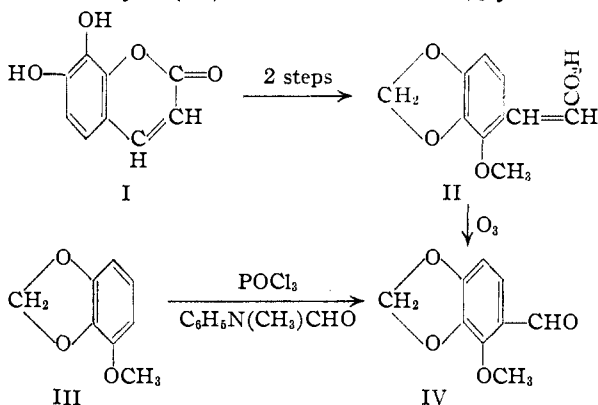


was desired. This aldehyde has been prepared² from daphnetin (I) by methylenation, followed by treatment with sodium hydroxide and dimethyl sulfate and ozonization of the resulting cinnamic acid (II).

As an approach to the synthesis of IV, 1-methoxy-2,3-methylenedioxybenzene (III) was treated with phosphorus oxychloride and N-methylformanilide.³ The aldehyde (IV) was obtained in a 46% yield.



If the aldehydes required for the preparation of the azlactones are available, this reaction has distinct advantages in comparison with procedures described previously.^{3,4,5}

Phenylactic Acid.—This process illustrates the general procedure. A mixture of 50 g. of azlactone (2-methyl-4-benzal-5-oxazalone), 100 g. of amalgamated zinc and 200 ml. of 6 N hydrochloric acid was refluxed for eight hours. The cold solution was saturated with sodium chloride and extracted repeatedly with ether. The ether was removed by distillation after drying over anhydrous sodium sulfate.

The crude acid recrystallized from carbon tetrachloride had m.p. 95.5–96.5° (uncor.).

Anal. Calcd. for C₉H₁₀O₂: C, 65.06; H, 6.02; neut. equiv., 166. Found: C, 64.81; H, 5.93; neut. equiv., 167.

p-Hydroxyphenylactic acid prepared using a similar procedure had m.p. 139–140° (uncor.).

Anal. Calcd. for C₉H₁₀O₄: C, 59.34; H, 5.49; neut. equiv., 182. Found: C, 59.25; H, 5.39; neut. equiv., 178.

A number of benzene-substituted phenylactic acids have been prepared; physical constants and microbial activity will be reported in a later paper.

(3) V. K. La Mer and J. Greenspan, *THIS JOURNAL*, **56**, 1492 (1934).

(4) F. F. Blicke and H. H. Kaplan, *ibid.*, **65**, 1967 (1943).

(5) E. Erlenmeyer, *Ber.*, **13**, 303 (1880).

DEPARTMENT OF AGRICULTURAL CHEMISTRY

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RECEIVED APRIL 23, 1951

Since III is readily prepared from *o*-vanillin by the method of Baker and co-workers,⁴ the present work offers a convenient synthesis of croweacin aldehyde (IV).

Experimental

Croweacin Aldehyde (IV).—To 13.5 g. (0.1 mole) of N-methylformanilide there was added 15.3 g. (0.1 mole) of phosphorus oxychloride. The solution was allowed to stand for 30 minutes and then 6 g. (0.04 mole) of 1-methoxy-2,3-methylenedioxybenzene^{4a} (III) was added. The reaction mixture was heated at 100° for two hours, cooled to room temperature and poured into ice-water. The solid product was collected by filtration and crystallized from dilute alcohol. The weight of material melting at 103° (lit.² 104°) was 3.3 g. (46%).

The 2,4-dinitrophenylhydrazone was prepared in the conventional manner and crystallized from ethyl acetate; m.p. 254–255° (lit.² 254°).

A portion of the aldehyde was oxidized with potassium permanganate to give croweacin acid, 2-methoxy-3,4-methylenedioxybenzoic acid, melting at 155° (lit.² 153°).

(2) A. R. Penfold, G. R. Ramage and J. L. Simonsen, *J. Chem. Soc.*, 756 (1938).

(3) L. N. Ferguson, *Chem. Revs.*, **38**, 231 (1946).

(4) (a) W. Baker, L. V. Montgomery and H. A. Smith, *J. Chem. Soc.*, 1281 (1932); (b) W. Baker and R. I. Savage, *ibid.*, 1607 (1938).

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RECEIVED APRIL 16, 1951

A Method of Synthesis of Phenylactic Acid and Substituted Phenylactic Acids¹

BY EDWARD C. BUBL AND JOSEPH S. BUTTS

The need for large quantities of phenylactic acid for the continuation of metabolic studies was met by the application of a reductive hydrolysis of the azlactone. The azlactones were prepared from the aldehyde and acetyl glycine using the well known general procedure.² When the azlactones were refluxed with amalgamated zinc and hydrochloric acid, they were converted into arylactic acids in good yields.

(1) Published as Technical Paper Number 658 with the approval of the Director of Oregon Agricultural Experiment Station.

(2) "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 1.

Amine-catalyzed Condensations of Benzaldehydes with Phenylacetic Acids¹

BY ROBERT E. BUCKLES, M. PETER BELLIS AND WILLIAM D. CODER, JR.

In an earlier report² the use³ of triethylamine and tripropylamine as catalysts in the condensations of benzaldehyde and *p*-nitrobenzaldehyde with phenylacetic acid to yield the corresponding α -phenylcinnamic acids was described. At the same time similar condensations with *p*-nitrophenylacetic acid were reported to give little or no product. Since that time improved methods for the isolation of products from these condensations have been developed, so that the yields of the few condensations originally reported have been raised substantially. A much more extensive survey of the condensations of phenylacetic acid and the nitrophenylacetic acids with various benzaldehydes in the presence of trialkylamines has now been carried out. The results of the reactions are summarized in Table I.

The method appears to be of general value for synthesizing α -phenylcinnamic acids. The yields obtained were not always as high as those few reported for the Ogialoro⁴ modification of the

(1) From the Ph.D. thesis of M. Peter Bellis and the M.S. thesis of William D. Coder, Jr.

(2) R. E. Buckles and E. A. Hausman, *THIS JOURNAL*, **70**, 415 (1948).

(3) M. Bakunin and D. Pecerillo, *Gazz. chim. ital.*, **65**, 1145 (1935).

(4) (a) A. Ogialoro, *ibid.*, **9**, 428, 533 (1879); (b) A. Ogialoro and E. Rosini, *ibid.*, **20**, 396 (1890).

TABLE I
 THE CONDENSATIONS OF BENZALDEHYDES WITH PHENYLACETIC ACIDS IN THE PRESENCE OF TRIALKYLAMINES

$$\text{ArCHO} + \text{Ar}'\text{CH}_2\text{COOH} \xrightarrow[\text{Ac}_2\text{O}]{\text{R}_3\text{N}} \text{ArCH}=\underset{\text{Ar}'}{\text{C}}-\text{COOH}$$

Ar	Ar'	R	Time of reaction, hr.	Crystn. solvent	Yield, %	M.p., ^a °C.
C ₆ H ₅	C ₆ H ₅	Et	5 ^b	EtOH-H ₂ O	58	172-173 ^c
C ₆ H ₅	<i>o</i> -NO ₂ C ₆ H ₄	<i>n</i> -Pr	17.5 ^d	EtOH	30	191.5-193.5 ^e
C ₆ H ₅	<i>p</i> -NO ₂ C ₆ H ₄	<i>n</i> -Pr	18 ^d	EtOH	32	224-225 ^e
<i>o</i> -NO ₂ C ₆ H ₄	C ₆ H ₅	<i>n</i> -Pr	17 ⁱ	EtOH	70	196.5-197.5 ^f
<i>o</i> -NO ₂ C ₆ H ₄	<i>o</i> -NO ₂ C ₆ H ₄	<i>n</i> -Pr	12 ^d	EtOH	35	206-206.5 ^g
<i>o</i> -NO ₂ C ₆ H ₄	<i>m</i> -NO ₂ C ₆ H ₄	<i>n</i> -Pr	22 ^d	EtOH	70	219-220 ^h
<i>o</i> -NO ₂ C ₆ H ₄	<i>p</i> -NO ₂ C ₆ H ₄	<i>n</i> -Pr	17 ^d	EtOH	14	185-186 ⁱ
<i>m</i> -NO ₂ C ₆ H ₄	C ₆ H ₅	<i>n</i> -Pr	18 ^d	EtOH	67	165-175 ^{j,k}
<i>m</i> -NO ₂ C ₆ H ₄	<i>p</i> -NO ₂ C ₆ H ₄	<i>n</i> -Pr	17.5 ^d	EtOH	32	214 (dec.) ^l
<i>p</i> -NO ₂ C ₆ H ₄	C ₆ H ₅	<i>n</i> -Pr	17.5 ^d	EtOH	79	212-214 ^k
<i>p</i> -NO ₂ C ₆ H ₄	<i>o</i> -NO ₂ C ₆ H ₄	<i>n</i> -Pr	16.5 ^d	EtOH	56	245-246 ^m
<i>p</i> -NO ₂ C ₆ H ₄	<i>m</i> -NO ₂ C ₆ H ₄	<i>n</i> -Pr	19 ^d	EtOH	38	216-218 ⁿ
<i>p</i> -NO ₂ C ₆ H ₄	<i>p</i> -NO ₂ C ₆ H ₄	<i>n</i> -Pr	3 ^d	EtOH-EtOAc	48	266-268 ^e
<i>o</i> -HOC ₆ H ₄	C ₆ H ₅	Et	48 ^b	EtOH	62	139.5-140.5 ^{o,p}
<i>o</i> -HOC ₆ H ₄	<i>p</i> -NO ₂ C ₆ H ₄	Et	48 ^b	HOAc	78	268.5-269 ^{e,o}
<i>m</i> -HOC ₆ H ₄	C ₆ H ₅	Et	56 ^b	...	0
<i>m</i> -HOC ₆ H ₄	<i>p</i> -NO ₂ C ₆ H ₄	Et	48 ^b	EtOH-H ₂ O	11	240-242 ^q
<i>p</i> -HOC ₆ H ₄	C ₆ H ₅	Et	48 ^b	EtOH-H ₂ O	73	220-222 (dec.) ^r
<i>p</i> -HOC ₆ H ₄	<i>p</i> -NO ₂ C ₆ H ₄	Et	48 ^b	EtOH	34	185-186 ^e
<i>o</i> -MeOC ₆ H ₄	C ₆ H ₅	Et	44 ^b	EtOH	45	185.5-186.5 ^t
<i>o</i> -MeOC ₆ H ₄	<i>p</i> -NO ₂ C ₆ H ₄	Et	24 ^b	EtOH	19	249-252 ^u
<i>m</i> -MeOC ₆ H ₄	C ₆ H ₅	Et	44 ^b	EtOH	65	187-188 ^t
<i>m</i> -MeOC ₆ H ₄	<i>p</i> -NO ₂ C ₆ H ₄	Et	44 ^b	...	0
<i>p</i> -MeOC ₆ H ₄	C ₆ H ₅	Et	48 ^b	EtOH	55	188-189 ^p
<i>p</i> -MeOC ₆ H ₄	<i>p</i> -NO ₂ C ₆ H ₄	Et	44 ^b	EtOH	8	235-236 ^v

^a All m.ps. corrected. ^b The reaction mixture was boiled under reflux. ^c Footnote 5, p. 252. ^d The reaction mixture was heated on a steam-bath. ^e W. Borsche, *Ber.*, **42**, 3596 (1909). ^f Footnote 4b. ^g P. Pschorr, *Ber.*, **39**, 3120 (1906). ^h *Anal.* Calcd. for C₁₅H₁₀O₆N₂: C, 57.3; H, 3.21. Found: C, 57.1; H, 3.15. ⁱ P. Ruggli and A. Dinger, *Helv. Chim. Acta*, **24**, 173 (1941). ^j This was crude product crystallized only once and then decarboxylated to the corresponding *m*-nitrostilbene. ^k M. Bakunin, *Gazz. chim. ital.*, **25I**, 137 (1895). ^l H. A. Harrison and H. Wood, *J. Chem. Soc.*, 1195 (1926). ^m *Anal.* Calcd. for C₁₅H₁₀O₆N₂: C, 57.3; H, 3.21. Found: C, 57.1; H, 3.19. ⁿ *Anal.* Calcd. for C₁₅H₁₀O₆N₂: C, 57.3; H, 3.21. Found: C, 57.0; H, 3.26. ^o The product was the corresponding 3-phenylcoumarin. ^p Footnote 4a. ^q Further crystallization gave m.p. 243-244°. *Anal.* Calcd. for C₁₅H₁₀O₆N: C, 63.2; H, 3.89. Found: C, 62.9; H, 3.97. ^r T. Zincke and W. Geibel, *Ann.*, **349**, 107 (1906). ^s This product appeared to be impure *p*-hydroxy-*p*'-nitrostilbene. It was dissolved in hot 10% sodium hydroxide, and the solution was acidified to give (68%) the stilbene, m.p. 209.5-210.5°. *Anal.* Calcd. for C₁₄H₁₁O₅N: C, 69.9; H, 4.60; N, 5.55. Found: C, 69.3; H, 4.63; N, 5.80. N. M. Cullinane, *J. Chem. Soc.*, **123**, 2053 (1923), reported m.p. 204°. ^t C. Funk and S. Kostanecki, *Ber.*, **38**, 939 (1905). ^u Further crystallization gave m.p. 257.5-258.5°. *Anal.* Calcd. for C₁₆H₁₃O₆N: C, 64.0; H, 4.38; N, 4.68. Found: C, 63.9; H, 4.36; N, 5.00. ^v Further crystallization gave m.p. 243-244°. *Anal.* Calcd. for C₁₆H₁₃O₆N: C, 64.0; H, 4.38. Found: C, 63.6; H, 4.36. J. T. Hewitt, W. Lewcock and F. G. Pope, *J. Chem. Soc.*, **101**, 608 (1912), reported m.p. 231° (uncor.).

Perkin reaction⁵ in which a salt of the phenylacetic acid is used in conjunction with acetic anhydride and the benzaldehyde. The reactions were simpler to carry out, however, because the preliminary preparation of the anhydrous salt was not necessary.

The geometric isomer, which is sometimes isolated as a by-product from similar condensations,⁶ was not obtained in any of the cases studied. No appreciable amount of the stilbene arising from the decarboxylation of the cinnamic acid could be isolated except in the case of the condensation of *p*-hydroxybenzaldehyde with *p*-nitrophenylacetic acid.

The general trend toward lower yields with *o*- and *p*-nitrophenylacetic acids as compared with phenylacetic acid and *m*-nitrophenylacetic acid is also apparent from Table I. A kinetic study of

the reaction will be necessary before any definite conclusion can be drawn concerning this effect of substitution on the aromatic ring.

Experimental

***o*-Nitrophenylacetic Acid.**—This material, m.p. 140-141°, was prepared in 20% over-all yield by the condensation of ethyl oxalate with *o*-nitrotoluene in the presence of sodium ethoxide, followed by oxidation of the condensation product with hydrogen peroxide.⁷

***m*-Nitrophenylacetic Acid.**—This material was prepared in very low yields from *m*-nitrotoluene. Bromination⁸ of *m*-nitrotoluene yielded a mixture of the benzyl and the benzal bromides. This mixture was converted in two steps to the *m*-nitrophenylacetic acid, m.p. 116-117°, by the method used for the synthesis of phenylacetic acid.⁹

***m*-Methoxybenzaldehyde.**—A mixture made up of 250 ml. of 10% aqueous sodium hydroxide, 200 ml. of 95% ethanol, 106 g. (0.57 mole) of methyl *p*-toluenesulfonate

(7) F. Mayer and G. Balle, *Ann.*, **403**, 167 (1914); Reissert, *Ber.*, **30**, 1036 (1897).

(8) C. Wachendorff, *Ann.*, **185**, 259 (1877).

(5) J. R. Johnson, *Organic Reactions*, **1**, 210 (1942).

(6) T. R. Lewis, M. G. Pratt, E. D. Homiller, B. F. Tullar and S. Archer, *This Journal*, **71**, 3749 (1949).

(9) R. Adams and A. F. Thal, "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1941, pp. 107, 436.

and 69.5 g. (0.57 mole) of *m*-hydroxybenzaldehyde¹⁰ was heated under reflux for 90 minutes. The product was distilled with steam, extracted with ether and finally extracted into 10% sodium bisulfite solution. The bisulfite addition complex was destroyed by acid and the product was extracted into ether. The solution was dried and distilled to yield 29.3 g. (38%) of *m*-methoxybenzaldehyde, b.p. 126–127° (25 mm.).

Other Reagents.—The other reagents used in the condensation reactions were redistilled or recrystallized commercial products, or they were synthesized by well-known methods given in the Organic Synthesis Series. The triethylamine was Sharples anhydrous grade. The tripropylamine was kindly donated by Sharples Chemicals, Inc.

Condensation Reactions.—Equimolar amounts of the benzaldehyde and the phenylacetic acid were mixed with from three-fourths to equal molar portions of the trialkylamine in 3–5 molar portions of acetic anhydride. The reaction mixture was either heated on a steam-bath or boiled under reflux. The reaction mixture was then heated with benzene, and in most cases a solution was obtained. This solution was extracted with portions of hot 10% sodium hydroxide until no more acidic material could be obtained. The combined basic extracts were acidified with hydrochloric acid to yield the crude acid. Crystallization from a suitable solvent, including any necessary treatment with decolorizing charcoal, completed the preparation.

The mother liquors from the crystallization gave no appreciable amounts of the isomeric acids as by-products. The benzene solutions of the original reaction mixtures yielded only tarry residues, which resisted purification, after the acids had been extracted.

In two of the preparations, α -phenylcinnamic acid and 3-phenylcoumarin, the reaction mixtures were freed of steam-volatile impurities by steam distillation. When cooled, the residues deposited crude crystals of the products which were then recrystallized. Such a method of product isolation has been described before for this type of reaction.¹¹

The results of these condensation reactions are presented in Table I.

(10) R. B. Woodward, *Org. Syntheses*, **25**, 55 (1945).

(11) R. E. Buckles, *J. Chem. Education*, **27**, 210 (1950).

DEPARTMENT OF CHEMISTRY
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RECEIVED JUNE 25, 1951

Isolation of Protactinium from a New Source¹

BY R. ELSON, G. W. MASON, D. F. PEPPARD, P. A. SELLERS
AND M. H. STUDIER

In the past, pure protactinium has not been readily available. The isotope of interest, Pa²³¹, occurs naturally only in uranium deposits. The weight ratio of Pa²³¹ to uranium is fixed by the relative half-lives and has a theoretical value of 3×10^{-7} . Workers at this and other laboratories have isolated small quantities of protactinium of varying purity by a variety of methods.² The following procedure differs from previously reported procedures for the isolation of protactinium in that concentration and preliminary purifications are accomplished by a liquid-liquid extraction technique. The source material exists in large quantities and is capable of yielding gram quantities of protactinium. The equipment requirements of the process are simple and the time and labor involved are small.

(1) The subject of this paper is discussed in greater detail in Argonne National Laboratory Reports ANL-4176, 4411 and 4469.

(2) A. von Grosse, *Nature*, **120**, 621 (1927), and G. Graue and H. Kading, *Angew. Chem.*, **47**, 650 (1934), used residues from pitchblende as their source of protactinium, while R. Thompson and co-workers, National Nuclear Energy Series, Div. IV, Vol. 17B, Paper No. 6.4, used the carbonate residue obtained from treatment of the acid solution of uranium ore with excess sodium carbonate. See also I. Katzin, *et al.*, *THIS JOURNAL*, **72**, 4815 (1950).

An aqueous waste stream of the Mallinckrodt process for the extraction of uranium from pitchblende concentrate was used as a source material.³ This aqueous waste is a concentrated nitrate solution of essentially all the acid-soluble gross components of the ore concentrate except uranium and contains between 25 and 50% of the protactinium originally present.

This source solution was contacted with tributyl phosphate. The tributyl phosphate extract was then contacted with hydrofluoric acid, which precipitated fluoride-insoluble impurities and left the protactinium in solution in the aqueous supernatant as the fluoride complex. The aqueous extract contained an average of 0.2 mg. of protactinium and 1 to 10-g. quantities of other elements (primarily calcium, rare earths and iron) per liter.

As protactinium cannot be extracted into organic solvents in the presence of fluoride ion it was necessary to complex all of the fluoride. It was found that diisopropylcarbinol was a suitable solvent for those solutions and the optimum acidity was found to be about 0.5 *M*. Protactinium was therefore extracted from the fluoride solution with diisopropylcarbinol after the fluoride was complexed with aluminum ion and the acidity adjusted with sodium aluminate. The carbinol extract was washed, and the protactinium re-extracted into aqueous hydrogen peroxide. Hydrogen peroxide was used, as protactinium forms an insoluble compound in the presence of peroxide in low acid solutions. By proper adjustment of the acidity, the protactinium could be removed quantitatively from the organic phase with a very small volume of peroxide resulting in a product containing primarily uranium and calcium and 4% protactinium. Further purification consisted of removal of uranium by ether extractions, precipitation of protactinium with tannic acid, and solvent-extraction cycles with diisopropyl ketone.

The over-all yield of protactinium obtained in this process was quite low, 5–35% of the content of the original source solution. This low yield was due primarily to the poor extractability of the protactinium from the Mallinckrodt waste into the tributyl phosphate. However, these low yields resulted from operations under conditions far from optimum for the extraction of protactinium, as the primary purpose of this step was the obtainment of elements other than protactinium. Proper adjustment of acidity and salt strength and removal of complexing ions such as sulfate and fluoride would improve the yield considerably. The yields in subsequent steps were quite good; the diisopropylcarbinol extraction yields were 70–90%, and subsequent operations were nearly quantitative.

Sodium aluminate was selected as the neutralizing agent in the carbinol extraction step because of its low equivalent weight, low heat of reaction and the complexing action afforded. Aluminum hydroxide or other alkaline reagents with low heat of reaction could be used in place of sodium aluminate. Preliminary investigations indicated that other solvents could be used in this step in place of diisopropylcarbinol; the most promising were thenoyltrifluoroacetone dissolved in benzene or other appropriate solvent and diisopropyl ketone. Other reagents to complex fluoride were investigated but proved less satisfactory than aluminum ion.

Experimental

Each sample of Mallinckrodt waste stream was contacted for about two hours with 5% of its volume of tributyl phosphate in a 55-gallon contactor. The tributyl phosphate extract was removed and contacted with one-fourth of its volume of 0.5 *M* hydrofluoric acid to precipitate fluoride-insoluble impurities. The aqueous fluoride supernatant solution contained 95–99% of the extracted protactinium and was 3–4.5 *M* in acid and approximately 0.2 *M* in fluoride.

Protactinium was extracted from this fluoride solution by contacting it with about 40% of its volume of diisopropylcarbinol. The acidity was adjusted to 0.5–0.8 *M* by the addition of sodium aluminate, and the fluoride was complexed by the addition of sufficient aluminum nitrate to give a final aluminum concentration approximately 0.6 *M* in excess over a 3:1 molar ratio of aluminum to initial fluoride.

The amounts of neutralizing and complexing agents to be added were determined easily and rapidly by titrating an aliquot of the solution to be processed to determine the total

(3) This process for the extraction of uranium differs from those previously described in that a carbonate precipitation is not made.