

ALKYLATION REACTIONS OF MANNICH BASES IN AQUEOUS MEDIUM

Part IV.—Some Reactions of β -morpholinoethyl-2-phenanthryl ketone hydrochloride

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Syntheses of skatyl-(phenanthroyl-2) methane, α -methylskatyl-(phenanthroyl-2)-methane, 1, 5-di phenanthroyl-2) 3-nitropentane, α , α' 1 di (phenanthroyl-2-ethyl)-furan, (phenanthryl-2)-vinyl ketone and Skatyl-(phenanthroyl-3)-methane are described.

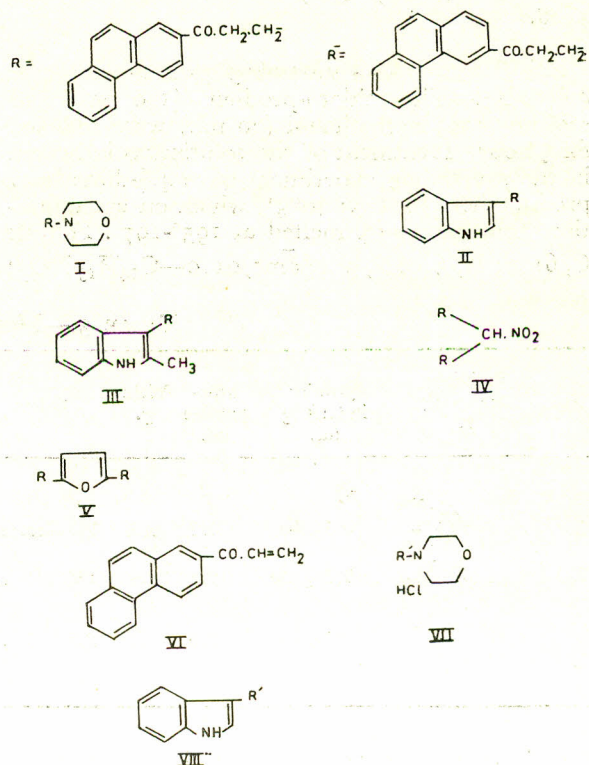
In the earlier communications we have described some alkylation reactions of Mannich bases, viz: Gramine,¹ phenyl - N,N - dimethyl - aminoethyl ketone,² N, N-dimethylamino-3 - keto - 5-phenyl-pent- Δ^4 -ene³ and N, N-dimethylamino-3-keto-5-phenylpentane in water.

In the present we communication describe the alkylation reaction of the Mannich base, β -morpholinoethyl-2-phenanthryl ketone hydrochloride (I) in aqueous medium.

When indole is alkylated with the Mannich base in water the product, skatyl-(phenanthroyl-2)-methane (II, m.p. 194°C.) is obtained in 85.7% yield based on the Mannich base. With 2-methyl-indole the corresponding α -methylskatyl (phenanthryl-2)- methane (III) is obtained in 79% yield (m.p. 210°C.). In the alkylation of nitromethane the dialkylated product, 1,5-di (phenanthroyl-2)-3-nitropentane (IV), is obtained in 54% yield and having m.p. 115°C. With furan the expected disubstituted product: α , α' -di (phenanthroyl-2-ethyl)-furan, (V) (m.p. 132°C.) is obtained in 76% yield.

Alkylation of methyl cyanide gave a product, m.p. 125°C which failed to give the test for elemental nitrogen, analysed for $C_{17}H_{12}O$ and decolorised aqueous potassium permanganate indicating the presence of a double bond. This can only be explained on the formation of (phenanthroyl-2) vinyl ketone (VI). The same product (VI) is also obtained when the alkylation of ammonium chloride, KCN and pyrrole is similarly tried.

With pyrrolidine no exchange of morpholine moiety takes place, as in the case of gramine, where-N $\begin{matrix} \text{CH}_3 \\ \diagdown \\ \text{C} \\ \diagup \\ \text{CH}_3 \end{matrix}$ is replaced.^{1b} The product (phenanthroyl-2)-vinyl ketone (VI) is obtained as before. The same product is obtained when the base hydrochloride (I) is boiled in water. A frequently proposed mechanism for alkylations with Mannich bases involves olefin forming elimination of a secondary amine from the Mannich



base as a first step. The reagent to be alkylated then adds to the conjugated olefinic bond in the Michael fashion. Since with CH_3CN , $NH_4^+Cl^-$ and pyrrole an elimination rather than an alkylation product is obtained and since the Michael addition of an active methylene compound to an activated olefinic species is known to be base-catalysed, it appears the present experimental conditions are not basic enough to lead to the second step in these cases.

Alkylation studies with the base, β -morpholinoethyl-3-phenanthrylketone hydrochloride (III) were not, however, successful in our hands. Attempted alkylation of furan, pyrrole, potassium

cyanide, methyl cyanide, nitromethane and ammonium chloride always resulted in a resinous material being formed which could not be crystallised. With the free base also resinous products were obtained. It was only with indole that the reaction took place giving the expected alkylation product, skatyl (phenanthroyl-3)-methane (VII) being obtained in 72% yield; m.p. 118°C.

Alkylation studies in water of other Mannich bases including those of cyclohexanone and acetone have been studied and will form the subject matter of separate communications.

Experimental

All melting points are corrected. U.V. absorption spectra were determined with a Beckman spectrophotometer model DK.2 in 95% ethanol. I.R. spectra were recorded with a Beckman I.R. 5 in KBr.

Skatyl - (phenanthroyl - 2) - methane (II).— β -Morpholinoethyl-2-phenanthryl ketone hydrochloride (I) (0.36 g.; 0.001 mole), indole (0.18 g.; 0.0015 mole) taken up in water (20 ml.) were refluxed on sand bath (8 hours). The separated pale yellow solid (0.34 g.) was filtered (suction) and crystallised from dioxane. Skatyl-(phenanthroyl-2)-methane (II) crystallised as pale yellow microscopic needles. M.P. 194°C.; yield: 0.30 g. (85.7% based on the Mannich base).

The product is soluble in ethanol, methanol, benzene, ethylacetate, furan, dioxane, and chloroform and insoluble in light petroleum (65-85°C.).

Analysis.—Skatyl-(phenanthroyl-2)-methane(II): $C_{25}H_{19}ON$ (349) requires: C, 85.93; H, 5.48; O, 4.58; N, 4.01%. Found: C, 85.66; H, 5.48; O, 4.59; N, 4.29% and mol. wt. (Rast) 305.

U.V. absorption bands at λ max 291 $m\mu$ ($\log \epsilon$ 4.0) and 265 $m\mu$ ($\log \epsilon$, 4.5) shoulder at 304 $m\mu$ ($\log \epsilon$ 3.8). I.R. absorption bands at 3448 cm^{-1} ($>NH$) and 1678 ($>CO$).

α -Methylskatyl - (phenanthroyl - 2) - methane (III).— β -Morpholinoethyl-2-phenanthryl ketone hydrochloride (I) (0.36 g.; 0.001 mole), 2-methylindole (0.196 g.; 0.0015 mole) were taken up in water (25 ml.) and refluxed on sand bath (6 hrs.). The solid was filtered off (suction) and crystallised from ethyl acetate. α -Methylskatyl-(phenanthroyl-2)-methane was obtained in yellow microscopic needles. M.P. 210°C.; yield 0.29 g., (79%, based on the Mannich base).

The product is soluble in ethyl acetate, ether, benzene chloroform, dioxane, ethyl and methyl alcohol and insoluble in light petroleum (65-85°C).

Analysis.— α -Methylskatyl-(phenanthroyl-2)-methane (III): $C_{26}H_{21}ON$, (363) requires: C, 85.92; H, 5.82; O, 4.40; N, 3.85%. Found: C, 85.62; H, 5.79; O, 4.41 and N, 4.08%.

U.V. absorption bands at λ max 295 $m\mu$ ($\log \epsilon$ 4.8) with shoulder at 300 $m\mu$ ($\log \epsilon$ 4.6). I.R. absorption bands at 3378 cm^{-1} ($>NH$) and 1667 cm^{-1} ($>CO$).

1,5-Di - (phenanthroyl - 2) - 3 - nitropentane (IV).— β -Morpholinoethyl-2-phenanthryl ketone hydrochloride (I) (0.355 g.; 0.001 mole) and nitromethane (0.183 g.; 0.003 mole) were taken up in water (20 ml.) and heated on water bath (reflux condenser) for 6 hours. The separated solid was filtered off (suction). 0.32 g. of 1,5-di-(phenanthroyl-2)-3-nitropentane crystallised from glacial acetic acid in tapering needles, m.p. 115°C.; yield 0.28 g. (54%, based on the Mannich base).

The product is soluble in ethyl and methyl alcohol, chloroform, ethyl acetate, glacial acetic acid, dioxane and tetrahydrofuran. It is insoluble in light petroleum (65-85°C.) and ether.

Analysis.—1,5-Di-(phenanthroyl-2)-3-nitropentane (IV): $C_{35}H_{27}O_4$ N, (525), requires: C, 79.98; H, 5.18; O, 12.81, N, 2.63%. Found: C, 79.47; H, 5.28; O, 12.42; N, 2.24% and mol. wt. (Rast) 553.

U.V. absorption bands at λ max 290 $m\mu$ ($\log \epsilon$ 4.2) and 264 $m\mu$ ($\log \epsilon$ 4.6) with shoulder at 299 $m\mu$ ($\log \epsilon$ 3.9). I.R. absorption bands at 1351 cm^{-1} ($C-NO_2$), 1667 cm^{-1} ($>CO$).

$\alpha\alpha'$ -Di - (phenanthroyl - 2 - ethyl) - furan (V).— β -Morpholinoethyl-2-phenanthryl ketone hydrochloride (I) (0.355 g.; 0.001 mole) and furan (0.41 g.; 0.006 mole) were taken up in water (20 ml.) and heated on water bath (7 hours). The separated solid was filtered by suction. α, α' -Di-(phenanthroyl-2-ethyl)-furan (V) crystallised from glacial acetic acid. Pale yellow leaflets. m.p. 132°C; yield 0.41 g. (76% based on the Mannich base).

The product is soluble in methyl and ethyl alcohol, ethyl acetate, chloroform, benzene, dioxane, glacial acetic acid and ether. It is insoluble in light-petroleum (65-85°C).

Analysis.— α, α' -Di (phenanthroyl-2-ethyl)-furan (V). $C_{38}H_{28}O_3$, (532), requires: C,

85.69; H, 5.30; O, 9.01. Found: C, 85.57; H, 5.54; O, 9.06%.

U.V. absorption bands at λ max 290 $m\mu$ ($\log \epsilon$ 4.8) and 265 $m\mu$ ($\log \epsilon$ 4.5) I.R. absorption bands at 1667 cm^{-1} ($>CO$).

(Phenanthroyl-2) vinyl ketone (VI).— β -Morpholinoethyl-2-phenanthryl ketone hydrochloride (I) (0.36 g.; 0.001 mole) and methyl cyanide (0.82 g.) g.; 0.002 mole taken in water (20 ml.) were heated on water bath (9 hours.). The separated solid was filtered (suction) and crystallised from ethyl acetate. (Phenanthroyl-2)vinyl ketone was obtained in pale microscopic needles, m.p. 125°C, yield, 0.24 g. (88%) based on the Mannich base).

The product is soluble in methyl and ethyl alcohol, ethyl acetate, chloroform, glacial acetic acid, dioxane and ether insoluble in benzene and light petroleum (65-85°C.).

Analysis:—(Phenanthroyl-2) vinyl ketone: $C_{17}H_{12}O$: (232): requires: C, 87.90; H, 5.21; O, 6.89%. Found: C, 87.86; H, 5.52; O, 6.63% and mol. wt.(Rast), 207.

U.V. absorption bands at λ max 291 $m\mu$ ($\log \epsilon$ 3.75), 265 $m\mu$ ($\log \epsilon$ 4.46) and 230 $m\mu$ ($\log \epsilon$ 3.74). I.R. absorption bands at 1667 cm^{-1} ($>CO$).

Skatyl-(phenanthroyl-3)-methane (VII).— The Mannich base, β -morpholinoethyl-3-phenanthryl ketone hydrochloride (0.355) g.; 0.001 mole) and indole (0.18 g.; 0.0015 mole), were taken up in water (25 ml.) and refluxed on sand bath (3 hours.). The solid was filtered off (suction) and crystallised from benzene. Skatyl-(phenan-

throyl-3)-methane was obtained in pale microscopic needles, m.p. 118°C, yield; 0.25 g. (72%).

The product is soluble in ethyl acetate, chloroform, ether, benzene, tetrahydrofuran and dioxane and insoluble in light petroleum (65-85°C.).

Analysis: Skatyl-(phenanthroyl-3)-methane: $C_{25}H_{19}ON$, (349), requires C, 85.93; H, 5.48; O, 4.58 and N, 4.01%. Found: C, 86.63; H, 5.72; O, 4.20; N, 3.70% and mol. wt. (Rast) 370.

U.V. absorption bands at λ max 320 $m\mu$ ($\log \epsilon$ 5.25) with shoulder at 251 $m\mu$ ($\log \epsilon$ 4.3). I.R. absorption bands at 3448 cm^{-1} ($>NH$) and 1678 cm^{-1} (CO).

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References

- (a) A. Kamal, A. Ali Qureshi and I. Ahmad, *Tetrahedron* **19**, 681 (1963).
(b) A. Kamal, (Miss.) Mussarat Anjum and (Miss.) Sooraiya Aziz, *Pakistan J. Sci. Ind. Res.*, **9**, April (1966).
- A. Kamal, (Miss.) Sooraiya Aziz, *Pakistan J. Sci. Ind. Res.*, **9** 217 1966.
- A. Kamal and Asadullah, *Pakistan J. Sci. Ind. Res.*, **9**(4), 1966.