EXPERIMENTAL

Materials. The 50% aqueous acetic acid was prepared from purified acetic acid as before.[8] Biphenyl (Distillation Products Industries) was recrystallized three times from ethanol (m.p. 69.1–69.7°, cor.); the purified *p*-bromobiphenyl[10] melted at 89.9–90.6°. All inorganic materials were best reagent grade chemicals.

Determination of percentage of 4-bromobiphenyl. The procedure, instrumentation and method of calculation were as described before.[8] The only difference was that the amount of 4-bromobiphenyl formed during reaction could not be neglected in relation to the amount of inactive material added and was taken into consideration in the final calculations. In a typical run, 12.5 ml. of a solution containing the radioactive bromine (about 5–10 μc) and a known, small amount of bromide, was added to 487.5 ml. of a solution containing the other reagents in such concentrations that the final solution was 0.01*M* in sodium bromide, 0.4*M* in sodium perchlorate, 0.006*M* in biphenyl, and 0.002194*M* in bromine as determined by titration of a 10-ml. sample. After about 50 hr., two 10-ml. samples were withdrawn and titrated for the extent of reaction (84.01%); the excess of bromine was destroyed with sodium bisulfite. Two 5-ml. samples were withdrawn for determining the activity of the total reaction mixture. Inactive 4-bromobiphenyl (1.8128 g.) was added to the reaction mixture followed by sufficient acetone to make the solution homogeneous. Ice and water was then added and the precipitated material was recrystallized from ethanol. After four recrystallizations there was obtained Sample A (0.7135 g.) of m.p. 90.0–90.6°, which, dissolved in acetone to exactly 5 ml., had an activity of 97.24 c/s. Assuming as a first approximation that all of the bromination products formed consisted of the *p*-isomer, the amount of total *p*-bromobiphenyl (added and formed) is 2.0104 g., and the recovery of pure isomer was therefore 35.49%. Hence the activity for total *p*-bromobiphenyl is 97.24/0.3549 = 274.0 c/s. The activity of the total amount of bromine that had reacted was 292.1 c/s. The amount of *p*-bromobiphenyl formed is therefore 93.8%. Using this value, the recalculated amount of total *p*-bromobiphenyl becomes 1.9981 g. and the percentage of *p*-isomer 93.2. No further correction was necessary. Sample A was recrystallized once more and 0.4780 g. of sample B of m.p. 90.2–90.7° was obtained; the per cent of *p*-isomer was similarly calculated to be 95.8. In all cases the specific activity was slightly higher after the last recrystallization and these values were used in the final average.

One of the major uncertainties was in the determination of the exact extent of reaction, because reaction is very slow, and a slight loss of bromine through reaction with the solvent is known to occur.[7] Under the present conditions this loss was about 2–3% at the end of the reaction period, as determined by a blank. To minimize this factor, the concentration of bromide was kept low, at 0.01*M*, in order to speed up the reaction, although the kinetics had previously been studied at at least 0.1*M* bromide ion concentrations.[7] In one case (sodium bromide = 0.1*M*), the extent of reaction was calculated from careful determinations of the rate constants under identical conditions with inactive materials. Since for this run the per cent of *p*-bromobiphenyl was the same as that for runs whose extent of reaction was found by titration, no blank corrections were applied.

Independent values for four runs were 91.9, 88.3, 96.0, and 95.8%. The weighted average is 94.0 ± 2.6%. The weighting was based on the estimated errors and uncertainties in the individual runs. Finally, the figure of 94.0% was used to recalculate the amount of 4-bromobiphenyl formed in all runs, and the new weighted average per cent thus obtained is 93.9 ± 2.4.

Acknowledgment. This work was supported by the National Science Foundation, Grant G-4474, which is gratefully acknowledged. We also express our thanks to the Committee on the Coordination of the Sciences of Bryn Mawr College for the purchase of the counting equipment and the isotopes.

DEPARTMENT OF CHEMISTRY
BRYN MAWR COLLEGE
BRYN MAWR, PA.

(9) R. E. Buckles, E. A. Hausman, and N. G. Wheeler, *J. Am. Chem. Soc.*, **72**, 2494 (1950). A fairly high value for *p*-bromination is also implicit in a private communication of H. C. Brown and L. M. Stock in P.B.D. de la Mare and J. H. Ridd, *Aromatic Substitution*, Butterworths Scientific Publications, London, 1959, p. 157.

(10) M. Gomberg and W. E. Bachmann, *Org. Syntheses*, Coll. Vol. I, 113 (1948).

β-Oxoadipic Esters

D. K. BANERJEE AND K. M. SIVANANDAIAH

Received August 22, 1960

β-Oxoadipic esters have been used as starting materials for the synthesis of several useful compounds.[1-5] Amongst the various methods[1,6-9] for the preparations of these esters, the best yields have been reported by Viscontini and co-workers.[8] Following their procedure we could obtain the reported yield (81%) of ethyl methyl or diethyl α-acetyl-β-oxoadipate, but ammonolysis of the crude α-acetyl esters according to their procedure, using 5% ethanolic ammonia, furnished ethyl methyl, or diethyl β-oxoadipate in an overall yield (36%) less than that reported (56–60%). However, we found that ammonolysis according to Ruggli and Maeder[6] by passing a stream of dry ammonia into an ethereal solution of the crude α-acetyl ester at 0° furnished ethyl methyl or dimethyl β-oxoadipate in an overall yield of 60%.

The dimethyl ester of β-oxoadipic acid, however, could not be prepared in quantity either by the aforementioned procedure or by Bardhan's method,[1] the yields being 5–7%. Korman[9] reported the preparation of this diester in 38% yield, but we found that the product obtained by his method was not

(1) J. C. Bardhan, *J. Chem. Soc.*, 1848 (1936).

(2) W. E. Bachmann and R. E. Holmen, *J. Am. Chem. Soc.*, **73**, 3660 (1951).

(3) A. J. Birch and A. R. Murray, *J. Chem. Soc.*, 1888 (1951).

(4) D. K. Banerjee and K. M. Sivanandaiah, *Tetrahedron Letters*, **5**, 20 (1960).

(5) (a) D. Nasipuri, A. C. Chaudhuri, and J. Roy, *J. Chem. Soc.*, 2734 (1958); (b) D. Nasipuri and J. Roy, *J. Chem. Soc.*, 1571 (1960).

(6) P. Ruggli and A. Maeder, *Helv. Chim. Acta*, **25**, 936 (1942).

(7) B. Riegel and W. M. Lilienfeld, *J. Am. Chem. Soc.*, **67**, 1273 (1945).

(8) M. Viscontini and N. Merckling, *Helv. Chim. Acta*, **35**, 2280 (1952); M. Viscontini and H. Kohler, *Helv. Chim. Acta*, **37**, 41 (1954).

(9) J. Korman, *J. Org. Chem.*, **22**, 848 (1957).

quite pure even after two distillations and was unsuitable for our work.[4] Therefore no satisfactory method was available for the preparation of the dimethyl ester. This compound could be conveniently prepared (75% yield) by transesterification[10] of ethyl methyl β-oxoadipate by refluxing its methanolic solution with a trace of sodium methoxide, or in a better yield (89%) by treating the methanolic solution with 1.05 g. atom of sodium methoxide at room temperature. Treatment of the latter solution, containing the sodio derivative, *in situ* with methyl iodide gave dimethyl α-methyl-β-oxoadipate in 83% yield.

EXPERIMENTAL

Diethyl β-oxoadipate. To magnesium ethoxide, prepared from 16.5 g. of magnesium and 94.6 ml. of absolute ethanol and suspended in 200 ml. of dry ether, was added a solution of 87 g. of ethyl acetoacetate in 100 ml. of dry ether followed by a solution of 109 g. of β-ethoxycarbonylpropionyl chloride in 100 ml. of dry ether.[8] The crude α-acetyl ester weighing 154 g. was dissolved in 300 ml. of dry ether and cooled to 0°, and a stream of dry ammonia was passed through it for 40 min.[6] The yield of diethyl β-oxoadipate was 86 g. (60%); b.p. 119–120°/1.5 mm. (reported 122–126° at 0.5 mm.[7]).

Ethyl methyl β-oxoadipate, b.p. 115–117°/1.5 mm. (reported b.p. 90°/0.06 mm. and 148–150°/12 mm.[8]) was similarly prepared in about the same yield.

Dimethyl β-oxoadipate. (i) To a solution of sodium methoxide, prepared from 0.35 g. of sodium and 100 g. of absolute methanol, was added ethyl methyl β-oxoadipate (20 g.), and the mixture was refluxed for 20 hr. The cooled product was taken up in ether, washed repeatedly with saturated ammonium sulfate solution, and dried over anhydrous sodium sulfate. After removal of the solvent, the residue was distilled to yield 14 g. (75%) of dimethyl β-oxoadipate; b.p. 125–126°/3 mm. (reported b.p. 122°/0.5 mm.[1] and 125–126°/3 mm.[5b]).

(ii) Ethyl methyl β-oxoadipate (20 g.) was added to a solution of sodium methoxide, from 2.4 g. of sodium and absolute methanol (120 g.), and allowed to stand at room temperature for 5 hr. It was then acidified with glacial acetic acid and most of the alcohol removed on a water bath under reduced pressure, the residue was taken up in ether and washed with sodium bicarbonate solution and water. After drying, the solvent was removed and the residue distilled, b.p. 125–126°/3 mm., yield 16.7 g. (89%).

Dimethyl α-methyl-β-oxoadipate. To a solution of sodium methoxide, from 3.63 g. of sodium and absolute methanol (180 ml.), was added ethyl methyl β-oxoadipate (30.3 g.) and left for 2 hr. at room temperature. Methyl iodide (19 g.) was added, and after 1 hr. at room temperature it was refluxed for 2 hr. A fresh quantity of methyl iodide (12 g.) was then added and the refluxing continued for 2 hr. Most of the alcohol was removed under reduced pressure, the residue taken up in ether and washed with water. The solvent was removed after drying and the residue distilled to yield 25.2 g. (83%) of dimethyl α-methyl-β-oxoadipate, b.p. 135–136°/3 mm.

Anal. Calcd. for $C_9H_{14}O_5$: C, 53.46; H, 6.93. Found: C, 53.03; H, 6.91.

DEPARTMENT OF ORGANIC CHEMISTRY
INDIAN INSTITUTE OF SCIENCE
BANGALORE-12, INDIA

(10) T. Peters, *Ann.*, **257**, 353 (1890).

Synthesis of *p*-Benzoylmandelic Acid

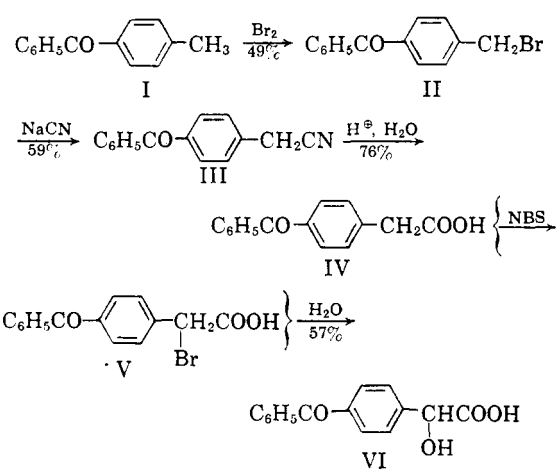
JOHN A. ZDERIC, MOTHER MARY J. KUBITSCHEK AND WILLIAM A. BONNER

Received September 2, 1960

In connection with a problem in the field of asymmetric synthesis we have been interested in the synthesis and resolution of *p*-benzoylmandelic acid (VI). Over the past several years we have developed several alternative syntheses for this substance. The purpose of the present note is to discuss these syntheses, to evaluate them and to describe several new compounds encountered in their development.

The first of these syntheses,[1] with yields given for each step, is shown in Chart I, where the overall yield of *p*-benzoylmandelic acid (VI) from

Chart I



p-methylbenzophenone (I) is 12.5%. In the preparation of *p*-benzoylbenzyl bromide (II) by bromination of I we obtained a sample of II having m.p. 112.5°. This bromide has been reported by Bourcet[2] to have m.p. 96.6°. The melting point discrepancy may be due to polymorphism, since this phenomenon has been observed with *p*-methylbenzophenone (I) itself.[3]

Since the development of the synthesis in Chart I Zelinski[4] has reported the preparation of our intermediate *p*-benzoylphenylacetic acid (IV) by an alternative method. We have employed Zelinski's procedure in the preparation of *p*-benzoylmandelic acid according to the sequence given in Chart II, where the yields from VIII to IV are those reported by Zelinski. The overall yield

(1) J. A. Zderic, M. S. thesis, Stanford University (1952).
(2) P. Bourcet, *Bull. soc. chim.*, **1**, 946 (1896).
(3) K. Schaum, K. Schaeling, and F. Klausing, *Ann.*, **411**, 188 (1916).
(4) R. P. Zelinski, B. W. Turnquest, and E. C. Martin, *J. Am. Chem. Soc.*, **73**, 5521 (1951).