[Contribution from the Kent Chemical Laboratory, University of Chicago]

THE PREPARATION OF *dl*-PARA-TRIMETHYLETHYLBENZOYL CHLORIDE AND THE RESOLUTION OF TRIMETHYLETHYLANILINE

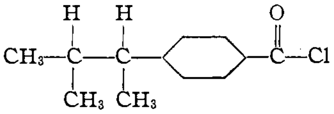
By J. W. E. Glattfeld, H. H. Hopkins and F. H. Thurber[1]

Received November 29, 1926 Published April 7, 1927

This paper reports some of the results that have been obtained in a continuation of work on the preparation and study of the eleven C_4-saccharinic acids and their derivatives, which has been undertaken in this Laboratory.[2] It has been pointed out in previous papers that need for resolving agents to supplement the alkaloids was felt in connection with the resolution of the synthesized saccharinic acids. Attempts are, therefore, being made to prepare optically active reagents[3] for this purpose and the work reported below was done in the hope that an optically active acid chloride might be obtained which could be used as a second supplementary resolving agent with these acids. The desired goal was not reached, however, as only the inactive acid chloride could be prepared in the available time.

Experimental Part

The acid chloride prepared has the formula



It will be referred to as *p*-trimethylethylbenzoyl chloride and the formula will serve to define "trimethylethyl" as used in this paper. This particular compound was chosen because some work had already been done on *p*-trimethylethylphenylhydrazine in this Laboratory[3a] and advantage could be taken of this experience. It is possible to report at present (*a*) the preparation of *dl*-*p*-trimethylethylbenzoic acid, of the corresponding nitrile and acid chloride, and (*b*) a more complete resolution of the corresponding amine than has hitherto been achieved. The acid, nitrile, and acid chloride are, so far as the authors are aware, new to the literature.

The preparation of *dl*-*p*-trimethylethylbenzonitrile required the preparation, in turn, of the following compounds: trimethylphenylethylene, trimethylethylbenzene, trimethylethylnitrobenzene and trimethylethyl-

---

[1] The dissertations of which this paper is a condensation were presented by Harris H. Hopkins and Francis H. Thurber, in partial fulfilment of the requirements for the degree of Doctor of Philosophy at the University of Chicago.

[2] (a) Glattfeld and Miller, This Journal, **42,** 2314 (1920). (b) Glattfeld and Sander, *ibid.*, **43,** 2675 (1921). (c) Glattfeld and Sherman, *ibid.*, **47,** 1742 (1925).

[3] (a) Glattfeld and Milligan, *ibid.*, **42,** 2322 (1920). (b) Glattfeld and Wertheim, *ibid.*, **43,** 2682 (1921).

aniline. All of these compounds have been previously prepared in this Laboratory by Glattfeld and Milligan. The methods of preparation used in the present work were essentially the same as those in the work cited, and the results obtained agreed in the main with those reported previously. A few points may be worthy of mention, however.

It was erroneously stated in the paper by Glattfeld and Milligan that trimethylphenylethylene is not mentioned in the literature. The references below have since been found.[4] Two new references to trimethylethylbenzene have also been discovered.[5]

It was found that the crude ethylene (residue after removal of ether from the undried ether extract of the hydrolyzed reaction mixture) could be used successfully for the reduction to trimethylethylbenzene; 250 g. of acetophenone gave from 320 to 365 g. of this residue. In those experiments in which this residue was fractionated, after first refluxing for four hours to convert any carbinol present into ethylene, it was found that the yield of ethylene, b. p. 175–200°, at atmospheric pressure, after three fractionations, was about 71% and that most of the product distilled in the neighborhood of 192°.

The trimethylethylbenzene was first prepared by hydrogen iodide reduction; yields of 51% (calculated on the basis of the acetophenone used) were obtained; b. p., 183–193°, at 760 mm. It was also prepared in equal yield by the sodium-alcohol reduction method (the sodium was added to a gently stirred ether solution of the unsaturated hydrocarbon which rested upon water). The saturated hydrocarbon, like the unsaturated one, had a slightly higher boiling point than that reported by Glattfeld and Milligan. A sample, proved to be pure by analysis, had a boiling range of 188–190° at atmospheric pressure.

In the preparations of trimethylethylnitrobenzene and trimethylethylaniline, the only departures from the procedure previously used were (a) the omission of fractionation of the crude nitro compound and the use of the residue from the ligroin extraction, after removal of the ligroin by distillation, for reduction, which change resulted in better yields of the desired aniline (24% of aniline, b. p., 123–125°, at 14 mm., calculated from the acetophenone used at the start); and (b) in the reductions, the hydrochloric acid was added in five portions to the mixture of tin and nitro compound with shaking and cooling after each addition, instead of being added all at once, which change prevented loss of control due to violence of reaction.

---

[4] (a) Klages, *Ber.*, **36**, 3691 (1903). (b) Ramart-Lucas, *Ann. chim. phys.*, [8] **30**, footnote, p. 379 (1913). (c) Auwers and Eisenlohr, *J. prakt. Chem.*, [2] **82**, 93 (1910); (d) [2] **84**, 33 (1911); (e) *Ber.*, **43**, 812 (1910). (f) Lepin, *Chem. Zentr.*, **83** [II], 2081 (1912).

[5] Konowaloff and Egoroff, *Chem. Centr.*, **70** [I], 776 (1899). Ref. 4a.

_p_-Trimethylethylbenzonitrile.—As this compound was obtained only in the crude condition, no detailed description of its preparation will be given. It was prepared by the Sandmeyer procedure and obtained as a yellow oil in 45% yield (calculated from the aniline); b. p., 125–126°, at 8 mm. This oil, in spite of its sharp boiling point, was high in nitrogen content (calcd., 8.09; found, 10.10, 9.94, 9.88). It may be worth while to state that the cold diazotized aniline solution was dropped into the mechanically stirred cuprous cyanide solution at 70° and that attempts to purify the nitrile were abandoned because of decomposition during distillation.

_p_-Trimethylethylbenzoic Acid.—The acid was obtained by alkaline hydrolysis of the nitrile and found to be a white solid, m. p. 77–78°, soluble in alcohol but almost completely insoluble in water. The yield, calculated on the basis of the nitrile used, was 56%; calculated on the basis of the original acetophenone, 4.5%.

A mixture of 8 g. of the crude nitrile with a solution of 20 g. of sodium hydroxide in 80 cc. of water was refluxed for 16 hours. The cooled, ether-extracted solution was then treated with an excess of dil. hydrochloric acid, whereupon the acid was precipitated together with much silicic acid. The precipitate was treated with a slight excess of sodium bicarbonate solution and heated; the silicic acid separated and the filtrate, clarified by means of charcoal, was treated with an excess of dil. hydrochloric acid. The precipitated organic acid was purified by solution in warm alcohol followed by precipitation by addition of water. The purified acid, after three such treatments, melted at 77–78°; yield, 5 g.

Anal. Subs., 0.1631, 0.1360: CO_2, 0.4475, 0.3733; H_2O, 0.1212, 0.0994. Calcd. for $C_{12}H_{16}O_2$: C, 74.95; H, 8.39. Found: C, 74.85, 74.87; H, 8.33, 8.19.

Samples were also titrated with alkali. Difficulty, due to the insolubility of the acid in water, was overcome by carrying out the titration at about 95–100°.

Titration. Subs., 0.3056, 0.3559: 15.90, 18.51 cc. of 0.1 *N* alkali. Calcd. for $C_{12}H_{16}O_2$: 15.91, 18.53 cc.

_p_-Trimethylethylbenzoyl Chloride.—The acid chloride was found to be a liquid of boiling range 118–120°, at 2 mm. A yield of 90%, calculated on the basis of the acid, and 4% calculated on the basis of the acetophenone originally used, was obtained.

Eight and three-tenths g. of dry trimethylethylbenzoic acid was treated with 12.5 g. of phosphorus pentachloride. The two solids were mixed as thoroughly as possible by shaking the flask. After the vigorous reaction had ceased, the reaction mixture was distilled at 2 mm. and yielded, after two fractionations, 10 g. of liquid; b. p., 118–120°. Samples of this liquid were analyzed for chlorine by a modification of the Rosanoff method (treatment of the sample with metallic sodium followed by precipitation of the chlorine as silver chloride) devised by Gladys Leavell in this Laboratory.

Anal. Subs., 0.7400, 0.3834: AgCl, 0.5080, 0.2624. Calcd. for $C_{12}H_{15}OCl$: Cl, 16.84. Found: 16.98, 16.93.

Further evidence that the material was actually the acid chloride sought was found in the fact that hydrolysis of a sample yielded the solid acid of proper melting point.

Resolution of _dl-p_-Trimethylethylaniline.—Resolution of this compound with *d*-oxymethylenecamphor has been reported by Glattfeld and Milligan.[6] We obtained practically identical results with this resolving agent (anilines of specific rotation +1.00° and —0.29° were obtained). With *d*-camphorsulfonic acid, however, more active anilines

---

[6] In the paper by Glattfeld and Milligan (Ref. 3a), there occurs a misprint on page 2328. The observed rotation of the *l*-aniline was —0.76 instead of +0.76 as recorded there.

were obtained ($[\alpha]_D$ = +3.85° and —3.5°). Whether or not these anilines were of the highest obtainable purity will have to be shown by work with other resolving agents. We could push the resolution no further with *d*-camphorsulfonic acid. The procedure used by Glattfeld and Wertheim[3b] was followed with practically no variation.

Twenty g. of the *dl*-aniline, with 22 g. of *d*-camphorsulfonic acid, etc., gave 48 g. of the *d*-camphorsulfonic acid-*dl*-aniline compound, $[\alpha]_D$ in chloroform, +24.5°; that is, 0.5216 g. of substance in 10 cc. of chloroform in a 1-dcm. tube gave α = +1.28°. Treatment with 20 cc. of ether, filtration, washing with ether and drying, yielded the crude *d*-camphorsulfonic acid-*l*-aniline compound (for filtrate see below). Recrystallization of the crude compound from a mixture of equal parts of acetone and ethyl acetate gave 19 g. of crystals; m. p., 179°; $[\alpha]_D^{20}$ +29.25°; that is, 0.3720 g. of substance in 10 cc. of chloroform in a 1-dcm. tube gave α = +1.09°. A recrystallization of these crystals did not appreciably alter the constants.

Eighteen g. of crystals, $[\alpha]_D$ = in chloroform +29.25°, was heated at 100° with 100 cc. of hydrochloric acid (d., 1.19) for five hours. The liquid was made strongly alkaline and subjected to steam distillation. Extraction of the distillate with low-boiling ligroin, and distillation of the residue from the ligroin extract at 14 mm. yielded 8 g. of crude aniline; b. p., 118–130°. This aniline was again made alkaline with sodium hydroxide, subjected to steam distillation and then recovered and fractionated as indicated above. Six g. of aniline was obtained; b. p., 124–126°, at 15 mm.; d., 0.905; $[\alpha]_D^{20}$ = —3.53; that is, α in a 1-dcm. tube, without solvent, = —3.2.

The "gummy" material which remained when the ether had evaporated from the filtrate from the crude *d*-camphorsulfonic acid-*l*-aniline compound was hydrolyzed and the aniline purified by exactly the same procedure as was used above for the *levo* isomer. Five g. of aniline was obtained; b. p., 132–134°, at 16 mm.; $[\alpha]_D^{20}$ = +3.85; that is, α in a 1-dcm. tube, without solvent, = +3.5.

Summary

In a continuation of efforts to prepare optically active reagents for the resolution of the C_4-saccharinic acids, (a) the preparation of *dl-p*-trimethylethylbenzonitrile, *dl-p*-trimethylethylbenzoic acid and *dl-p*-trimethylethylbenzoyl chloride and (b) a more complete resolution of *dl-p*-trimethylethylaniline, are reported.

CHICAGO, ILLINOIS