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SYNTHESIS OF 2-AMINO-5-NITRO-4H-PYRAN-3-CARBONITRILES

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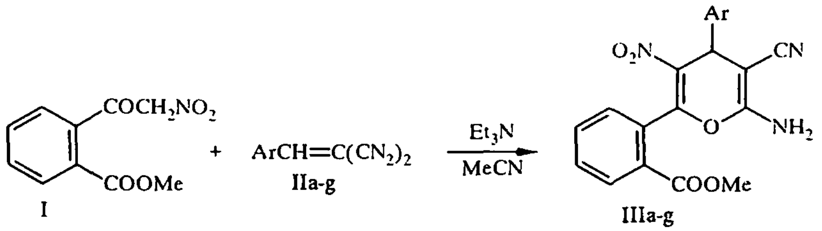
Reaction of 2-carbomethoxy-ω-nitroacetophenone with arylmethylenemalononitriles gives the previously unknown 2-amino-4-aryl-5-nitro-6-(2-carbomethoxyphenyl)-4H-pyran-3-carbonitriles.

Substituted 2-aminopyrans are of great interest for preparation of novel medicinal agents, pesticides, dyes, and analogs of natural products [1]. They can be quite readily converted to various heterocyclic compounds [2]. One of the basic methods for synthesis of 2-aminopyrans is the reaction of α,β-unsaturated nitriles with β-dicarbonyl compounds (β-diketones, β-ketoesters) [1]. At the same time, the possibility of using monocarbonyl compounds in this reaction has been little studied [3, 4]. In this work we have shown that the reaction of α-nitroketone (I) with arylmethylenemalononitriles (IIa-g) in acetonitrile in the presence of catalytic amounts of triethylamine at room temperature gives the previously unknown 2-amino-4-aryl-5-nitro-6-(2-carbomethoxyphenyl)-4H-pyran-3-carbonitriles (IIIa-g) in 40-60% yields.



II, III a Ar = Ph; b Ar = 2-BrC$_6$H$_4$; c Ar = 3-BrC$_6$H$_4$;
d Ar = 2-NO$_2$C$_6$H$_4$; e Ar = 3-NO$_2$C$_6$H$_4$;
f Ar = 4-ClC$_6$H$_4$; g Ar = 2,4-Cl$_2$C$_6$H$_3$

The IR spectra of the obtained compounds (see Table 1) show the presence of characteristic stretching and deformation bands for NH2 groups at 3306-3430 and 1647-1655 respectively, and stretching of the C≡N bonds at 2213-2225, C=O at 1687-1694, NO2 groups at 1510-1520 and 1338-1340, and C—O—C bonds at 1089-1090 cm^{-1} [5]. In addition, as discussed in [4], the IR spectra of all compounds showed intense bands at 1715-1725 cm^{-1} which are difficult to assign to a specific functional group.

The ^{1}H NMR spectra of IIIa-g are also characteristic. They show a singlet for the protons of the OMe group at 3.92-3.95 ppm, a singlet for the 4-H proton at 4.98-5.85 ppm, and a broad singlet for the NH2 protons at 6.35-6.62 ppm. It should be noted that the chemical shifts of the latter two signals depend significantly on the nature of the 4-aryl substituent in the pyran ring (see Table 1).

The reaction described in this work is the first example of the preparation of nitropyrans from α-nitroketones but the question of the limits of its use is still not completely resolved, in particular dinitrile IIa does not react with ω-nitroacetophenone PhCOCH2NO2 in the reported conditions.

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TABLE 1. IR and PMR Spectral Data for Compounds IIIa-g

Compound	IR spectrum, cm^{-1}					^1H NMR spectrum, δ, ppm
	NH_2	C≡N	C=O	NO_2	C—O—C	
IIIa	3407 3306 1647	2225	1687	1510 1345	1090	3,92 (3H, s, OMe); 4,99 (1H, s, 4-H); 6,46 (2H, br s, NH_2); 7,3...8,2 (9H, m, H_{arom})
IIIb	3425 3335 1655	2213	1690	1520 1340	1089	3,94 (3H, s, OMe); 5,03 (1H, s, 4-H); 6,56 (2H, br. s, NH_2); 7,3...8,2 (8H, m, H_{arom})
IIIc	3418 3343 1655	2223	1687	1520 1340	1090	3,93 (3H, s, OMe); 5,57 (1H, s, 4-H); 6,41 (2H, br. s, NH_2); 7,3...8,2 (8H, m, H_{arom})
IIId	3430 3315 1648	2213	1687	1520 1530 1358 1340	1090	3,93 (3H, s, OMe); 5,85 (1H, s, 4-H); 6,62 (2H, br. s, NH_2); 7,56...8,2 (8H, m, H_{arom})
IIIe						3,95 (3H, s, OMe); 5,23 (1H, s, 4-H); 6,48 (2H, br. s, NH_2); 7,6...8,2 (8H, m, H_{arom})
IIIf	3400 3325 1655	2213	1694	1520 1340	1090	3,94 (3H, s, OMe); 5,03 (1H, s, 4-H); 6,52 (2H, br. s, NH_2); 7,4...8,2 (8H, m, H_{arom})
IIIg	3390 1655	2220	1693	1520 1338	1089	3,93 (3H, s, OMe); 4,98 (1H, s, 4-H); 6,35 (2H, br. s, NH_2); 7,35...8,2 (7H, m, H_{arom})

EXPERIMENTAL

The starting nitroketone I was synthesized by a known method [6]. Confirmation of the purity of the compounds and monitoring of the reaction course was carried out by TLC on Silufol UV-254 plates in the system petroleum ether-ethyl acetate (3:2). IR spectra were taken on a Perkin-Elmer spectrophotometer for KBr tablets and PMR spectra on a Bruker WM-250 spectrometer using $(CD_3)_2CO$ solvent.

Preparation of Pyrans IIIa-g (general method). A mixture of nitroketone I (1 mmole) and nitrile IIa-g (1.02 mmole) in MeCN (6 ml for IIa-f, 15 ml for IIg) was heated gently until a clear solution was obtained. Et_3N (1 drop) was added to the product which was then stirred without heating for 10-15 min and left at room temperature (18-23°C) in an open flask for 1.5-2.5 days. The precipitate was filtered, washed with a small amount of cold MeCN (~0 °C), and purified using column chromatography on silica gel (100/160 mesh, eluent petroleum ether-ethyl acetate, 3:2).

2-Amino-6-(2-carbomethoxyphenyl)-5-nitro-4-phenyl-4H-pyran-3-carbonitrile (IIIa). Yield 58%. Mp 178-179°C. Found, %: C 63.5; H 3.91; N 11.34. $C_{20}H_{15}N_3O_5$. Calculated, %: C 63.66; H 4.01; N 11.14.

2-Amino-4-(2-bromophenyl)-6-(2-carbomethoxyphenyl)-5-nitro-4H-pyran-3-carbonitrile (IIIb). Yield 44%. Mp 182-183°C. Found, %: C 52.94; H 2.96; N 9.20; Br 17.37. $C_{20}H_{14}BrN_3O_5$. Calculated, %: C 52.65; H 3.09; N 9.21; Br 17.51.

2-Amino-4-(3-bromophenyl)-6-(2-carbomethoxyphenyl)-5-nitro-4H-pyran-3-carbonitrile (IIIc). Yield 46%. Mp 188-189°C. Found, %: C 52.51; H 3.22; N 9.09, Br 17.40. $C_{20}H_{14}BrN_3O_5$. Calculated, %: C 52.65; H 3.09; N 9.21; Br 17.51.

2-Amino-6-(2-carbomethoxyphenyl)-5-nitro-4-(2-nitrophenyl)-4H-pyran-3-carbonitrile (IIId). Yield 40%. Mp 184-185°C (decomp.). Found, %: C 56.72; H 3.38; N 13.13. $C_{20}H_{14}N_4O_7$. Calculated, %: C 56.88; H 3.34; N 13.27.

2-Amino-6-(2-carbomethoxyphenyl)-5-nitro-4-(3-nitrophenyl)-4H-pyran-3-carbonitrile (IIIe). Yield 45%. Mp 190-191°C (decomp.). Found, %: C 56.75; H 3.20; N 13.52. $C_{20}H_{14}N_4O_7$. Calculated, %: C 56.88; H 3.34; N 13.27.

2-Amino-6-(2-carbomethoxyphenyl)-5-nitro-4-(4-chlorophenyl)-4H-pyran-3-carbonitrile (IIIf). Yield 42%. Mp 185-186°C (decomp.). Found, %: C 58.54; H 3.22; N 10.06; Cl 8.99. $C_{20}H_{14}ClN_3O_5$. Calculated, %: C 58.33; H 3.43; N 10.20; Cl 8.61.

2-Amino-4-(2,4-dichlorophenyl)-6-(2-carbomethoxyphenyl)-5-nitro-4H-pyran-3-(carbonitrile) (IIIg). Yield 54%. Mp 178-179°C (decomp.). Found, %: C 53.66; H 3.05; N 9.30; Cl 15.71. $C_{20}H_{13}Cl_2N_3O_5$. Calculated, %: C 53.83; H 2.94; N 9.42 ; Cl 15.89.

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