2,6-dimethoxyphenol: mp 138-139.5°; nmr δ 1.35 (18 H, s, two *tert*-butyl), 3.84 (6 H, s, two methoxyl), 5.26 (1 H, s, phenolic hydroxyl), 6.79 (1 H, s, aromatic).

Anal. Calcd for $C_{16}H_{26}O_3$: C, 72.18; H, 9.77. Found: C, 72.15; H, 9.82.

Oxidation of 3-*tert*-Butyl-2,6-dimethoxyphenol (2) with Alkaline Potassium Ferricyanide. A solution of 1.20 g of the phenol 2 in 75 ml of benzene was stirred vigorously with a solution of 6.00 g of potassium ferricyanide and 5.60 g of potassium hydroxide in 50 ml of water at 25° for 5 hr. The benzene solution was washed twice with water, dried over sodium sulfate, and evaporated to dryness, and the residue was taken up in chloroform and precipitated with methanol. The precipitate was filtered and dissolved and reprecipitated twice more to give 1.01 g (*ca.* 85%) of the polyphenylene polymer **5**.

The lightly cream colored polymer softened and melted over the range 140-160°. The osmometrically determined molecular weight was 2923 using chloroform as solvent and measurements at three different concentrations. The ir (KBr) showed the following major peaks: 2950 (s), 1595 (s), 1480 (s), 1435 (s), 1383 (s), 1200 (s), 1108 (s), 1060 cm^{-1} (s). The nmr showed peaks at δ 1.57 (s, *tert*-butyl), 3.37 and 3.74 (both s, two different methoxyls), and 5.95 (s, aromatic) in the approximate ratio 9:3:3:1, respectively. One further small peak at δ 1.35 is probably due to the *tert*-butyl group on the terminal unit of the polymer. None of these peaks disappeared upon the addition of deuterium oxide to the sample.

Anal. Calcd for $C_{12}H_{16}O_3$: C, 69.23; H, 7.69. Found: C, 68.47; H, 7.65.

Oxidation of 3,5-Di-*tert*-butyl-2,6-dimethoxyphenol (3) with Alkaline Potassium Ferricyanide. A solution of 1.20 g of the phenol in 75 ml of benzene was stirred vigorously with a solution of 6.00 g of potassium ferricyanide and 5.60 g of potassium hydroxide in 50 ml of water at 70° for 5 hr. The benzene solution was washed twice with water, dried over sodium sulfate, and evaporated to dryness. The residue, a red-brown oil, was dissolved in 8 ml of acetone and allowed to stand in the refrigerator overnight. The precipitated product was filtered and the filtrate was diluted with 15 ml of 95% ethanol and filtered again to remove the second batch of precipitate. The combined precipitates were recrystallized from acetone to give 0.318 g (26%) of the orthoformate **6**: mp 152-153°; ir (KBr) 2960 (s), 1595 (w), 1485 (s), 1418 (s), 04 (s), 1358 (m), 1300 (m), 1230 (s), 1105 (s), 1070 (s), 1008 (s), 990 cm^{-1} (s); nmr δ 1.32 (36 H, narrowly split d, four *tert*-butyl), 3.80 (6 H, s, two methoxyl), 3.96 (3 H, s, methoxyl), 6.77 (1 H, s, trioxymethine), 7.03 (2 H, s, aromatic); none of these peaks disappears upon addition of deuterium oxide to the sample; nuclidic mass, 528.3389 (calcd for $C_{32}H_{48}O_6$, 528.3450); mass spectrum *m/e* (rel intensity) 528 (2.7), 513 (1.0), 266 (1.5), 265 (2.7), 264 (18.8), 263 (100.0), 251 (3.6).

Anal. Calcd for $C_{32}H_{48}O_6$: C, 72.85; H, 9.10. Found: C, 72.67; H, 9.10.

The structure of the orthoformate was confirmed by hydrolysis and subsequent acetylation of the products. Thus, 0.280 g of orthoformate was hydrolyzed in 20 ml of 95% ethanol-chloroform (1:1) containing 5 drops of concentrated hydrochloric acid. The solution was warmed on a steam bath for 1 hr and diluted with water, and the chloroform layer was removed. After drying over sodium sulfate, the chloroform was removed and the residue was acetylated with pyridine-acetic anhydride (1:1). After 24 hr the volatiles were removed under vacuum and ptlc of the residue using benzene-hexane (1:1) gave 0.127 g (76%) of the catechol diacetate **8** and 0.149 g (90%) of the phenol acetate **7**.

The phenol acetate, mp 144-145° from hexane, was identified by comparison of its melting point, mixture melting point, and ir with those of authentic material which was obtained by acetylation of phenol **3**.

Anal. Calcd for $C_{18}H_{28}O_4$: C, 70.10; H, 9.10. Found: C, 70.08; H, 9.19.

The catechol diacetate had mp 130-132° from hexane; ir (KBr) 2960 (m), 1770 (s), 1410 (s), 1200 (s), 1155 (s), 1062 cm^{-1} (s); nmr δ 1.27 and 1.32 (9 H each, both s, two *tert*-butyl), 2.22 and 2.24 (3 H each, both s, two acetyl), 3.77 (3 H, s, methoxyl), 7.21 (1 H, s, aromatic).

Anal. Calcd for $C_{19}H_{28}O_5$: C, 67.90; H, 8.34. Found: C, 68.01; H, 8.31.

Oxidation of 3,5-Di-*tert*-butyl-2,6-dimethoxyphenol (3) with Lead Dioxide in Ether. To a vigorously stirred suspension of lead dioxide (5.0 g) in 100 ml of dry diethyl ether, 2.45 g of the phenol was added. The reaction mixture was maintained at 25° for 4 hr and then filtered to remove the lead dioxide. The solution was washed with two 50-ml portions of water, dried over sodium sulfate, and evaporated to dryness. After tlc on silica gel using benzene-hexane (1:1), a compound was obtained as a partially crystallized oil. The oil was vacuum distilled to give 1.40 g (*ca.* 56%) of the acetal **9** which crystallized in the receiver: mp 36.3°; nmr δ 1.01 (3 H, t, methyl), 1.29 (18 H, s, *tert*-butyl), 1.44 (3 H, d, J = 5 Hz, methyl), 3.49 (2 H, m, methylene), 3.84 (6 H, s, methoxyl), 5.24 (1 H, q, J = 5 Hz, acetal), 6.94 (1 H, s, aromatic); mass spectrum *m/e* 338 (molecular ion), 266, 251, 235, 221, 166, 73, 45.

Anal. Calcd for $C_{20}H_{34}O_4$: C, 71.00; H, 10.07. Found: C, 71.16; H, 10.04.

Registry No.—**2**, 49746-11-4; **3**, 49746-12-5; **5**, 50322-12-8; **6**, 49746-13-6; **8**, 49746-14-7; **9**, 49746-15-8; 2,6-dimethoxyphenol, 91-10-1.

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A Facile Synthesis of 2-Aminonicotinaldehyde

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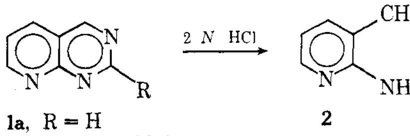
Aromatic *o*-aminoaldehydes are valuable starting materials for a wide variety of N-heterocyclic compounds. However, in spite of their seemingly simple array of functionality, they are difficult to synthesize and in fact relatively few compounds possessing this pair of functions have been described. In connection with our investigation of the Friedländer condensation as a synthetic method for the linear annellation of pyridine rings, large quantities of 2-aminonicotinaldehyde (**2**) were required.

The preparation of **2** had previously been accomplished by a multistep synthesis starting from 2-amino-3-picoline,[1,2] but this proved to be a tedious procedure with substantial loss of material upon purification. Therefore, an alternate route to **2** was sought. An attractive possibility was to employ the pyrimidine moiety of pyrido[2,3-*d*]pyrimidine (**1a**) as a source for the *o*-aminoaldehyde functionality. Covalent hydration of this heterocyclic system makes it susceptible to hydrolytic ring opening of the pyrimidine nucleus.[3] This reaction is of no synthetic value, since **1a** was synthesized from **2**.[3] However, sulfamation of nicotinamide with ammonium sulfamate[4] readily provided us with 2-(3′-pyridyl)pyrido[2,3-*d*]pyrimidine (**1b**) in 50% yield together with nicotinonitrile.



1a, R = H
b, R = 3-pyridyl

2

As anticipated, hydrolysis of this crude reaction mixture in 2 *N* HCl gave **2** and nicotinic acid. Separation was readily accomplished by extraction with ether, yielding pure **2** in 50% yield (based on nicotinamide). Proof of structure was obtained by spectroscopic data, by comparison with an authentic sample,[1] and by its conversion into derivatives of 1,8-naphthyridine by Friedländer condensation.[5]

Finally, it should be noted that the *o*-aminoaldehyde functionality in **2** is generated in one single reaction step, in contrast with previous routes to aromatic *o*-aminoaldehydes, where both functional groups are elaborated separately.

Experimental Section

A mixture of nicotinamide (36.5 g, 0.3 mol) and ammonium sulfamate[4] (52 g, 0.45 mol) was heated in an oil bath at 150°. After a clear melt was obtained, the temperature was raised slowly to 200°. The mixture was kept at this temperature for 6 hr, after which the content of the flask had completely solidified. Water was added and the precipitate collected and washed with ether to remove nicotinonitrile. The solid material thus obtained[6] was refluxed in 2 *N* HCl for 4 hr, made alkaline and extracted with ether. The resulting ether solution was dried (K_2CO_3) and evaporated to give pure 2-aminonicotinaldehyde (**2**) (9 g, 50%): mp 98-99° (lit.[2] 98°); ir (Nujol) 3440, 3250, 3125, 2750, 1650, 1625, 1575, 1540 cm^{-1}; nmr δ_{TMS} (DMSO-d_6) 9.96 (s, 1, HCO), 8.33 (dd, 1, H-α, $J_{\alpha-\beta}$ = 4 Hz, $J_{\alpha-\gamma}$ = 2 Hz), 8.08 (dd, 1, H-γ, $J_{\beta-\gamma}$ = 8 Hz), 7.6 (broad, 2, NH_2), 6.8 (dd, 1, H-β).

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Registry No.—**2**, 7521-41-7; nicotinamide, 98-92-0; ammonium sulfamate, 7773-06-0.

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(6) Purification of this material had no beneficial effect on the yield and purity of the final product. Its recrystallization from water gave pure **1b** (15.6 g, 50%), mp 224.

Enthalpy of the Diels-Alder Reaction of Cyclopentadiene and Maleic Anhydride

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In connection with a program of research on the energetics of cycloaddition reactions, we determined the enthalpy of the reaction between cyclopentadiene (CPD) and maleic anhydride (MA). Our report is prompted by the recent publication of similar data by Rogers and Quan.[1] These workers determined the heat for the DA reaction by standard solution calorimetric techniques. While the literature of thermal reactions abounds with kinetic data, measurement of enthalpies of reaction lags far behind. Where such data exist, they are often derived indirectly from heats of combustion or hydrogenation, or from van't Hoff data.[2] Our measurements provide an example of an application of flow calorimetry to the study of an organic reaction in solution.

The flow calorimeter and method employed have been described by Sturtevant.[3] The main components of the apparatus are a precision fluid delivery system capable of a wide range of delivery rates, a thermopile, and a massive aluminum heat sink. The reactant solutions are preequilibrated to the desired temperature and delivered through separate tubes to a junction where they are mixed just as they reach the thermopile. The heat evolved or absorbed upon mixing the solutions is quantitatively conducted through the thermopile to the heat sink. The output of the thermopile is integrated to yield the total heat transferred during a specified period.

Table I
Enthalpy of the Reaction of CPD and MA in Dioxane

Temp, °C	Run	CPD flow rate[a]	MA flow rate[a]	$-\Delta H_r$[b]
25.0	1[c]	2.8	2.8	24.14
	2	2.8	1.4	24.50
	3	2.8	1.0	24.56
	4[d]	2.0	2.0	24.92
	5	2.8	2.8	25.37
	6	1.4	1.4	24.27
	7	2.0	2.0	25.19
	8	2.8	2.8	25.24
	Average			24.8 ± 0.5[e]
40.0	1[f]	1.4	1.4	25.50
	2	2.0	2.0	25.59
	3	2.8	2.8	25.77
	4	2.0	1.4	25.62
	5	2.8	1.4	25.69
	6	1.4	2.0	25.36
	7[g]	1.4	1.4	25.78
	8	2.0	2.0	25.40
	9	2.8	2.8	25.39
	10	2.0	1.4	25.74
	11	2.8	1.4	25.45
	12	1.4	2.0	24.90
	Average			25.5 ± 0.3[c]

[a] A relative flow rate of 1 is 3.53 ml/min. [b] Kcal/mol. [c] Runs 1–3: [CPD] = 1.06 × 10^{-1} *M*; [MA] = 2.0 × 10^{-1} *M*. [d] Runs 4–8: [CPD] = 2.12 × 10^{-1} *M*; [MA] = 4.0 × 10^{-1} *M*. [e] The error is the standard deviation. [f] Runs 1–5: [CPD] = 1.88 × 10^{-1} *M*; [MA] = 4.0 × 10^{-1} *M*. [g] Runs 7–12: [CPD] = 1.98 × 10^{-1} *M*; [MA] = 4.0 × 10^{-1} *M*.

In the experiments performed, solutions of CPD (1-2 × 10^{-1} *M*)[4] and MA (2-4 × 10^{-1} *M*) in dioxane were allowed to react in the calorimeter. Upon mixing, an exothermic reaction ensued and the thermopile output increased to a steady-state value. The heat evolution was integrated for at least 5 min of the steady-state period. It should be noted that the flow rates of the two reactants were varied relative to one another, in order to demonstrate that the reaction was complete during the residence time in the calorimeter. Experiments were performed at 25 and 40°. The results of multiple runs are summarized in Table I. Control experiments indicated that there was negligible heat change on mixing of pure dioxane, or of dioxane with either reactant solution.

The enthalpy of reaction of CPD and MA in dioxane solution was found to be −24.8 ± 0.5 kcal/mol at 25.0°, and −25.5 ± 0.3 kcal/mol at 40° (the error quoted is the standard deviation). The precision of our values is not high enough to permit conclusions about the ΔC_p of this reaction, except to say that this term is probably small.

Comparison of our value of ΔH_r (25°) = −24.8 ± 0.5 kcal/mol for the reaction in dioxane and the value of Rogers and Quan of ΔH_r (25°) = −26.2 ± 0.1 kcal/mol for the reaction in dichloromethane indicates very good agreement after correction for solvent effects. Most of the data needed for solvent-effect corrections can be found in the work of Haberfield and Ray[5] as well as that of Rogers and Quan. The latter two investigators determined the heats of solution of CPD, MA, and the product *endo*-5-norbornene 2,3-dicarboxylic anhydride (N) in CH_2Cl_2.[6] The heat of solution of CPD in CH_2Cl_2 is 0.1 kcal/mol. This quantity is unknown in dioxane but it is almost certainly small, and can be assumed to be equal to the value in CH_2Cl_2 as a first approximation. The heat of solution of MA in dioxane is also known from the work of Haberfield and Ray.[5]