

## Oxidative Cyclization of 3-(3-Heterocycle-substituted 2-Propenoyl)tropolones

Masaaki HONDA and Kimiaki IMAFUKU\*

Department of Chemistry, Faculty of Science, Kumamoto University, Kurokami, Kumamoto 860

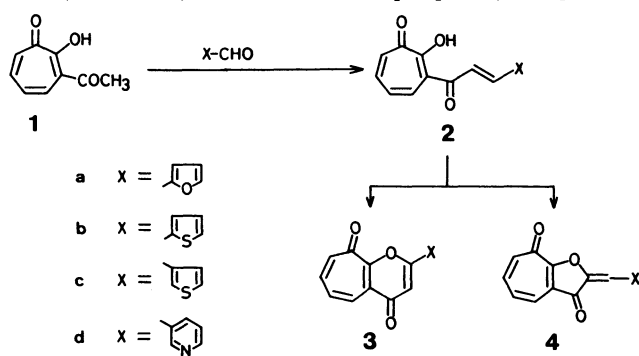
(Received August 11, 1984)

3-[3-(2-Furyl)-2-propenoyl]- (2a), 3-[3-(2-thienyl)-2-propenoyl]- (2b), 3-[3-(3-thienyl)-2-propenoyl]- (2c), and 3-[3-(3-pyridyl)-2-propenoyl]tropolone (2d) were prepared by the condensation of 3-acetyltropolone with the corresponding heterocyclic aldehydes. The compounds 2a—d were oxidized with selenium dioxide to afford 2-heterocycle-substituted cyclohepta[b]pyran-4,9-diones, while oxidation with both alkaline hydrogen peroxide and 2,3-dichloro-5,6-dicyano-*p*-benzoquinone gave 2-(heterocycle-substituted methylene)-2*H*-cyclohepta[b]furan-3,8-diones.

Previously, we reported that 3-cinnamoyltropolones were oxidized with selenium dioxide,<sup>1)</sup> alkaline hydrogen peroxide,<sup>2)</sup> and 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ)<sup>3)</sup> to afford flavonoid-like compounds. The present paper deals with the synthesis and oxidative cyclization of 3-(2-propenoyl)tropolones having a five- or six-membered heterocyclic ring at 3-position on the 2-propenoyl group and the effects of the heterocyclic ring on the cyclization.

## Results and Discussion

**Synthesis.** 3-Acetyltropolone (1) reacted with heterocyclic aldehydes at room temperature in the presence of potassium hydroxide solution to afford each of 3-(3-heterocycle-substituted 2-propenoyl)tropolones



Scheme 1.

TABLE I. CHARACTERISTICS FOR 3-(2-PROPENOYL)TROPOLONES (2a—d)

Compd	Yield	Mp	IR (CHCl <sub>3</sub> )	UV (CH <sub>3</sub> OH)	NMR (CDCl <sub>3</sub> )	Analysis (%)
	%	$\theta_m/^\circ\text{C}$	cm <sup>-1</sup>	$\lambda/\text{nm}(\log \epsilon)$	$\delta$	Found (Calcd)
2a	46	139—140	1710 1630	243 (4.51) 331 (4.47)	6.4—6.6 (1H, m) 6.7—7.9 (9H, m)	C <sub>14</sub> H <sub>10</sub> O <sub>4</sub> C 69.53 (69.42) H 4.25 (4.16)
2b	61	187—189	1675 1600	242 (4.34) 330 (4.28)	6.9—7.9 (10H, m)	C <sub>14</sub> H <sub>10</sub> O <sub>3</sub> S C 65.10 (65.10) H 3.61 (3.90)
2c	83	173—174	1670 1600	240 (4.40) 315 (4.24)	6.8—7.8 (10H, m)	C <sub>14</sub> H <sub>10</sub> O <sub>3</sub> S C 65.40 (65.10) H 3.86 (3.90)
2d	56	184—185	1690 <sup>a)</sup> 1605	245 (4.50) 305 (4.37) 360 (3.83)	4.8—6.0 (1H, br) <sup>b)</sup> 6.6—7.6 (6H, m) 7.6—7.8 (1H, m) 8.0—8.3 (1H, m) 8.5—8.7 (1H, m) 8.8—9.0 (1H, m)	C <sub>15</sub> H <sub>11</sub> NO <sub>3</sub> C 71.37 (71.14) H 4.42 (4.38) N 5.60 (5.53)

a) KBr. b) DMSO-*d*<sub>6</sub>.

(2a—d). Their structures were established by the spectral data and elemental analysis, which are summarized in Table 1.

**Oxidation with Selenium Dioxide.** In flavonoid chemistry, Mahal *et al.* found that 2'-hydroxychalcones were oxidized with selenium dioxide to give flavones.<sup>4)</sup>

When a solution of 3-(3-heterocycle-substituted 2-propenoyl)tropolones (2a—c) in dioxane were refluxed in the presence of selenium dioxide, 2-heterocycle-substituted cyclohepta[b]pyran-4,9-diones (3a—c) were isolated. Their structures were determined by the spectral data and elemental analysis, which are summarized in Table 2.

The reaction of 2d, which has a pyridine ring, did not give a desired product but a tarry material. The variation of the reaction conditions, such as molar ratio, solvent, reaction time, *etc.*, did not improve the reaction.

**Oxidation with Alkaline Hydrogen Peroxide.** It is well known that 2'-hydroxychalcones are oxidized with alkaline hydrogen peroxide to give the corresponding flavonols (Algar-Flynn-Oyamada reaction)<sup>5,6)</sup> and that, if a methoxyl group is present at the 6'-position of the chalcones, aurones rather than flavonols are obtained.<sup>7)</sup> In troponoid, we found that 3-cinnamoyltropolones were oxidized with alkaline hydrogen peroxide to give 2-arylmethylene-2*H*-cyclohepta[b]furan-3,8-diones.<sup>2)</sup>

TABLE 2. CHARACTERISTICS FOR THE PRODUCTS (3a—c)

Compd	Yield		Mp $\theta_m/^\circ\text{C}$	IR (CHCl <sub>3</sub> ) cm <sup>-1</sup>	UV (CH <sub>3</sub> OH) $\lambda/\text{nm}(\log \epsilon)$	NMR (CDCl <sub>3</sub> ) $\delta$	Analysis (%) Found (Calcd)
	%						
3a	31		210—211	1638 1602	255 (4.25) 327 (4.42)	6.6—6.9 (1H, m) 6.92 (1H, s) 7.0—8.3 (6H, m)	<i>m/z</i> M <sup>+</sup> for C <sub>14</sub> H <sub>8</sub> O <sub>4</sub> 240.0422 (240.0422)
3b	54		211—212	1640 1600	257 (4.30) 332 (4.42)	6.81 (1H, s) 6.9—8.2 (7H, m)	C <sub>14</sub> H <sub>8</sub> O <sub>3</sub> S C 65.71 (65.61) H 3.22 ( 3.15)
3c	56		212—214	1632 1598	223 (4.43) 253 (4.36) 317 (4.30)	6.91 (1H, s) 7.0—8.4 (7H, m)	<i>m/z</i> M <sup>+</sup> for C <sub>14</sub> H <sub>8</sub> O <sub>3</sub> S 256.0226 (256.0194)

TABLE 3. CHARACTERISTICS FOR THE PRODUCTS (4a—d)

Compd	Yield/%		Mp $\theta_m/^\circ\text{C}$	IR (CHCl <sub>3</sub> ) cm <sup>-1</sup>	UV (CH <sub>3</sub> OH) $\lambda/\text{nm}(\log \epsilon)$	NMR (CDCl <sub>3</sub> ) $\delta$	Analysis (%) Found (Calcd)
	H <sub>2</sub> O <sub>2</sub> Oxidn	DDQ Oxidn					
4a	37	45	211(dec)	1715 1645	235 (4.36) 282 (4.08) 395 (4.22) 440 (4.28)	6.5—6.8 (1H, m) 7.0—7.8 (7H, m)	C <sub>14</sub> H <sub>8</sub> O <sub>4</sub> C 69.68 (70.00) H 3.35 ( 3.36)
4b	12	33	191—192	1710 1640	230 (4.32) 285 (4.05) 391 (4.16) 446 (4.28)	6.8—8.0 (8H, m)	C <sub>14</sub> H <sub>8</sub> O <sub>3</sub> S C 65.77 (65.61) H 3.19 ( 3.15)
4c	42	15	214—215	1710 1650	228 (4.34) 290 (4.01) 375 (3.96) 423 (3.83)	6.7—8.3 (8H, m)	C <sub>14</sub> H <sub>8</sub> O <sub>3</sub> S C 65.67 (65.61) H 3.32 ( 3.15)
4d	7	8	230(dec)	1710 1645	228 (4.51) 274 (4.24) 368 (4.25) 412 (4.08)	7.0—8.0 (6H, m) 8.3—9.1 (3H, m)	<i>m/z</i> M <sup>+</sup> for C <sub>15</sub> H <sub>9</sub> NO <sub>3</sub> 251.0585 (251.0583)

When 3-(3-heterocycle-substituted 2-propenyl)tropolones (2a—d) were oxidized with hydrogen peroxide in the presence of sodium hydroxide, 2-(heterocycle-substituted methylene)-2*H*-cyclohepta[*b*]furan-3,8-diones (4a—d) were obtained. Their structures were determined by the spectral data and elemental analysis, which are summarized in Table 3.

In the reaction, large excess of hydrogen peroxide or alkali decreased the yields of the products. In addition, the heterocyclic aldehydes were detected in the reaction mixture by the NMR measurements.

**Oxidation with DDQ.** In dehydrocyclization of 3-cinnamoyltropolones with DDQ, we found that unsubstituted and 3-methoxy-substituted 3-cinnamoyltropolones gave the flavone-like compounds, while the other 2- and/or 4-methoxy-substituted ones gave aurone-like compound.<sup>9</sup> Thus, it was expected that  $\pi$ -rich five-membered heterocycle-substituted 3-(2-propenyl)tropolones might give the aurone-like products, while  $\pi$ -deficient six-membered heterocycle-substituted 3-(2-propenyl)tropolones might give the flavone-like products. However, a mixture of the compounds 2a—d and DDQ in dry benzene was refluxed to afford 4a—d in all the cases. The difference between the five- and six-membered heterocyclic ring was not observed.

## Experimental

The melting points were determined with a Yanagimoto MP-S2 apparatus and are uncorrected. The IR and UV spectra were taken on a JASCO IRA-1 and a Hitachi EPS-3T spectrophotometer, respectively. The NMR spectra were recorded with a Hitachi-Perkin-Elmer R-24 spectrometer (60 MHz). The high-resolution mass spectra were obtained with a JEOL DX-300 apparatus.

**3-(3-Heterocycle-substituted 2-Propenyl)tropolones (2a—d).** Potassium hydroxide solution (5%, 40 ml) was added to a mixture of 3-acetyltropolone (1) (1.6 g, 10 mmol) and heterocyclic aldehyde (20 mmol) in 50% aqueous methanol (60 ml). After stirring for 24 h at room temperature, the mixture was diluted with water (100 ml) and acidified with 3 M (1 M=1 moldm<sup>-3</sup>) hydrochloric acid to give a precipitate, which was recrystallized from ethanol to afford 3-(3-heterocycle-substituted 2-propenyl)tropolone (2a—d).

**Selenium Dioxide Oxidation.** A mixture of 2 (a, b, or c) (1.0 mmol) and selenium dioxide (584 mg, 5.0 mmol) in dioxane (10 ml) was refluxed for 36 h. The solvent was evaporated off, and the residue was diluted with ethanol (100 ml) and stirred for 2 h in the presence of Raney nickel (580 mg, 10 mmol). After filtration and removal of the ethanol, the residue was dissolved in chloroform, washed with a saturated sodium hydrogencarbonate solution and water, and dried over sodium sulfate. Evaporation residue was chromatographed on a Wakogel B-10 plate (30×30 cm) with diethyl ether and recrystallized from ethanol-dichloro-

methane to give 2-heterocycle-substituted cyclohepta[b]-pyran-4,9-dione (**3a—c**).

**Alkaline Hydrogen Peroxide Oxidation.** To a suspended solution of **2** (**a**, **b**, **c**, or **d**) (2.0 mmol) in ethanol (40 ml) was added 30% hydrogen peroxide (2 ml) under stirring at 0°C. After addition of 12% potassium hydroxide solution (10 ml), the stirring was continued for 5 h. The mixture was acidified with 3 M hydrochloric acid and extracted with chloroform. The extract was concentrated and chromatographed on a Wakogel B-10 plate (30×30 cm) with chloroform and recrystallized from benzene to give 2-(heterocycle-substituted methylene)-2H-cyclohepta[b]furan-3,8-dione (**4a—d**).

**DDQ Oxidation.** A mixture of **2** (**a**, **b**, **c**, or **d**) (1.0 mmol) and DDQ (450 mg, 2.0 mmol) in dry benzene (20 ml) was refluxed for 20 h. The reaction mixture was poured into a saturated sodium carbonate solution (100 ml) and extracted with chloroform. The extract was washed with water, dried over sodium sulfate, and brought to dryness by evaporation of the solvent. The residue was recrystallized from benzene to give **4a—d**.

We wish to thank Professor John F. W. McOmie,

University of Bristol, England, for his valuable suggestion. We are also grateful to Mr. Hiromichi Matsuura, Wakunaga Pharmaceutical Co., Ltd., Hiroshima, for his kind measurements of the high-resolution mass spectra.

#### References

- 1) K. Imafuku, A. Yamane, and H. Matsumura, *Yuki Gosei Kagaku Kyokai Shi*, **38**, 308 (1980).
- 2) K. Yamaguchi, K. Imafuku, and H. Matsumura, *Yuki Gosei Kagaku Kyokai Shi*, **38**, 998 (1980).
- 3) K. Imafuku and K. Yamaguchi, *Bull. Chem. Soc. Jpn.*, **54**, 2855 (1981).
- 4) H. S. Mahal, H. S. Rai, and K. Venkataraman, *J. Chem. Soc.*, **1935**, 966.
- 5) J. Algar and J. P. Flynn, *Proc. Roy. Irish Acad., (B)*, **42**, 1 (1934); *Chem. Abstr.*, **29**, 161 (1935).
- 6) T. Oyamada, *Nippon Kagaku Kaishi*, **55**, 1256 (1934).
- 7) T. A. Geissman and D. K. Fukushima, *J. Am. Chem. Soc.*, **70**, 1686 (1948).