by glpc comparison with known compounds or by collecting the glpc peaks for spectra. The percentage yields reported correspond to the peak area.

Hydrogenolyses with Alkoxychloroalanes.—Into the flask described above was weighed 2.40 g (18 mmol) of $AlCl_3$. In an ice bath 45 ml of Et_2O was syringed into the flask to dissolve the $AlCl_3$; 18 mmol of the standardized $LiAlH_4$ solution ($\sim$15 ml) was added by syringe. After 15 min without the ice bath it was returned, the alcohol was added, and the hydrogenolysis was run as above. For work-up the reaction mixture was poured into a separatory funnel containing 4 g of NaOH, 50 ml of H_2O, 50 g of ice, and 75 ml of Et_2O. The rest of the work-up was as above.

Materials.—THF and Et_2O were dried by distillation from $LiAlH_4$. Alcohols were distilled from CaH_2. The preparations of norcamphor dimethyl ketal, cycloheptanone dimethyl ketal, and cyclodecanone dimethyl ketal have been described.[4] The published preparation for 2,2,4,4-tetramethyl-1,3-dioxolane also yielded cyclohexanone isobutylene ketal and norcamphor isobutylene ketal.[18] The preparations of norcamphor diethyl ketal,[3] norcamphor ethylene ketal,[18] and trimethyl orthobenzoate[19] are reported. Benzaldehyde dimethyl acetal and heptanal dimethyl acetal were prepared from the aldehydes and trimethyl orthoformate.

Registry No.—**1,** 10395-51-4; **3,** 13372-34-4; methoxyalane, 36803-31-3.

[18] E. J. Salmi, *Ber.*, **71**, 1803 (1938).

[19] S. M. McElvain and J. T. Venerable, *J. Amer. Chem. Soc.*, **72**, 1661 (1950).

The Vapor Phase Pyrogenesis of Phenol

JOHN M. PATTERSON,* CHYNG-YANN SHIUE, AND WALTER T. SMITH, JR.

Department of Chemistry, University of Kentucky, Lexington, Kentucky 40506

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Phthalic acid and 3- and 4-methylphthalic acids (precursors of benzyne, methylbenzyne, water) were pyrolyzed at 700° and their interaction products were determined. From phthalic acid, the major products, in addition to benzyne interaction products, were benzoic acid, phenol, and phenyl benzoate. It is proposed that decarboxylation of phthalic acid competes with benzyne formation *via* the anhydride and that phenol and phenyl benzoate arise through a competitive addition of water and benzoic acid, respectively, to the benzyne intermediate. The vapor phase addition of water to methylbenzynes produces the expected isomeric cresols.

The high-temperature pyrolysis (*ca.* 800°) of a number of natural products such as tobacco,[1] lignin,[2] and carbohydrates[3] has been reported to produce significant amounts of phenol and substituted phenols. Because of the reported activity of phenols as tumor-promoting agents,[4] the origin of these substances in the pyrolytic process is of considerable interest. It was recently found that the pyrosynthesis of phenols occurs when both aromatic and nonaromatic substances, such as amino acids[5a] and maleic hydrazide,[5b] are pyrolyzed at high temperatures. The presence of hydrocarbons in the pyrolysate, which have been shown to arise from benzyne, suggested that benzyne might be a precursor to the phenols observed in the high-temperature pyrolyses. While the addition of water to benzyne in the liquid phase has been adequately demonstrated,[6] no evidence was available to indicate that the addition would occur in the vapor phase at high temperatures (700°) or in what way. Because of the recent reports that the addition of carbon disulfide to benzyne gives different products in the vapor phase[7] as compared to the liquid phase,[8] the possible vapor phase addition of water to benzyne was investigated.

Results and Discussion

The ease with which phthalic acid undergoes dehydration to phthalic anhydride and water and the fact that the thermal decomposition of phthalic anhydride at 700° produces benzyne[9] suggests that the pyrolysis of phthalic acid and methyl-substituted phthalic acids at 700° would provide convenient systems for observing the interaction of benzyne with water in the vapor phase.

When phthalic acid was pyrolyzed at 700°, phenol, phenyl benzoate, and benzoic acid were produced in addition to the usual benzyne products of biphenyl and naphthalene. Substituted phenols were likewise obtained from the thermolysis of 3- and 4-methylphthalic acids at 700°. The yields of these products as well as the relative concentrations of other pyrolysate constituents are summarized in Tables I and II.

TABLE I

YIELDS[a] OF SELECTED COMPONENTS OBTAINED FROM THE PYROLYSIS OF PHTHALIC ACID, BENZOIC ACID, AND METHYL-SUBSTITUTED DERIVATIVES AT 700°

Component	Phthalic acid	Benzoic acid	Toluic acids			Methylphthalic acids	
			o-	*m*-	*p*-	3-	4-
Naphthalene	1.2						
Biphenyl	1.8						
Phenol	3.9	0.4				0.09	0.14
o-Cresol			0.01	*b*	*b*	0.10	*b*
m-Cresol			*b*	0.02	*b*	0.11	
p-Cresol			*b*	*b*	0.01	*b*	1.25[c]
Phenyl benzoate	2.2						

[a] Yields are reported as moles of compound per mole of substance pyrolyzed × 100 and were determined by glpc using internal standards. [b] Not found. [c] Mixture of *m*- and *p*-cresol incompletely resolved by glpc. Ratio of para to meta isomer as determined by infrared spectroscopy was 0.83:1.

It is proposed that the major reaction products arise through a competitive decarboxylation and de-

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[1] R. L. Stedman, *Chem. Rev.*, **68**, 153 (1968).

[2] W. S. Schlotzhauer, I. Schmeltz, and L. C. Hickey, *Tobacco Sci.*, **11**, 31 (1967).

[3] E. B. Higman, I. Schmeltz, and W. S. Schlotzhauer, *J. Agr. Food Chem.*, **18**, 639 (1970).

[4] C. E. Searle, *Chem. Brit.*, **6**, 5 (1970).

[5] (a) J. M. Patterson, M. L. Baedecker, R. Musick, and W. T. Smith, Jr., *Tabacco Sci.*, **13**, 26 (1969); (b) J. M. Patterson, C. H. Issidorides, V. C. Groutas, and W. T. Smith, Jr., *Chem. Ind.* (*London*), 337 (1972).

[6] R. Howe, *J. Chem. Soc.*, 478 (1966); G. Wittig and R. W. Hoffman, *Chem. Ber.*, **95**, 2718 (1962).

[7] E. K. Fields and S. Meyerson, *Tetrahedron Lett.*, 629 (1970).

[8] I. Tabushi, K. Okazaki and R. Oda, *ibid.*, 3287 (1967).

[9] E. K. Fields and S. Meyerson in "Advances in Physical Organic Chemistry," Vol. 6, V. Gold, Ed., Academic Press, New York, N. Y., 1968, p 1.

SCHEME I

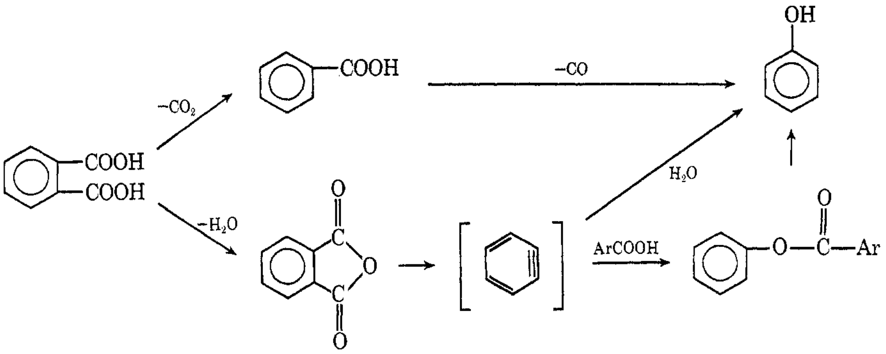

TABLE II

RELATIVE CONCENTRATIONS[a] OF SELECTED PYROLYSATE CONSTITUENTS OBTAINED FROM PHTHALIC, BENZOIC, TOLUIC, AND SOME METHYL-SUBSTITUTED PHTHALIC ACIDS

Component	Phthalic acid[e]	Benzoic acid[f]	Toluic acids[g]			Methylphthalic acids[h]	
			o-	*m*-	*p*-	3-	4-
			A. Neutral Fraction				
Benzene	3.4	61.0	0.2	0.3	0.1		0.8
Toluene	0.3	0.3	95.1	72.1	96.0	23.1	51.6
Styrene	1.2	0.5	0.1	0.2	0.2	1.7	0.5
o-Methylstyrene	0.5		0.1	0.2	0.2		0.1
β-Methylstyrene	0.8					4.0	0.4
Naphthalene	9.5	1.4	0.05		0.01	0.2	0.4
2-Methylnaphthalene					0.2	1.3	3.6
1-Methylnaphthalene						7.3	
Biphenyl	15.0	28.1		0.2	0.06		
3-Methylbiphenyl							0.9
4-Methylbiphenyl					0.6		0.8
Ditolyl				2.1			4.5
Fluorene			0.2			1.7	2.3
Anthracene						1.1	0.3
Phenylacetylene	0.7						
Dibenzofuran	3.5						
Phenyl benzoate	42.2	0.5					
Fluorenone	0.8						
Biphenylene	0.5						
Phenanthrene	7.5						
Wt neutral fraction	5.02	0.5	1.7	1.9	5.2	0.8	4.4
			B. Acidic Fraction				
Phenol	13.2	1.1				0.3	0.4
o-Cresol			0.4			2.7	
m-Cresol				0.5		2.4	26.2
p-Cresol					5.0		
o-Toluic Acid			99.1			0.7	
m-Toluic Acid				97.8		0.3	22.6
p-Toluic Acid					95.0		3.9
Benzoic Acid	53.5	98.9					
Phthalic acid[b]	21.2						
3-Methylphthalic acid[b]						92.8	
4-Methylphthalic acid[b]							35.2
Wt of acid fraction	3.65	9.94	1.30	15.8[c]	0.85[d]	1.60	2.15
Wt of substance pyrolyzed	43.65	16.00	7.90	21.70	11.80	9.60	18.40

[a] Relative concentrations are area per cent as determined by glpc analysis. [b] Compounds dehydrated to the anhydride during glpc analysis and percentages reported are for the anhydride. [c] Of the 15.8 g only 4.7 g was ether soluble. Concentrations reported are for the ether-soluble material. [d] Of the 0.85 g only 0.25 g was ether-soluble. Concentrations reported are for the ether-soluble material. [e] Registry no.: 88-99-3. [f] Registry no.: 65-85-0. [g] Registry no.: *o*-, 118-90-1; *m*-, 99-04-7; *p*-, 99-94-5. [h] Registry no.: 3-, 37102-74-2; 4-, 4316-23-8.

hydration of the phthalic acid followed by the addition of water or benzoic acid to the benzyne generated from the phthalic anhydride intermediate (see Scheme I).

Experiments carried out under the conditions used in the pyrolysis of phthalic acid demonstrated that the phenyl benzoate observed was produced primarily by the addition of benzoic acid to benzyne rather than by a thermal esterification of phenol by benzoic acid.[10] Benzoic acid, on pyrolysis with phthalic anhydride (benzyne precursor), gave 2.5% phenyl benzoate while

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[10] Benzoic acid has been reported to add to benzyne in the liquid phase. See M. Stiles, R. G. Miller, and U. Burckhardt, *J. Amer. Chem. Soc.*, **85**, 1792 (1963).

pyrolysis with phenol (equimolar mixture) gave only 0.3% phenyl benzoate.[11]

The facts that the pyrolysis of a mixture of benzoic acid and phthalic anhydride produced phenol (yield nearly equivalent to that of phenyl benzoate) and that neither the thermal decomposition of phthalic anhydride alone nor the previously reported[12] decarbonylation of benzoic acid produced significant quantities of phenol (0.05 and 0.3%, respectively)[11] suggest that phenyl benzoate decomposes at 700° to give mainly phenol along with naphthalene, biphenyl, benzene, dibenzofuran, and trace amounts of benzaldehyde. While the formation of naphthalene suggests that the addition of benzoic acid to benzyne is reversible, it is likely that the major decomposition pathway involves a homolytic acyl–oxygen cleavage as outlined in Scheme II (compare products from phthalic anhydride and phenyl benzoate in Table III).

SCHEME II

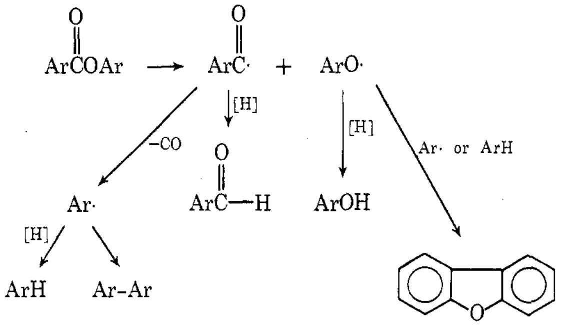

TABLE III

YIELDS[a] OF SELECTED COMPONENTS PRODUCED ON THE PYROLYSIS OF PHTHALIC ANHYDRIDE, PHENYL BENZOATE, PHTHALIC ANHYDRIDE–BENZOIC ACID MIXTURE, AND PHENOL–BENZOIC ACID MIXTURE AT 700°

Component	Phthalic anhydride[b]	Phenyl benzoate[c]	Phthalic anhydride–benzoic acid	Phenol–[d] benzoic acid
Naphthalene	0.7	0.6	0.7	0.3
Biphenyl	0.6	8.7	2.8	0.3
Dibenzofuran		6.5	0.5	0.4
Phenyl Benzoate		10.4	2.5	0.3
Phenol	0.05	18.0	2.2	62.8

[a] Yields are reported as moles of compound produced/mole of substance (or equimolar mixture) pyrolyzed × 100 and were determined by glpc using internal standards. [b] Registry no.: 85-44-9. [c] Registry no.: 93-99-2. [d] Registry no.: 108-95-2.

A measure of the extent of the competition between water and benzoic acid for benzyne can be obtained by a comparison of the yields of phenol and phenyl benzoate produced in the phthalic acid pyrolysis. The yields reported in Table I, however, must be corrected for the thermal conversion of phenyl benzoate into phenol. A rough estimate of the extent of this conversion in the phthalic acid reaction can be made by assuming in the reaction of phthalic anhydride with benzoic acid that the major portion of the phenol formed arises from the decomposition of the phenyl benzoate (see Tables I and III). Using the phenyl benzoate-phenol ratio (from the phthalic anhydride–benzoic acid reaction) and the phenyl benzoate concentration (phthalic acid reaction), the contribution of phenyl benzoate to the phenol yield in the phthalic acid reaction is obtained. A comparison of the corrected yields indicates that benzyne exhibits the same slight preference for the stronger acid in the vapor phase that was observed in the liquid phase.[10]

Further support for the participation of benzyne in the vapor phase pyrogenesis of phenol is obtained from experiments involving substituted benzyne precursors. The pyrolysis of 3-methylphthalic acid at 700° gave *o*- and *m*-cresol (but no *p*-cresol) in a ratio of 1.1:1. A similar ratio (1.07:1) was reported by Roberts[13] in the production of cresols in the liquid phase hydrolysis of *o*-chlorotoluene. Likewise, 4-methylphthalic acid at 700° produced *p*- and *m*-cresol (but no *o*-cresol) in the ratio of 0.8:1. 4-Methylbenzyne has been reported[14] to produce *p*- and *m*-cresyl phenyl ether in a similar ratio of 0.7:1.

As was true with phenol, cresol formation may occur by decarbonylation of the corresponding toluic acid. However, this path was found to be of minor importance when compared with the addition of water to methylbenzyne. *o*-, *m*-, and *p*-toluic acid gave 0.01, 0.02, and 0.01% of *o*, *m*, and *p*-cresol, respectively.

Experimental Section

Ultraviolet spectra were measured in cyclohexane using a Perkin-Elmer Model 202 spectrophotometer, and infrared spectra were measured in chloroform or carbon tetrachloride using a Beckman IR-8 spectrophotometer equipped with a mirror beam condenser. Mass spectra were determined on a Hitachi RMU-6E double-focusing mass spectrometer using 70 eV ionizing energy with the inlet system at 200°. Glpc analyses and preparative separations of the pyrolysate constituents were carried out on an F & M Model 810 gas chromatograph using a thermal conductivity detector.

Materials.—Benzoic and the toluic acids were commercially available samples and were used as received. Phthalic acid, mp 208–210°, and 4-methylphthalic acid, mp 150–151°, were produced by the alkaline hydrolysis of the available anhydrides. 4-Methylphthalic acid, mp 153–155°, was synthesized by the procedure of Smith and Kan[15] using *m*-toluyl chloride and lead isothiocyanate.

Pyrolyses.—The pyrolyses were carried out in the apparatus previously described[16] using 14 ml of Berl saddles or Vycor beads, a nitrogen flow of 100 ml/min, and a rotating screw device (driven by a Troemner monodrum unit) for the introduction of the solid samples into the pyrolysis tube. The liquid products were collected in two traps, each of which was cooled in a Dry Ice–chloroform–carbon tetrachloride mixture, dissolved in ether, and separated into a neutral and acidic fraction by extraction with 5% NaOH. See Table II.

Separation and Identification of Components.—Components of the neutral and acidic fractions were separated by glpc using a 25 ft × 0.375 in. 20% Apiezon L (Anakrom 50/60 U) column heated at 90° for 8 min and then programmed at 2°/min to 280°.

Identifications of components are based on comparisons of glpc retention times, ultraviolet spectra, and infrared spectra with those obtained from authentic samples. Estimation of relative abundances of constituents are based on area per cent values obtained from glpc using a 12 ft × 0.125 in. Hewlett-Packard Hipak Apiezon L column for the neutral fraction and a 12 ft × 0.125 in. 2% polyphenyl ether (six-ring) column for the acidic fraction.

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[11] The yields of compounds indicated represent the upper limits possible, since the reactants are present in considerably lesser amounts in the phthalic acid or phthalic anhydride pyrolyses.

[12] W. Moser, *Helv. Chim. Acta*, **14**, 971 (1931).

[13] A. T. Bottini and J. D. Roberts, *J. Amer. Chem. Soc.*, **79**, 1458 (1957).

[14] R. W. Hoffmann, *Chem. Ber.*, **97**, 2772 (1964).

[15] P. A. S. Smith and R. O. Kan, *J. Amer. Chem. Soc.*, **82**, 4753 (1960).

[16] J. M. Patterson, A. Tsamasfyros, and W. T. Smith, Jr., *J. Heterocycl. Chem.*, **5**, 727 (1968).

The results are reported in Table II. Yields of selected components were determined in the acidic and neutral fractions using the internal standard method. Naphthalene and/or biphenyl were used as internal standards in the acidic fraction analysis and 2-methylnaphthalene was used in the neutral fraction analysis. The results are reported in Tables I and III.

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The Synthesis of a Large-Ring Ketone Containing a Lactone Function. The Dieckmann Condensation *vs.* the Thorpe–Ziegler Condensation[1]

RICHARD N. HURD*[2] AND DINUBHAI H. SHAH

Research Department, Commercial Solvents Corporation, Terre Haute, Indiana 47808

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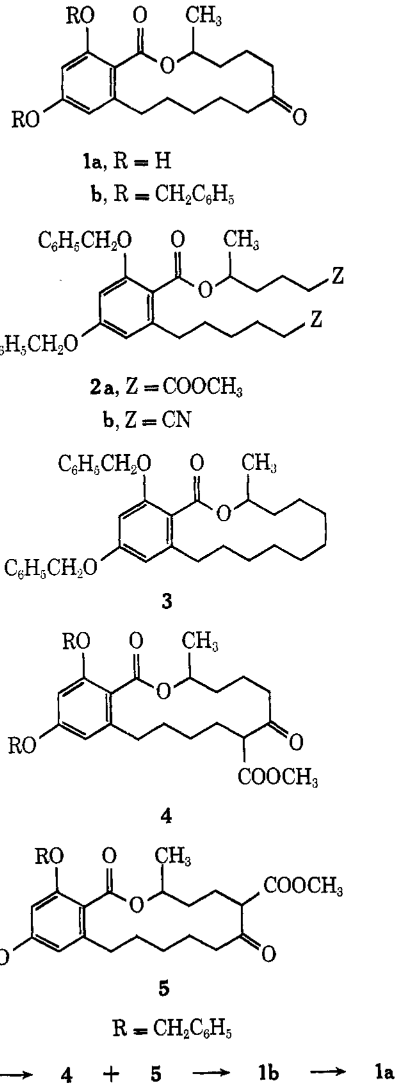
A method has been found for the synthesis in good yield of a large-ring ketone from an α,ω diester (**2a**) whose structure contains a third functional group that is susceptible to basic cleavage. This cyclization, an adaptation of the Dieckmann reaction, has been applied to the preparation of the 2,4-dibenzyl ethers of racemic 5′- and 7′-carbomethoxyzearalanone (**4** and **5**) which are necessary intermediates in the total synthesis of *R,S*-zearalanone (**1a**). This cyclization was compared to the Thorpe–Ziegler cyclization of the parallel α,ω-dinitrile (**2b**). In this case, the enamino nitriles first formed (**9** and **10**) were found to rearrange under the influence of base by nucleophilic attack of the enamino anion on the carbonyl carbon to give amides **11** and **12**. The physical and chemical properties of **11** and **12**, as well as those of the dimer (**19**) produced in this cyclization, are discussed.

The Thorpe–Ziegler condensation has been known for many years as a principal method for syntheses of large-ring ketones. In contrast, the Dieckmann condensation appears to be little known as a source of large-ring ketones[3] even though its application in useful yields has been demonstrated with a series of α,ω diesters.[4] Many modern texts and references[5–7] still continue to state that the scope of the Dieckmann cyclization is restricted to formation of five- or six-membered rings.

To our knowledge there is no reference in the literature to the synthesis of a large-ring ketone from an α,ω-difunctional compound by either the Thorpe–Ziegler or the Dieckmann reactions, where the starting dinitrile or diester, respectively, has a structure in which there is a third functional group that is susceptible to basic cleavage.

The problem of cyclizing such a structure became real to us in completing a total synthesis of zearalanone[8] (**1a**), where it became necessary to cyclize either triester **2a** or ester dinitrile **2b** to a 14-membered lactone intermediate that could be converted readily to **1a** (Scheme I).

SCHEME I



The Dieckmann Cyclization of 4-Carbomethoxy-1-methylbutyl 2,4-Bis(benzyloxy)-6-(5-carbomethoxypentyl)benzoate (2a).—The reaction conditions successfully used by Leonard and Schimelpfenig[4] for the cyclization of alkanedioic esters, namely, potassium *tert*-butoxide in refluxing xylene, did not appear promising for the cyclization of **2a**. The dibenzyl ether of zearalane (**3**) was completely destroyed in less than a day by this treatment, indicating that substantial

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[1] Part of this work was presented as a paper at the 157th National Meeting of the American Chemical Society, Minneapolis, Minnesota, April, 1969, MEDI 28.

[2] G. D. Searle International Co., P.O. Box 5486, Chicago, Ill. 60680.

[3] K. Ziegler, H. Eberle, and H. Ohlinger, *Justus Liebigs Ann. Chem.*, **504**, 94 (1933).

[4] N. J. Leonard and C. W. Schimelpfenig, Jr., *J. Org. Chem.*, **23**, 1708 (1958).

[5] J. Hendrickson, D. Cram, and G. Hammond, "Organic Chemistry," 3rd ed, McGraw-Hill, New York, N. Y., 1970, p 525.

[6] S. Patai, Ed., "The Chemistry of the Carbonyl Group," Interscience, New York, N. Y., 1966, p 274.

[7] A. Liberles, "Introduction to Theoretical Organic Chemistry," Macmillan, New York, N. Y., 1968, p 550.

[8] The total synthesis of zearalanone is the subject of a paper by us in *J. Med. Chem.*, in press.