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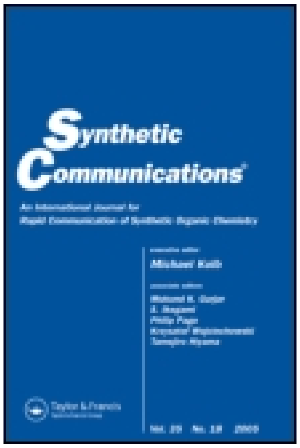

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A FACILE ONE POT SYNTHESIS OF PYRANO[2,3-*c*]PYRAZOLE DERIVATIVES UNDER MICROWAVE IRRADIATION

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ABSTRACT

A series of substituted pyrano[2,3-*c*]pyrazole derivatives were synthesized by the one pot reaction of aromatic aldehydes, malononitrile and 3-methyl-1-phenyl-2-pyrazolin-5-one under microwave irradiation in good yields.

Polyfunctionalized 4H-pyrans are a common structural unit in a number of natural products,[1] 4H-pyrans ring can be transformed to pyridine systems related to pharmacologically important calcium antagonists of the DHP type.[2–4] Substituted pyrazoles and condensed pyrazoles are important

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as pharmaceuticals[5,6] and biodegradable agrochemicals.[7,8] However, the synthesis of variety of substituted condensed pyrano[2,3-*c*]pyrazole derivatives were carried out by traditional heating with long time.[9,10]

Recently, the rate enhancement and wide applicability of microwave heating organic synthesis has been reviewed.[11,12] In our laboratory, we have researchered a facile synthesis of arylidenecyclo-alka[*b*]2-amino-4-aryl-3-cyano-4H-pyrans by the one pot reaction of malononitrile with 2,4-bisarylidenecyclopentanone or 2,6-bisarylidenecyclohexanone using piperidine as catalyst under microwave irradiation.[13] In this paper, we would like to report the synthesis of substituted condensed pyrano[2,3-*c*]pyrazole derivatives by the one pot reaction of aromatic aldehydes, malononitrile and 3-methyl-1-phenyl-2-pyrazolin-5-one under microwave irradiation. The reactions were generally finished in 2–8 min with good yields and easy work-up (Table 1).

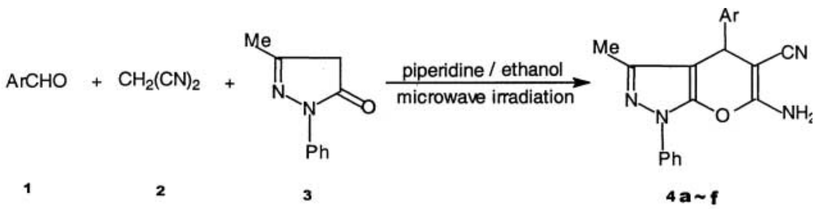
The synthetic route is shown as following (Sch. 1):

All of title compounds were characterized on the base of spectral data and elemental analysis. Also the product of **4d** were further confirmed by MS spectra.

Table 1. The Reaction Times and Yields of Compounds **4a–f**

Compounds	Ar	Reaction Time (min)	Yield (%)*
4a	C_6H_5	8	61
4b	$4\text{-}ClC_6H_4$	5	91
4c	$4\text{-}BrC_6H_4$	5	80
4d	$4\text{-}O_2NC_6H_4$	3	75
4e	$3\text{-}O_2NC_6H_4$	3	73
4f	$4\text{-}CH_3OC_6H_4$	2	66

*Yields of the isolated products.



a: Ar = C_6H_5; b: Ar = *4*-ClC_6H_4; c: Ar = *4*-BrC_6H_4;
d: Ar = *4*-$O_2NC_6H_4$; e: Ar = *3*-$O_2NC_6H_4$; f: Ar = *4*-$CH_3OC_6H_4$

Scheme 1.

EXPERIMENTAL

Melting points were determined in open capillaries and uncorrected. IR spectra were recorded on a Nicolet FT-IR 5DX instrument. ^{1}H NMR were measured on a Bruker 300 MHz spectrometer in $CDCl_3$ with TMS as internal standard. MS spectra were recorded on a VGZAB-HS (FAB). Elemental analyzer were determined using Perkin-Elmer 240 C elemental analyzer. The reactions were carried out with a modified commercial microwave oven (Sanle WP650D 650 w) under atmospheric pressure.

General Procedure for Pyrano[2,3-*c*]pyrazole Derivatives

Into an Erlenmeyer flask (25 mL) equipped with reflux condenser were introduced the aromatic aldehyde **1** (1 mmol), malononitrile **2** (1 mmol), 3-methyl-2-phenyl-2-pyrazolin-5-one **3** (1 mmol), dry ethanol (3 mL), and piperidine (0.05 mL). After irradiation with microwaves for 2–8 min (monitored by TLC), the reaction mixture was cooled. The precipitate was collected by suction filtration and washed with cold ethanol. The crude product was recrystallized from ethanol to give a pure sample. Specific details on each product are as follows:

4a: White solid, m.p. 168–170°C (167–168°C).[10] ^{1}H NMR (CD_3Cl) δ: 1.94 (s, 3H, CH_3), 4.69 (s, 1H, 4-H), 4.74 (br, s, 2H, NH_2), 7.75–7.31 (m, 10H, ArH). IR (KBr): 3450, 3320, 2200, 1660, 1590 cm^{-1}. Anal. calcd. for $C_{20}H_{16}N_4O$ (%): C, 60.98; H, 4.88; N, 17.07. Found: C, 60.70; H, 4.84; N, 16.95.

4b: White solid, m.p. 174–175°C (186–187°C).[10] ^{1}H NMR (CD_3Cl) δ: 1.95 (s, 3H, CH_3), 4.68 (s, 1H, 4-H), 4.75 (br, s, 2H, NH_2), 7.78–7.33 (m, 9H, ArH). IR (KBr): 3420, 3360, 2200, 1680, 1600 cm^{-1}. Anal. calcd. for $C_{20}H_{15}ClN_4O$ (%): C, 55.17; H, 4.14; N, 15.45. Found: C, 54.95; H, 4.10; N, 15.35.

4c: White solid, m.p. 183–184°C (184–185°C).[10] ^{1}H NMR (CD_3Cl) δ: 1.94 (s, 3H, CH_3), 4.70 (s, 1H, 4-H), 4.78 (br, s, 2H, NH_2), 7.71–7.30 (m, 9H, ArH). IR (KBr): 3420, 3360, 2200, 1680, 1600 cm^{-1}. Anal. calcd. for $C_{20}H_{15}BrN_4O$ (%): C, 58.68; H, 3.67; N, 13.69. Found: C, 58.45; H, 3.61; N, 15.23.

4d: White solid, m.p. 194–196°C. ^{1}H NMR (CD_3Cl) δ: 1.93 (s, 3H, CH_3), 4.77 (s, 1H, 4-H), 4.84 (br, s, 2H, NH_2), 8.20–7.35 (m, 9H, ArH). IR (KBr): 3420, 3330, 2200, 1680, 1600 cm^{-1}. Ms m/e: 373 (m + 1). Anal. calcd. for $C_{20}H_{15}N_5O_3$ (%): C, 64.34; H, 4.02; N, 18.77. Found: C, 64.02; H, 3.95; N, 18.66.

4e: White solid, m.p. 188–190°C (178–179°C).[10] ^{1}H NMR (CD_3Cl) δ: 1.93 (s, 3H, CH_3), 4.76 (s, 1H, 4-H), 4.88 (br, s, 2H, NH_2), 8.20–7.34 (m, 9H, ArH). IR (KBr): 3420, 3330, 2200, 1680, 1600 cm^{-1}. Anal. calcd. for $C_{20}H_{15}N_5O_3$ (%): C, 64.34; H, 4.02; N, 18.77. Found: C, 64.01; H, 3.95; N, 18.64.

4f: White solid, m.p. 170–172°C (177–178°C).[10] ^{1}H NMR (CD_3Cl) δ: 1.92 (s, 3H, CH_3), 4.68 (s, 1H, 4-H), 4.76 (br, s, 2H, NH_2), 7.63–7.28 (m, 9H, ArH). IR (KBr): 3450, 3320, 2200, 1660, 1600 cm^{-1}. Anal. calcd. for $C_{20}H_{18}N_4O_2$ (%): C, 70.39; H, 5.03; N, 18.87. Found: C, 70.02; H, 4.99; N, 18.62.

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