methyl cyclopentaneacetate: b.p. 51–79° at 30 mm.; $n^{25}\mathrm{D}$ 1.4369. Vapor–liquid partition of this material showed a much more volatile contaminant (not yet identified) in addition to the main, homogeneous product. The infrared spectrum (neat; 0.025 mm. cell) of this sample was completely superimposable on that of an authentic sample.

Methyl cyclopentaneacetate was made by condensing sodiomalonic ester with cyclopentyl bromide in boiling toluene (N. Chaudhuri). Saponification of the ester followed by two recrystallizations from ether gave diacid, m.p. 164–165°. Decarboxylation gave cyclopentaneacetic acid, b.p. 115–116° at 5 mm., $n^{25}\mathrm{D}$ 1.4524. The corresponding methyl cyclopentaneacetate, from the acid and diazomethane, boiled at 76–77° at 25 mm., $n^{25}\mathrm{D}$ 1.4368.

(c) ***n*-Pentane.**—From 10.0 g. of methyl diazoacetate and 900 ml. of pentane (*vide supra*) distillation gave 4.44 g. of liquid; b.p. 63–74° at 40 mm.; $n^{25}\mathrm{D}$ 1.4124. Vapor–liquid partition gave three clearly separated fractions: the first was obtained from *all* reactions and, in amount (19.3%), depended on the way distillation fractions were made; its structure is not yet known but is being determined. The second was not resolved, amounted to 50.0% and by making known mixtures of authentic materials was shown by infrared analysis to consist of 68 ± 2% of methyl 3-methylhexanoate and 32∓% of methyl 3-ethylpentanoate. The third and last fraction was infrared spectroscopically identical with pure methyl *n*-heptanoate.

Methyl *n*-heptanoate, from authentic acid and diazomethane, boiled at 174–175°, $n^{25}\mathrm{D}$ 1.4102.

Methyl 3-methylhexanoate was prepared (N. Chaudhuri) (1) by condensing 2-bromopentane and malonic ester to methyl (2-pentyl)-malonic ester (70% of th. yield); b.p. 109–110° at 1 mm.; (2) saponifying to the dicarboxylic acid, m.p. 92–93° after 4 recrystallizations from cyclohexane. Decarboxylation followed by esterification gave the ester, b.p. 163–164°, $n^{25}\mathrm{D}$ 1.4092.

Methyl β-ethylpentanoate was synthesized by N. Chaudhuri by the application of the Arndt–Eistert synthesis to diethylacetic acid. The ester had b.p. 164° and $n^{25}\mathrm{D}$ 1.4130.

(d) **2,3-Dimethylbutane.**—Distillation of the product from 10.0 g. of methyl diazoacetate and 900 ml. of 2,3-dimethylbutane gave 4.74 g. of ester, $n^{25}\mathrm{D}$ 1.4206. Vapor–liquid partition (N_2; 20 lb.; 135°) separated two fractions: the first was identical with the low-boiling impurity reported above. The second (23.5%) was presumed to be methyl 3,3,4-trimethylpentanoate, $n^{25}\mathrm{D}$ 1.4220. *Anal.* Calcd. for $C_9H_{18}O_2$: C, 68.3; H, 11.5. Found: C, 68.5; H, 11.6. The third component (76.5%) was methyl 4,5-dimethylhexanoate, $n^{25}\mathrm{D}$ 1.4198. Its infrared spectrum was identical with that of an authentic sample prepared by the method of Levin, Papa and Schwenk.[23a] The methyl ester (b.p. 181°, $n^{25}\mathrm{D}$ 1.4230) was prepared from the acid (b.p. 114–117° at 17 mm., $n^{25}\mathrm{D}$ 1.4378) by diazomethane.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF MARYLAND]

Disproportionative Condensations. III. Reciprocal Routes to β-Phenylpropiophenones

BY ERNEST F. PRATT AND ALLAN P. EVANS[1]

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It has been shown that a variety of *para*-substituted β-phenylpropiophenones may be prepared in good yield by the reaction of an acetophenone with a benzyl alcohol in the presence of a catalytic amount of the corresponding lithium benzylate. The reaction was facilitated and followed by distilling the by-product water into a trap. It was possible, by this means, to determine readily the effects on the rate of changing the main variables. Predictions, based on the proposed reaction course, that a given β-phenylpropiophenone would be formed as readily from a benzaldehyde and a phenylmethylcarbinol as from the corresponding benzyl alcohol and acetophenone were confirmed experimentally.

In preceding papers of this series the condensation of a primary alcohol at the *beta* carbon of a second alcohol molecule[2] and at the nitrogen of an aniline[3] were discussed. It has now been found that when a xylene solution containing benzyl alcohol, acetophenone and catalytic amounts of lithium benzylate is refluxed until the theoretical amount of water is removed β-phenylpropiophenone is obtained in about 70% yield.

$$C_6H_5CH_2OH + CH_3COC_6H_5 \longrightarrow C_6H_5CH_2CH_2COC_6H_5 + H_2O \quad (1)$$

The related condensation of normal aliphatic alcohols[4] and of benzyl alcohol[5] with fluorene has been reported recently.

Since, as shown in Table I, various *para*-substituted β-phenylpropiophenones are obtained in good yields in one step this method offers advantages over the two-step process *via* benzalacetophenones[6] and the four-step processes *via* dibenzyl[7] or di-*t*-butyl malonates.[8]

TABLE I

EFFECT OF CHANGING THE *para*-SUBSTITUENTS

para-Substit.	$t_{50\%}$, min.	Water, %	Product, % A[b]	Product, % B[c]
para-Substd. acetophenones and benzyl alcohol				
Cl–	355	105	62	75
H–	530	101	69	82
CH_3–	635	97	69	79
CH_3O–	690	99	74	81
CH_3O–[a]	490	100	65	71
para-Substd. benzyl alcohols and acetophenone				
Cl–	445	101	68	78
H–	530	101	69	82
CH_3–	350	105	67	71
CH_3O–	385	99	69	75

[a] In this experiment both reactants contained a *p*-methoxyl group. [b] The yield of pure recrystallized product obtained directly. [c] The yield including material obtained by treatment of by-product with chromic anhydride.

The action on acetophenone of potassium benzylate in dilute (1 *N*) solution in benzyl alcohol at the reflux temperature was studied by Mastagli.[9] 1,3-Diphenyl-1-propanol, the product desired in that study, was obtained free of β-phenylpropiophenone when the reaction time was two hours. From a single experiment, not described in detail, at a shorter reaction time a good yield of crude β-phenylpropiophenone was reported. It is evident

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[1] From the M.S. thesis of A. P. Evans, May, 1953.

[2] E. F. Pratt and D. G. Kubler, THIS JOURNAL, **76**, 52 (1954). See also H. Machemer, *Angew. Chem.*, **64**, 213 (1952).

[3] E. F. Pratt and E. J. Frazza, THIS JOURNAL, **76**, 6174 (1954).

[4] K. L. Schoen and E. I. Becker, *ibid.*, **77**, 6030 (1955).

[5] Y. Sprinzak, *ibid.*, **78**, 466 (1956).

[6] R. Adams, J. W. Kern and R. L. Shriner, "Organic Syntheses," Coll. Vol. I, 2nd Ed., John Wiley and Sons, Inc., New York, N. Y., 1954, p. 101.

[7] R. E. Bowman, *J. Chem. Soc.*, 325 (1950).

[8] G. S. Fonken and W. S. Johnson, THIS JOURNAL, **74**, 831 (1952).

[9] P. Mastagli, *Ann. chim.*, **10**, 281 (1938).

that the use of only the stoichiometric amount of alcohol in xylene solution and the continuous removal of the by-product water, as in the present study, offers decisive advantages when an alcohol other than benzyl alcohol itself is to be employed and when it is desired to stop the reduction at the ketone stage. The reciprocal route, described below, ordinarily would not be feasible under Mastagli's conditions.

In a number of preliminary experiments in which the standard procedure was altered only with respect to the specific variable being studied, the effects of varying the reactant ratio, the amount of lithium benzylate and the temperature (by changing the solvent) were determined. It was found (see Experimental) that an increase or decrease in the value of a variable from that of the standard procedure resulted in a decreased yield of β-phenylpropiophenone. In experiments with equimolar amounts of lithium, sodium or potassium benzylates the lithium benzylate gave the highest yield but, at least in part because of its limited solubility, it gave the lowest rate.

The reaction appears to take the course[9]

$$C_6H_5CH_2OH + CH_3COC_6H_5 \rightleftharpoons C_6H_5CHO + CH_3CHOHC_6H_5 \quad (2)$$

$$C_6H_5CHO + CH_3COC_6H_5 \longrightarrow C_6H_5CH{=}CHCOC_6H_5 + H_2O \quad (3)$$

$$C_6H_5CH{=}CHCOC_6H_5 + C_6H_5CH_2OH \longrightarrow C_6H_5CH_2CH_2COC_6H_5 + C_6H_5CHO \quad (4)$$

Reaction 4 may proceed by reduction of the carbonyl group followed by rearrangement.[2] The benzaldehyde reacting in 3 is regenerated in 4 so that addition of 3 and 4 gives the over-all reaction 1. As would be expected reaction 3 was found to proceed very rapidly under conditions similar to those described above. Since it has been shown that equilibrium 2 is rapidly attained[9] the over-all rate will be determined primarily by the rate of 4 and the position of equilibrium 2. In addition to its direct effect on the amount of reactants available for 3 and 4 the position of equilibrium 2 will influence the relative amounts of benzyl alcohol and phenylmethylcarbinol and hence the distribution of the lithium between them; both lithium alcoholates probably catalyze all three reactions.

Since several factors, some of which may well oppose others, influence the rate it is perhaps less surprising that a consistent change in rate with increasing electron releasing ability of the *para*-substituent of the benzyl alcohol was not obtained than it is that a consistent decrease in rate with increasing electron releasing ability of the *para*-substituent of the acetophenone was obtained (Table I). The results for the acetophenones may, perhaps, be explained in the same way as the similar effects encountered when the correspondingly substituted anilines were condensed with the benzyl alcohol.[3]

On the basis of the above reaction course it would be expected that β-phenylpropiophenone could be synthesized from benzaldehyde and phenylmethylcarbinol as well as from benzyl alcohol and acetophenone. A 73% yield of pure β-phenylpropiophenone was readily obtained by the reciprocal process. The advantages of having alternative routes to the same product are exemplified by the preparation of pure 3-(*p*-dimethylaminophenyl)-propiophenone in 60% yield from *p*-dimethylaminobenzaldehyde and phenylmethylcarbinol thus circumventing the need for the difficultly available *p*-dimethylaminobenzyl alcohol.

Experimental[10]

Experiments of Table I.—The solvent xylene was a commercial mixture of isomers which was redistilled and the lithium, stated by the manufacturer[11] to be 99% pure, was used as obtained. No refractive index was found in the literature for *p*-chloroacetophenone; the $n^{25}D$ for refractionated material was 1.5521. All other starting materials for the experiments of Table I were purified by standard methods until the refractive indices or melting points agreed closely with the literature values.

The standard procedure will be described for the reaction of benzyl alcohol with acetophenone; except for obvious modifications this procedure was used for all the experiments of Table I.

A 0.127 mole portion of benzyl alcohol was transferred to a flask with the aid of sufficient xylene to give a total volume of 25 ml. The 0.002 mole of clean lithium, weighed rapidly on an analytical balance, was added.[12] A water trap[13] filled with xylene was mounted on the flask and the trap was surmounted by a reflux condenser fitted with an "Anhydrone" filled drying tube. Rapid reaction of the lithium occurred upon heating the reaction mixture to about 160°. When reaction was complete 400 ml. of xylene was added and the solution was refluxed 0.5 hour to remove any adventitious water. One-eighth mole of acetophenone diluted to 50 ml. with xylene was then added along with the final 25 ml. of xylene. The solution was reheated rapidly and refluxing maintained at a rate just below that which would flood the condenser until no more water was evolved. Traces of white solid, probably lithium benzylate, carbonate or hydroxide remained suspended throughout the reaction period. Zero time was taken when refluxing resumed which was always between 5 and 10 minutes after the acetophenone was added. Frequent readings of water volume, time and temperature were taken. For the 25 to 75% portion of all reactions the temperature was 140.3 ± 1.1° and within a given experiment the temperature variation never exceeded ±0.35°.

After the solution was allowed to cool to about 100°, 100 ml. of water was added. The organic layer was separated and washed successively with 5% aqueous sodium bicarbonate, 5% hydrochloric acid and with water. The crude β-phenylpropiophenone was isolated by distillation through a 6-inch Vigreux column at reduced pressure and recrystallized from three times its weight of ethanol. Column A of Table I gives the yield of products which melted within 1° of the literature values.

The β-phenylpropiophenone was identified by ultimate analysis and by its known melting point and those of its semicarbazone and 2,4-dinitrophenylhydrazone. The β-(*p*-tolyl)-propiophenone which melted at 33–34° appears to be new.

Anal.[14] Calcd. for $C_{16}H_{16}O$: C, 85.67; H, 7.23. Found: C, 85.60; H, 7.23.

Acidification of the above mentioned sodium bicarbonate washings ordinarily gave traces of precipitate which were isolated and shown to be the benzoic acid corresponding to the benzyl alcohol used. It is apparent that during the later stages of the reaction conversion of the lithium benzylate to the lithium benzoate may have occurred to a significant extent.

Since the maximum change in rate resulting from varying the *para*-substituent of the benzyl alcohol was small (Table I) duplicate experiments were carried out for all four benzyl alcohols. The tabulated $t_{50\%}$ values are the averages of the

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(10) All melting points are corrected.

(11) The Lithium Corporation of America.

(12) It is noteworthy that as in the preceding studies (ref. 2 and 3) no serious etching of the flask occurred.

(13) Ace Glass, Inc., Cat. no. 7735.

(14) We are indebted to Professor Mary Aldridge for the microanalyses.

two which always agreed within ±4%. Plots of the percentage of water collected *vs.* time gave smooth curves of the same general shape showing constantly decreasing rates. Comparison of $t_{50\%}$ values are, therefore, valid.

In both of the preceding studies[2,3] the "rate curves" showed increasing rates during the early stages of the reaction and it was suggested[3] that during this period the aldehydes required to maintain the process were being formed by dehydrogenation of the alcohol. Since in the present study carbonyl groups are already present in a reactant no such induction period was expected or found. In agreement with this U. O. P. nickel[15] did not accelerate, in fact it retarded, the reaction and no hydrogen or other gas was evolved.

Oxidation of By-products.—Infrared absorption data on the ethanol-free material from the mother liquors of the above mentioned recrystallizations from ethanol indicated, as was expected from the work of Mastagli,[9] that 1,3-diphenyl-1-propanols were the principal by-products. Each residue was dissolved in 25 ml. of glacial acetic acid and for each 0.005 mole, calculated on the assumption it was all the 1,3-diphenyl-1-propanol, 1 ml. of a solution of 10.3 g. of chromium trioxide in 30 ml. of 80% aqueous acetic acid was added dropwise with stirring while the temperature was maintained below 40°. After 24 hours at room temperature the mixture was poured into 250 ml. of ice-water and extracted with two 50-ml. portions of ether. The ether solution was washed with water, the ether boiled off and the residue recrystallized from three times its weight of ethanol. Column B of Table I gives the yield of β-phenylpropiophenones including that from the oxidation.

Effects of Changing Important Variables.—The general procedure described above was followed for comparing the effects of potassium, sodium and lithium benzylates except that the 0.002 mole of lithium was replaced by 0.005 mole of the indicated metal hydroxide and 0.130 mole of benzyl alcohol was used. The reaction of the hydroxide with the benzyl alcohol to give the metal benzylate was forced to completion by refluxing one hour in the standard apparatus before adding the acetophenone. Reaction of the acetophenone with the benzyl alcohol gave a 50% yield of water from the three experiments in 19, 35 and 455 minutes, respectively. The total yields of water were 76, 100 and 100% and the yields of pure β-phenylpropiophenone, obtained directly upon recrystallization were 26, 45 and 58%.

In a series of three experiments using the standard procedure except that the amount of lithium metal was 0.001, 0.002 and 0.005 mole and the amount of benzyl alcohol correspondingly adjusted to 0.126, 0.127 and 0.130 mole the times for a 50% yield of water were 895, 550 and 440 minutes and the yields of recrystallized β-phenylpropiophenone obtained directly were 52, 69 and 59%.

The effect of varying the temperature was studied using toluene, xylene and *p*-cymene as solvents in experiments otherwise standard. The reflux temperatures were 112, 140 and 178°. A 50% yield of water was obtained in 3450, 550 and 180 minutes and the yields of pure product were 58, 69 and 53%.

For determining the effect of varying the reactant ratio three experiments were carried out with 0.252, 0.127 and 0.127 mole of benzyl alcohol and 0.125, 0.125 and 0.250 mole of acetophenone along with 0.002 mole of lithium so that the reactant ratios were 2:1, 1:1 and 1:2. The second experiment was standard and the amount of xylene was decreased in the first and third experiments to give the same total volume. A 50% yield of water was obtained in 280, 550 and 420 minutes and the total yield of water was 97 to 102% in all three cases. The yields of pure β-phenylpropiophenone obtained directly upon recrystallization were 48, 69 and 42%.

Reactions of Phenylmethylcarbinol with Benzaldehydes.—One-eighth mole of benzaldehyde, 0.133 mole of phenylmethylcarbinol and 0.008 mole of lithium were used under conditions otherwise standard. A 50% yield of water was obtained in 180 minutes and a 95% yield in 1900 minutes. A 73% yield of β-phenylpropiophenone was obtained directly upon recrystallization and an additional 7% by oxidation of material from the mother liquors as described above. The product melted at 70° both alone and when mixed with the product prepared from benzyl alcohol and acetophenone.

When *p*-dimethylaminobenzaldehyde replaced the benzaldehyde in the procedure of the preceding paragraph a 50% yield of water was obtained in 265 minutes and a 100% yield in 900 minutes. The white crystals, obtained in 60% yield, melted at 51°.

Anal.[14] Calcd. for $C_{17}H_{19}ON$: C, 80.58; H, 7.57. Found: C, 80.72; H, 7.50.

The 2,4-dinitrophenylhydrazone, prepared by standard methods, melted at 209–210°.

Anal.[14] Calcd. for $C_{23}H_{23}O_4N_5$: C, 63.71; H, 5.35. Found: C, 64.18; H, 5.36.

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[15] Universal Oil Products Co., 310 S. Michigan Ave., Chicago 4, Ill.

[CONTRIBUTION FROM THE CHEMISTRY DIVISION OF OAK RIDGE NATIONAL LABORATORY]

Molecular Rearrangements. IX. The *p*-Tolyl/Phenyl Migration Ratio in Deamination Reactions[1]

BY BEN M. BENJAMIN AND CLAIR J. COLLINS

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2-Phenyl-2-*p*-tolylethyl-1-C^{14}-amine (IV) and 2,2-diphenyl-2-*p*-tolylethyl-1-C^{14}-amine (VII) have been subjected to nitrous acid deamination. The *p*-tolyl/phenyl migration ratios have been found to be 1.18 ± 0.06.

Following the migratory aptitude work of Bachmann[2] and of Bailar,[3] and the "σ–ρ" correlation of Hammett,[4] much attention has been directed toward an understanding of the factors which determine the mobility sequence[5] of the various migrating groups which are involved in molecular rearrangements. We have obtained considerable quantitative information in this respect by the use of radioactive carbon,[6-11] with results indicating the expected preference for migration of those groups which are presumed to be better electron donors.[2-4]

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[1] This paper is based upon work performed under Contract Number W-7405-eng-26 for the Atomic Energy Commission at Oak Ridge National Laboratory.

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