Tetrahedron, 1966, Vol. 22, pp. 2475 to 2479. Pergamon Press Ltd. Printed in Northern Ireland

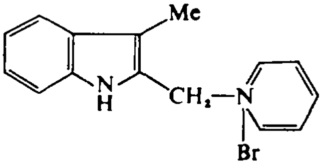
REACTIONS OF 2,3-DIMETHYLINDOLE AND TETRAHYDROCARBAZOLE WITH N-BROMOSUCCIMIDE

H. SAKAKIBARA and T. KOBAYASHI
Department of Chemistry, Faculty of Science, Gakushuin University, Mejiro, Tokyo, Japan

(*Received* 6 *May* 1965; *in revised form* 9 *March* 1966)

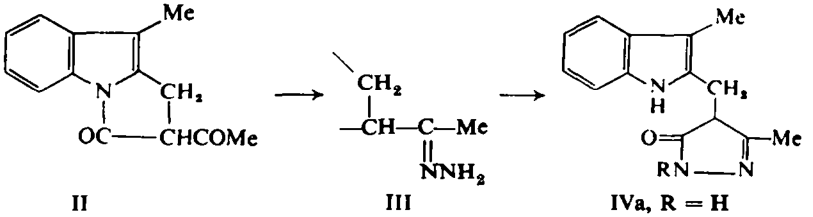
Abstract—Reaction of 2,3-dimethylindole and tetrahydrocarbazole with N-bromosuccimide in the presence of pyridine gave the corresponding pyridinium bromides (I and XI) which were condensed acetoacetic ester, benzoylacetic ester and malonic ester in the presence of potassium carbonate.

THE reaction of 3-substituted indoles with N-bromosuccimide (NBS) in the presence of pyridine affords the corresponding 2-pyridinium bromides.[1] Similarly, 2,3-dimethylindole reacts with NBS in the presence of pyridine to yield 3-methylindole-2-(N-methylenepyridinium bromide) (I) which was not isolated but the position of bromination was established by the reactions described.



The condensation of I with ethyl acetoacetate in the presence of potassium carbonate furnished in 30·6% yield a product, $C_{14}H_{13}NO$, which was assigned the structure, 2-acetyl-9-methyl-3-oxo-pyrrolidino[1,2-a]indole (II), by the lack of a sharp IR band expected for the indole hydrogen and the presence of three strong bands at 1680 (—CO—), 1653 (—NHCO—) and 1624 cm^{-1} ($>$C=C$<$).

Treatment of II with hydrazine afforded 3-methyl-2-(3′-methyl-2′-pyrazolin-5′-on-4′-ylmethyl)-indole, $C_{14}H_{15}N_3O$ (IVa). It was anticipated that the primary product of this condensation would be the corresponding hydrazone (III), but its conversion into IVa apparently took place spontaneously and was confirmed by a sharp IR band due to the indole hydrogen at 3480 cm^{-1}. Treatment of II with semicarbazide gave also the same product (IVa), and no semicarbazone was isolated.



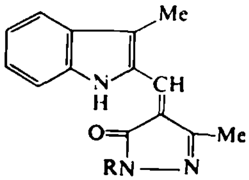
II III IVa, R = H
IVb, R = Ph

---

[1] T. Kobayashi and N. Inokuchi, *Tetrahedron* **20**, 2055 (1964).

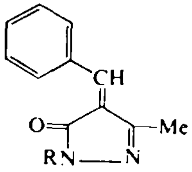
Heating IVa at 180° yielded orange crystals, $C_{14}H_{13}N_3O$, which indicated the IR bands of two hydrogens at 3500 and 3450 cm^{-1}, and was assigned the structure, 3-methyl-2-(3′-methyl-2′-pyrazolin-5′-on-4′-ylidenemethyl)-indole (Va).

Treatment of II with phenylhydrazine gave also 3-methyl-2-(3′-methyl-1′-phenyl-2′-pyrazolin-5′-on-4′-ylmethyl)-indole (IVb) and its heating at 180° yielded reddish orange crystals, $C_{20}H_{17}N_3O$, 3-methyl-2-(3′-methyl-1′-phenylpyrazolin-5′-on-4′-ylidenemethyl)-indole (Vb). 4-Benzylidene-3-methylpyrazolin-5-one (VIa)[2] and 4-benzylidene-3-methyl-1-phenylpyrazolin-5-one (VIb)[3], which are structurally analogous to Va and Vb, are respectively reddish orange and red.



Va, R = H

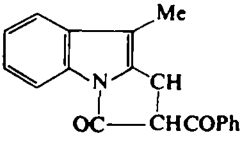
Vb, R = ph



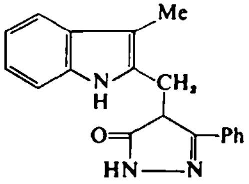
VIa, R = H

VIb, R = ph

Similarly the condensation of I with ethyl benzoylacetate gave 2-benzoyl-9-methyl-3-oxopyrrolidino[1,2-a]indole (VII) and its reaction with hydrazine yielded 3-methyl-2-(3′-phenyl-2′-pyrazolin-5′-on-4′-ylmethyl)-indole (VIII), $C_{19}H_{17}N_3O$, which showed the indole hydrogen absorption at 3450 cm^{-1}.

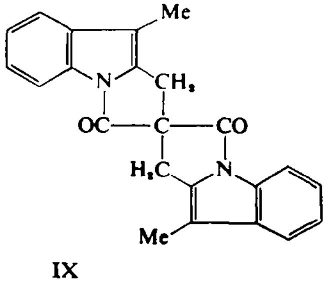


VII

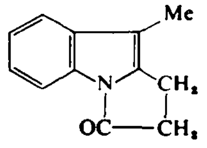


VIII

On treatment with ethyl malonate I yielded 2,2′-spirobi(9-methyl-3-oxopyrrolidino-[1,2-a]indole) (IX), $C_{23}H_{18}N_2O_2$ and 9-methyl-3-oxo-pyrrolidino[1,2-a]indole (X), $C_{12}H_{11}NO$. Both compounds showed the same IR absorption bands at 1730 (amide) and 1640 cm^{-1} (> C=C <).



IX



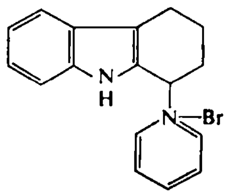
X

Similarly, the reaction of tetrahydrocarbazole with NBS yielded 1,2,3,4-tetrahydrocarbazole-1-(N′-pyridinium bromide) (XI) which condensed with ethyl acetoacetate yielding 2-acetyl-1-oxo-2a,3,4,5-tetrahydropyrrolidino[1,2,3-kl]carbazole (XIIa),

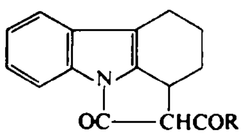
---

[2] T. Curtius, *J. Prakt, Chem.* **50**, 514 (1894).

[3] L. Knorr, *Liebigs Ann.* **238**, 179 (1887).



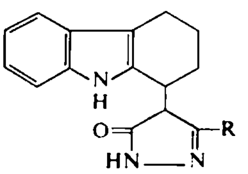
XI



XIIa, R = Me
XIIb, R = ph

$C_{16}H_{15}NO$. On refluxing with hydrazine or semicarbazide XIIa gave 1,2,3,4-tetrahydro-1-(3′-methyl-2′-pyrazolin-5′-on-4′-yl)-carbazole (XIIIa), $C_{16}H_{17}N_3O$. Pyrolysis of XIIIa at 210° afforded 3-methyl-2-pyrazolin-5-one and a mixture of carbazole and tetrahydrocarbazole.

The reaction of XI with ethyl benzoylacetate yielded 2-benzoyl-1-oxo-2a,3,4,5-tetrahydropyrrolidino[1,2,3-kl]carbazole (XIIb), $C_{21}H_{17}NO_2$, which on refluxing with hydrazine gave 1,2,3,4-tetrahydro-1-(3′-phenyl-2′-pyrazolin-5′-on-4′-yl)-carbazole (XIIIb), $C_{21}H_{19}N_3O$.



XIIIa, R = Me

XIIIb, R = ph

On treatment with diethyl malonate XI yielded diethyl tetrahydrocarbazole-1-malonate (XIV), $C_{19}H_{23}NO_4$, and its hydrolysis gave tetrahydrocarbazole-1-acetic acid (XV).

EXPERIMENTAL

3-*Methylindole-2-(N′-methylenepyridinium bromide)* (I) *and 2-acetyl-9-methyl-3-oxo-pyrrolidino* [1,2-a]-*indole* (II)

To a stirred solution of 2,3-dimethylindole (5 g) and pyridine (4 g) in dry C_6H_6 (60 ml), NBS (8 g) was added at 5° during 30 min. The mixture was stirred for additional 3 hr at 5° and at room temp overnight. The brown insoluble part was separated by decantation and washed with dry C_6H_6. A solution of this brown oil and ethyl acetoacetate (10 g) in abs. EtOH (50 ml) was stirred at 1° to 3°, while K_2CO_3 (5 g) was added during 20 min. The mixture was stirred for additional 2 hr at 3° and at room temp overnight, and after acidifing with AcOH the solvent was evaporated on a water bath. Upon the addition of water (100 ml), the product solidified and was extracted with C_6H_6. After evaporating C_6H_6 the residue was distilled *in vacuo* (2 mm); yield 4·65 g.

Recrystallization from MeOH gave colourless needles, m.p. 124–126°, 2·4 g (30·6%). The IR spectra (KBr) exhibited the characteristic three bands at 1680, 1653 and 1624 cm^{-1} (=NCO—, =CO). (Found: C, 74·19; H, 5·89; N, 6·26. $C_{14}H_{13}NO_2$ requires: C, 73·99; H, 5·77; N, 6·16%.)

The attempts to obtain II in the presence of Na_2CO_3, EtONa of KOH instead of K_2CO_3 failed and gave lower yields than in the above procedure.

3-*Methyl-2-(3′-methyl-2′-pyrazolin-5′-on-4′-ylmethyl)indole* (IVa)

(a) To a solution of II (1·0 g) in EtOH (30 ml, 95%) hydrazine hydrate (2·0 g, 80%) was added and the mixture refluxed on a water bath for 3 hr. After removal of EtOH on the water bath, water (50 ml) was added, and the precipitate was washed with water, and dried; yield 1·03 g (97%). Recrystallization from EtOH gave colourless crystals, m.p. 233–234°. (Found: C, 69·78; H, 6·59; N, 17·50. $C_{14}H_{15}N_3O$ requires: C, 69·69; H, 6·27; N, 17·42%.)

(b) To a solution of II (0·2 g) and AcONa (0·125 g) in EtOH (15 ml, 65 %) semicarbazide hydrochloride (0·15 g) was added and the mixture was refluxed on a water bath for 3 hr. After filtering off the insoluble part, the filtrate was concentrated to a small bulk on a water bath to remove EtOH. Upon the addition of water (3 ml), the product solidified and was washed with water and ether, and dried: yield 0·185 g (87 %), m.p. 230–232°. Recrystallization from EtOH gave colourless crystals, m.p. 233–234°. The IR spectra (KBr) showed the specific bands at 3480, (=NH), 2850, 2700, 1585 cm^{-1}.

3-*Methyl*-2-(3'-*methyl*-2'-*pyrazolin*-5'-*on*-4'-*ylidenemethyl*)*indole* (Va)

Compound IVa (0·36 g) was heated in an oil bath at 180° for 2·5 hr and distilled *in vacuo* (2 mm). The reddish orange distillate was recrystallized from EtOH; reddish orange needles, m.p. 249–250·5° (dec), yield, 0·25 g (69 %). (Found: C, 70·33; H, 5·82; N, 17·59. $C_{14}H_{13}N_3O$ requires: C, 70·27; H, 5·48; N, 17·56 %.) The IR spectra (KBr) showed the bands at 3500, 3450, 1660, 1615, (m), 1588, 1558 cm^{-1}.

3-*Methyl*-2-(3'-*methyl*-1'-*phenyl*-2'-*pyrazolin*-5'-*on*-4'-*ylmethyl*)*indole* (IVb)

The solution of II and phenylhydrazine in EtOH was refluxed for 2 hr. After removal of EtOH, waster was added and the precipitate washed with water and dried. The product was obtained almost in quantitative yield. Recrystallization from MeOH gave colourless needles, m.p. 183–184°. IR spectra (KBr) showed the bands at 3490, 1610, 1580, 1495 cm^{-1}. (Found: C, 75·62; H, 6·33; N, 13·06. $C_{20}H_{19}N_3O$ requires: C, 75·68; H, 6·03; N, 13·24 %.)

3-*Methyl*-2-(3'-*methyl*-1'-*phenyl*-2'-*pyrazolin*-5'-*on*-4'-*ylidenemethyl*) *indole* (Vb)

Compound IVb was heated at 180° for 2 hr and distilled *in vacuo* (2 mm). Recrystallization from MeOH gave orange-red needles, m.p. 154°, yield, 55 %. (Found: C, 75·80; H, 5·34; N, 13·14. $C_{20}H_{17}N_3O$ requires: C, 76·17; H, 5·43; N, 13·33 %.)

2-*Benzoyl*-9-*methyl*-3-*oxopyrrolidino*[1,2-a]*indole* (VII)

The reaction of I, obtained from 2,3-dimethylindole (2·5 g), with ethyl benzoylacetate (5·95 g) in the presence of K_2CO_3 (5 g) yielded 1·64 g (33 %), m.p. 141–143°. After recrystallization from MeOH colourless plates, m.p. 144° were obtained. IR spectra (KBr) showed three bands at 1735, 1680, 1630 cm^{-1}. (Found: C, 78·80; H, 5·65; N, 4·99. $C_{19}H_{15}NO_2$ requires: C, 78·87; H, 5·23; N, 4·84 %.)

3-*Methyl*-2-(3'-*phenyl*-2'-*pyrazolin*-5'-*on*-4'-*ylmethyl*)*indole* (VIII)

The alcoholic solution of VII (0·2 g) and hydrazine hydrate (80 %, 1 g) was refluxed for 3 hr, EtOH was removed by distilation and water added. The precipitate gave colourless needles, m.p. 204–206° (by recrystallization from dil. EtOH yield 0·17 g (81 %), IR spectra (KBr) showed the bands at 3450, 1620, 1595 and 1525 cm^{-1}. (Found: C, 75·41; H, 5·80; N, 14·01. $C_{19}H_{17}N_3O$ requires: C, 75·22; H, 5·65; N, 13·85 %.)

2,2-*Spirobi*(9-*methyl*-3-*oxo*-*pyrrolidino*[1,2-a]*indole*) (IX) *and* 9-*methyl*-3-*oxo*-*pyrrolidino*[1,2-a]*indole* (X)

The pyridinium salt (I), obtained from 2,3-dimethylindole (2·5 g), yielded 0·39 g, (12·8 %) of the product (IX) by the reaction with ethyl malonate (7·27 g) in the presence of K_2CO_3 (5 g). After vacuum distillation (2 mm) the product recrystallized from MeOH as colourless needles, m.p. 309–310°. (Found: C, 78·01; H, 5·21; N, 7·69. $C_{23}H_{18}N_2O_2$ requires: C, 77·95; H, 5·12; N, 7·91 %.)

The methanolic filtrate was mixed with 1 ml water and 0·5 g NaOH and the whole refluxed on a water bath for 3 hr and the EtOH was evaporated. Dil. HCl was added and the mixture extracted with C_6H_6. After evaporating the C_6H_6 the residue was distilled *in vacuo* (2 mm), yielding 0·53 g (16·6 %). Recrystallization from MeOH gave colourless needles, m.p. 175·5–176° (dec). (Found: C, 78·01; H, 6·29; N, 7·75. $C_{12}H_{11}NO$ requires: C, 77·81; H, 5·99; N, 7·56 %.)

Both IX and X showed the same IR spectra, bands (KBr) at 1740 and 1640 cm^{-1}.

1,2,3,4-*Tetrahydrocarbazole*-1-(N-*pyridinium bromide*) (XI) *and* 2-*acetyl*-1-*oxo*-2a,3,4,5-*tetrahydropyrrolidino*[1,2,3,kl]*carbazole* (XIIa)

To a stirred solution of tetrahydrocarbazole (3 g) and pyridine (3·6 g) in dry C_6H_6 (60 ml) at room temp, NBS (3·3 g) was added during 30 min. The mixture was stirred for an additional 3 hr, heated for 45 min at 62° and allowed to stand at room temp overnight.

The brown oily bromide (XI) was separated by decantation and washed with a little dry C_6H_6. A solution of the oily mass and ethyl acetoacetate (7·5 g) in abs EtOH (35 ml) was stirred at 1° to 3° while K_2CO_3 (4·5 g) was added during 20 min. The mixture was acidified with dil AcOH and the solvent was evaporated on a water bath. To the residue a little water was added, the brown oil extracted with C_6H_6, and after distillation of solvent the residue was distilled *in vacuo* (2 mm); yield 3·14 g.

Recrystallization from MeOH gave pale yellow needles. m.p. 116–117°, yield, 1·5 g (33·8 %). IR spectra (KBr) showed the bands at 2940, 2900 (w), 1741, 1709, 1670 cm^{-1}. (Found: C, 75·78; H, 6·21; N, 5·48. $C_{16}H_{15}NO_2$ requires: C, 75·87; H, 5·97; N, 5·53%.)

*2-Benzoyl-*1*-oxo-*2a,3,4,5*-tetrahydropyrrolidino*[1,2,3-kl]*carbazole* (XIIb)

The reaction of XI, obtained from tetrahydrocarbazole (3 g), with ethyl benzoylacetate (6 g) in the presence of K_2CO_3 (4·5 g) yielded 2·3 g (41·8%) of the product m.p. 158–161°, which after recrystallization from MeOH gave pale yellow needles, m.p. 163–164°. IR spectra (KBr) showed the bands at 1752, 1676 and 1657 cm^{-1}. (Found: C, 80·25; H, 5·73; N, 4·32. $C_{21}H_{17}NO_2$ requires: C, 79·98; H, 5·43; N, 4·44%.)

1,2,3,4*-Tetrahydro-*1*-*(3′*-methyl-*2′*-pyrazolin-*5′*-on-*4′*-yl*)*carbazole* (XIIIa)

The solution of XIIa (1 g) and hydrazine hydrate (80%, 3·2 g) in EtOH was refluxed for 3 hr yield, 0·9 g (85·5%). Recrystallization from C_6H_6 gave colourless crystal, m.p. 197–200°. The reaction with semicarbazide yielded the same product (XIIIa). IR spectra (KBr) showed the bands at 3460, 2930, 2850 (w), 1600, 1529, 1515 and 1462 cm^{-1}. (Found: C, 72·04; H, 6·60; N, 15·95. $C_{16}H_{17}N_3O$ requires: C, 71·88; H, 6·41; N, 15·72%.)

Pyrolysis of XIIIa

Compound XIIIa was heated in an oil bath for 3 hr at 210° under the N_2 atmosphere and distilled under red press (15 mm). The first sublimate, m.p. 209–222° (from MeOH) was the mixture of tetrahydrocarbazole and carbazole; this was proved by IR spectra and m.p. The second oily distillate was treated with ether, and the insoluble part (m.p. 206–208°) was recrystallized from dil EtOH, m.p. 212–213°. The mixed m.p. with 3-methyl-2-pyrazolin-5-one, m.p. 215°, was not depressed, and the both compounds showed the same IR spectra.

1-(3′*-Phenyl-*2′*-pyrazolin-*5′*-on-*4′*-yl*)-1,2,3,4*-tetrahydrocarbazole* (XIIIb)

The reaction of XIIb (0·8 g) with hydrazine hydrate (80%, 0·8 g) yielded 0·6 g (72·4%) of the product. Recrystallization from dil MeOH gave colourless needles, m.p. 217–219°. IR spectra (KBr) showed the bands at 3460, 3340, 2930, 1600, 1525 and 1460 cm^{-1}. (Found: C, 76·81; H, 6·55; N, 12·41. $C_{21}H_{19}N_3O$ requires: C, 76·56; H, 6·89; N, 12·76%.)

Diethyl 1,2,3,4*-tetrahydrocarbazole-*1*-malonate* (XIV) *and tetrahydrocarbazole-*1*-acetic acid* (XV)

The reaction of XI, obtained from tetrahydrocarbazole (2 g), with diethyl malonate (6·2 g) in the presence of K_2CO_3 (3 g) gave the product, 1·7 g by vacuum distillation (2 mm). Recrystallization from MeOH yielded 0·45 g (11·7%) of colourless crystals (XIV), m.p. 83–85°. IR spectra (KBr) showed the bands at 3450, 2930, 1749 and 1710 cm^{-1}. (Found: C, 69·35; H, 7·07; N, 4·22. $C_{19}H_{23}NO_4$ requires: C, 69·28; H, 7·04; N, 4·25%.)

The hydrolysis of the above filtrate with NaOH yielded 11 mg, carbazole and tetrahydrocarbazole-1-acetic acid, m.p. 137–138° after recrystallization from MeOH. IR spectra (KBr) showed the bands at 3450, 3030, 2930 and 1696 cm^{-1}. (Found: C, 73·56; H, 6·80; N, 6·53. $C_{14}H_{15}NO_2$ requires: C, 73·34; H, 6·59; N, 6·11%.)

The hydrolysis of XIV with NaOH gave also the same acid (XV).