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Synthesis and Herbicidal Activity of 2-Alkyl(aryl)-3-methylsulfonyl(sulfinyl)pyrano-[4,3-*c*]pyrazol-4(2*H*)-ones

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ABSTRACT: *Useful oxidation reaction of 2-alkyl-(aryl)-3-methylthiopyrano[4,3-c]pyrazol-4(2H)-ones, leading to either the corresponding sulfoxides or sulfones, using hydrogen peroxide and acetic acid in 1,2-dichloroethane, is described. Bioassay results showed that the products have some herbicidal activity.* © 2005 Wiley Periodicals, Inc. Heteroatom Chem 16:255–258, 2005; Published online in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/hc.20067

INTRODUCTION

We previously found that 3-(bis-methylthio)methylene-5,6-dihydro-6-methyl-2*H*-pyran-2,4-diones have interesting herbicidal activity. Considering good herbicidal activity of some pyrazole compounds, we combined β-keto-δ-valerolactone and pyrazole and hoped to find better lead compounds of herbicide. We have reported that the reaction of 5,6-dihydro-2*H*-pyran-2,4-dione-3-dithioacetals with (un)substituted hydrazines affords 2-alkyl(aryl)-3-methylthiopyrano[4,3-*c*]pyrazol-4(2*H*)-ones [1,2] (**1**), and we were interested in oxidation of 2-alkyl(aryl)-3-methylthiopyrano[4,3-*c*]pyrazol-4(2*H*)-ones and testing the herbicidal activity of title compounds.

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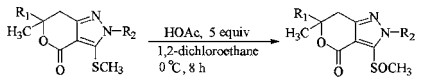
Various oxidative methods have been used for the preparation of sulfoxides or sulfones from the corresponding sulfides [3–7]. However, only few of them permit the oxidation in a selective manner. The simplest procedure for oxidation of sulfides to sulfoxides or sulfones involves hydrogen peroxide and acetic acid as the oxidative reagent. It was reported that it is necessary to use them in equivalent amounts with respect to sulfide in order to avoid the overoxidation. In our experiments, we used five equivalent amounts of hydrogen peroxide and acetic acid in 1,2-dichloroethane to oxidize the corresponding sulfides, and sulfoxides or sulfones were obtained respectively by controlling the oxidation temperature.

RESULTS AND DISCUSSION

2-Alkyl(aryl)-3-methylsulfinylpyrano[4,3-*c*]pyrazol-4(2*H*)-ones (**2a–i**) were prepared from 2-alkyl(aryl)-3-methylthiopyrano[4,3-*c*]pyrazol-4(2*H*)-ones (**1a–i**) [1]. The process is displayed in Scheme 1. At first, we failed to separate 2-alkyl(aryl)-3-methylsulfinylpyrano[4,3-*c*]pyrazol-4(2*H*)-ones by flash column chromatography because sulfoxides and sulfones were obtained at the same time and they have similar polarity, but sulfoxides or sulfones were obtained respectively by controlling the reaction condition and using 1,2-dichloroethane as the solvent.

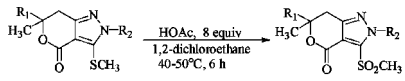
2-Alkyl(aryl)-3-methylsulfinylpyrano[4,3-*c*]pyrazol-4(2*H*)-ones (**2a–i**) were obtained in high yields (80–96%) (Table 1) by oxidizing the corresponding



1a-i **2a-i**

R_1 = H, Ph, Piperonyl, R_2 = H, CH_3, Ph, SO_2Ph.

SCHEME 1



1a-i **3a-i**

R_1 = H, Ph, Piperonyl, R_2 = H, CH_3, Ph, SO_2Ph.

SCHEME 2

sulfides with five equivalents of hydrogen peroxide-acetic acid in 1,2-dichloroethane at a temperature of 0°C for 8 h. In order to avoid overoxidation, low temperature is necessary.

2-Alkyl(aryl)-3-methylsulfonyl-pyrano[4,3-*c*] pyrazol-4(2*H*)-ones (**3a–i**) were prepared by the processes described in Schemes 2 and 3. Two different routes could be expected to lead to the required sulfones. Sulfones can be obtained in better yields (65–96%) (Table 2) by oxidizing the corresponding sulfides with eight equivalents of hydrogen peroxide-acetic acid in 1,2-dichloroethane at the temperature of 40°C for 6 h. On the other hand, we also got sulfones by over oxidation of sulfoxides (Scheme 3). Lower yields may result when water solubility of the product is higher.

The ^{1}H NMR spectra were consistent with the structure of new 2-alkyl(aryl)-3-methylsulfonyl-(sulfinyl)-pyrano[4,3-*c*]pyrazol-4(2*H*)-ones. A singlet of methylsulfinyl was shifted from higher field to lower field when the oxidation products were sulfones. When considering the advantages of hydrogen peroxide-acetic acid in 1,2-dichloroethane, overoxidation could be avoided and mild conditions could be employed.

Compounds **2** were tested in soil treatment against many herbs such as *Polygonum tataricum*, *Digitaria sanguinalis*, *Portulaca oleracea*, *Medicago sativa*, and *Rape* at 1.5 kg/ha. The bioassay results showed that they have some herbicidal activity. Especially, the inhibitory rate of **2g** toward *Portulaca oleracea* was 81.1% (Table 3). Considering the low-herbicidal activity of compound **3b**, we did not test the herbicidal activity of other compounds.

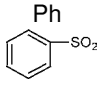
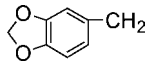
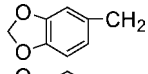
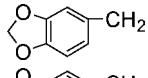
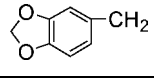
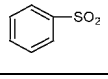
EXPERIMENTAL

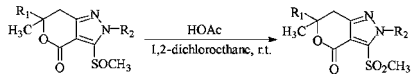
Melting points were conducted on a Yanaco MP-500 micromelting point apparatus. ^{1}H NMR spectra were recorded in $CDCl_3$ as solvent on AC-200 instrument using TMS as internal standard. Elemental analyses were performed on a Bruker MF-3 automatic elemental analyzer.

2-Alkyl(aryl)-3-methylsulfinyl-pyrano[4,3-c]-pyrazol-4(2H)-ones **2a–i**

2a: Compound **1a** (1.06 g, 0.005 mol) was dissolved in 20 mL 1,2-dichloroethane. With constant agitation, a solution of 2.9 g (0.025 mol, 30%) hydrogen

TABLE 1 Physical Data of Title Compounds **2a–i** and Elemental Analysis

					Elemental analysis % (Calcd, %)		
Compound **2**	R_1	R_2	*Yield (%)*	*mp (°C)*	*C*	*H*	*N*
a	H	CH_3	82	185–187	47.19 (47.36)	5.75 (5.30)	12.00 (12.27)
b	H	Ph	96	101–103	57.26 (57.92)	4.99 (4.86)	10.01 (9.65)
c	$PhCH_2$	H	86	123–125	59.12 (59.19)	4.90 (5.30)	9.45 (9.20)
d	$PhCH_2$	Ph	81	92.5–94	66.30 (66.30)	5.52 (5.30)	7.04 (7.36)
e	$PhCH_2$		93	85.5–86	56.52 (56.74)	4.58 (4.53)	6.35 (6.30)
f		H	88	204–206	55.23 (55.16)	4.62 (4.63)	8.09 (8.05)
g		CH_3	83	124–125	56.42 (56.34)	5.42 (5.01)	7.55 (7.73)
h		Ph	84	170–172	61.91 (62.25)	4.52 (4.75)	6.33 (6.60)
i			92	131–132	54.58 (54.09)	4.18 (4.13)	5.86 (5.74)



2a-i **3a-i**

R_1 = H, Ph, Piperonyl, R_2 = H, CH_3, Ph, SO_2Ph.

SCHEME 3

peroxide and 1.5 g (0.025 mol) acetic acid was added dropwise to the mixture, which was agitated for 8 h at a temperature of 0°C. After the agitation (monitored by TLC), the organic phase was separated and dried over anhydrous magnesium sulfate. After filtration, the solvent was evaporated in vacuo. The raw product was purified using *silica* gel column with ethyl acetate/petroleum ether (v/v, 1:1) as eluent and 0.93 g **2a** was obtained. Yield: 82%. mp 185–187°C. ^{1}H NMR ($CDCl_3$): 1.54 (d, 3H, J = 6.2, CH_3), 2.83 (m, 2H), 3.09 (s, 3H, $SOCH_3$), 4.22 (s, 3H, NCH_3), 4.75 (m, 1H).

2b: Following the above method and using 1.37 g **1b**, 1.39 g **2b** was obtained. Yield: 96%. mp 101–103°C. ^{1}H NMR ($CDCl_3$): 1.56 (d, 3H, J = 6.2, CH_3), 2.86 (m, 2H), 3.22 (s, 3H, $SOCH_3$), 4.75 (m, 1H), 7.51 (m, 5H).

2c: Following the above method and using 1.44 g **1c**, 1.30 g **2c** was obtained. Yield: 86%. mp 123–125°C. ^{1}H NMR ($CDCl_3$): 1.46 (s, 3H, CH_3), 3.03 (s, 2H, CH_2), 3.07 (m, 2H, CH_2), 3.11 (s, 3H, $SOCH_3$), 7.18 (m, 5H), 11.32 (bs, 1H, NH).

2d: Following the above method and using 1.82 g **1d**, 1.54 g **2d** was obtained. Yield: 81%. mp 92.5–94°C. ^{1}H NMR ($CDCl_3$): 1.53 (s, 3H, CH_3), 2.98 (s, 2H, CH_2), 3.05 (m, 2H, CH_2), 3.10 (s, 3H, $SOCH_3$), 7.20 (m, 5H), 7.49 (m, 5H).

2e: Following the above method and using 2.14 g **1e**, 2.06 g **2e** was obtained. Yield: 93%. mp 85.5–86°C. ^{1}H NMR ($CDCl_3$): 1.55 (s, 3H, CH_3), 2.91 (s, 2H, CH_2), 3.01 (m, 2H, CH_2), 3.33 (s, 3H, $SOCH_3$), 7.18 (m, 5H), 8.05 (m, 5H).

2f: Following the above method and using 1.66 g **1f**, 1.52 g **2f** was obtained. Yield: 88%. mp 204–206°C. ^{1}H NMR ($CDCl_3$): 1.45 (s, 3H, CH_3), 2.94 (s, 2H, CH_2), 3.06 (m, 2H, CH_2), 3.20 (s, 3H, $SOCH_3$), 5.88 (s, 2H, CH_2), 6.66 (m, 3H), 11.45 (bs, 1H).

2g: Following the above method and using 1.73 g **1g**, 1.49 g **2g** was obtained. Yield: 83%. mp 124–125°C. ^{1}H NMR ($CDCl_3$): 1.43 (s, 3H, CH_3), 2.88 (s, 2H, CH_2), 2.96 (m, 2H, CH_2), 3.08 (s, 3H, $SOCH_3$), 4.19 (s, 3H, NCH_3), 5.90 (s, 2H, CH_2), 6.68 (m, 3H).

2h: Following the above method and using 2.04 g **1h**, 1.78 g **2h** was obtained. Yield: 84%. mp 170–172°C. ^{1}H NMR ($CDCl_3$): 1.51 (s, 3H, CH_3), 2.88 (s, 2H, CH_2), 3.05 (m, 2H, CH_2), 3.14 (s, 3H, $SOCH_3$), 5.90 (s, 2H, CH_2), 6.62 (m, 3H), 7.48 (m, 5H).

2i: Following the above method and using 2.34 g **1i**, 2.22 g **2i** was obtained. Yield: 92%. mp 131–132°C. ^{1}H NMR ($CDCl_3$): 1.45 (s, 3H, CH_3), 2.88 (s, 2H, CH_2), 2.96 (s, 3H, $SOCH_3$), 3.25 (m, 2H, CH_2), 5.82 (s, 2H, CH_2), 6.52 (m, 3H), 7.68 (m, 5H).

2-Alkyl(aryl)-3-methylsulfonyl-pyrano[4,3-c]-pyrazol-4(2H)-ones **3a–i**

3a: Compound **1a** (1.06 g, 0.005 mol) was dissolved in 20 mL 1,2-dichloroethane. With constant agitation, a solution of 4.6 g (0.04 mol, 30%) hydrogen peroxide and 2.4 g (0.04 mol) acetic acid was added dropwise to the mixture, which was agitated for 6 h at a temperature of 40°C. After the agitation,

TABLE 2 Physical Data of Title Compounds **3a–i** and Elemental Analysis

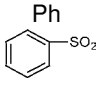
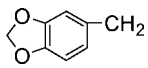
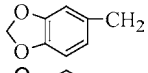
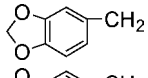
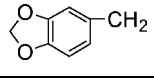
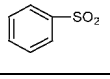
					Elemental analysis % (Calcd, %)		
Compound **3**	R_1	R_2	*Yield (%)*	*mp (°C)*	*C*	*H*	*N*
a	H	CH_3	96	155–157	44.34 (44.25)	4.93 (4.95)	11.3 (11.47)
b	H	Ph	92	148–150	54.78 (54.89)	4.71 (4.61)	10.10 (9.14)
c	$PhCH_2$	H	65	101–103	56.42 (56.24)	4.85 (5.03)	8.39 (8.74)
d	$PhCH_2$	Ph	83	99–101	63.58 (63.62)	5.37 (5.08)	7.12 (7.07)
e	$PhCH_2$		92	180–182	54.50 (54.77)	4.56 (4.38)	5.48 (6.08)
f		H	77	119–120	52.23 (52.74)	4.55 (4.43)	8.06 (7.69)
g		CH_3	68	126–127	53.41 (53.96)	4.84 (4.80)	7.54 (7.41)
h		Ph	89	165–167	60.05 (59.99)	4.33 (4.58)	6.51 (6.36)
i			93	186–188	52.67 (52.37)	4.32 (4.00)	5.56 (5.56)

TABLE 3 Inhibitory Rate (%) of Compounds **2** or **3** Against Many Herbs at 1.5 kg/ha (Soil Treatment)

Compound	*Polygonum tataricum*	*Digitaria sanguinalis*	*Portulaca oleracea*	*Medicago sativa*	*Rape*
2a	17.2	11.1	2.7	0	0
2c	0	0	0	12.6	0
2d	0	44.4	0	26.2	0
2f	15.6	11.1	0	0	17.6
2g	50	66.7	81.1	26.2	33.2
2h	1.6	0	5.4	9.8	0
2i	20.3	22.2	2.7	1.6	0
3b	11.0	0	0	7.1	0

the organic phase was separated off and dried over anhydrous magnesium sulfate. After filtration, the solvent was evaporated in vacuo. The raw product was purified using *silica* gel column with ethyl acetate/petroleum ether (v/v, 1:2) as eluent and 1.17 g **3a** was obtained. Yield: 96%. mp 155–157°C. ^{1}H NMR ($CDCl_3$): 1.53 (d, 3H, $J = 6.2$, CH_3), 2.82 (m, 2H), 3.54 (s, 3H, SO_2CH_3), 4.21 (s, 3H, NCH_3), 4.80 (m, 1H).

3b: Following the above method and using 1.37 g **1b**, 1.40 g **3b** was obtained. Yield: 92%. mp 148–150°C. ^{1}H NMR ($CDCl_3$): 1.56 (d, 3H, $J = 6.2$, CH_3), 3.05 (m, 2H), 3.46 (s, 3H, SO_2CH_3), 4.73 (m, 1H), 7.52 (m, 5H).

3c: Following the above method and using 1.44 g **1c**, 1.04 g **3c** was obtained. Yield: 65%. mp 101–103°C. ^{1}H NMR ($CDCl_3$): 1.50 (s, 3H, CH_3), 3.01 (m, 2H), 3.15 (s, 2H), 3.42 (s, 3H, SO_2CH_3), 6.43 (bs, 1H), 7.22 (m, 5H).

3d: Following the above method and using 1.82 g **1d**, 1.64 g **3d** was obtained. Yield: 83%. mp 99–101°C. ^{1}H NMR ($CDCl_3$): 1.56 (s, 3H, CH_3), 3.02 (s, 2H, CH_2), 3.12 (m, 2H, CH_2), 3.45 (s, 3H, SO_2CH_3), 7.12 (m, 5H), 7.55 (m, 5H).

3e: Following the above method and using 2.14 g **1e**, 2.11 g **3e** was obtained. Yield: 92%. mp 180–182°C. ^{1}H NMR ($CDCl_3$): 1.54 (s, 3H, CH_3), 3.00 (m, 2H, CH_2), 3.10 (s, 2H, CH_2), 3.33 (s, 3H, SO_2CH_3), 7.17 (m, 5H), 7.66 (m, 5H).

3f: Following the above method and using 1.66 g **1f**, 1.40 g **3f** was obtained. Yield: 77%. mp 119–120°C. ^{1}H NMR ($CDCl_3$): 1.49 (s, 3H, CH_3), 2.94 (s, 2H, CH_2), 3.15 (m, 2H, CH_2), 3.43 (s, 3H, SO_2CH_3), 5.86 (s, 2H, CH_2), 6.64 (m, 3H), 13.17 (bs, 1H, NH).

3g: Following the above method and using 1.73 g **1g**, 1.28 g **3g** was obtained. Yield: 68%. 126–127°C. ^{1}H NMR ($CDCl_3$): 1.40 (s, 3H, CH_3), 2.79 (s, 2H, CH_2), 2.93 (m, 2H, CH_2), 3.49 (s, 3H, SO_2CH_3), 4.15 (s, 3H, NCH_3), 5.87 (s, 2H, CH_2), 6.63 (m, 3H).

3h: Following the above method and using 2.04 g **1h**, 1.95 g **3h** was obtained. Yield: 89%. mp 165–167°C. ^{1}H NMR ($CDCl_3$): 1.45 (s, 3H, CH_3), 2.72 (s, 2H, CH_2), 2.97 (m, 2H, CH_2), 3.34 (s, 3H, SO_2CH_3), 5.82 (s, 2H, CH_2), 6.48 (m, 3H), 7.40 (m, 5H).

3i: Following the above method and using 2.34 g **1i**, 2.32 g **3i** was obtained. Yield: 93%. mp 186–188°C. ^{1}H NMR ($CDCl_3$): 1.54 (s, 3H, CH_3), 2.90 (s, 2H, CH_2), 3.01 (s, 2H, CH_2), 3.33 (s, 3H, SO_2CH_3), 5.90 (s, 2H, CH_2), 6.51 (m, 3H), 7.78 (m, 5H).

REFERENCES

[1] Li, Y. X.; Wang, Y. M.; Yang, X. P.; Wang, S. H.; Li, Z. M. Heteroatom Chem 2003, 14(4), 342.
[2] Li, Y. X.; Wang, Y. M.; Yang, X. P.; Wang, S. H.; Li, Z. M. Chin Chem Lett 2004, 15(1), 14.
[3] Drabowicz, J.; Mikoajczyk, M. Synth Commun 1981, 11(12), 1025.
[4] Tarbell, D. S.; Weaver, C. J Am Chem Soc 1941, 63, 2939.
[5] Overberger, C. G.; Cummins, R. W. J Am Chem Soc 1953, 75, 4250.
[6] Curci, R.; Giovine, A.; Modena, G. Tetrahedron 1966, 22, 1235.
[7] Carpion, L. A.; Chen, H. W. J Am Chem Soc 1979, 101, 390.