

## A New Anhydride Analog

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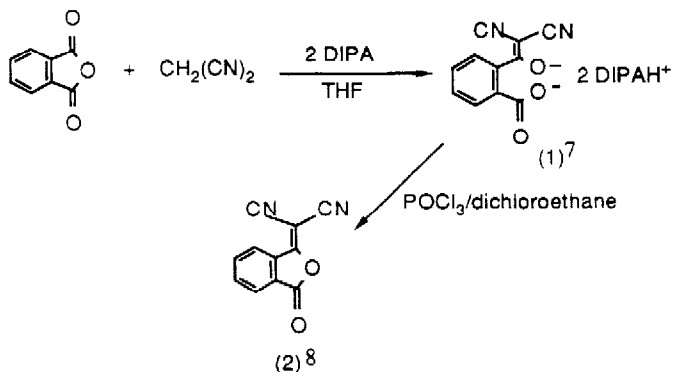
*Key words:* imide-forming reaction; pseudoanhydride

**Abstract:** A novel imide-forming reaction is described in which 3-(dicyanomethylidene) phthalide (pseudoanhydride) reacts with amines at room temperature. The pseudoanhydride was synthesized by condensation of phthalic anhydride with malononitrile followed by treatment with phosphorous oxychloride.

Recently we have been studying synthetic routes for the introduction of dicyanomethylidene groups in place of carbonyl oxygen atoms as a means of modifying reactivity as well as enhancing the solubility of such materials.<sup>1,2,3</sup>

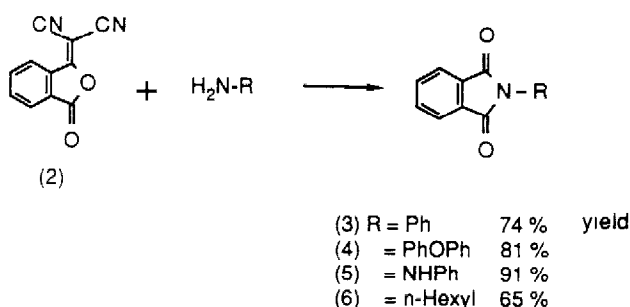
We have prepared, for the first time, a phthalic anhydride derivative (2) which exemplifies this approach from phthalic anhydride and malononitrile in high yield as shown in Scheme 1. Several model reactions disclosed unexpected chemistry producing the corresponding imide in tetrahydrofuran or N-methyl pyrrolidone solvent at room temperature. In contrast, it is known, generally, that imides are formed from stable amic acid precursors, the reaction product of an anhydride and an amine, only at elevated temperatures or by the addition of dehydration agents such as acetic anhydride. Details of this new imide forming reaction are described here and a tentative reaction mechanism is proposed. The structural assignment is secured by a single crystal X-ray diffraction analysis<sup>8</sup> as shown in Figure 1. The product (2), a pseudoanhydride, is expected to exhibit reactivity similar to that of phthalic anhydride. It was, however, of interest to know where nucleophilic attack would occur, at the carbonyl carbon atom or at the dicyanovinyl carbon atom.

Scheme 1



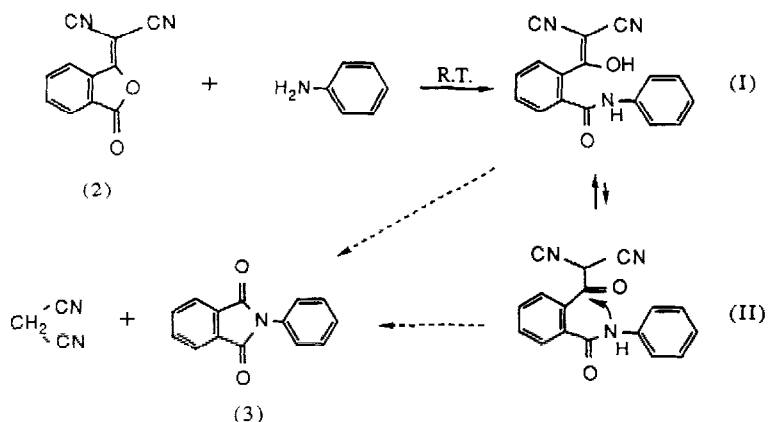
Two aromatic amines, *n*-hexylamine and phenyl hydrazine were used for model reactions with the pseudoanhydride (Scheme 2). Typically, to a pseudoanhydride solution in *N*-methyl pyrrolidone or THF, an amine solution in the same solvent was added slowly and the resulting amber solution was stirred for 24 hr or more at room temperature. The solution was then precipitated into water to give the corresponding imides, (3), (4), (5) as off-white powders, and (6) as viscous liquid in 65-91% yield. Even higher yields could be obtained by extended reaction time or by slightly warming the reaction. The reaction with phenyl hydrazine forms exclusively *N*-anilino phthalimide (5). The melting points and spectroscopic data (MS, IR,  $^1\text{H}$  and  $^{13}\text{C}$  NMR) matched well with those of the known compounds.<sup>4</sup> These model reactions are shown in Scheme 2. By conducting the model reaction with aniline in NMR tubes using tetrahydrofuran- $d_8$  as solvent, it was observed that the characteristic peaks of each component immediately disappeared when mixed and a pattern representative of an amic acid with amide  $\text{NH}$  at 9.8 ppm and a broad  $\text{OH}$  proton at 8.8 ppm (variable

Scheme 2



depending on concentration) appeared. The intensity of the  $\text{NH}$  proton peak from the amic acid intermediate at 9.8 ppm decreases and the broad  $\text{OH}$  peak moves upfield with decreasing intensity and a new peak at 4.0 ppm, which is assigned as the  $\text{CH}_2$  proton of malononitrile, increases as the reaction proceeds. The reaction probably proceeds by fast nucleophilic attack of the amine at the carbonyl carbon atom to produce the amic acid analog, intermediate (I). When aniline was reacted with (hydroxyphenylmethylene) propanedinitrile, the resulting salt was stable at room temperature and was converted to benzanilide only after heating at elevated temperatures.<sup>5</sup> Thus, the slow conversion of the amic acid-like intermediate (I) to product (3) may result from direct addition to the enol aided by the neighboring group effect or a small amount of reactive ketodinitrile may be in rapid equilibrium with the enol and may undergo addition followed by elimination of malononitrile (Scheme 3). In the case of reaction with *n*-hexylamine, it seems that an amic-acid-amine salt was formed first because of the more basic nature of this aliphatic amine and that this salt slowly dissociated to the amic-acid intermediate, followed by subsequent imidization. Experiments to clarify these possibilities are underway and will be reported subsequently. The difference in the chemistry of the pseudoanhydride compared to phthalic anhydride obviously rests on the dicyanomethylidene functionality. Attack at the carbonyl group yields a more stable enolate anion and the elimination of malononitrile anion rather than hydroxide ion is favored by the enhanced stability granted by the presence of two conjugated nitrile groups ( $\text{pK}_a$ , malononitrile = 11;  $\text{pK}_a$ ,  $\text{H}_2\text{O}$  = 15.74).<sup>6</sup>

Scheme 3



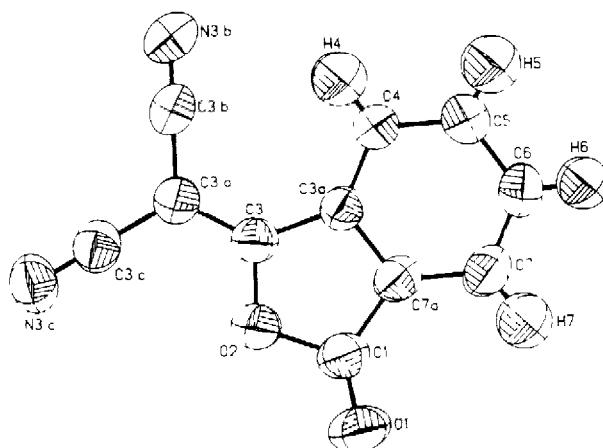
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#### References and Notes

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4. (3) 1H-Isoindole-1,3(2H)-dione,2-phenyl. [520-03-6], (4) 1H-Isoindole-1,3(2H)-dione,2-(4-phenoxy phenyl). [19357-24-5], (5) 1H-Isoindole-1,3(2H)-dione,2-(phenylamino). [4870-16-0] (6) 1H-Isoindole-1,3(2H)-dione,2-hexyl. [20320-48-3]
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7. Equimolar quantities of phthalic anhydride and malononitrile were reacted in THF at room temperature using diisopropylamine as base. After stirring for 5 h, a precipitate was filtered, washed with THF, and dried to yield product (I) which was purified by recrystallization from methanol to give an off-white crystalline solid (75 % yield): dec. above 140 °C, IR (KBr) 2202 cm<sup>-1</sup> (CN); <sup>1</sup>H NMR (D<sub>2</sub>O) δ 1.67 (d, 24H, CH<sub>3</sub>), 3.86 (heptet, 4H, CH), 5.11 (s, 4H, NH<sub>2</sub>), 7.7-8.1 (m, 4H, aromatic); <sup>13</sup>C NMR (D<sub>2</sub>O) δ 196.0, 175.1, 138.9, 136.9, 129.5(2C), 128.6, 127.1, [122.8, 120.7] (CN), 66.7 (C-CN), 47.4 (CH), 18.4 (CH<sub>3</sub>). Anal. Calcd. for C<sub>23</sub>H<sub>34</sub>N<sub>4</sub>O<sub>3</sub> (FW 416.56): C, 66.64; H, 8.27, N, 13.52. Found: C. 66.67; H. 8.49; N. 13.58.

- 8 8.0 g (19.2 mmol) of compound (1) was treated with 30 mL of  $\text{POCl}_3$  in dichloroethane. The clear solution was refluxed for 3 h and then  $\text{POCl}_3$  and dichloroethane were removed by distillation at reduced pressure. The product was separated by flash column chromatography on silica-gel using dichloromethane as eluent. An off-white crystalline solid was collected (84 %) and further purified by recrystallization from chloroform/hexane to provide an analytical sample (2): mp 157.5 °C (DSC); MS ( $M+1$ ) 197; IR (KBr) 2240 (CN), 1829 (anhydride CO)  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  8.47 (d, 1H), 8.14 (d, 1H), 7.98 (m, 2H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  168.6, 161.1, 136.8, 135.9, 134.0, 127.5, 125.8, 125.2, [110.9, 109.1] (CN), 66.0 (C-CN). Anal. Calcd. for  $\text{C}_{11}\text{H}_4\text{N}_2\text{O}_2$  (FW 196.16): C, 67.35, H, 2.06, N, 14.28. Found: C, 67.29; H, 2.05; N, 14.44. X-ray data. space group,  $P 2_1/n$ ;  $a = 6.944$  (2) Å,  $b = 7.995$  (2) Å,  $c = 16.388$  (2) Å,  $\beta = 93.75$  (1)°,  $Z = 4$ ;  $R = 5.26$ ;  $R_w = 6.36$  %. Detailed crystallographic data are available upon request.

**Figure 1**



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