mosphere of hydrogen. The theoretical volume of hydrogen was absorbed in 90 min. and the product (4.9 g.) was obtained in the usual manner, m.p. 81–85°. Two crystallizations from methanol and water afforded (in two crops) 3.9 g. of colorless crystals, m.p. 85–86°. The sample for analysis was obtained by sublimation at 80° (0.1 mm.) and had the same m.p., $[\alpha]^{19}\mathrm{D}$ +23.1° (1.38% in ethanol) (lit.[2] $[\alpha]\mathrm{D}$ +17°). The m.p. of a sample mixed with dihydroeudesmol[3] was unchanged.

Anal. Calcd. for $C_{15}H_{28}O$: C, 80.24; H, 12.58. Found: C, 80.33; H, 12.42.

Sagittol Acetate.—A mixture consisting of 10.0 g. of sagittol, 25 ml. of acetic anhydride and 1.0 g. of freshly fused sodium acetate was refluxed for 45 min. and then stirred with water (200 ml.) for 3 hr. Extraction with ether followed by distillation afforded 10.5 g. of the ester, b.p. 105–115° (0.75 mm.), which was contaminated with starting material. The only satisfactory means of purification consisted of passing this material in 50 ml. of petroleum ether (30–50°) through a column of acid-washed alumina (30 g.). After washing the column with 300 ml. of 10% ether in petroleum ether (30–50°) the combined solutions were freed from solvent by distillation through a 30-cm. bead-packed column. Upon further distillation through a 10-in. Vigreux column there was obtained 7.5 g. of sagittol acetate, b.p. 107.5–109.5° (0.75 mm.), $n^{20}\mathrm{D}$ 1.4915, $[\alpha]^{19}\mathrm{D}$ +30.2° (1.15% in ethanol). This compound is reported[12] to have $n^{20}\mathrm{D}$ 1.49204 and $[\alpha]^{20}\mathrm{D}$ +31°.

Anal. Calcd. for $C_{17}H_{28}O_2$: C, 77.22; H, 11.18. Found: C, 77.45; H, 11.21.

Treatment of Sagittol with Formic Acid.—Six grams of sagittol was refluxed for 45 min. with 30 ml. of 90% formic acid. Extraction with ether and isolation in the usual manner afforded 5.3 g. of colorless liquid, b.p. 77–78° (1.0 mm.), $n^{20}\mathrm{D}$ 1.5149, $[\alpha]^{19}\mathrm{D}$ −7.14° (1.18% in ethanol).

Anal. Calcd. for $C_{16}H_{26}O_2$: C, 76.75; H, 10.47. Found: C, 76.97; H, 10.41.

[12] F. W. Semmler and E. Tobias, *Ber.*, **46**, 2026 (1913).

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The Synthesis of Nitrogen-containing Ketones. III. Studies with 2-Methyl-5-ethylpyridine, 2,4-Lutidine and Lepidine[1]

BY NEWTON N. GOLDBERG AND ROBERT LEVINE

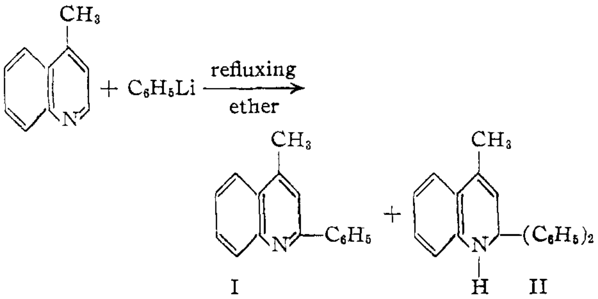
RECEIVED MARCH 3, 1955

Earlier papers from this Laboratory[2,3] have been concerned with the acylation of 2-picoline, quinaldine and 2,6-lutidine. The present report is an extension of our work to other tar bases.

Reaction of two equivalents of the lithium derivative of 2,4-lutidine or 2-methyl-5-ethylpyridine with one equivalent of methyl benzoate as described earlier[2,3] gave 2-phenacyl-4-methylpyridine (89%) and 2-phenacyl-5-ethylpyridine (83%), respectively. Both of these ketones gave copper salts when treated with copper(II) acetate solution and may have some application as chelating agents.

The acylation of lepidine has been studied by other investigators.[4,5] Although Bergstrom and Moffat[4] reported that they were unable to acylate lepidine with ethyl benzoate using sodium amide as the condensing agent, a reinvestigation of this reaction by Weiss and Hauser[5] has shown that the benzoylation and other acylations of lepidine may be effected in low yields in the presence of sodium amide.

We have attempted to metalate the methyl group of lepidine by treating it with phenyllithium in refluxing ether. However, metalation did not take place since the reaction of the mixture with esters, acid halides or carbon dioxide did not result in acylation or carboxylation of the methyl group. In all cases a mixture of 2-phenyl-4-methylquinoline (I) (61–66%) and 2,2-diphenyl-4-methyl-1,2-dihydroquinoline (II) (24–26%) was obtained.



I II

These results show the importance of temperature on the course of the reaction since Tarbell and co-workers[6] have shown that when this reaction is effected at ice-bath temperature only I (54%) is obtained.

The structure of II was established by oxidizing it with potassium ferricyanide[7,8] to give the corresponding carboxylic acid which was then decarboxylated by calcium oxide[9] to give the known 2,2-diphenyl-1,2-dihydroquinoline.[10]

Experimental[11]

The Benzoylation of 2,4-Lutidine and 2-Methyl-5-ethylpyridine.—Using the method described earlier for similar reactions,[2,3] the interaction of phenyllithium (0.2 mole) and methyl benzoate (13.6 g., 0.1 mole) gave 18.8 g. (89%) of 2-phenacyl-4-methylpyridine, b.p. 159–160° at 1.8 mm. *Anal.* Calcd. for $C_{14}H_{13}NO$: C, 75.59; H, 6.20; N, 6.68. Found: C, 79.58; H, 6.11; N, 6.83. The ketone gave a yellow picrate, m.p. 167–168° (from 95% ethanol). *Anal.* Calcd. for $C_{20}H_{16}N_4O_8$: N, 12.72. Found: N, 12.91. The ketone also gave a tan copper salt, m.p. 171–172° dec. *Anal.* Calcd. for $C_{28}H_{24}N_2O_2Cu$: N, 5.79. Found: N, 5.54.

From a similar sized run involving 2-methyl-5-ethylpyridine there was obtained 18.7 g. (83% of 2-phenacyl-5-ethylpyridine, b.p. 169–171° at 1.8 mm., m.p. 64–65° (from 60–70° petroleum ether). *Anal.* Calcd. for $C_{15}H_{15}NO$: C, 79.97; H, 6.71; N, 6.22. Found: C, 79.99; H, 6.95; N, 5.97. The ketone gave a yellow picrate, m.p. 163.8–164.2° (from 95% ethanol). *Anal.* Calcd. for $C_{21}H_{18}N_4O_8$: N, 12.33. Found: N, 12.12. The ketone also gave a brown copper salt, m.p. 168–169° dec. *Anal.* Calcd. for $C_{30}N_{28}N_2O_2Cu$: N, 5.47. Found: N, 5.26.

Reaction of Lepidine with Phenyllithium.—An ether solution of phenyllithium (0.4 mole) and lepidine (0.4 mole) was refluxed for 30 minutes and then poured onto 150 ml.

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[1] This work was performed under Contract No. AT(30-1)-670 between the U. S. Atomic Energy Commission and the University of Pittsburgh.

[2] N. N. Goldberg, L. B. Barkley and R. Levine, THIS JOURNAL, **73**, 4301 (1951).

[3] N. N. Goldberg and R. Levine, *ibid.*, **74**, 5217 (1952).

[4] F. W. Bergstrom and A. Moffat, *ibid.*, **59**, 1494 (1937).

[5] M. J. Weiss and C. R. Hauser, *ibid.*, **71**, 2023 (1949).

[6] D. S. Tarbell, J. F. Bunnett, R. B. Carlin and V. P. Wystrach, *ibid.*, **67**, 1584 (1945).

[7] L, Ruzicka, G. B. R. de Graaff and J. R. Hosking, *Helv. Chim. Acta*, **9**, 976 (1926); **14**, 238 (1931).

[8] R. Weissgerber and O. Kruber, *Ber.*, **52**, 352 (1919).

[9] W. Koenigs, *ibid.*, **12**, 98 (1879).

[10] H. Gilman and G. C. Gainer, THIS JOURNAL, **69**, 877 (1947).

[11] The tar bases for this study were supplied through the courtesy of Dr. F. E. Cislak, Reilly Tar and Chemical Corp.

of 6 *N* hydrochloric acid and 500 g. of crushed ice. The mixture of solids (*i.e.*, 2,2-diphenyl-4-methyl-1,2-dihydroquinoline and 2-phenyl-4-methylquinoline hydrochloride) which precipitated was filtered and separated into its components in the following way. The mixed solids were treated with 5% sodium hydroxide to free the 2-phenyl-4-methylquinoline from its salt and the mixture then extracted with several portions of ether. In this way the ether-soluble 2-phenyl-4-methylquinoline was separated from the ether-insoluble 2,2-diphenyl-4-methyl-1,2-dihydroquinoline. Thus, 14.9 g. (25%) of 2,2-diphenyl-4-methyl-1,2-dihydroquinoline, m.p. 163–164° (from 95% ethanol) was obtained. *Anal.* Calcd. for $C_{22}H_{19}N$: C, 88.85; H, 6.44; N, 4.71. Found: C, 88.42; H, 6.83; N, 4.62. This dihydroquinoline gave a yellow picrate, m.p. 198–200° dec. *Anal.* Calcd. for $C_{28}H_{22}N_4O_7$: C, 63.87; H, 4.21; N, 10.64. Found: C, 63.51; H, 3.89; N, 10.72.

From the ether solution mentioned above there was obtained (56.6 g., 64.6%) of 2-phenyl-4-methylquinoline, b.p. 161–164° at 1.3 mm. This amine gave a methiodide, m.p. 183.5–185°.[6] It also gave a yellow picrate, m.p. 212–213.5° (from 95% ethanol) and a hydrochloride, m.p. 233–235°. *Anal.* of picrate: Calcd. for $C_{22}H_{16}N_4O_7$: C, 58.93; H, 3.60; N, 12.50. Found: C, 58.96; H, 3.31; N, 12.42. *Anal.* of the hydrochloride: Calcd. for $C_{16}H_{14}NCl$: N, 5.49. Found: N, 5.48.

Similar results were obtained when the ether solution of the tar base and phenyllithium was treated with methyl benzoate, benzoyl chloride or carbon dioxide.

Proof of Structure of 2,2-Diphenyl-4-methyl-1,2-dihydroquinoline.—Using the procedure described for similar compounds[7-9] 5.0 g. of 2,2-diphenyl-4-methyl-1,2-dihydroquinoline was oxidized to give a mixture of 4.2 g. of starting material and 0.02 g. of 2,2-diphenyl-1,2-dihydroquinoline, m.p. 86–87°[10] (from 95% ethanol).

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The Preparation of Some ω-Bromoalkyl Quaternary Ammonium Salts

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In conjunction with the investigation of unsymmetrical bis-quaternary salts, which is being carried on in these laboratories, a convenient route to ω-bromoalkyl monoquaternary intermediates was required. A preliminary search of the literature revealed that little had been done in this field. Maréchal and Bagot,[1] who adequately reviewed the earlier literature, prepared two of the desired type of bromoalkylammonium bromide salts by what appeared to be the simplest approach: reaction of a dibromoalkane with a slight excess of trimethylamine in benzene solution. In our hands, however, their procedure afforded salt mixtures containing a high proportion of the bis-quaternary derivative.[2] After some experimentation a modification was adopted, which afforded the monoquaternary salts in yields of 50 to 90%. The technique involved the slow addition of 65 to 75% of the calculated amount of the appropriate tertiary amine to a benzene solution of the dibromoalkane. In this way, a large excess of the dihalide was maintained in solution throughout the operation and the mono salt precipitated before it was given the opportunity to react further. Unreacted dibromide was recovered from combined mother liquors. Even under these conditions appreciable amounts of the bis-quaternary by-products often formed; these were isolated in a few instances. Occasionally, the crude mono salt containing (as indicated by ionic halogen determination) roughly 5 to 10% of bis-quaternary material, was not purified and was found to be satisfactory for the preparation of desired derivatives.

An alternative approach was attempted for the synthesis of some of the propyl salts. This, involving the reaction of a hydroxypropyl quaternary ammonium bromide with 48% hydrobromic acid, was found to be less satisfactory and not generally applicable. V and VIII were successfully prepared by both methods.

There was, of course, no difficulty in the preparation of mono salt derivatives of dibromoethane.

Experimental[3]

Tertiary Amines.—N-Methylpyrrolidine, b.p. 78.5–79.5°, n^{26}D 1.4204,[4] picrate m.p. 219–221°, was prepared from pyrrolidine by the Eschweiler–Clarke process[5] or, less satisfactorily, from 1,4-dibromobutane and methylamine.[6]

Anal. Calcd. for $C_5H_{11}N$: N, 16.34. Found: N, 16.59.

N-Methylpiperidine, b.p. 105–107°, n^{25}D 1.4355, and methyldiethylamine, b.p. 65°, were prepared by the Eschweiler–Clarke method.

3-Bromopropyltrimethylammonium Bromide (III).—This compound was prepared a number of times in yields of 50 to 90%. As an example, anhydrous trimethylamine was bubbled slowly into a solution of 135 g. (0.67 mole) of 1,3-dibromopropane in 300 ml. of benzene at room temperature until 26.4 g. (0.45 mole) had been absorbed. This took approximately 5 hours. After 16 hours the white crystalline precipitate, 99.5 g. (85% yield) of analytically satisfactory III, m.p. 205° dec., was collected. Occasionally, the precipitate obtained directly from the reaction mixture was found to be contaminated with bis salt; in the event of this, one recrystallization from alcohol afforded pure III.[7]

3-Bromopropylmethyldiethylammonium Bromide (V).—Over a period of 1.5 hours a solution of 14.3 g. (0.16 mole) of methyldiethylamine in 50 ml. of benzene was added dropwise with stirring to 50.5 g. (0.25 mole) of 1,3-dibromopropane, warmed on a steam-bath. After completion of the addition, the reaction mixture was allowed to stand overnight at room temperature. The supernatant liquid was decanted from the oily product which was washed with fresh benzene, taken to dryness twice under reduced pressure with the addition of more benzene, and finally dried *in vacuo* over phosphorus pentoxide. There was obtained 27.9 g. (59% yield) of white, hygroscopic material, melting 120–130°.

6-Bromohexyltrimethylammonium Bromide (XIII).—Into a solution of 14.6 g. (0.06 mole) of dibromohexane in 25 ml. of benzene at room temperature, was bubbled slowly 2.4 g. (0.04 mole) of trimethylamine. The reaction mixture was allowed to stand overnight, the white precipitate was collected and recrystallized from *t*-butyl alcohol. A yield of 11.5 g. (95%) of XIII, m.p. 106–108°, was obtained.

3-Bromopropylmethylpiperidinium Bromide (Alternative Procedure) (VIII).—3-Piperidinopropanol, b.p. 109–110° (19 mm.), was prepared by the reaction of 3-bromopropanol with piperidine and sodium carbonate in aqueous alcohol. The methobromide, prepared in benzene, melted at 128–129°.

A solution of 10.7 g. of the methobromide salt in 20 ml.

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[1] R. Maréchal and J. Bagot, *Ann. pharm. franç.*, **4**, 172 (1946).

[2] See also, K. J. M. Andrews, F. Bergel and A. L. Morrison, *J. Chem. Soc.*, 2998 (1953).

[3] Melting points are corrected for stem exposure.

[4] N. D. Zelinsky and J. K. Jurjew, *Ber.*, **62**, 2589 (1929), report n^{20} 1.4480. Their product may have been contaminated with N-methylpyrrole.

[5] H. T. Clarke, H. B. Gillespie and S. Z. Weisshaus, THIS JOURNAL, **55**, 4571 (1933).

[6] J. v. Braun, *Ber.*, **49**, 966 (1916).

[7] When present in appreciable amounts, the bis-quaternary impurities sometimes crystallized first out of alcoholic solvents. The mono salts were obtained from the mother liquors by the addition of ether. In the purification of longer chain monoquaternaries, advantage could be taken of their relatively high solubility in acetone