

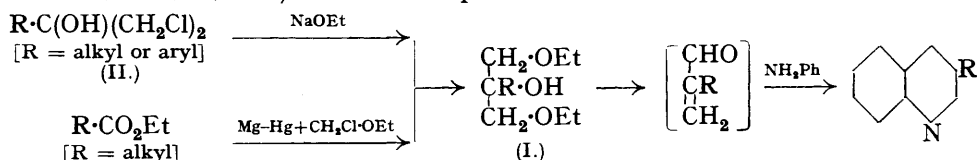
295. *The Synthesis of 3-Alkyl- and 3-Aryl-quinolines.*

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SKRAUP'S synthesis of quinoline (*Monatsh.*, 1880, **1**, 317) has been widely applied to the preparation of quinolines substituted in the benzene nucleus, and has been extended by Delaby and Hiron (*Compt. rend.*, 1930, **191**, 845) to include the use of aliphatic α -substituted glycerols. By means of the latter, mixtures of 2- and 4-substituted quinolines have been obtained, from which the predominating 2-compounds have been isolated. The method consists virtually of the reaction between an aromatic amine and a substituted acraldehyde generated *in situ*, and thus avoids difficulties due to polymerisation of the aldehydes (especially the α -substituted ones). The preparation of pure substituted glycerols from the corresponding glycerol dibromohydrin has the disadvantage of requiring the isolation of the diacetates and their subsequent hydrolysis (Delaby, *Compt. rend.*, 1922, **175**, 967), and several of the aryl derivatives of glycerol are jellies.

The present communication describes a method for the preparation of 3-substituted quinolines from the readily obtainable $\alpha\gamma$ -diethyl ethers of β -substituted glycerols—the alkyl-substituted compounds are known to decompose on heating with oxalic acid into easily polymerisable acraldehydes (Sommelet, *Ann. Chim. Phys.*, 1906, **9**, 484). The method gives a purer product and is more easily applicable to fused-ring systems than that of Friedländer and Göhring (*Ber.*, 1883, **16**, 1833).

The conditions of the experiment are essentially those of the Skraup reaction; replacement of nitrobenzene by arsenic acid (except when the base is aniline) (Knueppel, *Ber.*, 1896, **29**, 703), and dilution of the reactants with acetic acid (Cohn and Gustavson, *J. Amer. Chem. Soc.*, 1928, **50**, 2707) have been adopted in some cases.



The preparation of the β -substituted glycerol ethers (I) is effected almost quantitatively from the $\alpha\gamma$ -dichlorohydrin (II), obtained from a Grignard reagent and dichloroacetone

(Baeyer and Co., D.R.P. 168,941; *Centr.*, 1906, **1**, 1471), by the action of sodium ethoxide, although Roubel (*Annalen*, Suppl., **1**, 238) found that this reaction with the unsubstituted chlorohydrin is not complete. The alkyl compounds can be synthesised by Sommelet's method (*loc. cit.*).

The constitution of the final products as 3-substituted quinolines was established by comparison of their m. p.'s and those of their picrates with those given in the literature; but 3-ethylquinoline had to be oxidised to the carboxylic acid, since Kahn (*Ber.*, 1885, **18**, 3371) gives the m. p. of its picrate as 163° whereas that of the specimen now obtained, as well as that of the substance prepared by the synthetic method of Friedländer and Göhring (*loc. cit.*), was 196°.

EXPERIMENTAL.

3-Ethylquinoline.—Nitrobenzene (6.0 g.; 0.5 mol.), aniline (9.3 g.; 1 mol.), β -ethylglycerol $\alpha\gamma$ -diethyl ether (42 g.; 2.4 mols.), and concentrated sulphuric acid (25 g.; 2.5 mols.) were carefully mixed, and heated under reflux until reaction started. When the first violent reaction had subsided, the whole was boiled for 3 hours. The black solution was poured into water, the excess nitrobenzene and ether removed in steam, the solution made alkaline, and again steam-distilled. The excess aniline in the distillate was removed by diazotisation and boiling, the alkaline solution again steam-distilled, and the distillate extracted with ether. The ethereal solution, dried over potassium hydroxide, gave a colourless oil (yield 4 g., equivalent to 25% calc. on the aniline taken), b. p. 269° (corr.); d_4^{20} 1.0343; n_D^{20} 1.5949; n_a 1.5872; $[R_L]_D$ 51.60; $[R_L]_a$ 51.06 {Calc. from $[R_L]_a$ for quinoline (Brühl, *Z. physikal. Chem.*, 1895, **16**, 218) and $2 \times CH_2$ (Eisenlöhr, *ibid.*, 1910, **75**, 585): 51.09, 50.58 respectively}. The picrate forms long yellow needles from hot, and yellow plates from cold, methyl alcohol; m. p. 196—197°, undepressed on admixture with an authentic specimen (see below) (Found: C, 52.8; H, 3.9. Calc. for $C_{17}H_{14}O_7N_4$: C, 52.8; H, 3.7%). The base was oxidised with chromic acid (Riedel, *Ber.*, 1883, **16**, 1613) to quinoline-3-carboxylic acid, m. p. 273.5° (Found, by titration: *M*, 174.5. Calc.: *M*, 173).

This compound was also prepared from *o*-aminobenzaldehyde (2.2 g.; 1 mol.) in 50% alcohol (20 c.c.), *n*-butaldehyde (1.8 g.; 1.4 mols.), and 2*N*-sodium hydroxide (5 drops) according to Friedländer and Göhring (*loc. cit.*). The liquid product distilled at about 250°. The picrate separated from methyl alcohol as long yellow needles, m. p. 196—197° (Found: C, 52.8; H, 3.8%).

β -Phenylglycerol $\alpha\gamma$ -Diethyl Ether.— $\alpha\gamma$ -Dichloro- β -hydroxy- β -phenylpropane (1 mol.) in absolute alcohol (10 mols.) was slowly added to a solution of sodium ethoxide (2.5 mols.) in absolute alcohol (14 mols.), and the whole boiled under reflux for 4 hours. The separated sodium chloride (2 mols.) was filtered off and washed with dry ether. Most of the solvent was distilled off in a vacuum, and the residue, after being heated at 170° for one hour to remove the last traces of chloro-compounds which have nearly the same b. p. as the ethyl ether, was poured into water, extracted with ether, and the ethereal solution dried over sodium sulphate. β -Phenylglycerol $\alpha\gamma$ -diethyl ether was obtained in 80% yield as a colourless mobile liquid, b. p. 155°/21 mm. (Found: C, 69.8; H, 8.9. $C_{13}H_{20}O_3$ requires C, 69.6; H, 9.0%).

3-Phenylquinoline.—Aniline (3.0 g.; 0.7 mol.), nitrobenzene (2.0 g.; 0.37 mol.), the foregoing ether (10 g.; 1.0 mol.), 80% acetic acid (10 c.c.), and concentrated sulphuric acid (5 g.; 1.1 mols.) were carefully mixed in this order and heated under reflux on an oil-bath at 130° for 2 hours. More sulphuric acid (5 g.) was added to the cooled solution, which was then heated at 150—160° for a further 4 hours. The product was worked up as before, the phenylquinoline being distilled off in superheated steam, in which it was slightly volatile. The product was precipitated from the acidified bulky distillate as the picrate, which separated from hot methyl alcohol in a jelly-like mass, m. p. 205° (Hübner, *Ber.*, 1908, **41**, 482, gives 205°); yield 1.7 g., equivalent to 12% calculated on the amine taken (Found: C, 57.9; H, 3.4. Calc. for $C_{21}H_{14}O_7N_4$: C, 58.0; H, 3.3%). The base regenerated from the picrate had m. p. 52° (Hübner, *loc. cit.*, gives 52°).

3-Ethyl- α -naphthaquinoline.— α -Naphthylamine (10.0 g.; 1.0 mol.), arsenic acid (9.3 g.; 0.5 mol.), β -ethylglycerol $\alpha\gamma$ -diethyl ether (38 g.; 2.0 mols.), 80% acetic acid (15 g.), and concentrated sulphuric acid (22 g.; 2.0 mols.) were mixed in this order and heated at 150° on an oil-bath for 5 hours. The product was poured into water and steam-distilled, and the residue was filtered from the dark insoluble powder, which was extracted many times with dilute acid. The combined acid extracts were concentrated, made alkaline, and distilled in superheated steam, in which the base was difficultly volatile. Attempts to precipitate the base from the acid extract as the dichromate (Bamberger, *Ber.*, 1891, **24**, 2474) or the picrate, or to steam-distil

it directly from the resinous material, were less satisfactory. The distillate (5 l.) was acidified, filtered from a small quantity of insoluble material, and the base precipitated as the *picrate*. This crystallised from methyl alcohol in long needles containing 1 MeOH, which was removed in a vacuum. The alcohol-free compound had m. p. 188°; yield 4.4 g., equivalent to 12% calculated on the amine taken (Found : loss in weight in a vacuum, 6.78. $C_{21}H_{16}O_7N_4 \cdot CH_3 \cdot OH$ requires $CH_3 \cdot OH$, 6.84%. Found for residue : C, 57.9; H, 3.8. $C_{21}H_{16}O_7N_4$ requires C, 57.8; H, 3.7%). The regenerated 3-ethyl- α -naphthaquinoline crystallised from light petroleum in almost cubic crystals modified by the octahedron faces (doubly refracting), m. p. 75.5° (Found : C, 86.9; H, 6.3. $C_{15}H_{13}N$ requires C, 86.9; H, 6.3%).

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