effect of replacement of alkoxyl by methyl or ethyl has been studied in the case of the 2,4,6-substituted phenethylamines,[3] but all compounds in this series produced markedly different effects on the respiratory enzymes present in brain homogenates than did compounds substituted in the 3,4- or 3,4,5-positions. Accordingly, 3,4,5-trimethyl-β-phenethylamine should provide a more reliable indication of the change in psychochemical activity brought about by replacement of methoxyl by methyl in the mescaline nucleus.

The key reaction in the synthesis of 3,4,5-trimethyl-β-phenethylamine was the isomerization of 2,4,6-trimethylacetophenone, readily obtained by Friedel-Crafts acetylation of mesitylene, to 3,4,5-trimethylacetophenone by heating with anhydrous aluminum chloride.[4] Transformation of the acetyl group to the β-aminoethyl side-chain was readily accomplished *via* the Kindler modification of the Willgerodt reaction. Conversion of the 3,4,5-trimethylphenylacetic acid so obtained to the corresponding amide, and reduction with lithium aluminum hydride, afforded the desired 3,4,5-trimethyl-β-phenethylamine. This route to β-phenethylamines is convenient when the corresponding acetophenones are available and is worthy of further exploitation.

Results of the physiological evaluation of 3,4,5-trimethyl-β-phenethylamine will be published elsewhere.

EXPERIMENTAL[5]

3,4,5-Trimethylphenylacetothiomorpholide. 2,4,6-Trimethylacetophenone, b.p. 109–111°/9 mm., was obtained in 88% yield by the action of acetic anhydride on mesitylene in the presence of anhydrous aluminum chloride in carbon disulfide solution.[6] Isomerization to 3,4,5-trimethylacetophenone was accomplished as described[4] by heating a mixture of 71 g. of 2,4,6-trimethylacetophenone with 116 g. of anhydrous aluminum chloride at 170° for 1.5 hr.; yield, 56.6 g. (80%) of a pale yellow oil, b.p. 135–140°/12 mm. A mixture of 48.6 g. of 3,4,5-trimethylacetophenone, 39 g. of redistilled morpholine, and 14.4 g. of sulfur was refluxed for 12 hr. The warm reaction mixture was poured into 175 ml. of hot ethanol and allowed to cool to permit the product to crystallize; yield, 62.6 g. (79%) of 3,4,5-trimethylphenylacetothiomorpholide, m.p. 120–122°, sufficiently pure for the next step. A sample recrystallized from ethanol melted at 123–124°.

Anal. Calcd. for $C_{15}H_{21}NOS$: N, 5.3; S, 12.2. Found: N, 5.2; S, 12.0.

3,4,5-Trimethylphenylacetic acid. A mixture of 51 g. of 3,4,5-trimethylphenylacetothiomorpholide, 110 ml. of acetic acid, 16 ml. of sulfuric acid, and 25 ml. of water was heated under reflux for 5 hr. and decanted from the small amount of tar formed into 850 ml. of water with stirring. The precipitated crude product was collected, washed with water, and heated with 225 ml. of 5% aqueous sodium hydroxide. Filtration from a small amount of insoluble matter and acidification with dilute hydrochloric acid gave 30 g. (88%) of 3,4,5-trimethylphenylacetic acid sufficiently pure for the next step. A sample recrystallized from benzene-petroleum ether melted at 125–126°.

Anal. Calcd. for $C_{11}H_{14}O_2$: C, 74.1; H, 7.8; Neutr. Equiv. 178. Found: C, 74.0; H, 7.9; Neutr. Equiv. 180.

3,4,5-Trimethylphenylacetamide. After the initial vigorous reaction had subsided, a mixture of 21.3 g. of 3,4,5-trimethylphenylacetic acid and 25 g. of phosphorus pentachloride was warmed on the steam bath for 10 min. The mixture was distilled under reduced pressure to remove phosphorus oxychloride, and the residue was added gradually to 100 ml. of ice-cooled concentrated aqueous ammonia. The precipitated amide was collected, washed with water, and air dried; recrystallization from benzene plus a small amount of ethanol afforded 18 g. (85%) of the pure amide, m.p. 183–184°.

Anal. Calcd. for $C_{11}H_{15}NO$: C, 74.6; H, 8.5; N, 7.9. Found: C, 74.4; H, 8.6; N, 7.9.

3,4,5-Trimethyl-β-phenethylamine. To a stirred suspension of 8.6 g. of lithium aluminum hydride in 500 ml. of absolute ether, was added a solution of 10 g. of 3,4,5-trimethylphenylacetamide in 600 ml. of boiling reagent benzene, using additional hot benzene to redissolve material which crystallized during the addition. The reaction mixture was stirred and refluxed for 22 hr. and then hydrolyzed by cautious addition of water and 10% sulfuric acid. A white solid insoluble in both the ether and aqueous layers was formed and collected by filtration. This material proved to be the insoluble sulfate of 3,4,5-trimethyl-β-phenethylamine contaminated with aluminum salts. Upon heating with concentrated hydrochloric acid, the crude product dissolved, and the hydrochloride of 3,4,5-trimethyl-β-phenethylamine crystallized in the form of colorless lustrous plates on cooling. The yield was 10.1 g. (89%), m.p. 249–250° after recrystallization from methanol-ethyl acetate.

Anal. Calcd. for $C_{11}H_{15}ClN$: Cl, 17.8; N, 7.0. Found: Cl, 17.7; N, 6.9.

The *benzoyl derivative* melted at 153–154°.

Anal. Calcd. for $C_{18}H_{21}NO$: C, 80.9; H, 7.9. Found: C, 80.6; H, 7.7.

BATTELLE MEMORIAL INSTITUTE
COLUMBUS 1, OHIO
FELS RESEARCH INSTITUTE
YELLOW SPRINGS, OHIO

(3) F. Benington, R. D. Morin, and L. C. Clark, Jr., *J. Org. Chem.*, **20**, 1292 (1955).
(4) G. Baddeley, *J. Chem. Soc.*, 232 (1944).
(5) Melting points are uncorrected.
(6) Shirley, *Preparation of Organic Intermediates*, John Wiley & Sons, Inc., New York, 1951, p. 190.

A Convenient Synthesis of *m*-Anisidine

PANKAJA K. KADABA AND SAMUEL P. MASSIE

Received July 16, 1956

In studies on the preparation of ring derivatives of phenothiazines[1] beginning with the corresponding anilines, *m*-anisidine was required. This compound is not commercially available, in spite of its relative importance as a starting material, particularly in the synthesis and degradative studies of some indole alkaloids, notably harmine[2] and reserpine.[3] The conventional method of preparing *m*-

(1) S. P. Massie and P. K. Kadaba, *J. Org. Chem.*, **21**, 347 (1956).
(2) W. O. Kermack, W. H. Perkin, and R. Robinson, *J. Chem. Soc.*, **199**, 1641 (1921); E. Spath and E. Lederer, *Ber.*, **63**, 123 (1930).
(3) C. F. Huebner, H. B. McPhillany, A. F. St. Andre, and E. Schlitter, *J. Am. Chem. Soc.*, **77**, 473 (1955).

anisidine,[4] using *m*-nitroaniline as the starting material, is long and tedious, and involves diazotization, hydrolysis, methylation, and reduction. Its preparation by rearrangement of the product from *o*-chloroanisole with sodium amide in liquid ammonia is not very convenient.[5] A convenient method of making *m*-anisidine, starting with *m*-aminophenol, has been reported by Reverdin,[6] and involves acylation of the amino group, followed by methylation with dimethyl sulfate and subsequent hydrolysis. However, in spite of the apparent simplicity of this method it has not been widely used by other workers, and in recent studies on the constitution of tazettine,[7] as lycoris alkaloid, the above described conventional method for the synthesis of *m*-anisidine was used.

We wish to report here the details of a single step synthesis of *m*-anisidine by direct methylation of the easily available and inexpensive *m*-aminophenol using dimethyl sulfate, as well as the results of reinvestigation of the earlier procedure of Reverdin.[6] The use of methyl *p*-toluenesulfonate as a methylating agent was also successful but offered no advantage.

We acknowledge the financial support of the National Cancer Institute (Grant C-2450) and we thank them very much.

EXPERIMENTAL

m-Anisidine from m-Aminophenol. A mixture of *m*-aminophenol (25 g.), dimethyl sulfate, technical grade (50 g.), anhydrous potassium carbonate (100 g.), and potassium hydroxide (25 g.) was refluxed in anhydrous methyl ethyl ketone (500 ml.) for 120 hr. The cooled reaction mixture was poured into an excess of cold water and let stand overnight to decompose excess dimethyl sulfate. It was then extracted with ether and the ether extract dried and distilled to remove solvent. The oily residue was distilled under reduced pressure to give 25.5 g. (91%) of pale yellow *m*-anisidine, b.p. 81–86°/2 mm.

m-Anisidine from m-acetylaminophenol. A mixture of *m*-acetylaminophenol (43 g.), dimethyl sulfate, technical grade (50 g.) and anhydrous potassium carbonate (100 g.) was refluxed in anhydrous methyl ethyl ketone (500 ml.) for 48 hr. The mixture was then cooled, filtered, and the residual potassium carbonate washed with ether. The washings were combined with the filtrate and the solvents removed by distillation. The syrupy residue of *m*-acetaniside (a portion was crystallized from benzene petroleum ether to give colorless, shining crystals, m.p. 79–80°)[6] was hydrolyzed by refluxing with concentrated hydrochloric acid for 4 hr. The cooled mixture was made strongly alkaline with sodium hydroxide solution, and extracted with ether. Removal of the ether, subsequent to drying and distillation of the residue, gave 20 g. (57%) of pale yellow *m*-anisidine, distilling at 79° under 1 mm. pressure. The reaction time could be reduced to 6 hr., but the yield was lower.

m-Acetylaminophenol was methylated and hydrolyzed following the procedure of Reverdin. The yields were in order of 50–55% as against the 90% claimed by Reverdin.

DEPARTMENT OF CHEMISTRY
FISK UNIVERSITY
NASHVILLE 8, TENN.

(4) D. A. Shirley, *Preparation of Organic Intermediates*, John Wiley and Sons, New York, N. Y., 1951, p. 213.
(5) H. Gilman and R. H. Kyle, *J. Am. Chem. Soc.*, **74**, 3028 (1952).
(6) F. Reverdin and A. de Luc, *Ber.*, **47**, 1537 (1914).
(7) H. Kondo, T. Ikada, and J. Taga, *Ann. Rept. ITSUU Lab. Japan*, **3**, 659 (1952); [*Chem. Abstr.* **47**, 7417 (1953)].

Analogs of Hexaphenylethane. VI. Triphenylgermyltriphenyltin[1]

HENRY GILMAN AND CLARE W. GEROW

Received August 7, 1956

There has been reported only one organic compound containing a germanium-tin bond. This was triphenylgermyltrimethyltin reported by Kraus and Foster.[2] We have prepared triphenylgermyltriphenyltin as a member of a series to compare the strengths of the bonds between various Group IV-B elements. The preparation was carried out by coupling triphenylgermylpotassium with triphenyltin chloride according to the equation

$$(C_6H_5)_3GeK + (C_6H_5)_3SnCl \rightarrow (C_6H_5)_3GeSn(C_6H_5)_3 + KCl$$

The mode of addition was found to be important in this reaction, for it was found that when the triphenyltin chloride was added to the triphenylgermylpotassium a 60% yield of triphenylgermyltriphenyltin was isolated; however, when the triphenylgermylpotassium was added to the triphenyltin chloride only a mixture of products was formed which could not be separated into its components. A mixture was also formed when triphenyltinlithium was allowed to react with triphenylchlorogermane, and when triphenylgermyllithium was allowed to react with triphenyltin chloride. It is believed that the mixtures obtained above contain hexaphenyldigermane, triphenylgermyltriphenyltin, and possibly hexaphenylditin. The presence of hexaphenyldigermane and probably triphenylgermyltriphenyltin was confirmed by treating the mixture obtained from the reaction of triphenylgermyllithium and triphenyltin chloride with iodine. Hexaphenyldigermane, which is unaffected by iodine, was isolated in 46% yield and triphenyliodogermane was found in 14% yield. The triphenyliodogermane probably arose from the cleavage of triphenylgermyltriphenyltin, and the nonisolation of a tin compound was probably due to the cleavage of more than one phenyl group from the tin atom.

The above mixtures could have been formed from a coupling of the many species present in the

(1) For paper V of this series see H. Gilman and C. W. Gerow, *J. Am. Chem. Soc.*, **78**, 5823 (1956).
(2) C. A. Kraus and L. S. Foster, *J. Am. Chem. Soc.*, **49**, 457 (1927).