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NITRILES IN ORGANIC SYNTHESIS

SYNTHESIS OF NEW FUNCTIONALLY SUBSTITUTED PYRAZINES AND PYRROLES

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Abstract - Whereas the reaction of 1a,b with 2a-c afforded pyrazines, compound 1c reacted with 2a-c to yield diaminopyrroles. Compound 1c reacted with 2a to yield triazacenaphthene derivative.

Nitriles are versatile reagents and their chemistry is now receiving a considerable attention. In the last decade we were involved in a program directed to developing new approaches for synthesis of polyfunctionally substituted azoles and azines utilizing laboratory available starting materials.[1,2] During this phase of our research we have described a novel synthesis of polyfunctionally substituted pyrazines via reacting 1a,b with 2a,b.[3,4] Since polyfunctional pyrazines are not readily accessible compounds and there is no general route for their preparation we became interested to see if this reaction can be developed to constitute a new general route to polyfunctional pyrazines. It has been found that 1a,b also react with 2c to yield products of condensation via p-toluenesulphonic acid elimination. These were assigned the pyrazine structures 3e,f as they revealed uv similar to those of the known[3] pyrazines 3a-d. Thus, the uv spectra of compounds 3e,f revealed in each case two maxima at λ_{max} = 222, 256 nm comparable to those obtained by us for (6-amino-3,5-dicyano-pyrazin-2-yl) malononitrile (3a) prepared as described earlier.[3] The formation of 3 from 1a,b and 2 is assumed to proceed via cyclization of intermediately formed acyclic condensation product 4.

Compounds 3e,f (0.01 mole) were converted into the pyridopyrazine derivatives 5a,b on refluxing (2h) in acetic (30 ml)-(34 %) hydrochloric acid (2 ml) mixture.

Compound 1c reacted with 2a-c to yield also products of condensation via p-toluenesulphonic acid elimination. Although it seemed logical to assume the pyrazine structure for these products based on analogy to well established behaviour of 1a,b toward 2a-c. The reaction product revealed uv pattern that can hardly be correlated to that of 3a-f. It was suggested that unlike 1a,b compound 1c firstly rearranged with loss of p-toluenesulphonyl anion under reaction conditions to yield 6. The carbonium ion, so formed, then reacted with 2a to yield 7 which cyclised into the intermediate 8. The latter was then converted into the triazacenaphthene derivative 9. Structure 9 was assigned based on ir spectra which revealed one CN band at 2220 and (M^+ 227). In support of this view, 1c was found to rearrange readily in basic media in contrast to 1a,b which are recovered unchanged after being left for long periods in basic solution.

Compound 1c reacted with 2b to yield a product of molecular formula $C_{12}H_{14}N_4O_4$ and (M^+ 279). This was assumed to be the pyrrole derivative 10a. The formation of 10a from the reaction of 1c and 2b is assumed to proceed via sequence shown in chart 2. The formation of pyrrole derivative 10a from reaction of 1c and 2b finds analogy to reported pyrrole formation on reacting 1a,b with enamino esters.[5]

Similar to behaviour of 1c and 2b, compound 1c reacted with 2c to yield the pyrrole derivative 10b. Compounds 3e,f, 9 and 10a,b were prepared by treating a solution of 0.1 mole of each of 2a, 2b or 2c in acetonitrile (30 ml) with the appropriate 1a-c (0.1 mole) and triethylamine (0.2 mole). The reaction mixture was stirred for 24 h at room temperature, then poured into water and acidified with concentrated hydrochloric acid (5 ml). The solid products, so formed, were collected by filtration and crystallized from the proper solvent.

Table 1: List of compounds newly synthesized

Compound*	Solvent of crystallization	Colour	Mp [°C]	Yield [%]	Mol. formula	M^+
3e	ethanol	yellow λ_{max} = 222, 256 nm $\epsilon = 4\times10^3, 4.9\times10^3$	>300	70	$C_{11}H_8N_6O_2$	256
3f	ethanol	yellow	142	80	$C_{13}H_{13}N_5O_4$	303
5a	acetic acid	brown	>300	60	$C_9H_8N_6O_4$	
5b	acetic acid	brown	>300	60	$C_9H_7N_5O_5$	
9	ethanol	yellow	>300	80	$C_9H_5N_7O$	227
10a	ethanol	yellow	182	70	$C_{12}H_{14}N_4O_4$	278
10b	ethanol	yellow λ_{max} = 244 nm $\epsilon = 4.6\times10^3$	220	80	$C_{10}H_9N_5O_7$	231

* Satisfactory elemental analyses for all the newly synthesized compounds were obtained.

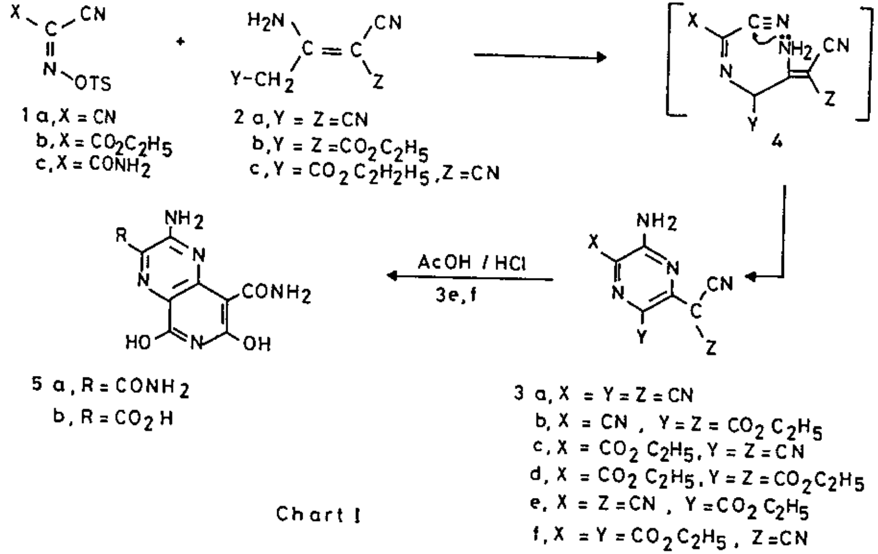

Chart I

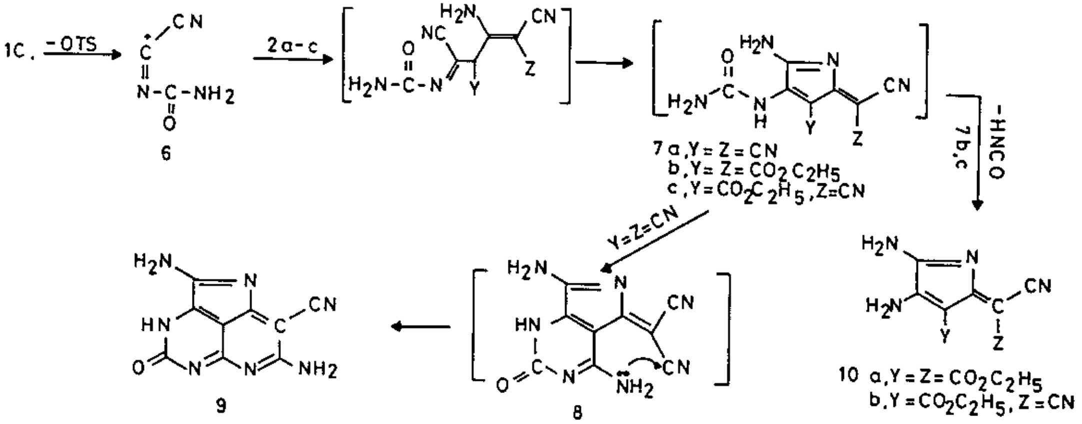

Chart II

Table 2: Ir and ^{1}H-nmr data of compounds newly synthesized

Compound	Ir, cm^{-1}	^{1}H-nmr ppm
3e	3460, 3420, 3260, (NH_2, NH), 2220 (CN), 1720 (ester CO); 1620 (C=C, C=N).	1.16 (m, 6H, $2CH_3$), 4.16 (m, 4H, $2CH_2$), 8.31 (s, 2H, NH_2).
3f	3460, 3420, 3160 (NH_2, NH), 2230, 2220 (CN), 1720 (ester CO), 1620 (C=C, C=N).	1.17 (t, J=8 Hz, 3H, CH_3), 4.16 (q, J=8 Hz, 2H, CH_2), 6.35 (s, 2H, NH_2).
5a	3380, 3220, 3160 (NH_2, NH), 1680 (amide CO).	
5b	3410, 3320, 3260 (NH_2, NH), 1680 (amide CO).	
9	3460, 3410, 3240 NH_2, NH), 2220 (CN), 1710 (CO), 1610 (C=C, C=N).	7.45 (s, 2H, NH_2), 7.82 (s, 1H, NH), 8.13 (s, 2H, NH_2).
10a	3460, 3410, 3220 (NH_2), 2220 (CN), 1710 (ester CO).	1.16 (m, 6H, $2CH_3$), 3.25 (s, 2H, NH_2), 4.18 (m, 4H, $2CH_2$).
10b	3440, 3420, 3210 (NH_2), 2220, 2210 (CN), 1710 (ester CO).	1.16 (t, J=8 Hz, 3H, CH_3), 4.21 (q, J=8 Hz, 2H, CH_2), 6.34 (s, 2H, NH_2).

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