

ways were recovered unchanged. No olefins or condensation products of the haloethanes could be found, either in the reaction mixture, or as gaseous products of the reaction.

1,2-Dichloro-1,1,2-trifluoro-2-iodoethane.—Chlorotrifluoroethylene (88 g.) was bubbled through a mixture of 162 g. of iodine monochloride and 500 ml. of 1,1,2-trichloro-1,2,2-trifluoroethane (Freon-113) during the course of 5 hours. As the reaction proceeded the iodine chloride passed into solution, and the temperature of the reaction mixture rose to 35°. After the absorption of the olefin had ceased, the reaction mixture was washed with sodium thiosulfate solution, and then with sodium carbonate solution until colorless, and was dried over sodium carbonate. Fractional distillation of the solution gave 119 g., 57% of theory, of 1,2-dichloro-1,1,2-trifluoro-2-iodoethane boiling 43–44° at 100 mm., n_D^{25} 1.4474, d_4^{25} 2.1959. *Anal.* Calcd. for $C_2Cl_2F_3I$: C, 9.29; mol. wt., 279; MR_D 34.3. Found: C, 8.87; mol. wt., 271, determined in $n-C_7F_{16}$; MR_D 34.0. This material was stored in the dark at room temperature for several months without excessive decomposition. The above structure was assigned by analogy to other addition reactions with this olefin.⁴

A much less stable compound, thought to be 1-chloro-1,2,2-trifluoro-1,2-diiodoethane, was obtained in 30–35% yield by the distillation of a mixture of equal weights of chlorotrifluoroethylene and iodine which had stood at room temperature for several days sealed in a Pyrex reactor. This material, boiling 54–55° at 20 mm., with slight decomposition, and having a density of greater than 2.5, decomposed readily upon standing to yield crystals of iodine, but no other residue. A reliable analysis or refractive index could not be obtained because of this instability.

(4) W. E. Hanford and G. W. Rigby, U. S. Patent 2,409,274, issued October, 1946; C. W. Huskins and P. Tarrant, "Preparation and Reactions of Certain Chlorofluoroethylenes," Report of Office of Naval Research under Contract N8onr503, June 15, 1946; J. A. Young and P. Tarrant, *THIS JOURNAL*, **71**, 2432 (1949); K. E. Rapp, *et al.*, *ibid.*, **72**, 3642 (1950); R. L. Pruett, *et al.*, *ibid.*, **72**, 3646 (1950); J. T. Barr, *et al.*, *ibid.*, **72**, 4480 (1950).

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An Improved Synthesis of Mescaline

BY FRED BENINGTON AND RICHARD D. MORIN

In connection with certain studies of the synthesis of phenethylamines, we have had the occasion to prepare mescaline, β -(3,4,5-trimethoxyphenyl)-ethylamine, an alkaloid which occurs naturally in the cacti *Anhalonium*. The literature cites the synthesis of this alkaloid by two methods, neither of which gives a satisfactory yield.

Slotta and Heller¹ synthesized mescaline in four steps from 3,4,5-trimethoxybenzaldehyde in an over-all yield of 28%. A more direct method *via* the condensation of 3,4,5-trimethoxybenzaldehyde with nitromethane, followed by the reduction of the resulting nitrostyrene, was employed by Späth.² The nitrostyrene was first reduced to the corresponding aldoxime, which on further reduction gave mescaline. The two-stage reduction gave a 24.9% yield, and the over-all yield of mescaline from the aldehyde was only 20.8%.

An elegant method for reduction of β -nitrostyrenes to phenethylamines with lithium aluminum hydride has been reported.³ Reduction of 3,4,5-

trimethoxy- β -nitrostyrene by this method resulted in an 89% yield of mescaline hydrochloride. The over-all yield from 3,4,5-trimethoxybenzaldehyde has been increased to 65%.

Experimental⁴

3,4,5-Trimethoxybenzaldehyde.—Gallic acid was converted to trimethylgallic acid in 80% yield by methylation with methyl sulfate.⁵ Trimethylgalloyl chloride was prepared in 81% yield by the action of phosphorus pentachloride on trimethylgallic acid.¹ The acid chloride was purified by distillation and redistillation under reduced pressure; b.p. 131–133° (2 mm.); m.p. 83–84°. Rosenmund reduction of 3,4,5-trimethoxybenzaldehyde was carried out as described¹ using 52 g. of 3% Pd-BaSO₄ catalyst per mole of acid chloride. Dry xylene was the solvent. The product was recovered by removal of the catalyst by filtration, stripping off the xylene and fractional distillation of the residue under reduced pressure. A forerun of pyrogallol trimethyl ether, b.p. 82–100° (0.1 mm.), was obtained, and 3,4,5-trimethoxybenzaldehyde was collected as the fraction boiling at 106–112° (0.1 mm.). After crystallization from alcohol the aldehyde melted at 73–74°; yield 59%.

3,4,5-Trimethoxy- β -nitrostyrene.—This compound was prepared by the procedure of Späth² in 82.7% yield; m.p. 121–122° after recrystallization from alcohol.

Mescaline Hydrochloride.—Reduction of 7.2 g. (0.03 mole) of 3,4,5-trimethoxy- β -nitrostyrene with 5.7 g. of lithium aluminum hydride was carried out as described^{3a} for 4-hydroxy-3-methoxy- β -nitrostyrene. The yield of mescaline picrate, m.p. 210–212°, was 11.4 g. (86%). After recrystallization from alcohol, the picrate melted at 214–216°; reported³ 216–218°. The mescaline picrate was converted to mescaline hydrochloride as described^{3a} in 92% yield; m.p. 180–181° (after recrystallization from alcohol); reported¹ 181°.

(4) All melting and boiling points uncorrected.

(5) H. Gilman and A. H. Blatt, "Organic Syntheses," John Wiley and Sons, Inc., New York, N. Y., 1941, Coll. Vol. I, 2nd Ed., p. 537.

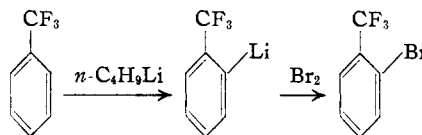
BATTELLE MEMORIAL INSTITUTE
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Preparation of *o*-Bromobenzotrifluoride

BY ROBERT A. BENKESER AND ROLAND G. SEVERSON

In view of the recent interest in ortho and para derivatives of benzotrifluoride,^{1,2} we are hereby reporting a two-step synthesis of *o*-bromobenzotrifluoride.

Metallation of benzotrifluoride with *n*-butyllithium has been shown to yield largely the ortho isomer.³ Treatment of the metallated product with bromine vapor forms *o*-bromobenzotrifluoride in a 28% over-all yield.



This procedure is more direct than the six-step synthesis outlined by Jones¹ and the yield might conceivably be improved since the optimum reaction conditions were not investigated. As a proof of structure, *o*-bromobenzotrifluoride was found to undergo halogen-metal interconversion with *n*-butyllithium. The product upon carbonation was *o*-trifluoromethylbenzoic acid. It is of interest that

(1) R. Jones, *THIS JOURNAL*, **69**, 2346 (1947).

(2) M. Lilyquist, J. G. Wisler and P. Tarrant, Abstracts of 118th Meeting of the American Chemical Society, Chicago, Illinois, 1950.

(3) J. D. Roberts and D. Y. Curtin, *THIS JOURNAL*, **68**, 1658 (1946).

(1) K. H. Slotta and H. Heller, *Ber.*, **63**, 3029 (1930).

(2) E. Späth, *Monatsh.*, **40**, 144 (1919).

(3) (a) F. A. Ramirez and A. Burger, *THIS JOURNAL*, **72**, 2781 (1950);

(b) R. F. Nystrom and W. G. Brown, *ibid.*, **70**, 3738 (1948); (c) K. E. Hamlin and A. W. Weston, *ibid.*, **71**, 2210 (1949).

o-bromobenzotrifluoride does not appear to react with lithium metal using the conventional procedure and yet it undergoes halogen-metal interconversion in high yields. This parallels the observations made on *m*-bromotrifluoromethylbenzene.⁴

Experimental

***o*-Bromobenzotrifluoride.**—To a solution of *n*-butyllithium prepared from 278 g. (3 moles) of *n*-butyl chloride and 43 g. (6.2 g. atoms) of lithium in 1 l. of dry ether, was added 438 g. (3 moles) of trifluoromethylbenzene. This mixture was refluxed for 12 hours after the spontaneous evolution of butane had ceased. Bromine vapor was then carried into the reaction flask by a stream of nitrogen until approximately 400 g. had been added. The reaction mixture was poured into 1 l. of water with thorough mixing. The organic layer was washed with dilute sodium hydroxide, a sodium thiosulfate solution, and then with water. The resulting material was steam distilled to remove a rather large amount of tar. The organic layer from this operation was dried and fractionated giving 134 g. (30% recovery) of trifluoromethylbenzene, b.p. 100–101°, and after a relatively small intermediate fraction, 129 g. (28% yield) of *o*-bromobenzotrifluoride, b.p. 167–168°, n_D^{25} 1.4806.

To 6.75 g. (0.03 mole) of the *o*-bromotrifluoromethylbenzene thus prepared was added 66 ml. of an ether solution containing 0.03 mole of *n*-butyllithium at such a rate as to allow gentle reflux. The mixture was stirred for an additional 30 minutes and then carbonated with Dry Ice. Working up in the usual manner gave 4.73 g. (83%) of material, melting at 106–108°. Recrystallization from petroleum ether gave 4 g. (70%) of *o*-trifluoromethylbenzoic acid, m.p. 108–109.5°.

(4) H. Gilman and L. Woods, *THIS JOURNAL*, **66**, 1981 (1944).

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Preparation of Pure Secondary Bromides

BY JAMES CASON AND ROBERT H. MILLS

It has long been realized that conversion of a secondary alcohol to the corresponding bromide is likely to be accompanied by rearrangement of the intermediate carbonium ion to yield an isomeric

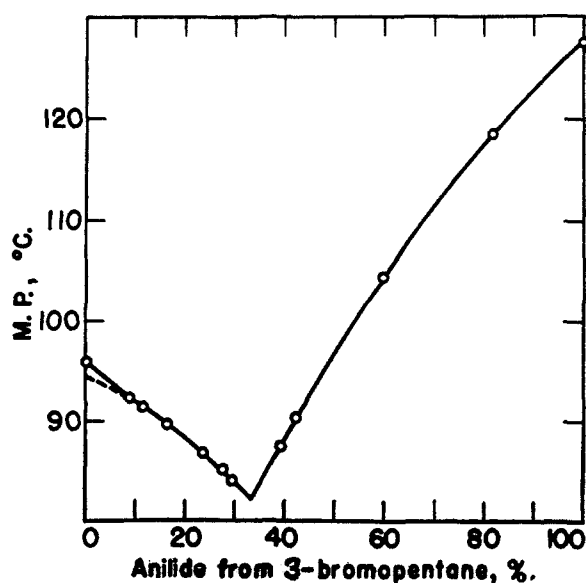


Fig. 1.—Binary melting point diagram of mixtures of the anilides prepared by reaction of 2-pentyl- and 3-pentylmagnesium bromide with phenyl isocyanate.

secondary bromide. In this connection, the *s*-amyl bromides have been studied carefully^{1,2} for there are only two possible isomers. Lauer and Stodola³ have made a careful study of the analysis of mixtures of the isomeric *s*-amyl bromides, and have concluded that analysis based on the index of refraction is quite unreliable but that the binary melting point diagram of the anilides may be used for reliable analysis of mixtures of the bromides. These investigators prepared 2-bromo- and 3-bromopentane by the methods judged to be most reliable for furnishing the pure bromides, but there has actually been no evidence that these "best" samples are entirely homogeneous isomers.

Evidence has been presented⁴ that the reaction of bromine with the silver salt of a carboxylic acid, to give an alkyl halide, proceeds by way of a free radical mechanism. If this is the case, since free radicals are much less prone to rearrangement than carbonium ions, the reaction of bromine with the silver salt of an α -alkylalkanoic acid should lead to an isomerically pure *s*-alkyl halide. In the present investigation, this reaction has been carried out with silver 2-methylpentanoate and silver 2-ethylbutanoate to give, respectively, 2- and 3-bromopentane. The anilides obtained from these compounds proved to melt significantly higher than the best samples obtained by Stodola and Lauer,³ who prepared the bromides from the alcohols with hydrogen bromide. Also, a direct comparison has been made with a sample of the bromide prepared by reaction of phosphorus tribromide with synthetic 2-pentanol, according to the procedure⁵ considered best. The anilide from this bromide exhibited a melting point in agreement with the value reported by Stodola and Lauer, thus below the melting point of a sample prepared from bromide obtained *via* the silver salt reaction. It thus appears that a pure secondary bromide cannot be obtained from the corresponding alcohol in instances where isomeric secondary bromides are structurally possible.

Since analysis of mixtures of the *s*-amyl bromides is often desirable,³ a binary melting point diagram has been constructed by use of mixtures of the pure anilides prepared from the *s*-amyl bromides obtained from the silver salt reactions. From this diagram (Fig. 1), it is indicated that the best sample of 2-bromopentane obtained previously³ was of about 92% purity, and the best sample of 3-bromopentane was of about 87% purity. The right side of this curve (anilide from 3-bromopentane crystallizing) has a form normally characteristic of such diagrams, but the left side (anilide from 2-bromopentane crystallizing) does not. A characteristic curve (terminal portion dotted) may be drawn through all points except the upper one, and it is felt that the actual curve bends up at this point on account of association in the concentrated solution of a molecular compound of the *d*- and *l*-forms of the anilide. In another instance⁶ in which the optical

(1) Sherrill, Otto and Pickett, *THIS JOURNAL*, **51**, 3027 (1929).

(2) Sherrill, Baldwin and Hass, *ibid.*, **51**, 3036 (1929).

(3) Lauer and Stodola, *ibid.*, **56**, 1215 (1934).

(4) Arnold and Morgan, *ibid.*, **70**, 4248 (1948); Dauben and Tilles, *ibid.*, **72**, 3185 (1950); Smith and Hull, *ibid.*, **72**, 3309 (1950).

(5) Hsueh and Marvel, *ibid.*, **50**, 855 (1928).

(6) Cason and Winans, *J. Org. Chem.*, **15**, 157 (1950).