Nitriles in Organic Synthesis. The Chemical Behavior of [1-(2-Furyl)ethylidene]- and [1-(2-Thienyl)ethylidene]malononitriles

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The chemical behavior of [1-(2-furyl)ethylidene]- and [1-(2-thienyl)ethylidene]malononitriles **1a** and **b** toward electrophilic reagents, active methylene reagents and (arylmethylene)malononitriles is described.

The chemistry of nitriles has received considerable recent attention.[1,2] A variety of new systems has been efficiently synthesized utilizing simple nitriles as starting components.[3,4] In conjunction with our program directed for developing utility of polycyano compounds in organic synthesis we have recently reported a novel synthesis of pyridazines and 3,5-disubstituted-2,6-dicyanoanilines utilizing (1-phenylethylidene)malononitrile (**1c**) as starting material.[5] In order to see if reactions of the type reported above can be extended to constitute general route for the synthesis of pyridazines and 3,5-disubstituted-2,6-dicyanoanilines , we report here the results of our investigations to conduct similar reactions with [1-(2-furyl)], and [1-(2-thienyl)ethylidene]malononitriles (**1a** and **b**).

In contrast to the reported formation of [1-phenyl-2-(phenylhydrazono)ethylidene]malononitrile on coupling **1c** with benzenediazonium chloride, compounds **1a** and **b** coupled with the same reagent to yield (phenylazo)malononitrile (**2**). The formation of **2** in this reaction is assumed to proceed via coupling of benzenediazonium chloride with malononitrile, the latter is assumed to be formed via action of water on **1a** or **b** (cf. route (a)). Possible formation of **2** via route (b) seems unlikely, although it cannot be ruled out. The difference in behavior between **1a,b** and **1c** can be attributed to a decrease in the acidity of the methyl group in **1a** and **b** by the effect of the electron-rich heterocycles which counterbalance the electron-attracting effect of the two cyano functions.[6]

Compound **1a** reacted with (arylmethylene)malononitriles 3a—c to yield products of condensation via HCN elimination. Two isomeric structures seemed possible for the reaction product (cf. structures **4** and **5**). Structures **4a—c** were established for the reaction products based on their syntheses via reactions of **6** with malononitrile. Compounds **6** were obtained in turn via reaction of **1a**, **b** with furfural and 2-thiophenecarbaldehyde. Compound **4a** was also found identical with authentic sample prepared as has been previously described.[5] Similarly, compound **1b** rected with (arylmethylene)malononitriles **3a** and **b** to yield the 3,5-disubstituted-2,6-dicyanoanilines **4c** and **d**. In contrast, compound **1b** reacted with **3c** to yield 1 : 1 adduct. The pyridine structure **7** was established for the reaction product based on its analytical and spectral data (cf. Experimental).

The behavior of **1a** and **b** toward malononitrile was also investigated. It has been found that **1a** reacted with malononitrile to yield a compound of molecular formula $C_{12}H_8ON_4$ (M^+=224; m/z). This compound can be formulated as the pyridine derivative **8** or the isomeric benzene derivative **9**. Structure **8** was readily eliminated based on ^{1}H NMR which revealed the absence of CH_2 function. Thus, structure **9** was considered for the reaction product. Attempts at addition of **1b** to malononitrile under the same experimental conditions were unsuccessful. The reactants were recovered almost unchanged after reflux in sodium-dioxane mixture.

In contrast to the reported addition of **1c** to trichloroacetonitrile,[5] attempts at addition of **1a** and **b** to the same reagents has failed.

The results obtained in our investigation clearly reveal the effect of C-1 substituent on the reactivity of methyl grorup in [1-substitutedethylidene]malononitriles. Electron-rich substituents counterbalance the electron-attracting force of the cyano groups which result in the decrease of the reactivity of methyl group.

Experimental

All melting points were uncorrected. IR spectra were recorded (potassium bromide) on a Shimadzu-408 spectrophotometer. ^{1}H NMR were measured in DMSO on a Varian EM-390 spectrophotometer at 90 MHz with TMS as internal reference and chemical shifts were expressed as δ (ppm). Microanalytical data (C, H, N, S.) were obtained from the Microanalytical Data Unit at Cairo University.

[1-(2-Furyl)ethylidene]- and [1-(2-Thienyl)ethylidene]-malononitriles (1a and b). General Procedure: Malononitrile (0.01 mol) was added to a suspension of 2-acetylfuran or 2-acetylthiophene (0.01 mol) in a mixture of benzene–acetic acid (50 : 5) in the presence of β-alanine (2 g). The reaction miture was heated under reflux in the presence of a water separator until complete removal of water (2 h) then evaporated in vacuo. The solid product, so formed, was collected by filtration and crystallized from the appropriate solvent (see Table 1).

Coupling of Compounds 1a and b with Benzenediazonium Chloride: An ice cold solution of 0.01 mol of benzenediazonium chloride (prepared from 0.01 mol of aniline

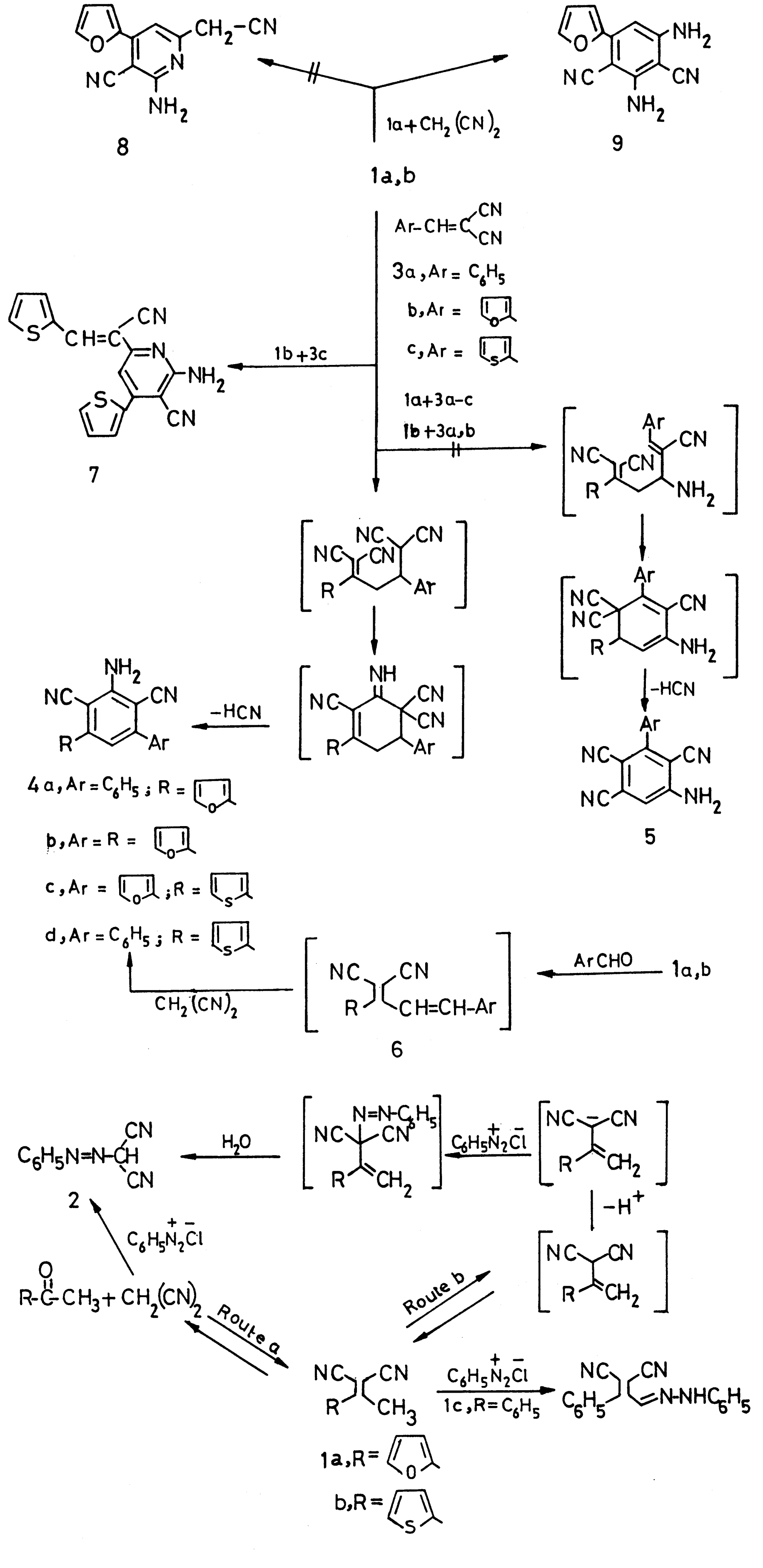
8
9
1a+CH2(CN)2
1a,b
Ar-CH=C(CN)CN
3a,Ar = C6H5
b,Ar =
c,Ar =
1b+3c
7
1a+3a-c
1b+3a,b
-HCN
4a,Ar=C6H5 ; R =
b,Ar = R =
c,Ar = ;R =
d,Ar = C6H5 ; R =
5
ArCHO
1a,b
CH2(CN)2
6
H2O
C6H5N2Cl
-H+
2
R-C(O)-CH3+CH2(CN)2
Route a
Route b
1c,R=C6H5
1a,R=
b,R=

Table 1. List of the Newly Synthesized Compounds

Compd.	Cryst. solvent	Mp θ_m/°C	Yield %	Mol. form. mol. Wt.	Calcd (Found)/%				ν_{max}/cm^{-1}	δ_H
					C	H	N	S		
1a	Methanol	75	70	$C_9H_6N_2O$ (158.15)	68.35 (68.2	3.82 3.6	17.71 17.8)		2970(CH_3), 2190, 2200(CN bands), and 1580(C=C)	1.3(s, 3H, CH_3), 7.3—8.2(m, $3H_{furan}$)
1b	Methanol	82	72	$C_9H_6N_2S$ (174.15)	62.07 (62.6	3.47 3.5	16.09 16.2	18.37 18.1)	2900(CH_3), 2190, 2200(CN bands), and 1550(C=C)	1.2(s, 3H, CH_3), 7.0—7.66(m, $3H_{thiophene}$)
4a	Ethanol	235	82	$C_{18}H_{11}N_3O$ (285.29)	75.78 (75.7	3.89 3.8	14.73 14.5)		3350(NH_2), 2200(CN bands), and 1630(δ NH_2)	3.7(br, 2H, NH_2), 7.2—8.2(m, 9H, aromatic protons)
4b	Acetone	255	85	$C_{16}H_9N_3O_2$ (275.26)	69.81 (69.7	3.30 3.2	15.27 15.5)		3390(NH_2), 2190, 2200(CN bands), and 1635(δ NH_2)	3.5(br, 2H, NH_2), 6.8—8.2(m, 7H, aromatic protons)
4c	Acetone	250	83	$C_{16}H_9N_3OS$ (291.26)	65.97 (66.4	3.11 3.5	14.43 14.4	11.0 11.0)	3350(NH_2), 2190, 2200(CN bands), and 1630(δ NH_2)	3.3(s, 2H, NH_2), 6.8—8.0(m, 7H, aromatic protons)
4d	Ethanol	237	75	$C_{18}H_{11}N_3S$ (301.29)	71.75 (71.5	3.68 3.5	13.95 14.0	10.62 10.8)	3340(NH_2), 2190, 2200(CN bands), and 1635(δ NH_2)	3.4(br, 2H, NH_2), 7.0—7.9(m, 9H, aromatic protons)
7	Acetone	270	75	$C_{17}H_{10}N_4S_2$ (334.28)	61.08 (61.1	3.02 3.5	16.76 16.9	19.15 19.1)	3350(NH_2), 2200(CN bands), and 1640(δ NH_2)	3.8(br 2H, NH_2), 6.2(s, 1H, ylidene CH), 7.2—8.0(m, 7H, aromatic protons)
9	Ethanol-water	228	77	$C_{12}H_8ON_4$ (224.22)	64.29 (64.8	3.60 3.5	24.99 25.0)		3350, 3150(NH_2 bands), 2200 (CN bands)	3.3(br 4H, $2NH_2$), 6.6—8.2(m, 4H, aromatic protons)

and the appropriate amount of sodium nitrite and hydrochloric acid) was added to a solution of **1a** or **b** (0.01 mol) in ethanol (50 ml) containing sodium acetate (5 g). The precipitate was filtered off and crystallized from ethanol. The product was identical with authentic sample of (phenylazo)malononitrile.

Condensation of Compounds 1a and b with (Arylmethylene)malononitrile Derivatives 3a—c. General Procedure: A solution of compound **1a** or **b** (0.01 mol) and the appropriate (arylmethylene)malononitrile derivatives **3a—c** (0.01 mol) in ethanol (50 ml) was treated with piperidine (1.0 ml). The reaction mixture was heated under reflux for 3 h and then evaporated in vacuo. The solid product, so formed, was collected by filtration and recrystallized from the appropriate solvent (see Table 1).

The same products were obtained by the follwing procedure: To a solution of compound **1a** or **b** (0.01 mol) in ethanol (50 ml) was added to the appropriate aromatic aldehyde in the presence of piperidine (1.0 ml). The reaction mixture was heated under reflux for 1—2 h (TLC monitor). To this solution, malononitrile (0.01 mol) was added and the reaction mixture was heated under reflux for additional 2 h. The solvent was then evaporated in vacuo and the solid product, so formed, was collected by filtration.

Compound **4a** was also found identical with authentic sample prepared as was previously described.[5]

Reaction of 1a with Malononitrile. Equimolecular amounts (0.01 mol) of **1a** and malononitrile were heated under reflux in 50 ml of dioxane with 0.01 mol of sodium metal for 4 h. The mixture was then evaporated in vacuo and neutralized with HCl. The solid product, so formed was collected by filtration and recrystallized from the appropriate solvent (see Table 1).

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