tetrahydropyridine (I) have already been described.[3,4]

4-p-Tolyl-1,2,3,6-tetrahydropyridine (II) was prepared by reacting p,α-dimethylstyrene, formaldehyde, and ammonium chloride and then treating the reaction mixture with excess hydrochloric acid to effect rearrangement and dehydration.

4-p-Tolylpyridine (III) was obtained by dehydrogenation of either I or II with palladium and nitrobenzene.

EXPERIMENTAL[5]

1-Methyl-4-p-tolyl-1,2,3,6-tetrahydropyridine (I). This compound, b.p. 110–115° (0.9 mm.), m.p. 76–78°, was prepared in 61% yield from methylamine hydrochloride, formaldehyde, and p,α-dimethylstyrene using the procedure (Method C) described previously[4] for the preparation of 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine.

Anal. Calc'd for $C_{13}H_{17}N$: C, 83.37; H, 9.15; N, 7.48. Found: C, 82.95; H, 9.08; N, 7.36.

4-p-Tolyl-1,2,3,6-tetrahydropyridine (II). This compound, b.p. 110–125° (0.75 mm.), m.p. 55–57°, was prepared in 33% yield from ammonium chloride, formaldehyde, and p,α-dimethylstyrene using the direct preparation procedure described previously[1] for the preparation of 4-phenyl-1,2,3,6-tetrahydropyridine.

Anal. Calc'd for $C_{12}H_{15}N$: C, 83.19; H, 8.73; N, 8.09. Found: C, 83.06; H, 8.71; N, 8.30.

The *hydrochloride* melted at 193–195° after recrystallization from a 10:1 mixture of acetone and isopropyl alcohol.

Anal. Calc'd for $C_{12}H_{16}ClN$: C, 68.72; H, 7.69; N, 6.68; Cl, 16.9. Found: C, 68.65; H, 7.54; N, 6.77; Cl, 16.8.

4-p-Tolylpyridine (III). *A. From 1-methyl-4-p-tolyl-1,2,3,6-tetrahydropyridine* (I). This compound (III) was prepared from 76 g. (0.41 mole) of 1-methyl-4-p-tolyl-1,2,3,6-tetrahydropyridine (I), 5 g. of 5% palladium on alumina catalyst, and 150 g. (1.22 moles) of nitrobenzene at 150–60° during 2$^1/_2$ hours using the procedure described previously[1] for the preparation of 4-phenylpyridine from 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine. There was obtained 37 g. (54%) of 4-p-tolylpyridine (III), b.p. 122–127° (0.7 mm.). This solidified and melted at 90–91° after recrystallization from heptane.

Anal. Calc'd for $C_{12}H_{11}N$: C, 85.17; H, 6.55; N, 8.28. Found: C, 84.89; H, 6.45; N, 8.28.

The *picrate* melted at 199–201° after recrystallization from ethanol containing a small amount of acetone.

Anal. Calc'd for $C_{18}H_{14}N_4O_7$: C, 54.27; H, 3.54; N, 14.07. Found: C, 54.49; H, 3.87; N, 13.80.

B. From 4-p-tolyl-1,2,3,6-tetrahydropyridine (II). A mixture of 5 g. of 5% palladium on alumina catalyst, 190 g. (1.54 moles) of nitrobenzene, and 46 g. (0.27 mole) of 4-p-tolyl-1,2,3,6-tetrahydropyridine (II) was stirred in a nitrogen atmosphere at 130–160° during two hours while water was removed by a water separator. The mixture was cooled, filtered, and distilled to give 39 g. (87%) of 4-p-tolylpyridine (III), b.p. 90–110° (0.1 mm.). This solidified and melted at 90–91° after recrystallization from heptane. The m.p. of a mixture with III prepared from I was 90–91°.

Anal. Calc'd for $C_{12}H_{11}N$: C, 85.17; H, 6.55; N, 8.28. Found: C, 85.14; H, 6.53; N, 8.43.

The *picrate* melted at 199–201° after recrystallization from ethanol containing a small amount of acetone. The m.p. of a mixture with the picrate of III prepared from I was 199–201°.

Anal. Calc'd for $C_{18}H_{14}N_4O_7$: C, 54.27; H, 3.54; N, 14.07. Found: C, 54.52; H, 3.78; N, 14.15.

Acknowledgment. We wish to thank Mr. C. W. Nash and his staff for analytical data reported.

RESEARCH LABORATORIES
ROHM AND HAAS COMPANY
PHILADELPHIA 37, PENNSYLVANIA

The Aminomethylation of *p*-Isopropyl-α-methylstyrene

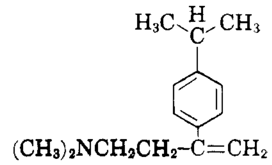
CLAUDE J. SCHMIDLE, JOHN E. LOCKE, AND
RICHARD C. MANSFIELD

Received June 21, 1956

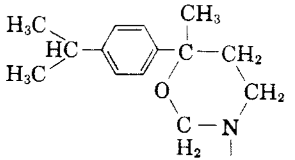
It is the purpose of this paper to report the aminomethylation of p-isopropyl-α-methylstyrene. The reaction of dimethylamine, formaldehyde, and p-isopropyl-α-methylstyrene gave N,N-dimethyl-3-p-isopropylphenyl-3-butenylamine (I).

The reaction of p-isopropyl-α-methylstyrene, formaldehyde, and methylamine hydrochloride gave 3,6-dimethyl-6-p-isopropylphenyltetrahydro-1,3-oxazine (II) and 1-methyl-4-p-isopropylphenyl-4-piperidinol (III). Rearrangement and dehydration of the crude reaction mixture in the presence of excess sulfuric acid gave 1-methyl-4-p-isopropylphenyl-1,2,3,6-tetrahydropyridine (IV). This substance was dehydrogenated and demethylated, using nitrobenzene and palladium on alumina, to 4-p-isopropylphenylpyridine (VI).

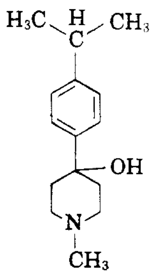
Treatment of the reaction product of p-isopropyl-α-methylstyrene, formaldehyde, and ammonium chloride with excess hydrochloric acid gave 4-p-



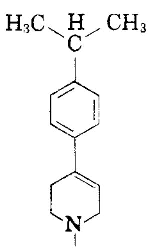
I



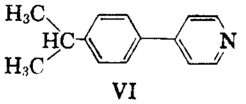
II



III



IV; R=CH₃
V; R=H



VI

---

[3] Schmidle and Mansfield, *J. Am. Chem. Soc.*, **77**, 5698 (1955).

[4] Schmidle and Mansfield, *J. Am. Chem. Soc.*, **78**, 425 (1956).

[5] All melting points are uncorrected.

isopropylphenyl-1,2,3,6-tetrahydropyridine (V). This compound also was dehydrogenated to 4-*p*-isopropylphenylpyridine (VI).

This is an extension of our work on the aminomethylation of olefins in which an analogous series of reactions was carried out using α-methylstyrene and p-α-dimethylstyrene.[1–5]

EXPERIMENTAL[6]

N,N-Dimethyl-3-p-isopropylphenyl-3-butenylamine (I). A 15-g. (0.125 mole) portion of N,N,N′,N′-tetramethyldiaminomethane was added slowly with stirring and cooling to a mixture of 4 g. (0.125 mole) of 95% paraformaldehyde and 150 g. of glacial acetic acid. Then 40 g. (0.25 mole) of *p*-isopropyl-α-methylstyrene was added and the mixture was refluxed for 15 hours. After cooling, the mixture was poured into 500 ml. of water and was extracted with toluene. The aqueous layer was made basic with excess sodium hydroxide solution. The amine was taken up in toluene, dried, and distilled to give 32.3 g. (60%) of N,N-dimethyl-3-*p*-isopropylphenyl-3-butenylamine (I), b.p. 100–110° (1.2 mm.), n_D^{25} 1.5162.

Anal. Calc'd for $C_{15}H_{23}N$: C, 82.89; H, 10.66; N, 6.45. Found: C, 82.86; H, 10.69; N, 6.69.

3,6-Dimethyl-6-p-isopropylphenyltetrahydro-1,3-oxazine (II) *and 1-methyl-4-p-isopropylphenyl-4-piperidinol* (III). A mixture of 70 g. (1.04 moles) of methylamine hydrochloride, 200 g. (2.46 moles) of 37% aqueous formaldehyde, and 160 g. (1.00 mole) of *p*-isopropyl-α-methylstyrene was stirred at 95–100° for 1 hour, cooled, diluted with 1 l. of water, extracted with toluene, and made basic with excess 50% sodium hydroxide. The amine was taken up in toluene, dried, and distilled. The fraction boiling at 120–130° (0.7 mm.) was redistilled to give 76 g. (33%) of 3,6-dimethyl-6-*p*-isopropylphenyltetrahydro-1,3-oxazine (II), b.p. 115–117° (0.7 mm.).

Anal. Calc'd for $C_{15}H_{23}NO$: C, 77.21; H, 9.93; N, 6.00. Found: C, 77.77; H, 9.95; N, 6.02.

The fraction boiling at 130–140° (0.7 mm.) solidified, was combined with the residue, and was recrystallized from toluene twice to give 25 g. (11%) of 1-methyl-4-*p*-isopropylphenyl-4-piperidinol (III), m.p. 143–144°.

Anal. Calc'd for $C_{15}H_{23}NO$: C, 77.21; H, 9.93; N, 6.00. Found: C, 76.98; H, 9.91; N, 6.05.

The foreruns, residues, and mother liquors from the purification of II and III were combined, stripped free of toluene, and stirred at 95–100° for 6 hours with a mixture of 10 g. of water and 100 g. of concentrated hydrochloric acid. The mixture was cooled, diluted with 500 ml. of water, extracted with heptane, and made basic with excess 50% sodium hydroxide. The amine was taken up in toluene, dried, and distilled to give 52 g. (24%) of 1-methyl-4-*p*-isopropylphenyl-1,2,3,6-tetrahydropyridine (IV), b.p. 125–135° (0.8 mm.). This material solidified and melted at 63–65° after recrystallization from heptane.

Anal. Calc'd for $C_{15}H_{21}N$: C, 83.66; H, 9.83; N, 6.51. Found: C, 82.89; H, 10.01; N, 6.49.

The *hydrochloride* sintered about 200° and melted at 218–220° after recrystallization from acetone containing about 3% of ethanol.

Anal. Calc'd for $C_{15}H_{22}ClN$: C, 71.54; H, 8.81; N, 5.56; Cl, 14.1. Found: C, 71.02; H, 8.85; N, 5.47; Cl, 14.0.

1-Methyl-4-p-isopropylphenyl-1,2,3,6-tetrahydropyridine (IV). A mixture of 130 g. (1.93 moles) of methylamine hydrochloride, 370 g. (4.56 moles) of 37% aqueous formaldehyde, and 300 g. (1.88 moles) of *p*-isopropyl-α-methylstyrene was stirred at 95–100° for 1 hour and then was cooled. There was slowly added 150 g. (1.47 moles) of concentrated sulfuric acid and the mixture was stirred at 95–100° for 4 hours, cooled, extracted with heptane, and made basic with excess 50% sodium hydroxide. The amine was taken up in toluene, dried, and distilled to give 159 g. (39%) of 1-methyl-4-*p*-isopropylphenyl-1,2,3,6-tetrahydropyridine (IV), b.p. 120–130° (0.5 mm.). This compound solidified and melted at 64–66° after recrystallization from heptane.

Anal. Calc'd for $C_{15}H_{21}N$: C, 83.66; H, 9.83; N, 6.51. Found: C, 83.47; H, 10.02; N, 6.45.

The *hydrochloride* sintered about 200° and melted at 218–220° after recrystallization from acetone containing a small amount of ethanol.

Anal. Calc'd for $C_{15}H_{22}ClN$: C, 71.54; H, 8.81; N, 5.56; Cl, 14.1. Found: C, 70.99; H, 9.01; N, 5.37; Cl, 13.9.

4-p-Isopropylphenyl-1,2,3,6-tetrahydropyridine (V). A stirred mixture of 108 g. (2.02 moles) of ammonium chloride and 334 g. (4.12 moles) of 37% aqueous formaldehyde was warmed to 60°. There was added 160 g. (1.00 mole) of *p*-isopropyl-α-methylstyrene during 15 minutes while the temperature was controlled at 60–65° by external cooling. After the exotherm had ceased the mixture was stirred for 2 hours while the temperature fell to 45°. There was added 225 g. (7.0 moles) of methanol and the mixture was stirred for one hour and then was allowed to stand overnight. The methanol was removed by heating to 85° at about 200 mm. pressure. After cooling, 300 g. (3.08 mole) of concentrated hydrochloric acid was added and the mixture was stirred for four hours at 96–98°, cooled, poured into 700 ml. of water, made basic with excess 50% sodium hydroxide, and extracted with toluene. The toluene extract was dried and distilled to give 96 g., b.p. 128–179° (0.75 mm.). This product was dissolved in excess 8% hydrochloric acid, extracted with heptane, and made basic with excess 50% sodium hydroxide. The amine was taken up in toluene, dried, and distilled to give 48 g. (24%) of 4-*p*-isopropylphenyl-1,2,3,6-tetrahydropyridine (V), b.p. 110–125° (0.3 mm.). The fraction boiling at 120–125° (0.3 mm.), which consisted of 25 g., was used for analysis.

Anal. Calc'd for $C_{14}H_{19}N$: C, 83.53; H, 9.51; N, 6.96. Found: C, 83.15; H, 9.52; N, 6.98.

The *hydrochloride* melted at 184–186° after one recrystallization from acetone containing a small amount of isopropyl alcohol.

Anal. Calc'd for $C_{14}H_{20}ClN$: C, 70.72; H, 8.48; N, 5.89; Cl, 14.9. Found: C, 70.53; H, 8.63; N, 5.84; Cl, 15.0.

4-p-Isopropylphenylpyridine (VI). *A. From 1-methyl-4-p-isopropylphenyl-1,2,3,6-tetrahydropyridine* (IV). A mixture of 37 g. (0.17 mole) of 1-methyl-4-*p*-isopropylphenyl-1,2,3,6-tetrahydropyridine (IV), 150 g. (1.22 moles) of nitrobenzene, and 4 g. of 5% palladium on alumina catalyst was stirred in an atmosphere of nitrogen at 140–150° for $2^1/_2$ hours with a water-removal trap attached to the reaction flask. The mixture was cooled, diluted with excess dilute hydrochloric acid and toluene, and filtered. The organic layer was washed with dilute hydrochloric acid and then with water. The combined aqueous phases were extracted twice with a toluene-heptane mixture and then were made basic with excess 50% sodium hydroxide. The amine was taken up in toluene, dried, and distilled to give 19 g. (56%) of 4-*p*-isopropylphenylpyridine (VI), b.p. 130–137° (0.7 mm.). This substance solidified and an analytical sample, recrystallized from heptane, melted at 70–72°.

Anal. Calc'd for $C_{14}H_{15}N$: C, 85.23; H, 7.67; N, 7.10. Found: C, 85.21; H, 7.72; N, 7.10.

---

(1) Schmidle and Mansfield, *J. Am. Chem. Soc.*, **77**, 4636 (1955).

(2) Schmidle and Mansfield, *J. Am. Chem. Soc.*, **77**, 5698 (1955).

(3) Schmidle and Mansfield, *J. Am. Chem. Soc.*, **78**, 425 (1956).

(4) Schmidle and Mansfield, *J. Am. Chem. Soc.*, **78**, 1702 (1956).

(5) Schmidle, Locke, and Mansfield, *J. Org. Chem.*, **21**, 1194 (1956).

(6) All melting points are uncorrected.

The *picrate* melted at 184–186° after recrystallization from ethanol containing a small amount of acetone.

Anal. Calc'd for $C_{20}H_{18}N_4O_7$: C, 56.34; H, 4.25; N, 13.14. Found: C, 56.38; H, 4.37; N, 13.02.

B. From 4-p-isopropylphenyl-1,2,3,6-tetrahydropyridine (V). A mixture of 4 g. of 5% palladium on alumina catalyst, 61 g. (0.30 mole) of 4-*p*-isopropylphenyl-1,2,3,6-tetrahydropyridine (V), and 250 g. (2.03 moles) of nitrobenzene was stirred at 140–150° for two hours in an atmosphere of nitrogen with a water-removal trap attached to the reaction flask. The mixture was cooled, filtered, and distilled to give 45 g. (75%) of 4-*p*-isopropylphenylpyridine (VI), b.p. 112–125° (0.1 mm.). This product solidified and an analytical sample, recrystallized from heptane, melted at 70–72°. The melting point of a mixture with VI prepared from IV was 70–72°.

Anal. Calc'd for $C_{14}H_{15}N$: C, 85.23; H, 7.67; N, 7.10. Found: C, 84.96; H, 7.82; N, 7.18.

The *picrate* melted at 184–186° after recrystallization from ethanol containing a small amount of acetone. The melting point of a mixture with the picrate of VI prepared from IV was 184–186°.

Anal. Calc'd for $C_{20}H_{18}N_4O_7$: C, 56.34; H, 4.25; N, 13.14. Found: C, 56.43; H, 4.22; N, 13.02.

Acknowledgment. We wish to thank Mr. C. W. Nash and his staff for analytical data reported.

RESEARCH LABORATORIES
ROHM AND HAAS COMPANY
PHILADELPHIA 37, PENNSYLVANIA