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

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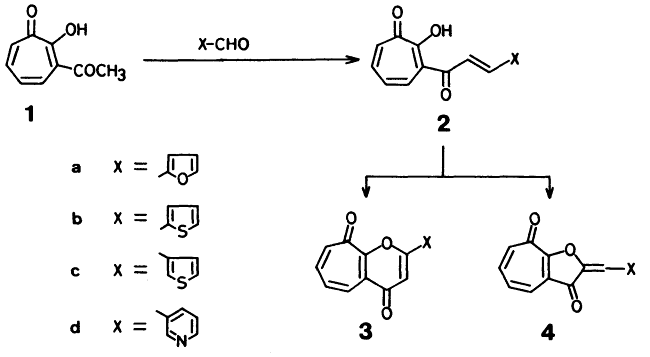
3-[3-(2-Furyl)-2-propenoyl]- (**2a**), 3-[3-(2-thienyl)-2-propenoyl]- (**2b**), 3-[3-(3-thienyl)-2-propenoyl]- (**2c**), and 3-[3-(3-pyridyl)-2-propenoyl]tropolone (**2d**) were prepared by the condensation of 3-acetyltropolone with the corresponding heterocyclic aldehydes. The compounds **2a—d** were 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,[1] alkaline hydrogen peroxide,[2] and 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ)[3] 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 (**2a—d**). Their structures were established by the spectral data and elemental analysis, which are summarized in Table 1.



Scheme 1.

Oxidation with Selenium Dioxide. In flavonoid chemistry, Mahal *et al.* found that 2′-hydroxychalcones were oxidized with selenium dioxide to give flavones.[4]

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)[5,6] and that, if a methoxyl group is present at the 6′-position of the chalcones, aurones rather than flavonols are obtained.[7] 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.[2]

Table 1. Characteristics for 3-(2-propenoyl)tropolones (**2a—d**)

Compd	Yield	Mp	IR ($CHCl_3$)	UV (CH_3OH)	NMR ($CDCl_3$)	Analysis (%)
	%	θ_m/°C	cm^{-1}	λ/nm(log ε)	δ	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)	$C_{14}H_{10}O_4$ 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)	$C_{14}H_{10}O_3S$ 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)	$C_{14}H_{10}O_3S$ C 65.40 (65.10) H 3.86 (3.90)
2d	56	184—185	1690[a)] 1605	245 (4.50) 305 (4.37) 360 (3.83)	4.8—6.0 (1H, br)[b)] 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)	$C_{15}H_{11}NO_3$ C 71.37 (71.14) H 4.42 (4.38) N 5.60 (5.53)

a) KBr. b) DMSO-d_6.

Table 2. Characteristics for the products (**3a**—**c**)

Compd	Yield	Mp	IR (CHCl$_3$)	UV (CH$_3$OH)	NMR (CDCl$_3$)	Analysis (%)
	%	θ_m/°C	cm^{-1}	λ/nm(log ε)	δ	Found (Calcd)
3a	31	210—211	1638	255 (4.25)	6.6—6.9 (1H, m)	m/z M$^+$ for $C_{14}H_8O_4$
			1602	327 (4.42)	6.92 (1H, s)	240.0422 (240.0422)
					7.0—8.3 (6H, m)	
3b	54	211—212	1640	257 (4.30)	6.81 (1H, s)	$C_{14}H_8O_3S$
			1600	332 (4.42)	6.9—8.2 (7H, m)	C 65.71 (65.61)
						H 3.22 (3.15)
3c	56	212—214	1632	223 (4.43)	6.91 (1H, s)	m/z M$^+$ for $C_{14}H_8O_3S$
			1598	253 (4.36)	7.0—8.4 (7H, m)	256.0226 (256.0194)
				317 (4.30)		

Table 3. Characteristics for the products (**4a**—**d**)

Compd	Yield/%		Mp	IR (CHCl$_3$)	UV (CH$_3$OH)	NMR (CDCl$_3$)	Analysis (%)
	H_2O_2 Oxidn	DDQ Oxidn	θ_m/°C	cm^{-1}	λ/nm(log ε)	δ	Found (Calcd)
4a	37	45	211(dec)	1715	235 (4.36)	6.5—6.8 (1H, m)	$C_{14}H_8O_4$
				1645	282 (4.08)	7.0—7.8 (7H, m)	C 69.68 (70.00)
					395 (4.22)		H 3.35 (3.36)
					440 (4.28)		
4b	12	33	191—192	1710	230 (4.32)	6.8—8.0 (8H, m)	$C_{14}H_8O_3S$
				1640	285 (4.05)		C 65.77 (65.61)
					391 (4.16)		H 3.19 (3.15)
					446 (4.28)		
4c	42	15	214—215	1710	228 (4.34)	6.7—8.3 (8H, m)	$C_{14}H_8O_3S$
				1650	290 (4.01)		C 65.67 (65.61)
					375 (3.96)		H 3.32 (3.15)
					423 (3.83)		
4d	7	8	230(dec)	1710	228 (4.51)	7.0—8.0 (6H, m)	m/z M$^+$ for $C_{15}H_9NO_3$
				1645	274 (4.24)	8.3—9.1 (3H, m)	251.0585 (251.0583)
					368 (4.25)		
					412 (4.08)		

When 3-(3-heterocycle-substituted 2-propenoyl)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 deterimed 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.[3] Thus, it was expected that π-rich five-membered heterocycle-substituted 3-(2-propenoyl)tropolones might give the aurone-like products, while π-defficient six-membered heterocycle-substituted 3-(2-propenoyl)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-Propenoyl)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 mol dm^{-3}) hydrochloric acid to give a precipitate, which was recrystallized from ethanol to afford 3-(3-heterocycle-substituted 2-propenoyl)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–dichloromethane 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 to give 2-(heterocycle-substituted methylene)-2*H*-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**.

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