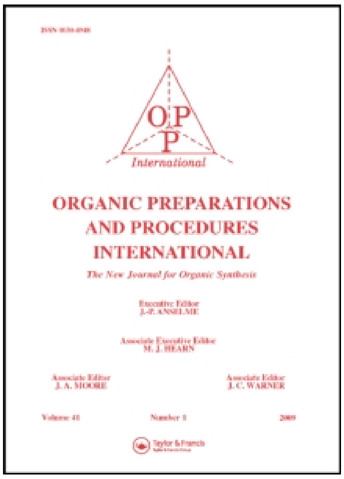

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3,4-DIALKYLQUINOLINES BY AN EXTENSION OF THE BEYER SYNTHESIS

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189-191°. NMR [$(CD_3)_2SO$] δ 7.58-7.95 (m, 4, aromatic), δ 5.57 (pair of d, 1, CHBr) δ 4.17-4.57 (m, 2, CH_2Br) δ variable with concentration and amount of water contamination (s, 2, OH).

Anal. Calcd. for $C_8H_9Br_2O_3P$: C, 27.94; H, 2.64; P, 9.01.
Found: C, 27.69; H, 2.65; P, 8.68.

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   (b) Masters' Candidate (Teaching).
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3,4-DIALKYLQUINOLINES BY AN EXTENSION OF THE BEYER SYNTHESIS

Submitted by (8/30/73)
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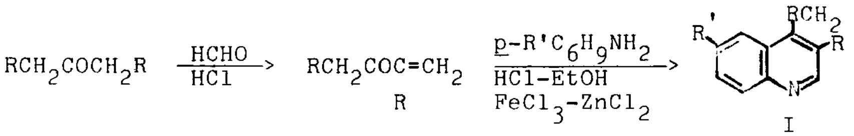
An extension of the Beyer synthesis[1,2] has been developed into a simple one-step procedure, useful for the preparation of 3,4-dialkylquinolines (I), starting from any simple ketone. Prior to this work, only methyl ketones had been used.[1,3-5]



I

a) R=CH_3, R'=H; b) R=R'=CH_3; c) R=C_2H_5, R'=H

Although the yields obtained in the present synthesis are low, the reaction has the advantage both in its simplicity and in the ready availability of reactants and hence may be preferred over the multistage syntheses reported previously.[6,7]

EXPERIMENTAL

Nmr spectra were determined at 100 MHz on a Varian model HA-100D spectrometer for solutions in CCl_4 (10% w/v). Tetramethylsilane (TMS) was used as an internal standard. Mass spectra were recorded at 70 eV on an A.E.I. model MS902 spectrometer.

3-Methyl-4-ethylquinoline (Ia). - A mixture of ethanol (60 ml.), 3-pentanone (30 ml.), ferric chloride hexahydrate (50 g.), anhydrous zinc chloride (5 g.) and conc. hydrochloric acid (30 ml.) was placed in a three necked round-bottomed flask fitted with two separatory funnels and a reflux condenser. In one of the funnels was placed a mixture of aniline (30 ml.), 3-pentanone (30 ml.) and ethanol (10 ml.) and in the other a solution of paraformaldehyde (9.2 g.) in a mixture of conc. hydrochloric acid (5 ml.) and ethanol (65 ml.). The contents of the flask were heated to gentle reflux, and then at 2 minute intervals ca. 1 ml. of each of the solutions in the funnels was added; the total period of addition was about 2 hours. When the addition was complete the reaction mixture was refluxed for another hour.

Excess solvent was removed by distillation to a miximum temperature of 100°. Solid sodium hydroxide was added to the residue. The alkaline mixture was steam distilled to obtain the crude product. Primary and secondary amine impurities were removed by diazotization[8] and the final product isolated by steam distillation. Ia (2.6 g., 5%) was obtained as a yellow oil.

NMR(CCl_4): 1.54 τ (1H, s, H_2), 2.00-2.26 τ (2H, m, H_5, H_8), 2.47-2.77 τ (2H, m, H_6, H_7), 7.11 τ (2H, q, J=7.5 Hz, $C\underline{H}_2CH_3$), 7.70 τ 3H, s, $C\underline{H}_3$), 8.85 τ (3H, t, J=7.5 Hz, $CH_2C\underline{H}_3$).

The picrate crystallized from ethanol as slender, yellow needles, mp. 199-200°, lit.[7] mp. 190-2°, lit.[6] mp.196-7°.

Anal. Calcd. for $C_{18}H_{16}N_4O_7$: C, 54.0; H, 4.0; N, 14.0.
Found: C, 54.2; H, 3.9; N, 13.9.

3,6-Dimethyl-4-ethylquinoline (Ib). - The procedure used for the preparation of Ia was employed, except that p-toluidine (32.8 g.) was substituted for aniline. Ib (13.9 g., 25%) was initially obtained as a tan solid, which was recrystallized from hexane to afford colorless prisms, mp. 68-9°.

Anal. Calcd. for $C_{13}H_{15}N$: C, 84.3; H, 8.2; N, 7.6.
Found: C, 84.4; H, 8.1, N, 7.7.

NMR(CCl_4); 1.55 τ (1H, s, H_2), 2.16 τ (1H, d, J_{78}=8.4 Hz, H_8), 2.40 τ (1H, bs, H_5), 2.69 τ (1H, d of d, J_{78}=8.4 Hz, J_{57}=1.8 Hz, $H_7$0, 7.03 τ (2H, q, J=7.5 Hz, $C\underline{H}_2CH_3$), 7.49 τ (3H, s, $C\underline{H}_3$), 7.61 τ (3H, s, $C\underline{H}_3$), 8.77 τ (3H, t, J=7.5 Hz, $CH_2C\underline{H}_3$).
(lit.[9] J_{78}=8.2 Hz, J_{57}=1.8 Hz).

The picrate crystallized from ethanol as yellow prisms, mp. 205-6°.

Anal. Calcd. for $C_{19}H_{18}N_4O_7$: C, 55.1; H, 4.4; N, 13.5.
Found: C, 55.2; H, 4.6; N, 13.3.

3-Ethyl-4-n-propylquinoline (Ic). - The procedure used for the preparation of Ia was employed, except that 4-heptanone (2 x 40 ml.) was substituted for 3-pentanone and the quantity of ethanol for the paraformadehyde solution was increased to 65 ml. to maintain the two reactant solutions at equal volume. Ic (0.9 g., 1.5%) was obtained as a yellow oil.

NMR(CCl_4): 1.30 τ (1H, s, H_2), 1.90-2.06 τ (2H, m, H_5, H_8), 2.31-2.60 τ (2H, m, H_6, H_7), 6.96 τ (2H, t, J=7.5 Hz, $C\underline{H}_2CH_2CH_3$), 7.17 τ (2H, q, J=7.5 Hz, $C\underline{H}_2CH_3$), 8.34 τ (2H, sextet, J=7.5 Hz, $CH_2C\underline{H}_2CH_3$), 8.71 τ (3H, t, J=7.5 Hz, $CH_2C\underline{H}_3$), 8.91 τ (3H, t, J=7.5 Hz, $CH_2CH_2C\underline{H}_3$).

Mass Spectrum: m/e 199.1359 (M^+, Calcd. for $C_{14}H_{17}N$: 199.1361), 184 ($M^+ - CH_3$), 170 ($M^+ - C_2H_5$).

The picrate crystallized from ethanol as slender, yellow needles, mp. 173-4°, (lit.[7] mp. 172-3°).

Anal. Calcd. for $C_{20}H_{20}N_4O_7$: C, 56.1; H, 4.7; N, 13.1.
Found: C, 55.9; H, 4.9; N, 12.9.

Erratum. - In a previous report[10] of our work in this series of compounds, a typographical error was made in reporting some of the chemical shifts of aromatic H atoms of 2,4,5,8-tetramethylquinoline. The signal at τ 2.81 should be assigned to H_7 and that at 3.06 to H_6.

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2-CYCLOHEXYLIDENECYCLOPENTANONE

Submitted by (6/28/73)

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Calcium carbide catalyses the self-condensation of cyclopentanone[1] but not that of cyclohexanone[2] while the reverse is true with sulfuric acid;[2,3] sodium hydroxide catalyses the self-condensation of both ketones.[4] Crossed condensations are brought about by all three catalysts,[2] but the calcium