# ACTIVATED NITRILES IN HETEROCYCLIC SYNTHESIS: A NEW APPROACH FOR THE SYNTHESIS OF PYRAN DERIVATIVES

Nadia S. Ibrahim

Department of Chemistry, Faculty of Science, Cairo University, Giza, A.R. Egypt

**Abstract**— The reaction of cinnamonitriles with acetylacetone and ethyl acetoacetate is reported. Several new polyfunctional pyrans could be prepared. Spectral data of the synthesised products is reported.

Polyfunctional nitriles are highly reactive reagents that have been extensively used in heterocyclic synthesis.[1,2] In continuation of our program directed towards the development of new procedures for the synthesis of polyfunctional heterocycles from simple laboratory available starting materials,[3-5] we report here a new synthesis of substituted pyrans from polyfunctional nitriles. Although the reaction of cinnamonitriles with active methylene heterocycles and with benzoylacetonitrile has recently been utilized as a source for polyfunctional pyrans,[6-8] the utility of simple β-diketones and β-ketoesters in the same reaction has never been reported. As the pyrans, that may be formed, seems interesting for further chemical transformations, we have investigated the reaction of 1a,b with 2a-f.

Thus, it has been found that ethyl acetoacetate 1a reacted with benzylidene malononitrile 2a to yield a product of molecular formula $C_{16}H_{16}N_2O_3$ ($M^+$ = 284). The pyran structure 3a was assigned for this product based on spectral data. Thus, $^1$HNMR revealed a one proton singlet at δ 4.50 ppm for pyran H-4, a singlet at δ 2.22 ppm ($CH_3$) and at δ 6.88 ppm ($NH_2$) in addition to signals corresponding to ester and aromatic protons. Moreover, $^{13}$CNMR can be only interpreted in terms of proposed structure (cf. chart 1). Other alternative possible isomeric forms would show completely different $^1$HNMR and $^{13}$CNMR.

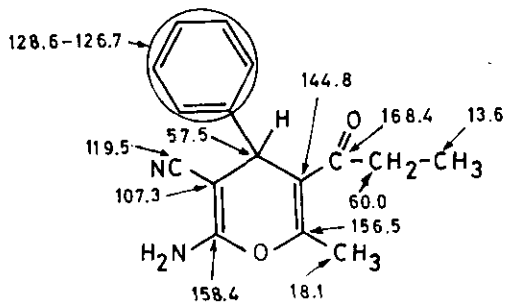


Chart 1

Similarly, 1a reacts with 2b-e yielding the corresponding pyrans 3b-e via Michael addition reaction.

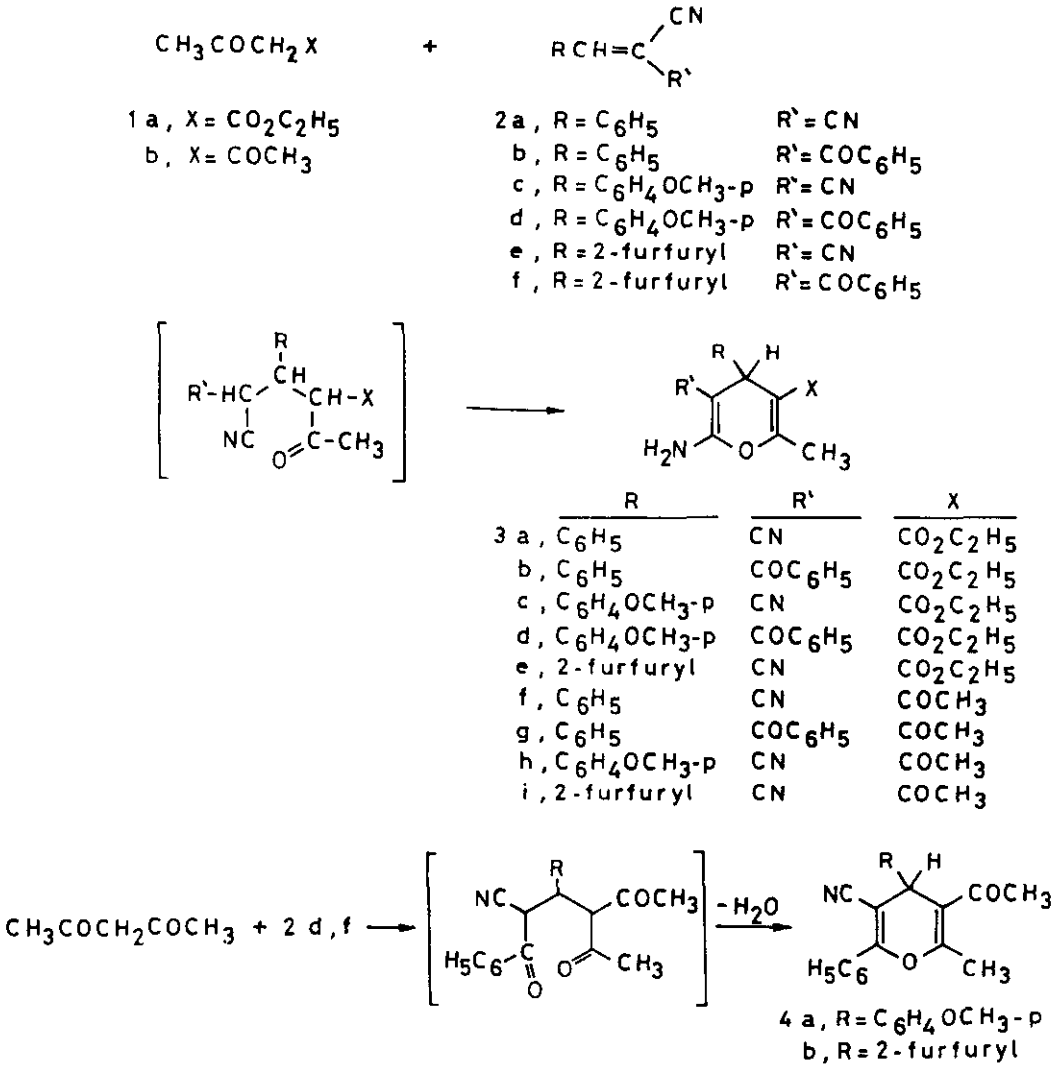


Chart 2

Acetylacetone 1b reacts also with 2a,b,c,e to yield the corresponding pyrans 3f-i. In case of 2d,f acetylacetone underwent condensation reaction yielding 5a,b via loss of water molecule.

As a general procedure, equimolecular amounts of either 1a or 1b were reacted with 2a-f in refluxing ethanol (30 ml) with catalytic amount of triethylamine for 3h. The solvent was then reduced to half its volume and the reaction mixture was left to cool. The products, so formed, were collected by filtration and crystallized from the proper solvent.

Table 1: List of compounds 3a-i; 4a-b.

| Compound* | Solvent of Crystallization | Colour | Mp. (°C) | Yield % | Mol. Formula |
|---|---|---|---|---|---|
| 3a | acetic acid | colourless | 176 | 80 | $C_{16}H_{16}N_2O_3$ |
| 3b | DMF/$H_2O$ | colourless | 245 | 85 | $C_{22}H_{21}NO_4$ |
| 3c | ethanol | yellow | 110 | 70 | $C_{17}H_{18}N_2O_4$ |
| 3d | DMF/$H_2O$ | colourless | 234 | 80 | $C_{23}H_{23}NO_5$ |
| 3e | ethanol | colourless | 195 | 80 | $C_{14}H_{14}N_2O_4$ |
| 3f | DMF/$H_2O$ | colourless | 210 | 70 | $C_{15}H_{14}N_2O_2$ |
| 3g | ethanol | yellow | 190 | 75 | $C_{21}H_{19}NO_3$ |
| 3h | ethanol | yellow | 205 | 60 | $C_{16}H_{16}N_2O_3$ |
| 3i | ethanol | buff | 220 | 75 | $C_{13}H_{12}N_2O_3$ |
| 4a | ethanol | yellow | 195 | 65 | $C_{22}H_{19}NO_3$ |
| 4b | acetic acid | buff | 140 | 70 | $C_{19}H_{15}NO_3$ |

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

Table 2: IR and $^1$HNMR data of compounds 3a-i; 4a-b.

| Compound | IR, $cm^{-1}$ | $^1$HNMR ppm |
|---|---|---|
| 3a* | 3420, 3340, 3280 ($NH_2$); 2200 (CN); 1700 (CO). | 1.18 (t, 3H, $CH_3$); 2.22 (s, 3H, $CH_3$); 3.95 (q, 2H, $CH_2$); 4.50 (s, 1H, H-4); 6.88 (s, 2H, $NH_2$), 7.12-7.37 (m, 5H, aromatic protons). |
| 3b | 3360, 3100($NH_2$); 1750, 1720 (CO) | 1.18 (t, 3H, $CH_3$); 2.4 (s, 3H, $CH_3$), 3.3 (s,2H, $NH_2$); 4.2 (q, 2H, $CH_2$); 4.6 (s, 1H, H-4); 7.2 - 7.6 (m, 10H, aromatic protons). |
| 3c | 3400, 3320, 3200 ($NH_2$); 2200 (CN); 1710 (CO) | 1.2 (t, 3H, $CH_3$); 2.5 (s, 3H, $CH_3$); 3.8 (s,3H, $OCH_3$); 4.2 (q, 2H, $CH_2$); 4.6 (s, 1H, H-4); 6.2 (s, 2H, $NH_2$); 7.2 - 7.6 (m, 4H, aromatic protons). |
| 3d | 3320 ($NH_2$); 1750, 1740, 1720 (CO) | 1.17 (t, 3H, $CH_3$); 2.4 (s, 3H, $CH_3$); 3.8(s, 3H, $OCH_3$);4.2(q,2H,$CH_2$);4.4(s,1H,H-4);6.9(s,2H,$NH_2$); 7.1-7.8 (m,9H, aromatic protons). |

| | | |
|---|---|---|
| 3e | 3400, 3340, 3200 ($NH_2$); 2200 (CN); 1690 (CO). | 1.2 (t, 3H, $CH_3$); 2.3 (s, 3H, $CH_3$); 4.2 (q, 2H, $CH_2$); 4.5 (s, 1H, H-4); 6.17 (d, 1H, furan H-3); 6.39 (m, 1H, furan H-4);6.9 (s, 2H,$NH_2$); 7.6 (d, 1H, furan H-5). |
| 3f | 3500, 3400 ($NH_2$); 2220 (CN); 1720 (CO). | 2.1 (s, 3H, $CH_3$); 2.2 (s, 3H, $CH_3$); 4.5 (s, 1H, H-4); 5.1(s, 2H, $NH_2$); 7.2 - 7.4 (m, 5H, aromatic protons). |
| 3g | 3400 ($NH_2$); 1770, 1760 (CO). | 1.17 (t, 3H, $CH_3$); 2.2 (s, 3H, $CH_3$); 3.6 (s,2H, $NH_2$); 4.4 (s, 1H, H-4); 7.4-7.9 (m, 10H, aromatic protons). |
| 3h | 3300, 3200 ($NH_2$); 2220 (CN); 1730 (CO). | |
| 3i | 3450, 3350 ($NH_2$); 2200 (CN); 1720 (CO). | |
| 4a | 2200 (CN); 1720 (CO) | 1.2 (t, 3H, $CH_3$); 1.9 (s, 3H, $CH_3$); 3.7(s,3H, $OCH_3$); 4.5 (s, 1H, H-4); 7.1-7.9 (m, 9H, aromatic protons). |
| 4b | 2200 (CN); 1690 (CO). | |

* 3a ($M^+$ = 284); $^{13}$CNMR (Chart 1).

## REFERENCES


1. F.M. Abdelrazek, N.S. Ibrahim, Z.E. Kandeel and M.H. Elnagdi, Synthesis,970 (1984).
2. M.H. Elnagdi, H.A. Elfahham and G.E.H. Elgemeie, Heterocycles,20, 519 (1983).
3. N.S. Ibrahim, N.M. Abed and Z.E. Kandeel, Heterocycles,22, 1677 (1984).
4. N.S. Ibrahim, K.U. Sadek, S.I. Aziz and M.H. Elnagdi, Zeitschrift Fur Naturforschung, 40b, 129 (1985).
5. N.S. Ibrahim, F.M. Abdelrazek, S.I. Aziz and M.H. Elnagdi, Monatsh. Chem., 116, 551 (1985).
6. M.R.H. Elmoghayer, M.A.E. Khalifa, M.K.A. Ibraheim and M.H. Elnagdi, Monatsh. Chem., 113,53 (1982).
7. S.I. Aziz, B.Y. Riad, H.A. Elfahham and M.H. Elnagdi, Heterocycles,19, 2251 (1982).
8. H.A.F. Daboun, S.E. Abdou, M.M. Hussein and M.H. Elnagdi, Synthesis,502 (1982).


Received, 30th October, 1985