

Microwave-prompted Reaction of Cinnamitrile Derivatives with 5,5-Dimethyl-1,3-cyclohexanedione

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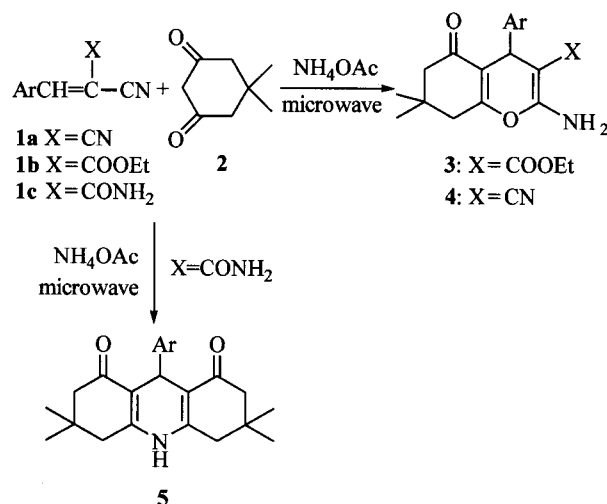
In the reactions of α -cyanocinnamitrile or β -cyano- β -carboxy styrene with 5,5-dimethyl-1,3-cyclohexanedione in the presence of ammonium acetate under microwave irradiation without solvent, the 2-amino-5,6,7,8-tetrahydro-5-oxo-4-aryl-7,7-dimethyl-4H-benzo-[*b*]-pyran derivatives were obtained. However, in the reactions of arylidenecyanoacetamide with 5,5-dimethyl-1,3-cyclohexanedione under the same reaction conditions, the acridine derivatives were obtained. The structures of the products were determined by single crystal X-ray diffraction analysis.

Keywords cinnamitrile, dimedone, microwave

Polyfunctionalised benzo-[*b*]-4H-pyrans are the structural unit of a number of natural products and are used as versatile synthons¹ because of the inherent reactivity of the inbuilt pyran ring. Their conventional preparation was the reaction of cinnamitrile derivatives with dimedone, which was catalyzed by acid or base. Kamaljit *et al.* reported² that ethyl 2-amino-5,6,7,8-tetrahydro-5-oxo-4-aryl-7,7-dimethyl-4H-benzo-[*b*]-pyran-3-carboxylates (**3**) were prepared by the reaction of β -cyano- β -carboxy styrene with 1,3-cyclohexanedione in refluxing acetonitrile-acetic acid (10 : 1, *V/V*), or through one-pot reaction of dimedone, aromatic aldehydes and malonitrile in ethanolic piperidine (or ammonium acetate as catalyst instead of piperidine).^{3,4} Recently, we found that **3** and **4** could also be prepared by the reaction of α -cyanocinnamitrile (**1a**) and β -cyano- β -carboxy

(**1b**) styrene, respectively, with 5,5-dimethyl-1,3-cyclohexanedione (**2**) in the presence of ammonium acetate under microwave irradiation without solvent. The reactions were completed in 4—8 min with 76%—96% yield. While arylidenecyanoacetamide (**1c**) was reacted with **2** under similar reaction conditions giving acridine derivatives (**5**) in 83%—92% yield, instead of the expected benzo-[*b*]-pyrans derivatives (Scheme 1).

Scheme 1



The structures of these products were determined by

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Received September 13, 2001; revised and accepted March 4, 2002.

Project supported by the Natural Science Foundation of Jiangsu Province (No. BK2001142) and the Natural Science Foundation of Education Ministry of Jiangsu Province (No. 01KJB150008).

single crystal X-ray diffraction analysis (Fig. 1—3). The selected crystallographic data were shown Table 1. X-ray analysis reveals that in the structure of **3** and **4** the benzo-*[b]*-pyran ring exhibits envelope configurations. In the structure of **3** (Fig. 1), the dihedral angle between plane 1 [C(5), C(6), C(9), O(1)] and plane 2 [C(1), C(2), C(4), C(5), C(6)] is 2.9° , the dihedral angle between furan ring and plane 1 is 84.7° , the dihedral angle between furan ring and plane 2 is 85.9° . In the structure of **4** (Fig. 2), the plane [C(7), C(8), C(9), O(1), C(10), C(11)] forms an angle of 92.5° with the phenyl plane. In the structure of **5** (Fig. 3), there exists a flattened-boat conformation in which the aryl substituent is in pseudo-axial position, orthogonal to the dihydropyridine plane. The dihydropyridine plane is approximately bisected by the plane of the phenyl ring, as indicated by the magnitude of the dihedral angle between the two planes, which is 87.2° . The two fused rings are in the same plane, with atoms C(3) and C(11) displaced from this plane.

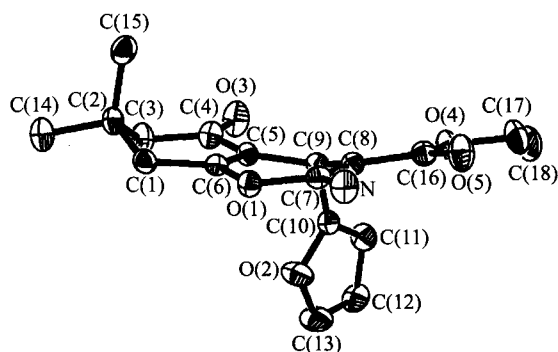


Fig. 1 Crystal structure of **3**.

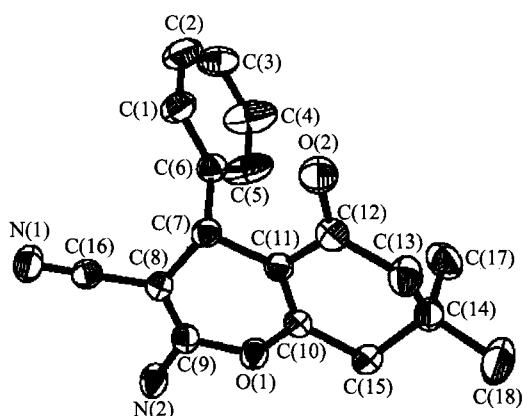


Fig. 2 Crystal structure of **4**.

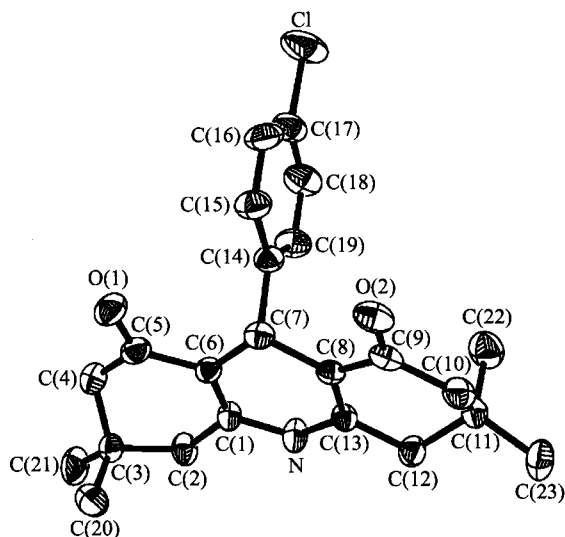


Fig. 3 Crystal structure of **5**.

Typical experimental procedure

Cinnamitrile derivatives (**1**) (5 mmol), 5,5-dimethyl-1,3-cyclohexanedione (**2**) (5 mmol) (when X = CONH₂, 10 mmol) and ammonium acetate (7 mmol) were thoroughly mixed with silica (2 g) in an agate mortar. The resulting fine powder was transferred to a flask (50 mL) connected with refluxing equipment. After irradiation for several minutes, the reaction mixture was cooled to room temperature and washed with ethanol. The solvents were removed under reduced pressure. The crude products were purified by recrystallization from 95% EtOH to give **3**, **4** or **5**.

Selected spectral data

3 M. p. 128—129 °C; ¹H NMR (CDCl₃) δ: 1.02 (s, 3H, CH₃), 1.09 (s, 3H, CH₃), 1.21 (t, *J* = 7.11 Hz, 3H, CH₃), 2.25 (s, 2H, CH₂), 2.41 (s, 2H, CH₂), 4.10 (q, *J* = 7.05 Hz, 2H, CH₂), 4.98 (s, 1H, CH), 6.27 (brs, 2H, NH₂), 6.05—7.17 (m, 3H, furanH); IR (KBr) ν: 3452, 3321, 1696, 1660 cm⁻¹. Anal. calcd for C₁₈H₂₁NO₅: C 65.24, H 6.39, N 4.22; found C 65.32, H 6.44, N 3.99.

4 M. p. 150—152 °C; ¹H NMR (CDCl₃) δ: 1.07 (s, 3H, CH₃), 1.11 (s, 3H, CH₃), 2.16—2.24 (m, 2H, CH₂), 2.45 (s, 2H, CH₂), 4.64 (s, 2H, NH₂), 4.90 (s, 1H, CH), 7.03—7.52 (m, 4H, ArH); IR (KBr) ν: 3394, 3282, 2197, 1649 cm⁻¹.

Anal. calcd for $C_{18}H_{17}BrN_2O_2$: C 57.91, H 4.56, N 7.51; found C 57.98, H 4.47, N 7.48.

5 M. p. 296—298 °C, 1H NMR ($DCCl_3$) δ : 0.93 (s, 6H, 2CH₃), 1.05 (s, 6H, 2CH₃), 2.21—2.25 (m, 8H, 4CH), 5.06 (s, 1H, CH), 7.12—7.32

(m, 4H, ArH), 7.72 (s, 1H, NH); IR (KBr) ν : 3383 (NH), 1623 (C=O), 1603 cm^{-1} (N-C=O). Anal. calcd for $C_{23}H_{26}ClNO_2$: C 71.96, H 6.83, N 3.65; found C 72.03, H 6.72, N 3.50.

Table 1 Crystallographic data for **3**, **4** and **5**

Crystallographic parameter	3	4	5
Molecular formula	$C_{18}H_{18}N_2O_2$	$C_{18}H_{21}NO_5$	$C_{23}H_{26}ClNO_2$
Formula weight	294.34	332.36	383.90
Crystal system	monoclinic	triclinic	orthorhombic
Space group	$P2_1/c$	$P\bar{1}$	$Pna2_1$
<i>a</i> (nm)	1.1307(1)	1.1232(2)	1.4125(3)
<i>b</i> (nm)	0.9475(1)	1.3048(2)	1.4118(3)
<i>c</i> (nm)	1.492(2)	1.3274(3)	1.0719(2)
α (°)		105.730(1)	
β (°)	99.340(1)	95.68(2)	
γ (°)		109.56(1)	
<i>V</i> (nm ³)	1.5771(3)	1.7254(6)	2.1375(7)
<i>Z</i>	4	2	4
<i>D_c</i> (g/cm ³)	1.240	1.276	1.193
λ (Mo K α) (nm)	0.071073	0.071073	0.071073
μ (mm ⁻¹)	0.082	0.083	0.20
<i>F</i> (000)	624	704	816
θ (°)	1.83 to 25.00		2.0 to 25.0
Final <i>R</i> indices	<i>R</i> = 0.0381, <i>wR</i> = 0.0961	<i>R</i> = 0.0431, <i>wR</i> = 0.0973	<i>R</i> = 0.051, <i>wR</i> = 0.208
Goodness-of fit	1.021	0.937	1.03
Largest difference peak and hole (e/nm ³)	186 and -135	186 and -188	340 and -320

Table 2 Synthetic data of **3**, **4** and **5**

Entry	Ar	Time (min)	m. p. (lit. °C)	Yield (%)	Product
1	C ₆ H ₅	4	146—148	76	3a
2	2-Furyl	5	128—129	87	3b
3	2-ClC ₆ H ₄	7	166—168	90	3c
4	4-ClC ₆ H ₄	6	149—150	75	3d
5	3,4-(OCH ₂ O)C ₆ H ₃	8	142—144	82	3e
6	3-O ₂ NC ₆ H ₄	7	172—174	86	3f
7	3,4-(CH ₃ O) ₂ C ₆ H ₃	7	155—157	80	3g
8	4-BrC ₆ H ₄	6	160—162	80	3h
9	C ₆ H ₅	3	232—233	91	4a
10	2-BrC ₆ H ₄	2	150—152	92	4b
11	4-BrC ₆ H ₄	2	196—198	96	4c
12	2-O ₂ NC ₆ H ₄	2	220—222	89	4d
13	4-(CH ₃) ₂ NC ₆ H ₄	4	208—210	90	4e
14	4-HOC ₆ H ₄	4	206—208	89	4f
15	3-HO-4-CH ₃ OC ₆ H ₃	3	228—230	92	4g
16	C ₆ H ₅	5	190—192 (190—192) ⁵	90	5a
17	2-ClC ₆ H ₄	4	221—223 (222—224) ⁶	85	5b
18	4-ClC ₆ H ₄	4	296—298	92	5c
19	4-(CH ₃) ₂ NC ₆ H ₄	7	263—265 (264—266) ⁵	91	5d
20	3-O ₂ NC ₆ H ₄	4	283—285 (285—286) ⁶	83	5e
21	3,4-(CH ₃ O) ₂ C ₆ H ₃	6	258—260	89	5f
22	3,4-(OCH ₂ O)C ₆ H ₃	6	324—326	91	5g
23	4-CH ₃ OC ₆ H ₄	7	269—270 (270—272) ⁵	89	5h

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(E0109131 SONG, J. P.; DONG, H. Z.)