (II), a similar alkylation of ammonium carbonate yields tri-(α-methylskatyl)-amine (VIII), m.p. 86°, in 79% yield.

Reaction of levulinic acid with 3-diethylaminomethylindole in boiling water results in the elimination of one molecule of carbon dioxide and separation of a crystalline product which analysed for $C_{12}H_{22}ON_2$ and may be 3,3,diskatylbutan-2-one (IX). A similar alkylation levulinic acid with 3-(diethylaminomethyl)-2-methylindole (II), yields 1,3,3, tri-(α-methylskatyl) butan-2-one product m.p. 140°, with the elimination of a molecule of carbon dioxide.

In these reactions the first point of attack is the active methylene group adjacent to the keto group: (β-carbon[9–11]). If this carbon is fully substituted, the next vulnerable carbon is δ- and not α- to the carboxyl group. According to Borsche[12] and Sen and Roy[13] condensation takes place at the α-position, if the reaction of benzaldehyde is carried out with the sodium salt of levulinic acid in acetic anhydride. In the presence of alkali, however, condensation of aldehyde with levulinic acid takes place on the δ carbon.[14,15]

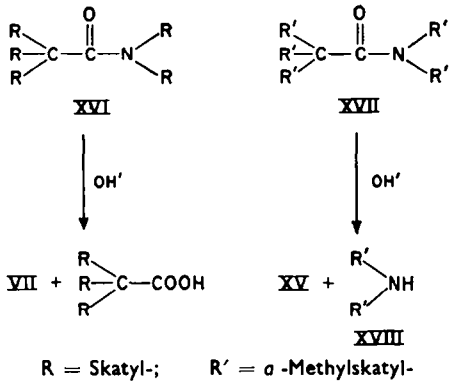
3-Indolepropionitrile has been prepared by a number of methods, (a) by reaction of β-chloropropionitrile with indolyl magnesium-iodide,[16] and (b) by cyanoethylation of indole.[17] In the present investigation reaction of methyl cyanide with 3-diethylaminomethylindole in boiling water yields 3-indolepropionitrile (XI; m.p. 67°; 61·7%) as confirmed by mixed melting point (undepressed) with an authentic sample.[16] The identity of 3-indolepropionitrile was further confirmed by alkaline hydrolysis to indolepropionic acid[18] (XII) m.p. 134° identical with a sample, prepared according to the method of Johnson and Crosby,[19] and by reduction to 3-indolepropylamine[20] (XIII), m.p. 64°.

[8] R. Mozingo, *Org. Syntheses*, **21**, 15 (1941).
[9] H. Erdmann, *Ber.*, **18**, 3441 (1885).
[10] E. A. Kehrer and W. Kleberg, *Ber.*, **26**, 345 (1893).
[11] E. Erlenmeyer, *Ber.*, **23**, 74 (1890).
[12] W. Borsche, *Ber.*, **48**, 842 (1915).
[13] R. N. Sen and B. C. Roy, *J. Indian Chem. Soc.*, **7**, 401 (1930).
[14] Meigash, *Montash*, **26**, 2675 (1905).
[15] A. Ludwig and E. A. Kehrer, *Ber.*, **24**, 2776 (1891).
[16] R. Majima and T. Hoshino, *Ber.*, **58**, 2044 (1925).
[17] W. Reppe and H. Ufer, German Patent, 698273. French Patent, 48570, addition to French Patent 742358.
[18] R. Majima and T. Hoshino, *Ber.*, **58**, 2045 (1925).
[19] Herbert E. Johnson and Donald G. Crosby, *J. Org. Chem.*, **25**, 569 (1960).
[20] R. W. Jackson and R. H. Manske, *J.A.C.S.*, **52**, 5033 (1930); R. Majima and T. Hoshino, *Ber.*, **58**, 2046 (1925).

A similar reaction carried out with 3-(diethylaminomethyl)-2-methylindole (II) yields tri-(α-methylskatyl)methylcyanide (XIV; m.p. 190°; 84%) which on alkaline hydrolysis, gives tri-(α-methylskatyl)-acetic acid (XV); m.p. 197° in 78% yield.

Hahn *et al.*[21] failed to alkylate several amides including acetamide with gramine in boiling toluene. However, alkylation of acetamide with 3-diethylaminomethylindole (I) and 3-(diethylaminomethyl)-2-methylindole (II) in water proceeds readily to yield what are believed to be (N,N-diskatyl)-(tri-skatyl)-acetamide (XVI) m.p. 107°, and N,N-Di-(α-methylskatyl)-tri-(α-methyl-skatyl)-acetamide (XVII); m.p. 220° respectively.

In order to confirm the constitutions of XVI and XVII the compounds were hydrolysed with 10% alcoholic potassium hydroxide, XVI yielding a product m.p. 88° which is identical with diskatylamine (VII) by mixed m.p. and comparison of U.V. absorption spectra with an authentic sample. The other moiety which should be tri-skatyl acetic acid, could not be sufficiently purified for identification.



N,N-Di-(α-methylskatyl)-tri-(α-methylskatyl) acetamide (XVI) in a similar manner yields two products viz; compound m.p. 100° which analysed for di-(α-methylskatyl)-amine and compound m.p. 197° which was identified as tri-(α-methylskatyl)-acetic acid (XV).

All attempts to alkylate nitromethane, ammonium carbonate, methylcyanide, levulinic acid and acetamide with 2-(diethylaminomethyl)-3-methylindole (III) in water failed; the original 3-methylindole was recovered almost quantitatively. The presence of the other two components viz., formaldehyde and diethylamine was also established.

EXPERIMENTAL

All m.p.s are corrected. U.V. absorption spectra were determined with a Beckman Spectrophotometer Model D.B., in 95% ethanol. I.R. Spectra were recorded with a Leitz double beam instrument Model 105.

2-(*Diethylaminomethyl*)-3-*methylindole* (III)

An ice cold mixture of diethylamine (7·3 g; 10·2 ml: 0·1 mole), acetic acid (21 g; 21 ml) and formaldehyde (40%; 7·5 ml; 0·1 moles) were added to the 3-methylindole (13·1 g; 0·1 mole), allowed to stand overnight, and made alkaline with 10% aqueous potassium hydroxide. An oily separated product was isolated with ether and purified by vacuum distillation; pale-yellow viscous oil; 13·91 g;

[21] G. Hahn, S. K. Qureshi, K. Rasheed and A. K. Mekheri, *Pak. J. Sci. Ind. Research*, **1**, No. 2; 104 (1958).

(65%); b.p. 146–148°/0·5 mm $(n)_D^{32°} = 1·57$. 2-(*Diethylaminomethyl*)-3-*methylindole* is easily soluble in acetone, benzene, chloroform, ethyl acetate and insoluble in water and light-petroleum (60–80°). (Found: C, 77·47; H, 9·34; N, 12·82; $C_{14}H_{20}N_2$ (M.W. 216) requires: C, 77·73; H, 9·32; N, 12·95%). U.V. absorption bands at λ_{max} 283 mμ (log ε 3·99); 226 mμ (log ε 4·63); λ_{min} 248 mμ (log ε 3·46) and shoulder at 290 mμ (log ε 3·95) and I.R. absorption bands at 3400 cm^{-1} (>NH). 3-Diethylaminomethylindole (I) shows absorption bands at λ_{max} 280 mμ (log ε 4·52), 220 mμ (log ε 4·60) and λ_{min} 244 mμ (log ε 3·92), with shoulder at 288 mμ (log ε 4·38). 3-(Diethylaminomethyl)-2-methylindole (II) shows absorption bands at λ_{max} 280 mμ (log ε 4·40), 224 mμ (log ε 4·63) and λ_{min} 250 mμ (log ε 4·09) with shoulder at 288 mμ (log ε 4·33).

Alkylation reaction of Mannich bases in aqueous medium

General method. The mannich base: 3-Diethylaminomethyl-indole (I) or 3-Diethylaminomethyl 2-methylindole (II) and the reactant to be alkylated, were suspended in water and the mixture refluxed on sand bath. After completion of reaction the product if oily was isolated with ether or ethyl acetate, and if solid through filtration, and crystallized from appropriate solvent.

The quantities (in g and molar ratios) of the mannich bases and the reactants alkylated, period of refluxing, the name of the solvent from which the products were crystallized etc., are shown in Table 1.

The elemental analyses as well as the U.V. and I.R. Spectral analyses are shown in Table 2.

The alkylated products reported are generally moderately to easily soluble in acetone, benzene, ethyl acetate, chloroform, ether, ethanol and methanol and insoluble in light-petroleum (60–80°) and water.

Reduction of diskatylnitromethane

Diskatylmethylamine (V). Diskatylnitromethane (0·319 g; 0·001 mole) was dissolved in absolute ethanol (50 ml) Raney-nickel (½ tea spoon-full) was added and shaken in the atmosphere of hydrogen (3 hr). On filtration and removal of solvent, *diskatylmethylamine* was obtained in long needles; m.p. 190°; 0·22 g; (73%). Recrystallized from ethanol; light brown microscopic needles; 0·20 g; (70%); m.p. 195° (clear melt). *Diskatylmethylamine* is easily soluble in acetone, benzene, ethyl acetate; sparingly in ethanol and is insoluble in water and ligroin. (Found: N, 14·67°; $C_{19}H_{19}N_3$ (M.W. 289) requires: N, 14·52%). U.V. absorption bands were at λ_{max} 290 mμ (log ε 3·99); and λ_{min} 250 mμ (log ε 3·10).

Hydrolysis of 3-indolepropionitrile

3-*Indolepropionic acid* (XII). 3-Indolepropionitrile (1·70 g; 0·01 mole) was taken up in alcoholic potassium hydroxide (20%; 50 ml) and the contents refluxed (12 hr). The solvent was removed and water (25 ml) added. Isolation with ether gave crystalline material; 1·45 g; (76%), m.p. 130° which recrystallized from dil. methanol in colourless needles; 1·29 g; (68%), m.p. 134° (clear melt), undepressed on admixture with an authentic sample.[19] U.V. absorption bands at λ_{max} 292 mμ (log ε 3·04); 283 mμ (log ε 3·15); 223 mμ (log ε 3·98) and λ_{min} 287 mμ (log ε 3·08); 245 mμ (log ε 2·26). I.R. absorption band at 1681 cm^{-1} (—COOH), in nujol.

Reduction of 3-indolepropionitrile

3-*Indolepropylamine* (XIII). 3-Indolepropionitrile (1·70 g; 0·01 mole) dissolved in absolute ethanol (50 ml), was shaken in hydrogen atmosphere with Raney nickel (1 teaspoon-full) (4 hr), then filtered, the solvent removed and the product crystallized from ether-ligroin in long needles; 1·35 g; (77%); m.p. 64° (clear melt), undepressed with an authentic sample.[20] The U.V. absorption bands at λ_{max} 280 mμ (log ε 4·46); 227 mμ (log ε 4·63) and λ_{min} 250 mμ (log ε 3·99) with shoulder at 288 mμ (log ε 4·43). I.R. absorption bands at 3425 cm^{-1} (—NH_2) in chloroform.

Hydrolysis of tri-(α-methylskatyl)-methylcyanide

Tri-(α-methylskatyl)-acetic acid (XV). To tri-(α-methylskatyl)-methylcyanide (0·468 g; 0·001 mole) dissolved in ethanol (25 ml), alcoholic potassium hydroxide (10%; 20 ml) was added. After refluxing (8 hr), the solvent was removed, water (20 ml) added and the product isolated with ether. It crystallized from benzene–ligroin in colourless microscopic needles which change to brown on standing; 0·32 g; (65%); m.p. 197° (dec). *Tri-(α-methylskatyl)-acetic acid* is easily soluble in

TABLE 1

Mannich base	Reactant alkylated	Water (ml)	Period of reflux (hr)	State of the reaction product in medium	Name of product and molecular formula	Degree of alkylation	Crystallizing medium colour and shape of the crystals.	Yield (g) (%)	M.P.
(I) 1·21 g; (0·006 mole)	Nitromethane 0·48 g (0·003 mole)	50	6	Oil	Diskatylnitromethane (IV); $C_{19}H_{17}O_2N_3$.	di	Dil. ethanol; colourless microscopic needles.	0·71 74%	206° (dec) lit[7] 206°
(II) 1·30 g; (0·006 mole)	Nitromethane 0·12 g; (0·002 mole)	50	6	Viscous oil	Tri-(α-methylskatyl)-nitromethane (VI); $C_{31}H_{30}O_2N_4$	tri	Dil. methanol; light brown microscopic needles, change to dark brown on standing.	0·81 83%	222° (dec)
(I) 1·212 g; (0·006 mole)	Saturated aqueous solution of ammonium carbonate 50 ml	—	6	Crystalline solid	N,N-Diskatylamine; (VII); $C_{18}H_{17}N_3$	di	Benzene-light petroleum (60–80°); colourless microscopic needles; sensitive to light: change to brown colour.	0·68 83%	88°
(II) 1·30 g; (0·006 mole)	Saturated solution of ammonium carbonate 50 ml	—	4–6	Crystalline solid	Tri-(α-methylskatyl)-amine: (VIII); $C_{30}H_{30}N_4$	tri	Ether–light petroleum (60–80°), pale yellow microscopic leaflets.	0·71 79%	86°
(I) 1·2 g; (0·006 mole)	Levulinic acid 0·35 g; (0·003 mole)	50	8 (evolution of CO_2. $BaCO_3$ collected: 1·81 g; Theory: 1·97 g)	Oil	3,3-Diskatylbutan-2-one (IX); $C_{23}H_{23}O_1N_2$	di	Dil. ethanol; light brown microscopic needles.	0·83 84%	270° (dec)

(II) 1·30 g; (0·006 mole)	Levulinic acid 0·232 g; (0·002 mole)	50	8	Viscous oil	1,3,3-Tri-(α-methyl skatyl)-butan-2-one: (X): $C_{34}H_{35}O_1N_3$	tri	Dil. ethanol; light brown, microscopic needles.	0·79 77%	140°
(I) 2·02 g; (0·01 mole)	Methyl-cyanide. 0·41 g; (0·01 mole)	100	6–8	Viscous oil	3-Indolepropionitrile: (XI); $C_{11}H_{10}N_2$	mono	Dil. methanol; colourless microscopic needles sensitive to light.	1·05 61·7%	67° (lit.[18] 67°
(II) 0·65 g; (0·003 mole)	Methylcyanide. 0·04 g; (0·001 mole)	50	6–8	Oil	Tri-(α-methylskatyl)-methylcyanide: (XIV) $C_{32}H_{30}N_4$	tri	Ethyl acetate–light petroleum (60·80°); golden yellow needles.	0·41 84%	140°
(I) 2·02 g; (0·01 mole)	Acetamide 0·12 g; (0·002 mole)	50	6	Viscous oil	(N,N-Diskatyl)-(tri-Skatyl)-acetamide (XVI); $C_{47}H_{40}O_1N_6$	penta	Dil. methanol; microscopic leaflets.	0·62 44%	190°
(II) 1·08 g; (0·005 mole)	Acetamide 0·06 g; (0·001 mole)	50	6–8	Oil	N,N-Di (α-methyl-skatyl-tri-(α-methyl skatyl)-acetamide; (XVII); $C_{52}H_{50}O_1N_6$.	penta	Ethyl acetate–light petroleum (60–80°); colourless long needles.	0·52 67%	222° (dec)

I = 3-Diethylaminomethylindole.
II = 3-(Diethylaminomethyl)-2-methylindole.

TABLE 2

Product	Molecular formula (Mol. wt.)	Analysis Requires C%	Analysis Requires H%	Analysis (Found) O%	Analysis (Found) N%	U.V. absorption bands in 95% ethanol λ_{max} in mμ (log ε)	U.V. absorption bands in 95% ethanol λ_{min} in mμ (log ε)	I.R. absorption bands cm^{-1}
Diskatylnitromethane (IV)	$C_{19}H_{17}O_2N_3$ (319)	*71·45 (71·61) (71·64)	5·37 (5·58) (5·62)	10·02 (10·03) (9·74)	13·16 (12·78) (13·01)	292 (4·37) 280 (4·43)	288 (4·34) 243 (4·02)	1550 (—NO_2) in $CHCl_3$
Tri-(α-methylskatyl)-nitromethane (VI)	$C_{31}H_{30}O_2N_4$ (490)	75·89 (75·24)	6·16 (6·27)	6·52 (6·98)	11·42 (11·48)	280 (5·82) with shoulder at 287 (5·76)	250 (5·43)	1550 (—NO_2) in $CHCl_3$
N,N-Diskatylamine (VII)	$C_{18}H_{17}N_3$ (275)	78·51 (79·09)	6·22 (6·37)	—	15·26 (14·55)	276 (4·63) 218 (3·44) with shoulder at 285 (4·53)	245 (4·20)	3425 (>NH) in $CHCl_3$
Tri-(α-methylskatyl)-amine (VIII)	$C_{30}H_{30}N_4$ (446)	80·68 (80·23)	6·77 (6·34)	—	12·55 (12·68)	282 (5·72) with shoulder at 287 (5·63)	250 (5·32)	—
3:3-diskatylbutan-2-one (IX)	$C_{22}H_{22}O_1N_2$ (330)	79·97 (80·29)	6·71 (5·97)	4·84 (4·89)	8·48 (8·96)	280 (4·30) 225 (4·80) with shoulder at 287 (4·25)	254 (4·02)	1618 (>C=O) in $CHCl_3$

1,3,3-tri (α-methylskatyl)-butan-2-one (X)	$C_{34}H_{35}O_1N_3$ (501)	81·40 (81·40)	7·02 (7·02)	3·19 (3·23)	8·38 (8·80)	285 (4·04) 255 (3·74) 227 (4·70) with shoulder at 288 (4·02)	1620 (>C=O) in $CHCl_3$
3-Indolepropionitrile (XI).	$C_{11}H_{10}N_2$ (170)	*77·62 (77·42)	5·92 (5·71)	—	16·46 (17·07)	283 (3·25) 252 (3·43) 222 (4·43) with shoulder at 287 (3·61)	2242 (—CN) in Nujol.
Tri-(α-methylskatyl)-methylcyanide (XIV).	$C_{32}H_{30}N_4$ (470)	81·67 (81·04)	6·43 (7·07)	— —	11·91 (11·89)	285 (4·48) 255 (4·07) 228 (5·09) with shoulder at 288 (4·35)	2280 (—CN) in Nujol.
(N,N-Diskatyl)-(tri-skatyl)-acetamide. (XVI)	$C_{47}H_{40}O_1N_6$ (704)	80·11 (79·41)	5·68 (5·79)	2·28 (3·02)	11·93 (11·78)	290 (5·35) 260 (5·06) 225 (5·94) with shoulder at 298 (5·27)	1645 and 1709 (—CO of tertiaryamide), in Nujol.
N.N-di-(α-methylskatyl)-tri-(α-methylskatyl)-acetamide. (XVII).	$C_{52}H_{50}O_1N_6$ (774)	80·62 (80·65)	6·46 (6·59)	2·06 (2·16)	10·86 (10·69)	284 (4·68) 255 (4·19) 226 (5·41) with shoulder at 288 (4·69)	—

* = Calculated for.

acetone, chloroform, ethylacetate; sparingly in benzene and insoluble in light-petroleum (60–80°) and ligroin. (Found: C, 78·91; H, 6·51; O, 6·90; N, 7·89; $C_{32}H_{31}O_2N_3$; (M.W. 489); requires: C, 78·50; H, 6·38; O, 6·54; N, 8·58%).

U.V. absorption bands at λ_{max} 280 mμ (log ϵ 4·73); 225 mμ (log ϵ 5·45) and λ_{min} 255 mμ (log ϵ 4·59) with shoulder at 287 mμ (log ϵ 4·69). I.R. absorption bands at 3425 cm^{-1} (>NH); 1681 cm^{-1} (—COOH) in chloroform.

Hydrolysis of (N,N-*diskatyl*)-(*triskatyl*)-*acetamide* (XVI)

N,N-Diskatyl-(triskatyl) acetamide (XVI) (0·352 g; 0·0005 mole), in ethanolic potassium hydroxide (10%; 20 ml) was refluxed (48 hr). Ethyl alcohol was removed (vac.), water (14 ml) added and the contents extracted with ethyl acetate, the extract dried and the solvent removed. The oily residue crystallized from Benzene–light petroleum (60–80°) in colourless microscopic needles; m.p. 88° (clear melt), undepressed on admixture with N,N-Diskatylamine (VII). It also gave identical U.V. absorption bands. The alkaline aqueous solution was carefully acidified with dil. hydrochloric acid and the brown red-coloured product isolated with ethyl acetate. The product m.p. 172° (dec.) on removal of solvent could not be sufficiently purified for analysis.

Hydrolysis of N,N-*di*-(α-*methylskatyl*)-*tri*-(α-*methylskatyl*)-*acetamide* (XVII)

N,N-Di-(α-methylskatyl)-tri-(α-methylskatyl)-acetamide (XVII); 0·39 g; 0·0005 mole) in ethanolic potassium hydroxide (10%; 20 ml) was refluxed (48 hr). Ethanol was removed (vac.), water (15 ml) added and the contents extracted with ethyl acetate. After drying and removal of ethyl acetate N,N-*di*-(α-*methylskatyl*)-*amine* (XVIII); 0·15 g; m.p. 96° (dec.) was obtained and crystallized from dil. ethanol in colourless needles; 0·10 g; m.p. 100° (dec.). N,N-*Di*-(α-*methylskatyl*)-*amine* is soluble in acetone, chloroform, ethyl acetate, methanol and ethanol sparingly soluble in benzene and ether and insoluble in carbon tetrachloride and light-petroleum (60–80°). (Found: C, 80·04; H, 6·78; $C_{20}H_{21}N_3$; (M.W. 303) requires: C, 79·27; H, 6·98. U.V. absorption bands at λ_{max} 280 mμ (log ϵ 4·43); 224 mμ (log ϵ 4·90) and λ_{min} 250 mμ. (log ϵ 4·18) and 214 mμ (log ϵ 4·87) with shoulder at 288 mμ (log ϵ 4·23).

The alkaline aqueous solution left after extraction with ethyl acetate, was acidified with dil. hydrochloric acid and extracted with ethyl acetate. Drying and removal of solvent gave 0·08 g of material which crystallized from benzene–ligroin; m.p. 197° (dec.), undepressed on admixture with *tri*-(α-*methylskatyl*)-*acetic acid* (XV), the U.V. bands were also identical.

Acknowledgement—Our thanks are due to Mr. A. Rauf Anwar for carrying out I.R. determinations. The assistance of Mr. Jan Muhammad is also thankfully acknowledged. All analyses were carried out by Dr. A. Bernhardt, Microanalytisches Laboratorium, 22 a, Mulheim, (Rtihr), West Germany.