TABLE XVII

GAS CHROMATOGRAPHY CONDITIONS

Method	Column	Temp., °C.	He flow rate (ml./min.)
A1	Tritolyl phosphate (15%), 8 ft.	95	85
A2	Apiezon L (14%), 12 ft.	180	75
A3	Apiezon L (14%), 12 ft.	120	60
A4	Apiezon L (14%), 12 ft.	130	55
A5	Apiezon L (14%), 12 ft.	150	100
A6	Apiezon L (14%), 12 ft.	125	120
A7	Apiezon L (14%), 12 ft.	135	90
A8	DEGS (15%), 15 ft.	130	120
A9	*m*-Phenyl ether, 5-ring (15%), 12 ft	140	120
A10	Apiezon L (14%), 12 ft.	110	120
A11	*m*-Phenyl ether, 5-ring (5%), 4 ft., and terephthalic acid–Carbowax (5% reacted), 4 ft.	150	80

used were *ortho*, 13.3–13.8; *meta*, 12.8–13.1; and *para*, 12.1–12.5. The determinations were made with products which were isolated by one of several methods: B1, gas chromatography (20% Apiezon L grease) (known mixtures of authentic materials were subjected to infrared analysis before and after collection in order to ascertain that the collection was essentially quantitative; the isomer distributions represent the mean of at least two collections and a minimum of three determinations for each sample); and B2, distillation (the isomer distributions represent the mean of at least three determinations on each of two distillations).

C. **Distillation.**—A large-scale run was carried out for each set of reaction conditions in order to determine the amount of distillation residue. After fractionation of the volatile products, the residue comprised <4% of the total product.

Acknowledgment.—We wish to acknowledge support provided by the National Science Foundation and the donors of the Petroleum Research Fund, administered by the American Chemical Society.

A Quantitative Study of the Perkin Synthesis of α-Phenyl-*trans*-cinnamic Acid

ROBERT E. BUCKLES AND JOHN A. COOPER

Department of Chemistry, University of Iowa, Iowa City, Iowa

Received August 28, 1964

Quantitative product isolations were carried out on the triethylamine-catalyzed Perkin condensation of phenylacetic anhydride with benzaldehyde. A 96% recovery of purified major product, α-phenyl-*trans*-cinnamic acid (1), was possible. Variations of the yield of this product with reaction conditions led to an optimum procedure (96% yield) involving phenylacetic acid, acetic anhydride, and triethylamine in a 2:3:4 molar ratio reacting at 65° in benzaldehyde as a solvent. The amine was best added slowly as the reaction progressed. The results were consistent with a slow aldol-type condensation of phenylacetic anhydride with benzaldehyde followed by an irreversible, stereoselective dehydration promoted by anhydrides and catalyzed by the amine. The main competing reactions were Claisen condensations of the anhydrides. Self-condensation of phenylacetic anhydride gave varying yields of phenylacetic acid, 1,3-diphenyl-2-propanone (2), and the enol phenylacetate of 2.

In an earlier investigation[1] it was suggested on the basis of kinetic results that the apparent condensation of phenylacetic acid with benzaldehyde in acetic anhydride was an aldol-type condensation of the mixed anhydride of acetic acid and phenylacetic acid with benzaldehyde. It was further implied that the benzylmethylene group of this mixed anhydride was more reactive to the base than was the methyl group so that the major product isolated from such a reaction is always α-phenylcinnamic acid (α,β-diphenylacrylic acid) rather than cinnamic acid. Because of the leveling effect of the acetic acid in the medium it appeared that the only effective basic catalyst was acetate ion whether a tertiary amine or an acetate salt was added initially as the catalyst.

A similar conclusion concerning the nature of the Perkin condensation can be drawn from the kinetic study reported[2] for the amine-catalyzed condensation of benzaldehydes with acetic anhydride in kerosine. Of course no comparison of the relative reactivity of benzyl groups and methyl groups could be made in this case. Also no test was made of the possibility that the catalytic activity of the amine could be lessened by the acid formed during the reaction. Essentially only initial rates were studied.

Admittedly the reaction is more complex than was assumed originally.[1] Product-isolation experiments[1,3] led to only about 60% yield of pure α-phenyl-*trans*-cinnamic acid (*cis*-α,β-diphenylacrylic acid, 1), m.p. 172–173°. Other investigators,[4–6] using amine-catalyzed condensations under conditions vigorous enough to cause some isomerization[5,6] to α-phenyl-*cis*-cinnamic acid (*trans*-α,β-diphenylacrylic acid), m.p. 138–139°, isolated this acid as a by-product. Also from these condensations *trans*-stilbene has often been isolated.[4] The possibility of Claisen-type self-condensations of the anhydride to give 1,3-diphenyl-2-propanone (2) as a side reaction to the Perkin condensation has also been demonstrated[7] with a carboxylate ion as a catalyst.

The best isolated yields (92–95%) of α-phenyl-*trans*-cinnamic acid (1) were reported[6] for the stereoselective dehydration of either *erythro*- or *threo*-2,3-diphenylhydracrylic acid in a mixture of boiling acetic anhydride and triethylamine for 35 min. Under the same conditions the apparent Perkin condensation of phenylacetic acid with benzaldehyde gave an 83% yield of essentially pure 1. It was also shown[6] that the hydroxy acids did not undergo any appreciable reversal of the aldol condensation. It was proposed[6] that the dehydration

---

(1) R. E. Buckles and K. G. Bremer, *J. Am. Chem. Soc.*, **75**, 1487 (1953).

(2) Y. Ogata and M. Tsuchida, *J. Org. Chem.*, **24**, 78 (1959).

(3) R. E. Buckles and K. G. Bremer, "Organic Syntheses," Coll. Vol. IV, John Wiley and Sons, Inc., New York, N. Y., 1963, p. 857.

(4) L. F. Fieser, *J. Chem. Educ.*, **31**, 291 (1954); "Experiments in Organic Chemistry," 3rd Ed., D. C. Heath and Co., 1957, pp. 182–185.

(5) R. Ketcham and D. Jambotkar, *J. Org. Chem.*, **28**, 1034 (1963).

(6) H. E. Zimmerman and L. Aramijian, *J. Am. Chem. Soc.*, **81**, 2086 (1959).

(7) D. S. Breslow and C. R. Hauser, *ibid.*, **61**, 786 (1939).

part of this Perkin condensation involved a stereoselective, base-catalyzed elimination of acetic acid from the acetylated aldol product (the mixed anhydride of 2,3-diphenylhydracrylic acid and acetic acid).

In the present investigation a quantitative product-isolation study of the Perkin synthesis of 1 was carried out. It was the purpose of the study to correlate the quantitative data with the reaction mechanism and thereby to establish conditions for the minimum production of side-products.

The results of these quantitative experiments are summarized in Tables I and II. In general the reactions were carried out under much milder conditions than those usually used[1,3-6] for this Perkin condensation. The reaction temperatures were 30 ± 5 and 65 ± 5°. In preliminary experiments at 100° such as those used in the earlier investigation[1] of kinetics the reaction mixtures became colored a deep red-brown. This color developed when no Perkin condensation was even carried out if phenylacetic acid was heated in acetic anhydride with triethylamine. Such experiments indicated the necessity of running experiments with a minimum of Claisen-type condensations of the anhydrides as side reactions. For this reason the condensations were carried out in various amounts of benzaldehyde as a solvent. The advantage of a lowered concentration of anhydride had been commented[8] upon for the Perkin condensation in general, but the application[4] of this idea to the synthesis of 1 led to no particular improvement in yield of product because of the vigorous reaction conditions used. In general the reaction mixtures summarized in Tables I and II were no more deeply colored than a pale yellow.

TABLE I

YIELD OF α-PHENYL-*trans*-CINNAMIC ACID (1) FROM THE APPARENT CONDENSATION OF PHENYLACETIC ACID WITH BENZALDEHYDE[a]

R in $(RCO)_2O$	Et_3N Mole	Et_3N Addn. time, hr.	PhCHO, ml.	Yield, %
CH_3	0.20	0	75	45
CH_3	0.20	1.5	75	53[b]
CH_3[c]	0.40	1.5	75	76
CH_3	0.40	3.0	75	64
CH_3[d]	0.40	3.0	75	83
CH_3	0.60	4.5	75	72
CH_3[e]	0.40	0	75	89[f]
CH_3[e]	0.40	3.0	75	96[f]
CH_3[e,g]	0.80	3.0	150	95[f]
CH_3[h]	0.40	0	. . .	58[i]
Ph	0.40	1.5	75	83
Ph	0.40	3.0	75	82
Ph	0.60	4.5	75	82
Ph[d]	0.60	4.5	75	88
Ph[e]	0.60	4.5	75	85
Ph[e]	0.60	4.5	150	92[f]
Ph[e,j]	0.60	4.5	150	88[f]
Ph[e,j]	0.60	5.0	200	92[f]
CF_3	0.60	4.5	150	0
d, k	0.20	1.5	100	0
CH_3[l]	0.20	1.5	75	0
CH_3[e,l]	0.20	1.5	75	0.3

[a] The reactions were carried out at 30 ± 5° with 27.2 g. (0.20 mole) of phenylacetic acid and 0.3 mole of the anhydride, $(RCO)_2O$, in benzaldehyde as a solvent. The total reaction time was 5 hr. [b] From one such experiment about 1 g. (7%) of 1-phenyl-2-propanone was also isolated. [c] In these experiments the reaction temperature went considerably above 30 ± 5° during the addition of the amine. [d] The total reaction time in this case was 7.5 hr. [e] The reactions were run at 65 ± 5°. [f] Low yields (0.2–2%) of *trans*-stilbene were isolated. [g] The quantities of all reagents were doubled. [h] This experiment was carried out at about 140° for 4 hr. with 0.40 mole each of phenylacetic acid, benzaldehyde, and triethylamine in 80 ml. of acetic anhydride. The procedure was that described[1,3] for the product isolation experiments in the earlier investigation. [i] About 3 g. (7%) of 1,3-diphenyl-2-propanone (2) was also isolated. [j] Instead of 0.30 mole of benzoic anhydride a mixture of 0.30 mole each of benzoic acid, triethylamine, and benzoyl chloride in benzaldehyde which had been allowed to react at 65° for 1.5 hr. was used. [k] Phthalic anhydride was used. [l] No phenylacetic acid was used; the expected product was cinnamic acid.

TABLE II

YIELD OF α-PHENYL-*trans*-CINNAMIC ACID (1) FROM THE CONDENSATION OF PHENYLACETIC ANHYDRIDE WITH BENZALDEHYDE[a]

R in $(RCO)_2O$	Et_3N Mole	Et_3N Addn. time, hr.	PhCHO, ml.	Yield, %
CH_3	0.10	0.75	50	53
CH_3	0.20	1.5	50	79
CH_3 ,	0.30	2.25	50	78
CH_3	0.40	3.0	50	76
CH_3[b]	0.20	3.0	100	65
Ph	0.20	1.5	50	77
Ph	0.40	3.0	50	82
Ph[c]	0.40	3.0	75	86
Ph[d]	0.40	4.0	200	89[e]
Ph[d]	0.40	4.0	250	87[e]
$PhCH_2$[f]	0.20	0	50	28[e]
$PhCH_2$[f]	0.20	1.5	50	32
CF_3[c,g]	0.20	1.5	150	0

[a] The reactions were carried out at 65 ± 5° with 25.4 g. (0.10 mole) of phenylacetic anhydride and 0.10 mole of the other anhydride, $(RCO)_2O$, in benzaldehyde as solvent. The total reaction time was 4 hr. [b] The total reaction time in this case was 8 hr. [c] In this case 0.20 mole of the second anhydride was used. [d] In this case 0.20 mole of phenylacetic acid, 0.10 mole of benzoic acid, and 0.30 mole of triethylamine reacted with 0.30 mole of benzoyl chloride in the reaction medium to give the equivalent of 0.10 mole of phenylacetic anhydride and 0.20 mole of benzoic anhydride before the amount of amine used as catalyst was added. [e] Low yields (0.2–1%) of *trans*-stilbene were isolated. [f] In these cases the only anhydride was phenylacetic anhydride (0.20 mole). [g] These experiments were carried out at 30 ± 5°.

The isolation procedure developed for the experiments summarized in Tables I and II was capable of giving at least a 96% recovery of all of the 1 in the reaction mixture. The recovery is as good as that reported[6] for the dehydration of the 2,3-diphenylhydracrylic acids. In some cases low yields of *trans*-stilbene were isolated from the neutral fraction. In others 1,3-diphenyl-2-propanone (2) and 1-phenyl-2-propanone were isolated from the neutral fraction or from the base-soluble fraction after acidification and apparent decarboxylation. In no cases were conditions apparently vigorous enough to lead to the formation of α-phenyl-*cis*-cinnamic acid for none of this acid was isolated. This product would be expected[4] to be precipitated at a lower pH than that (pH 5) used for the precipitation of the *trans* isomer, but precipitation at such lower pH values gave only benzoic acid as an identifiable product. No cinnamic acid could be isolated when acetic anhydride was used with either phenylacetic acid or phenylacetic anhydride. Even with acetic anhydride alone very little cinnamic acid could be isolated.

---

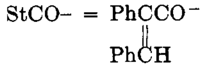
(8) J. R. Johnson, *Org. Reactions*, 1, 236 (1942).

The results summarized in Tables I and II are consistent with the composite view of the reaction which was reached in the earlier kinetic investigation[1] and the investigation[6] of the stereoselective dehydration step. According to this view both the amine and the acetate ion can promote the aldol condensation and the dehydration but the amine would be expected to be the more effective catalyst.

Although the presence[1,6] of the mixed anhydride of phenylacetic acid and acetic acid in the reaction mixture is entirely reasonable, all attempts to synthesize this compound led to phenylacetic anhydride. Since this anhydride is a solid (m.p. 72°), it is possible that it crystallized selectively during the isolation procedure. Attempts to prepare the mixed anhydride of phenylacetic acid and benzoic acid by the method described[9] for aromatic anhydrides yielded only phenylacetic anhydride also. In any event the Perkin condensation can be written as involving either mixed anhydrides or symmetrical anhydrides. It was assumed, however, that the anhydride of the strongest acid would always be preferentially hydrolyzed or that of the weakest acid would be favored in anhydride-interchange equilibria.[10] Since all of the anhydrides used in the experiments outlined in Tables I and II were anhydrides of acids stronger than **1** ($pK_a = 6.1$ in 60% ethanol[4]), the product was assumed to be mostly in the anhydride form before the reaction mixture was quenched. The overall reactions showing the stoichiometry based on symmetrical anhydrides are given in eq. 1 and 2. These equations were used in designing many of the experiments of Tables I and II. These equations do not represent the exact stoichiometry since the anhydride interchanges would be equilibria. Obviously a considerable amount of the anhydride product must have been hydrolyzed before the reaction mixture was quenched in the experiments (Table II) in which only 0.1 mole of acetic anhydride or benzoic anhydride was used with 0.1 mole of phenylacetic anhydride. Equation 2 requires 0.2 mole of the second anhydride to take care of the water formed in the dehydration step. In the equilibrium mixture of anhydrides enough of the phenylacetyl group must have been present in the anhydride form in order to give rise to reasonably high yields of product even though the anhydride of **1** would be expected to be favored over phenylacetic anhydride.

$$2PhCH_2COOH + 2PhCHO + 6Et_3N + 3(RCO)_2O \longrightarrow (StCO)_2O + 6RCO_2^- + 6Et_3NH^+ \quad (1)$$

$$(PhCH_2CO)_2O + 2PhCHO + 4Et_3N + 2(RCO)_2O \longrightarrow (StCO)_2O + 4RCO_2^- + 4Et_3NH^+ \quad (2)$$



$$StCO\text{–} = \underset{\underset{PhCH}{\|}}{PhC}CO^-$$

The results of the experiments support the view that we are dealing with a base-catalyzed Perkin condensation accompanied by slower Claisen condensations. When phenylacetic acid was used, more triethylamine was necessary than when the anhydride was used because more of the amine was neutralized by the acid and the carboxylate ion was a poorer basic catalyst than the amine. This situation was apparent especially when the carboxylate ion was benzoate ion and more amine was necessary than with corresponding experiments involving the more basic acetate ion. On the other hand, excess amine, especially early in the reaction when anhydride concentrations were highest, presumably led to lower yields because of competing Claisen-type condensations. Such an effect was especially apparent with benzoic anhydride which would be expected to condense better than either acetic anhydride or phenylacetic anhydride with an enolate anion. In such cases it was necessary to use larger volumes of benzaldehyde as solvent in order to minimize side reactions. With phthalic anhydride and trifluoroacetic anhydride no **1** could be isolated at all, presumably because of Claisen condensations. In fact in the case of phthalic anhydride a Claisen condensation with phenylacetic anhydride would be expected to be one of the steps in the synthesis[11] of 3-benzylidenephthalide.

The optimum conditions for the synthesis of **1** involve a compromise of the factors discussed above. Best results were obtained with 0.2 mole of phenylacetic acid and 0.3 mole of acetic anhydride in 75 ml. of benzaldehyde at 65°. A 0.4-mole sample of triethylamine was added over a 3-hr. or longer period. The yields in such an experiment were consistently around 95%. These conditions make use of the superior catalysis by the amine as opposed to the carboxylate ions. Claisen condensations are minimized by the relatively low concentration of phenylacetic anhydride, by the slow addition of amine, by the limitation on the amount of the amine, and by the relatively low temperature. The low temperature also limits the isomerization of the product to α-phenyl-*cis*-cinnamic acid and the formation of *trans*-stilbene. The reactions carried out under these conditions are also convenient because no special anhydrides must be synthesized and no large amounts of solid acid such as benzoic acid must be separated from the product.

In a separate series of experiments the self-condensation of phenylacetic anhydride catalyzed by triethylamine in ether, benzene, or excess catalyst was investigated. Although no quantitative measurements were carried out, the reaction was considerably slower than the Perkin condensation as would be expected. Varying amounts of phenylacetic acid, 1,3-diphenyl-2-propanone (**2**), and the enol phenylacetate of **2** were isolated. Part of the **2** often arose from the base-soluble fraction rather than from the neutral fraction. This same observation was made concerning the 1-phenyl-2-propanone isolated from the Perkin condensation. Such observations support the intermediate formation of β-keto acids rather than the concerted elimination of carbon dioxide which has been suggested[12] as the driving force for such a condensation. None of the β-keto acid could be isolated, however. Higher condensations were suggested by the deep reddish color of the reaction mixtures. It was bleached to some extent on acidification. Also from the neutral fraction it was possible to precipitate a copper chelate in some cases, but no diketone could be isolated from it. In eq. 3 are summarized the reaction steps which appear to account best for the results of these Claisen condensations.

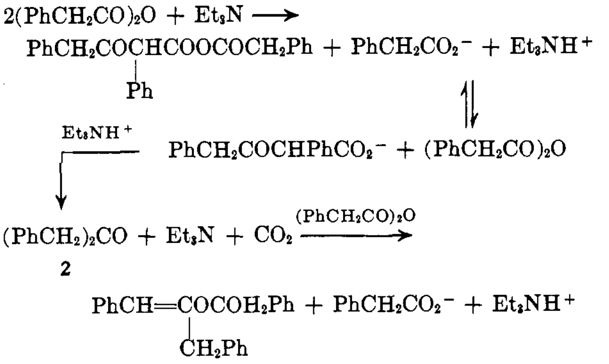
---

[9] D. B. Denney and M. A. Greenbaum, *J. Am. Chem. Soc.*, **79**, 979 (1957).

[10] N. F. Albertson, *Org. Reactions*, **12**, 157 (1962).

[11] R. Weiss, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons; Inc., New York, N. Y., 1943, p. 61.

[12] J. King and F. McMillan, *J. Am. Chem. Soc.*, **73**, 4911 (1951).



$$2(\mathrm{PhCH_2CO})_2\mathrm{O} + \mathrm{Et_3N} \longrightarrow \mathrm{PhCH_2CO\underset{\substack{|\\ \mathrm{Ph}}}{C}HCOOCOCH_2Ph} + \mathrm{PhCH_2CO_2^-} + \mathrm{Et_3NH^+} \rightleftharpoons \mathrm{PhCH_2COCHPhCO_2^-} + (\mathrm{PhCH_2CO})_2\mathrm{O} \xrightarrow{\mathrm{Et_3NH^+}} \underset{\mathbf{2}}{(\mathrm{PhCH_2})_2\mathrm{CO}} + \mathrm{Et_3N} + \mathrm{CO_2} \xrightarrow{(\mathrm{PhCH_2CO})_2\mathrm{O}} \mathrm{PhCH{=}\underset{\substack{|\\ \mathrm{CH_2Ph}}}{C}OCOH_2Ph} + \mathrm{PhCH_2CO_2^-} + \mathrm{Et_3NH^+} \qquad (3)$$

The product of the condensation, the enol phenylacetate of **2**, is a hitherto undescribed enol ester. Hydrolysis in 96% sulfuric acid yielded phenylacetic acid and **2**. Its infrared absorption spectra in carbon tetrachloride and in carbon disulfide showed the intense carbonyl frequency at 1760, the weaker carbon–carbon double bond frequency at 1680, and the intense antisymmetric and symmetric C–O–C stretching frequencies at 1230 and 1120 cm.$^{-1}$ which are characteristic[13,14] of enol esters. The n.m.r. spectrum (measured on a Varian Model A-60 in carbon tetrachloride) was consistent with the structure of the enol ester. It consisted of the following singlets or very close multiplets given as δ in p.p.m.: the phenylacetate methylene, 3.55; the allyl methylene, a partially resolved doublet with $J \sim 0.8$ c.p.s. centered at 3.66; the vinyl proton, a partially resolved triplet with $J \sim 0.8$ c.p.s. centered at 5.83; one phenyl, 7.10; and the other two, 7.20. The resonance of the vinyl proton at 5.83 p.p.m. is quite far upfield. Vinyl protons in a similar environment—α to a phenyl and β to an acetoxy group—in the *cis*- and *trans*-enol acetate of phenylacetaldehyde have been found[15] to have doublets in the n.m.r. spectra (in carbon tetrachloride) centered at $\delta = 5.55$ and 6.26 p.p.m., respectively. Usually a vinyl proton α to a phenyl group tends to have its resonance farther downfield than these values even when the phenyl group is not completely coplanar with the double bond, as with *cis*-β-bromostyrene (6.86 p.p.m.),[15] *cis*-cinnamic acid (7.08 p.p.m.), and *cis*-stilbene (6.55 p.p.m.) (all in carbon tetrachloride). In aliphatic enol acetates vinyl protons β to the acetoxy group have been found[14] to have the expected resonances (~5 p.p.m.) for vinyl protons in general, while those α to the acetoxy group show resonances quite far downfield (~7). These low-field resonances were also observed[15] for the enol acetates of phenylacetaldehyde.

Experimental

Phenylacetyl Chloride.—A mixture of 546 g. (4.00 moles) of dry phenylacetic acid, m.p. 75–77°, and 475 g. (4.00 moles) of freshly distilled thionyl chloride, b.p. 76° (745 mm.), was allowed to react spontaneously at room temperature for 20 hr. The reaction mixture was warmed to 35–40° until no more gas was evolved. Thionyl chloride was distilled at reduced pressure from the mixture with the aid of 125 ml. of anhydrous benzene. Distillation of the residue yielded 498 g. (81%), b.p. 55–57 (approximately 1 mm.), of colorless phenylacetyl chloride.

Sodium Phenylacetate.—A solution of 120 g. (3.00 moles) of sodium hydroxide and 408 g. (3.00 moles) of phenylacetic acid in 150 ml. of water was adjusted to pH 6.5 (nitrazine paper) by the addition of a small amount of either the acid or the base. The solution was evaporated and the residue was ground and washed with anhydrous ether. Drying in an oven at 10 mm. pressure yielded 460 g. (97%) of anhydrous sodium phenylacetate.

Phenylacetic Anhydride. The reaction of 110 g. (0.69 mole) of sodium phenylacetate with 108 g. (0.69 mole) of phenylacetyl chloride in 400 ml. of anhydrous benzene essentially as described by King and Macmillan[12] yielded 151 g. (86%) of phenylacetic anhydride, m.p. 70–72°.

In other experiments 157 g. (2.00 moles) of acetyl chloride in 100 ml. of anhydrous ether was added dropwise over a period of 22 hr. to 316 g. (2.00 moles) of sodium phenylacetate which was stirred with 1 l. of anhydrous ether. After an additional 22-hr. reaction period the ether solution was washed with four 25-ml. volumes of cold, saturated aqueous ammonium chloride. The inorganic solid was removed by filtration. The ether solution was separated from the water layer and dried over anhydrous magnesium sulfate. The ether was evaporated at room temperature under reduced pressure. The residue was crystallized from a benzene–hexane mixture to yield about 176 g. (70%) of phenylacetic anhydride, m.p. 71–72°. No evidence of the presence of the mixed anhydride of phenylacetic acid and acetic acid was observed during the isolation procedure.

In a series of similar experiments on a smaller scale equimolar amounts of sodium phenylacetate reacted with benzoyl chloride to give relatively small yields of phenylacetic anhydride (m.p. 72–74°) as the only product isolated. Similar results were obtained from equimolar amounts of phenylacetic acid, benzoyl chloride, and pyridine used in a modification of the method of Denney and Greenbaum[9] for the synthesis of mixed anhydrides.

Anhydrides.—Commercial grade acetic anhydride was purified by distillation just before it was used. The fraction with a 0.1° boiling range at about 139° (745 mm.) was used. Phthalic anhydride was crystallized from benzene to give material of m.p. 130°. Benzoic anhydride, m.p. 41–42°, b.p. 148–150° (approximately 1 mm.), was synthesized in 90% yield by means of the reaction of the complex between benzoyl chloride and pyridine with a 0.5-molar amount of water.[16] Trifluoroacetic anhydride, b.p. 39° (745 mm.), was prepared in 69% yield by the reaction of trifluoroacetic acid with phosphorus pentoxide.[17]

Other Reagents.—Benzaldehyde was dried over magnesium sulfate, filtered, and distilled (from a small amount of hydroquinone), b.p. 178–179° (745 mm.). Benzoyl chloride was purified by distillation, b.p. 196–197° (745 mm.). Anhydrous triethylamine was treated with acetyl chloride, filtered, and distilled twice (the second time just before it was used) from fresh barium oxide. The distillate with a 0.1° boiling range around 89° (745 mm.) was used.

Benzoic acid (m.p. 120–121°) and phenylacetic acid (m.p. 75–77°) were dried over phosphorus pentoxide in a desiccator. Further purification of the phenylacetic acid of this melting point by crystallization or by distillation gave no improvement in yield in the various experiments in which it was used.

Eastman practical grade 1,3-diphenyl-2-propanone (**2**) was distilled, b.p. 153–155° (4 mm.), m.p. 30°, for use as an authentic sample.

Procedure for the Perkin Condensation.—The following procedure was used for the experiments summarized in Tables I and II. Most entries in these tables involved at least two runs each with the average per cent yields of relatively pure product showing standard deviation of about 2%.

A 500-ml. round-bottomed three-necked flask was placed in an oil bath and was fitted with a reflux condenser equipped with a calcium chloride drying tube, a dropping funnel, and a mechanical stirrer. The specified amounts of phenylacetic acid or phenylacetic anhydride, benzaldehyde, and the indicated anhydride were mixed in the flask. During the course of 15 min. the oil bath was regulated to 30 ± 5 or 65 ± 5°. The specified amount of amine was placed in the dropping funnel. The amine was added dropwise to the reaction mixture during the time specified in the tables. At the completion of the reaction period, the reaction mixture was quenched by the addition of 350 ml. of 10% aqueous sodium hydroxide solution. The reaction mixture

---

[13] K. Nakanishi, "Infrared Absorption Spectroscopy," Holden-Day, Inc., San Francisco, Calif., 1962, pp. 44, 181.

[14] H. O. House and V. Kramar, *J. Org. Chem.*, **28**, 3362 (1963).

[15] D. T. Witiak and B. B. Chaudhari, *ibid.*, **30**, 1467 (1965).

[16] C. F. H. Allen, C. J. Kibler, D. M. McLachlin, and C. V. Wilson, "Organic Syntheses," Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1955, p. 28.

[17] E. J. Bourne, M. Stacey, J. C. Tatlow, and J. A. Tedder, *J. Chem. Soc.*, 719 (1951).

was placed in a 2-l. round-bottomed flask arranged for steam distillation with external heating. Steam distillation was continued until the distillate was no longer cloudy. The crude product was precipitated from the steam distillation residue when it was acidified to pH 5 (nitrazine paper) with concentrated hydrochloric acid. The product was collected by suction filtration and was pressed firmly on the filter. The moist solid was placed in a 1-l. round-bottomed flask and approximately 400 ml. of benzene was added. The remaining water was removed with the aid of a Dean–Stark water separator. Hexane was added to the boiling benzene solution until the solid product was just about to precipitate. The hot benzene–hexane solution was filtered and allowed to cool. The product was filtered and washed in the funnel with 75–100 ml. of hot hexane. An additional amount of product formed when the combined hexane rinse and filtrate were chilled. The filtrate was evaporated and the residual solid was recrystallized from a hexane–benzene mixture. The combination of these fractions made up the yield of 1, m.p. 172–174, listed in Tables I and II.

At the low temperatures of 30 or 65° the reaction mixtures in benzaldehyde as a solvent turned only a light yellow. At 100° in acetic anhydride as a solvent the reaction mixture turned red-brown. This color change was observed when no benzaldehyde was present so that Claisen condensation side reactions appear to be indicated. It was shown by experiments in a nitrogen atmosphere that air oxidation did not account for the color. Reaction mixtures with either the amine or anhydride missing did not become colored.

Little difference in yield was observed if 200 ml. of concentrated hydrochloric acid was used to quench the reaction mixture and the pH was adjusted with aqueous sodium hydroxide after the steam distillation.

During the steam distillation a small amount of solid sometimes appeared in the condenser. The steam distillation was continued until no more of this material appeared. Its presence was detected by its characteristic fluorescence under ultraviolet radiation. Ether extraction of the aqueous distillate followed by evaporation yielded small amounts of *trans*-stilbene identified by the melting point of mixtures with an authentic sample of m.p. 123–124°.

In one experiment a lower yield (58%) of 1 was prepared by the procedure used in the product-isolation experiments described for the earlier investigation.[1,3] This reaction was carried out in boiling acetic anhydride and the temperature was about 140°. The steam distillate from this preparation was extracted with ether and the ether solution was then extracted with 30% aqueous sodium bisulfite to remove benzaldehyde. Evaporation of the ether yielded 3 g. of a brown oil which was identified as 1,3-diphenyl-2-propanone (2) by its infrared absorption spectrum and by the following derivatives which were identical with authentic samples: 2,4-dinitrophenylhydrazone, m.p. 94–96°; phenylhydrazone, m.p. 117–120°; and oxime, m.p. 124–125°.

After precipitation of 1 at pH 5, further acidification yielded little product unless benzoic anhydride was used, in which case benzoic acid was isolated. In one experiment, in which phenylacetic acid and acetic anhydride were the reagents, acidification to below pH 2 after the major product had been isolated yielded 1 g. of an oil which would not redissolve in base. Its boiling point (210–213°) and its infrared absorption spectrum were the same as those of an authentic sample of 1-phenyl-2-propanone.

In two experiments where only acetic anhydride was condensed with benzaldehyde the steam distillation residue was acidified to pH 1. Only 2–3 g. of product precipitated. It proved to be benzoic acid. At 65°, however, 0.27 g. (0.3%) of cinnamic acid, m.p. 132–133°, was isolated from this crude product by fractional crystallization.

Self-Condensation of Phenylacetic Anhydride.—A number of experiments were carried out. In general a solution of 19.1 g. (0.075 mole) of phenylacetic anhydride in 100 ml. of anhydrous ether was boiled vigorously with amounts of triethylamine varying from 3.5 (0.035 mole) to 7.6 g. (0.076 mole) for periods of time varying from 24 to 48 hr. In one experiment 75 ml. of triethylamine was used as the solvent. In another 38.1 g. (0.15 mole) of phenylacetic anhydride and 12.2 g. (0.12 mole) of triethylamine in 250 ml. of benzene were heated at 60° for 161 hr. In each case the reaction mixture was extracted with enough 2 *M* hydrochloric acid to dissolve the triethylamine. The organic layer was then extracted with 5% aqueous sodium bicarbonate. Acidification of this extract to pH 4 (nitrazine paper) gave phenylacetic acid. Further acidification to pH 1 yielded a little red oil which was not soluble in base. This oil proved to be 2 as identified by infrared absorption spectrum. Evaporation of the organic layer gave a red-brown oil. Crystallization of this oil from 95% ethanol yielded the enol phenylacetate of 2. The mother liquor, on addition of water, yielded more liquid 2. The variation in yields of these products was quite haphazard and bore no relationship to the variation in amounts of amine, the nature of the solvent, or length of reaction time. An equimolar amount of phenylacetic acid was expected (eq. 3) to accompany the enol ester of 2 which was isolated. This amount was subtracted from the total amount of acid isolated, and the remainder was assumed to arise from the hydrolysis of the anhydride. These yields varied from 3.3 (17%) to 10.7 g. (51%). Yields of 2 varied from 1.3 (8%) to 6.9 g. (44%) and of the enol ester of 2 from 0.5 (4%) to 4.0 g. (33%). The total material accounted for in the experiments ranged from 45 to 94%.

The enol phenylacetate of 2 was a new compound of m.p. 63–64°.

Anal. Calcd. for $C_{23}H_{20}O_2$: C, 84.1; H, 6.14. Found: C, 84.5; H, 6.05.

A mixture of 0.57 g. (1.74×10^{-3} mole) of the enol phenylacetate of 2 in 35 ml. of 96% sulfuric acid was stirred at room temperature for 4 hr. The mixture was poured over 100 g. of ice. Extraction with five 75-ml. portions of ether gave an ether solution which in turn was extracted with four 100-ml. portions of 5% sodium bicarbonate. Evaporation of the ether yielded 0.25 g. (68%) of yellow oil which was identified by its infrared absorption spectrum as 2. The aqueous bicarbonate solution on acidification and ether extraction yielded 0.12 g. (50%) of phenylacetic acid, m.p. 72–73°. A mixture of 0.60 g. of the enol ester with 0.4 g. of potassium carbonate in 25 ml. of water was boiled for 4 hr. Ether extraction yielded 0.57 g. (95%) of the enol ester, m.p. 59–61°.

Acknowledgment.—The authors would like to thank Dr. D. T. Witiak and Mr. B. B. Chaudhari, College of Pharmacy, University of Iowa, for making information on their research available to us prior to its publication