

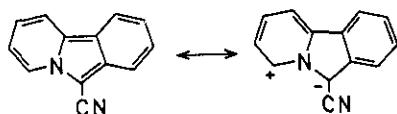
SYNTHESES AND CYCLOADDITIONS OF 1,2-AROMATIC RING-FUSED 3-CYANO-INDOLIZINES

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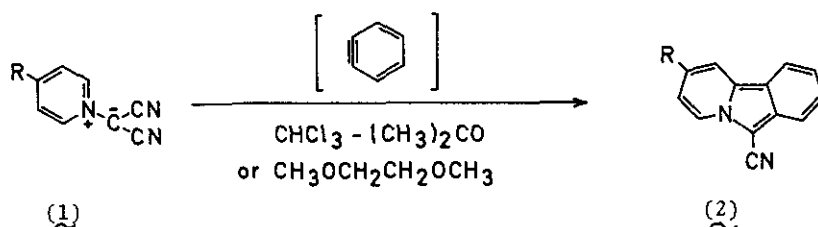
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Abstract--The syntheses and 1,3-dipolar and Michael type cycloaddition reactions of 1,2-aromatic ring-fused 3-cyanoindolizines such as benzo[c]pyrrolo[1,2-a]pyridines, 1,3-diphenylthieno[3',4':3,4]pyrrolo[1,2-a]pyridines, and 1,4-diphenylpyrido[1',2':1,2]pyrrolo[3,4-d]pyridazines are described.

Bicyclic bridgehead-nitrogen containing heterocycles like indolizines¹ and azapentalenes² whose resonance hybrids involve an ylid structure could serve as a bicycloimmonium ylid. Indeed, we have found that 1,2-unsubstituted 3-cyanoindolizines undergo both/either 1,3-dipolar and/or Michael type cycloaddition to electron deficient acetylenes to afford the cycl[2.2.3]azine and/or cycl[2.3.4]azine systems.³ Annulation of carbo- or hetero-aromatic nucleus to indolizine at 1,2-positions is expected to activate 3-cyanoindolizines by means of aromatic stabilization in favor of azomethine ylid structure. Here we describe preparation and some cycloaddition reactions of 3-cyanoindolizines fused at 1,2-positions by benzene, thiophene and pyridazine ring.

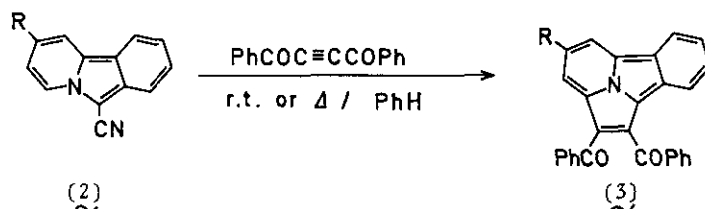
A. Benzo[a]indolizines⁴

Reaction of pyridinium dicyanomethylid (1a) with benzyne,⁵ generated from anthranilic acid and *iso*-amyl nitrite, gave 6-cyanobenzo[a]indolizine (2a)⁶ in 35 % yield. Similar 1,3-dipolar reactions of 4-methyl-, 4-phenyl-, and 4-benzoylpyridinium methylids (1b-1d) produced the corresponding 6-cyanobenzo[a]indolizines (2b: 12 %, 2c: 10 %, 2d: 24 %) along with benzo[a]isoindolo[1,2,3-cd]indolizines as



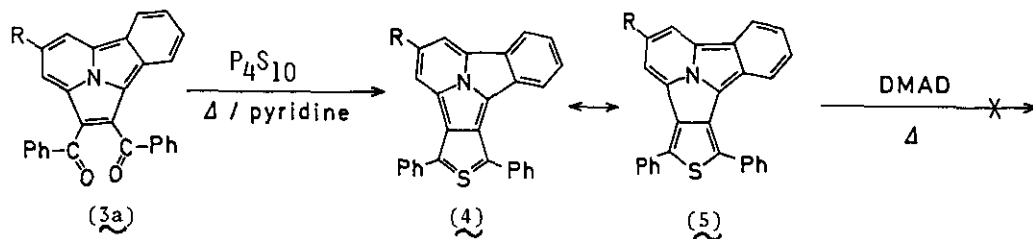
(2)	R	Mp (°C)	ν (cm ⁻¹)	δ (ppm) C-6	δ (ppm) pmr
a	H	126-128	2170	86.1	8.14-8.26 8.50-8.68
b	CH ₃	149-150	2180	84.9	2.45 6.8-7.6 7.69 7.90 8.27
c	C ₆ H ₅	154-155	2220	85.8	7.16-7.92 8.18 8.33 8.60
d	C ₆ H ₅ CO	216-217	2220 1640	—	7.27-8.0 8.19 8.61 8.64

a minor product.⁷ As expected, the C-6 ¹³C resonances are at considerably higher field than those (C-3 in this case) of the 1,2-unsubstituted 3-cyanoindolizines,⁸ thus suggesting more carbanionic character of the azomethine carbon. Indeed, these 6-cyanobenzo[a]indolizines (2a-d) readily underwent 1,3-dipolar cycloaddition onto dibenzoylacetylene giving the corresponding 1,2-benzocycl[2.2.3]azines (3a-d) in



(3)	R	%	Mp (°C)	M ⁺	ν (cm ⁻¹)	δ (ppm) pmr (CDCl ₃)
a	H	82 (r.t. 46 h)	214-215	399	1640 (br)	6.98-7.90 (m, 12 H) 7.94-8.42 (m, 5 H)
b	CH ₃	82 (r.t. 24 h)	256-257	413	1655	2.82 (s, 3 H) 7.01-7.84 (m, 12 H) 7.90-8.53 (m, 4 H)
c	C ₆ H ₅	69 (r.t. 24 h)	227-228	475	1657 (sh) 1630 (br)	7.23-8.21 (m, 19 H) 8.42 (s, 1 H) 8.63 (d, J=3.6 Hz, 1 H)
d	C ₆ H ₅ CO	59 (Δ 5.5 h)	248-251	503	1660 (sh) 1650 (br) 1624	7.07-8.60 (m, 19 H) 8.70 (s, 2 H)

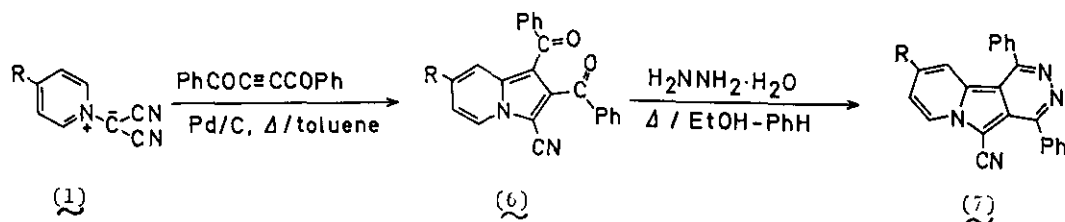
good yields. Treatment of 3a with P₄S₁₀ in pyridine produced a new 18 π thiophene system (4)⁹ in 32 % yield. This system was almost inert to dimethyl acetylenedicarboxylate (DMAD), therefore (5) being assumed to be a major contributor



to the ground state, though steric factors can not be neglected.

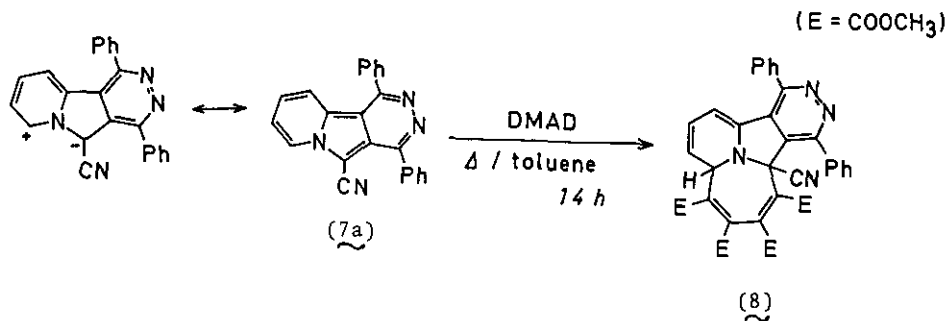
B. Pyridazino[4,5-a]indolizines¹⁰

1,3-Dipolar reactions of 1a-d with dibenzoylacetylene afforded the 1,2-dibenzoyl-3-cyanoindolizines (6a-d),¹¹ treatment of which with hydrazine gave the 6-cyano-1,4-diphenylpyridazino[4,5-a]indolizines (7a-d) in good yield. 7a with DMAD



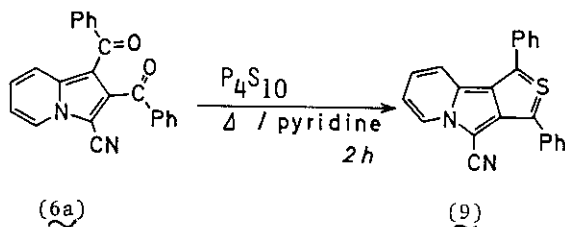
(7)	R	Mp (°C)	M ⁺	ν (KBr)	%
a	H	284-286	346	2205 1625	87
b	CH ₃	284-286	360	2190 1640	85
c	C ₆ H ₅	279-282	422	2175 1630	91
d	C ₆ H ₅ CO	245-247	450	2205 1630	95

produced the 1:2 adduct¹² in 43 % yield, whose structure is supposed to be (8).

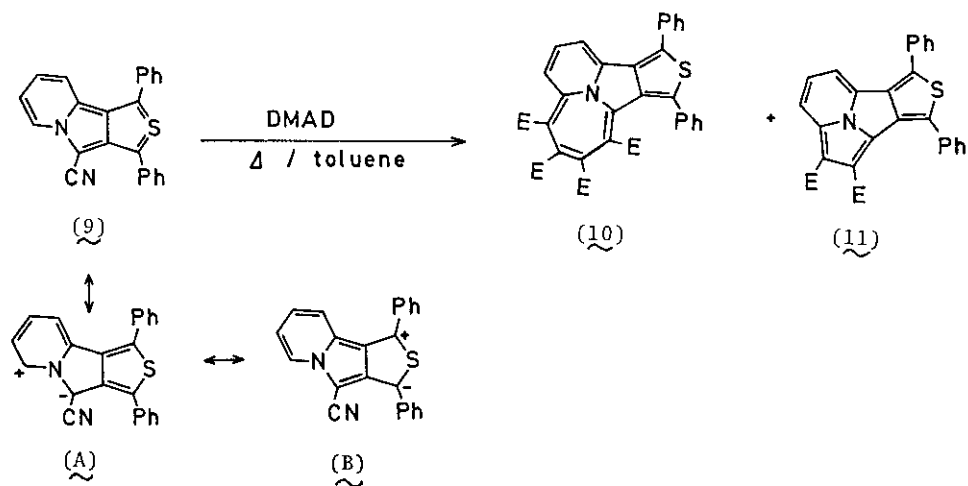


C. Thieno[3,4-a]indolizines¹³

P_4S_{10} treatment of **6a** in refluxing pyridine gave a new nonclassical thiophene, 5-cyano-1,3-diphenylthieno[3,4-a]indolizine (**9**)¹⁴ albeit only in 3 % yield.



Such a system offers an interesting possibility for the development of two kinds of 1,3-dipolar forms, an azomethine ylid (**A**) and a thiocarbonyl ylid (**B**) within the fused ring system.¹⁵ DMAD underwent cycloaddition with **9** in refluxing toluene to afford the dehydrocyanated 1:2 adduct (**10**)¹⁶ along with a trace amount of the dehydrocyanated 1:1 adduct,¹⁷ possibly (**11**).



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2. Review: K. T. Potts, Chem. Heterocycl. Compd., 30, 317 (1977); C. A. Ramsden, Tetrahedron, 33, 3203 (1977). An example: K. Matsumoto et al., Heterocycles, 19, 1483 (1982).
3. T. Uchida and K. Matsumoto, Chem. Lett., 1980, 149; An analogous example : Y. Yamashita, D. Suzuki, and M. Masumura, Tetrahedron Lett., in press.
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5. A review on the reactions of benzyne with heterocycles: M. R. Bryce and J. M. Vernon, Adv. Heterocycl. Chem., 28, 183 (1981).
6. All the new compounds except 11 gave satisfactory elemental analyses.
7. K. Matsumoto and T. Uchida, Chem. Lett., 1982, 869.
8. For instance, the ^{13}C signal of 3 position of 7-methyl-3-cyanoindolizine appears at 94.4 downfield from TMS.
9. mp 202 °C; m/e 399(M^+); $^1\text{H-NMR}(\text{CDCl}_3)$ δ 7.1-7.7(m, 10H), 7.8-8.8(m, 7H); UV (CHCl_3) $\lambda_{\text{max}}(\log \epsilon)$ 251(4.64), 314(4.43), 365(sh), 385(3.86), 446(4.04).
10. Pyrido[1',2':1,2]pyrrolo[3,4-d]pyridazines.
11. e.g. 6a: 89 %; mp 158-159 °C; m/e 350 (M^+); IR(KBr) 2220 cm^{-1} (CN); $^1\text{H-NMR}(\text{CDCl}_3)$ δ 7.03(m, 12H), 8.27(d, J=9.6 Hz, 1H), 8.48(d, J=6.6 Hz, 1H).
12. mp. 282-283 °C; m/e 630(M^+); IR(KBr) 2200 (CN), 1740, 1725 (C=O) cm^{-1} .
13. Thieno[3', 4':3,4]pyrrolo[1,2-a]pyridines.
14. mp 221-223 °C (red crystals); IR(KBr) 2160 cm^{-1} (CN).
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16. mp 225 °C (red brown crystals); m/e 607(M^+); IR(KBr) 1720 cm^{-1} (C=O).
17. m/e 465(M^+).

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