

REACTION OF 3-ACYLINDOLES WITH DIETHYL PHOSPHOROCYANIDATE.  
 A FACILE SYNTHESIS OF 2-CYANO-3-INDOLEACETONITRILES

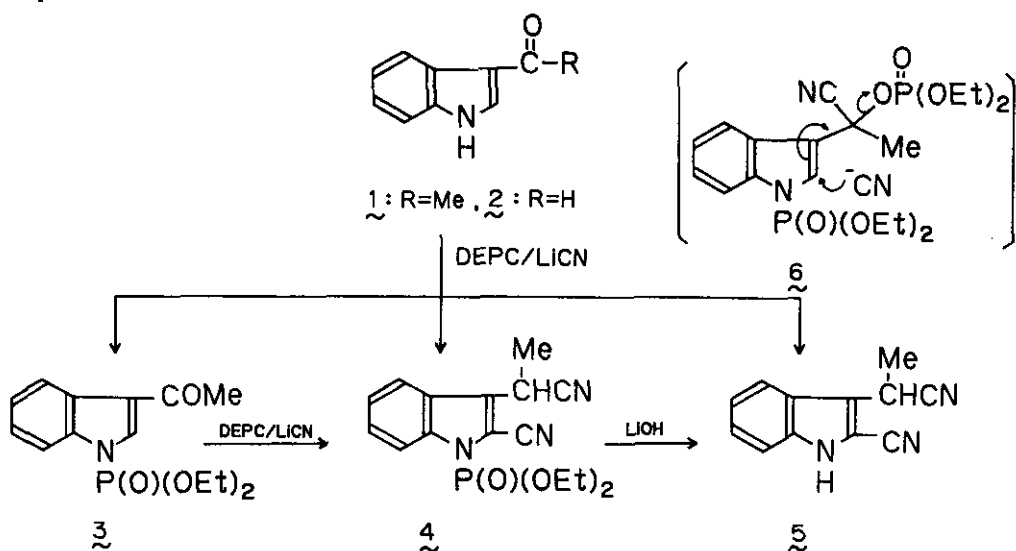
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**Abstract** — 3-Acylindoles (1, 7a-7d) were easily converted into 2-cyano-3-indoleacetonitriles (5, 9a-9d) by treatment with diethyl phosphorocyanidate in the presence of lithium cyanide in excellent yields. Treatment of 9a with acetylenic esters in the presence of sodium hydride in tetrahydrofuran afforded 1-amino-4-cyanocarbazoles (10a and 10b). The compound 9a also reacted with benzyne in the presence of lithium di-isopropylamide to give 6-amino-11-cyano-5-methylbenzo[b]-carbazole (11) in 64% yield, together with a small amount of 6,11-o-benzenobenzo[b]carbazole (12).

Recent studies in our laboratory have been concerned with reaction of  $\alpha, \beta$ -unsaturated ketones involving aromatic ketones with diethyl phosphorocyanidate [DEPC,  $(\text{EtO})_2\text{P}(\text{O})\text{CN}$ ] in the presence of lithium cyanide (LiCN) for the synthesis of  $\alpha, \beta$ -unsaturated nitriles.<sup>1,2</sup> In continuation of our studies on the synthetic use of DEPC, we investigated the reaction of indole-3-carboxaldehydes with DEPC/LiCN and found a novel synthesis of 2-cyano-3-indoleacetonitriles. Some of them could be used for the generation of indole-2,3-quinodimethane, which has been implicated in the synthesis of carbazole derivatives.<sup>3</sup>

Treatment of 3-acetylindole (1) with DEPC (3 equiv.) and LiCN (3 equiv.) in tetrahydrofuran (THF) at room temperature afforded a mixture of 3-acetyl-1-diethylphosphoroindole (3) (3%) [oil;  $M^+$  295;  $\nu_{\text{max}}$  1660, 1280-1310, 960-1040  $\text{cm}^{-1}$ ;  $\delta$  ( $\text{CDCl}_3$ ) 2.57 (3H, s,  $\text{COCH}_3$ ), 8.16 (1H, s,  $\text{C}_2\text{-H}$ )], 2-cyano-1-diethylphosphoro-3-( $\alpha$ -methyl)indoleacetonitrile (4) (2%) [oil;  $M^+$  331;  $\nu_{\text{max}}$  2215, 1280-1320, 960-1050;  $\delta$  ( $\text{CDCl}_3$ ) 1.83 (3H, d,  $J=7$  Hz,  $\text{CHCH}_3$ )], and 2-cyano-3-( $\alpha$ -methyl)indoleacetonitrile (5) (87%) [mp 96-97 C;  $M^+$  195;  $\nu_{\text{max}}$  3330, 2210, 2240  $\text{cm}^{-1}$ ;  $\delta$  ( $\text{CDCl}_3$ ) 1.83 (3H, d,  $J=7$  Hz,  $\text{CHCH}_3$ ), 4.35 (1H, q,  $J=7$  Hz,  $\text{CHCH}_3$ )]. Treatment of 3 with DEPC/LiCN in anhydrous THF gave 4 which was easily hydrolyzed with lithium hydroxide in 95% ethanol into 5

quantitatively. Thus, a plausible mechanism for the formation of 5 is as follows : the initial step is the formation of cyanophosphate (6) via 3 and the nucleophilic attack of cyanide anion, followed by leaving of the diethyl phosphonoxy function and then aromatization results in the formation of 4, which is hydrolyzed to 5 in the presence of water.



Although the reaction of indole-3-carboxaldehyde (2) with DEPC/LiCN resulted in a formation of complex mixture, N-substituted indole-3-carboxaldehydes (7a-7d)<sup>4</sup> were found to give the corresponding 2-cyano-3-indoleacetonitriles (9a-9d)<sup>5</sup> in excellent yields, respectively. The results are summarized in the Table.

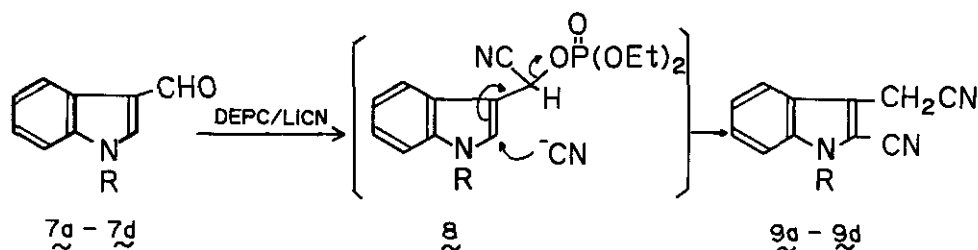
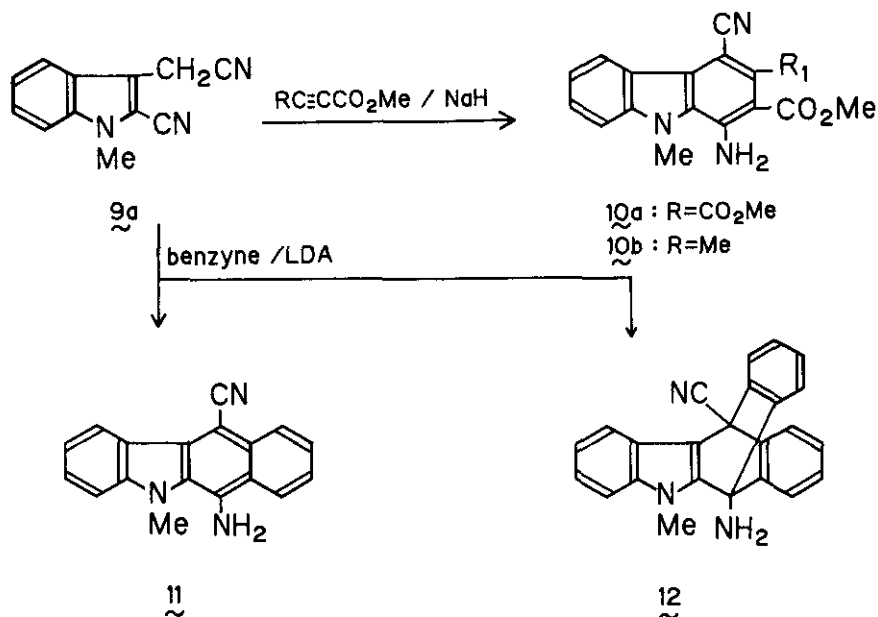


Table.

	R	Product	Yield (%)	mp (°C)
<u>7a</u>	Me	<u>9a</u>	92	165
<u>7b</u>	Et	<u>9b</u>	86	95-96
<u>7c</u>	CH <sub>2</sub> Ph	<u>9c</u>	100	135-137
<u>7d</u>	Ph	<u>9d</u>	96	109-110

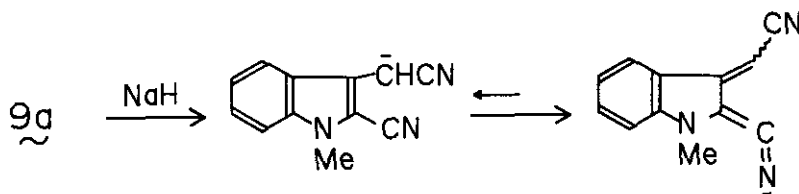
Recently Tamura et al.<sup>6</sup> reported a strong base induced cycloaddition of homophthalic anhydride leaving to peri-hydroxy polycyclic compounds. In this connection, addition of sodium hydride to a solution of 9a and acetylenic dienophiles (dimethyl acetylenedicarboxylate and methyl propiolate) in THF at 0~-5°C was tried and found to give a dark-red colored solution, presumably due to a formation of an anionic indole-2,3-quinodimethane.<sup>7,8</sup> The solution was stirred at 0°C for 1 h and then quenched with saturated ammonium chloride solution and dil. acetic acid to yield 1-amino-4-cyano-9-methylcarbazoles (10a and 10b)<sup>9</sup> in 69% and 45% yields, respectively. Compound 9a reacted with benzyne (1.1 equiv.), generated *in situ* by reaction of bromobenzene with lithium di-isopropylamide,<sup>10</sup> in THF at -60~0°C to give 6-amino-11-cyano-5-methylbenzo[*b*]carbazole (11)<sup>11</sup> in 64% yield, together with a small amount of 6,11-*q*-benzenobenzo[*b*]carbazole (12).<sup>12</sup>

In summary we have described a convenient and one-pot synthesis of 2-cyano-3-indoleacetonitriles, some of which were used for the synthesis of 1-amino-4-cyanocarbazole derivatives.



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5. 9a:  $\nu_{\max}$  2240, 2210  $\text{cm}^{-1}$ ;  $\delta$  (DMSO- $d_6$ ) 3.89 (3H, s, NCH<sub>3</sub>), 4.35 (2H, s, CH<sub>2</sub>CN), 7.27-7.83 (4H, m, Ar-H).
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7. a) Y. Tamura, S. Mohri, H. Maeda, T. Tsugoshi, M. Sasho, and Y. Kita, Tetrahedron Lett., 1984, 25, 309; b) B. Saraja and P.C. Srinivasan, ibid., 1984, 25, 5429.
8. When 1-methylindole-3-acetonitrile was treated with sodium hydride in THF at 0°C, a dark-red coloration in the solution was not observed. Thus, a dark-red coloration of 9a suggested the presence of anionic quinodimethane structure.



9. 10b: mp 259-260 °C (CH<sub>3</sub>CN); M<sup>+</sup> 279;  $\nu_{\max}$  3500 and 3340, 2220, 1670  $\text{cm}^{-1}$ ;  $\delta$  (DMSO- $d_6$ ) 3.94 (3H, s, CO<sub>2</sub>CH<sub>3</sub>), 4.23 (3H, s, NCH<sub>3</sub>), 6.86 (2H, bs, NH<sub>2</sub>), 7.32-7.59 (3H, m, Ar-H), 8.26 (1H, s, C<sub>3</sub>-H), 8.59 (1H, d, J=8 Hz, C<sub>5</sub>-H).
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11. mp 282-285 °C (CH<sub>3</sub>CN); M<sup>+</sup> 347;  $\nu_{\max}$  3400, 2210  $\text{cm}^{-1}$ ;  $\delta$  (DMSO- $d_6$ ) 4.19 (3H, s, NCH<sub>3</sub>), 6.70 (2H, s, NH<sub>2</sub>), 7.29-8.59 (8H, m, Ar-H).
12. mp 175-177 °C (benzene); M<sup>+</sup> 347;  $\nu_{\max}$  3450, 3400, 2230  $\text{cm}^{-1}$ ;  $\delta$  (DMSO- $d_6$ ) 4.23 (3H, s, NCH<sub>3</sub>), 5.76 (2H, s, NH<sub>2</sub>), 6.40-8.40 (12H, m, Ar-H).

Received, 27th May, 1985