Synthesis and Oxidative Cyclization of 3-(1-Cycloalkenyl)tropolones

Kimiaki IMAFUKU* and Kyoko INOUE

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

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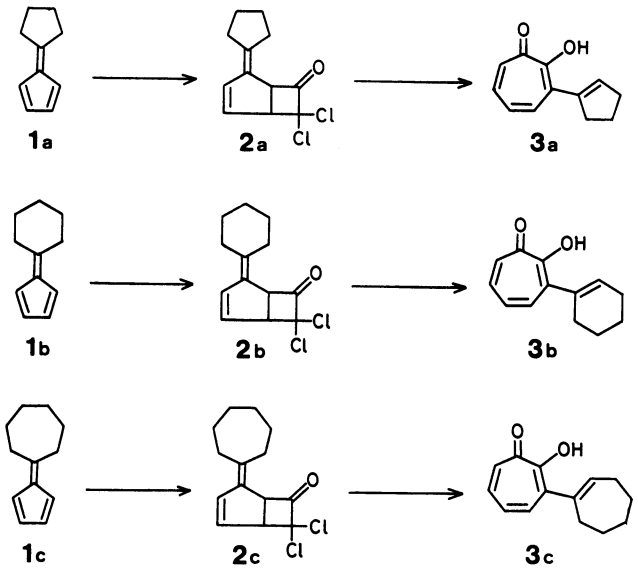
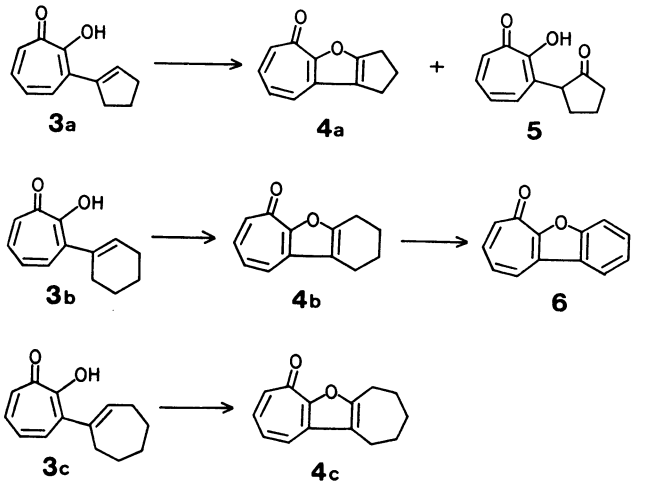
3-(1-Cyclopentenyl)-, 3-(1-cyclohexenyl)-, and 3-(1-cycloheptenyl)tropolones (**3a**, **3b**, and **3c**) were prepared by the hydrolysis of cycloadducts of dichloroketene to cyclopentylidene-, cyclohexylidene-, and cycloheptylidenecyclopentadiene, respectively. Compound **3a** was oxidized with performic acid to give 1,2,3,5-tetrahydrocyclohepta[*b*]cyclopenta[*d*]furan-5-one and 3-(2-oxocyclopentyl)tropolone. Oxidation of **3b** and **3c** gave 1,2,3,4-tetrahydro-6*H*-cyclohepta[*b*]benzofuran-6-one (**4b**) and 5,7,8,9,10,11-hexahydrodicyclohepta[*b*,*d*]furan-5-one, respectively. Dehydrogenation of **4b** with palladium catalyst gave 6*H*-cyclohepta[*b*]benzofuran-6-one.

Halogenated ketenes are versatile intermediates in organic synthesis.[1-3] In 1965, Stevens *et al.*[4,5] obtained tropolone in good yield by hydrolysis of the cyclopentadiene–dichloroketene adduct. This method is most interesting and useful synthetic method of tropolone and has been applied to synthesis of a variety of alkyl-substituted tropolones.[6-8] Hydrolysis of the fulvene–dichloroketene adducts also gave 3-alkenyltropolones.[9,10] These 3-alkenyltropolones were oxidized with peroxy acid or 2,3-dichloro-5,6-dicyano-1,4-benzoquinone to afford 8*H*-cyclohepta[*b*]furan-8-one.[10] On the other hand, hydrolysis of the spiro[2.4]hepta-4,6-diene–dichloroketene adduct gave 2,3-dihydro-8*H*-cyclohepta[*b*]furan-8-one.[11]



Scheme 1.



Scheme 2.

In this communication, we wish to report the synthesis of 3-(1-cycloalkenyl)tropolones by the hydrolysis of the cycloalkylidenecyclopentadiene–dichloroketene adducts and their oxidative cyclization with peroxy acid.

Results and Discussion

Synthesis of 3-(1-Cycloalkenyl)tropolones. The cycloaddition reaction of cyclopentylidenecyclopentadiene (**1a**)[12] with dichloroketene, produced *in situ* by the reaction of dichloroacetyl chloride with triethylamine, afforded a 1 : 1 adduct (**2a**) as a pale yellow oil. The IR spectrum shows a strong carbonyl absorption at 1800 cm^{-1}, which is reasonable for a cyclobutanone.[13] The assignment of the ^1H NMR spectrum was done in comparison with the spectra of 6,6-dimethyl-[9] and 6,6-diphenylfulvene–dichloroketene adducts.[14] The assignments are fit for the structure (**2a**): δ=1.5—2.0 (m, 4H, H-3′×2, H-4′×2), 2.1—2.6 (m, 4H, H-2′×2, H-5′×2), 3.95—4.20 (m, 1H, H-1), 4.62 (d, 1H, $J_{1,5}$=7.2 Hz, H-5), 5.8—6.0 (m, 1H, H-2), 6.49 (dd, 1H, $J_{2,3}$=6.0, $J_{1,3}$=1.8 Hz, H-3). Similarly, by the reactions of cyclohexylidenecyclopentadiene (**1b**)[12] and cycloheptylidenecyclopentadiene (**1c**) with dichloroketene, oily 1 : 1 adducts (**2b** and **2c**) were obtained, respectively. Their structures were also confirmed by the ^1H NMR spectral data.

Hydrolysis of the adduct (**2a**) with sodium hydroxide in aqueous acetic acid was carried out to give 3-(1-cyclopentenyl)tropolone (**3a**) in 26% yield. The ^1H NMR spectrum shows peaks at δ=1.7—2.3 (m, 2H, H-4′×2), 2.4—3.0 (m, 4H, H-3′×2, H-5′×2), 6.8—7.7 (m, 5H, H-2′,4,5,6,7), 9.50 (br, 1H, OH), supporting the structure. The elemental analysis also gave a satisfactory result. The adducts (**2b** and **2c**) were also hydrolyzed to afford 3-(1-cyclohexenyl)tropolone (**3b**) and 3-(1-cycloheptenyl)tropolone (**3c**) in 42 and 16% yields, respectively.

Oxidative Cyclization of 3-(1-Cycloalkenyl)tropolones with Peroxy Acid. Previously, we reported that the 3-alkenyltropolones were oxidized with peroxy acid or 2,3-dichloro-5,6-dicyano-1,4-benzoquinone to give 8*H*-cyclohepta[*b*]furan-8-one.[10]

3-(1-Cyclopentenyl)tropolone (**3a**) was oxidized with performic acid to give **4a** (mp 217—218 °C) and **5** (mp 97—99 °C) in 4.5 and 7.7% yields, respectively. From the elemental analysis and spectral data, the compound (**4a**) was assigned to 1,2,3,5-tetrahydrocyclohepta[*b*]cyclopenta[*d*]furan-5-one. This compound gave no coloration with iron(III) chloride. The IR spectrum shows a characteristic absorption at 1642 cm^{-1} for tropone carbonyl group. The ^1H NMR spectrum shows six protons at $\delta=2.3$—3.1 corresponding to three methylene groups in the five-membered ring and four protons for the aromatic seven-membered ring. On the other hand, the compound (**5**) was determined to be 3-(2-oxocyclopentyl)tropolone from its elemental analysis, spectral data, and coloration with iron(III) chloride. The IR spectrum shows a characteristic carbonyl absorption at 1745 cm^{-1} for a cyclopentanone. The ^1H NMR spectrum is also reasonable for the structure.

The 3-(1-cycloalkenyl)tropolones (**3b** and **3c**) were also oxidized with performic acid to afford 1,2,3,4-tetrahydro-6*H*-cyclohepta[*b*]benzofuran-6-one (**4b**) and 5,7,8,9,10,11-hexahydrodicyclohepta[*b*,*d*]furan-5-one(**4c**) in 38 and 26% yields, respectively. Their structures were determined by their elemental analysis and spectral data.

The compound (**4b**) was dehydrogenated with palladium catalyst to afford 6*H*-cyclohepta[*b*]benzofuran-6-one (**6**), which was confirmed by its elemental analysis and spectral data. The IR spectrum shows a tropone carbonyl absorption at 1635 cm^{-1}, the ^1H NMR spectrum showing aromatic protons as complex multiplet at $\delta=6.90$—8.05.

Experimental

The melting points were determined with a Yanagimoto MP-S2 melting-point measuring apparatus and are uncorrected. The IR spectra were taken on a JASCO IRA-1 spectrophotometer, the UV spectra on a Hitachi EPS-3T spectrophotometer. The ^1H NMR spectra were recorded with a Hitachi-Perkin-Elemer R-24 spectrometer (60 MHz).

*Cyclopentylidenecyclopentadiene (**1a**).* A mixture of cyclopentadiene (105 g, 1.6 mol) and cyclopentanone (143 g, 1.7 mol) was stirred overnight at room temperature in the presence of 40% methylamine solution (35 ml). The organic layer was washed with 1 M hydrochloric acid until the mixture was made slightly acidic. Then, the organic layer was washed with water and with saturated sodium chloride solution, dried over anhydrous sodium sulfate, and distilled under reduced pressure to give 77 g (36%) of cyclopentylidencyclopentadiene (**1a**) as an orange oil: bp 103—104 °C/18 Torr (lit,[12] 55—57 °C/2 Torr); NMR (CCl_4) $\delta=1.6$—1.9 (m, 4H), 2.5—2.9 (m, 4H), 6.20 (s, 4H).

*Cyclohexylidenecyclopentadiene (**1b**).* A mixture of cyclopentadiene (80 g, 1.2 mol) and cyclohexanone (127 g, 1.3 mol) was stirred overnight at room temperature in the presence of 40% methylamine solution (26 ml) and worked up, as mentioned above, to give 83 g (57%) of cyclohexylidenecyclopentadiene (**1b**) as an orange oil: bp 118—120 °C/17 Torr (lit,[12] 78—80 °C/2.5 Torr; NMR (CCl_4) $\delta=1.4$—1.9 (m, 6H), 2.3—2.8 (m, 4H), 6.36 (s, 4H).

*Cycloheptylidenecyclopentadiene (**1c**).* A mixture of cyclopentadiene (66 g, 1.0 mol) and cycloheptanone (134 g, 1.2 mol) was stirred overnight at room temperature in the presence of 40% methylamine (22 ml) and worked up, as mentioned above, to give 105 g (66%) of cycloheptylidenecyclopentadiene (**1c**) as an orange oil: bp 124—126 °C/18 Torr; NMR (CCl_4) $\delta=1.3$—1.9 (m, 8H), 2.2—2.9 (m, 4H), 6.2—6.5 (m, 4H).

*4-Cyclopentylidene-7,7-dichlorobicyclo[3.2.0]hept-2-en-6-one (**2a**).* A solution of triethylamine (56 g) in anhydrous hexane (500 ml) was added dropwise to a solution of **1a** (35 g) and dichloroacetyl chloride (41 g) in anhydrous hexane (700 ml) over a period of 3 h with stirring at room temperature. After additional stirring for 1 h, the mixture was allowed to stand overnight. The reaction mixture was washed with 1 M hydrochloric acid and with water, and dried over anhydrous sodium sulfate. After the evaporation of the solvent, the residue was distilled under reduced pressure to give 20 g (31%) of 4-cyclopentylidene-7,7-dichlorobicyclo[3.2.0]hept-2-en-6-one (**2a**) as a pale yellow oil: bp 125—127 °C/0.45 Torr; IR (neat) 1800 cm^{-1} (C=O); NMR (CCl_4) $\delta=1.5$—2.0 (m, 4H), 2.1—2.6 (m, 4H), 3.95—4.20 (m, 1H, H-1), 4.62 (d, 1H, $J_{1,5}=7.2$ Hz, H-5), 5.8—6.0 (m, 1H, H-2), 6.49 (dd, 1H, $J_{2,3}=6.0$, $J_{1,3}=1.8$ Hz, H-3).

*4-Cyclohexylidene-7,7-dichlorobicyclo[3.2.0]hept-2-en-6-one (**2b**).* A solution of triethylamine (40 g) in anhydrous hexane (250 ml) was added dropwise to a solution of **1b** (33 g) and dichloroacetyl chloride (32 g) in anhydrous hexane (250 ml) over a period of 3 h with stirring at room temperature. The reaction mixture was worked up, as mentioned above, to give 17 g (29%) of 4-cyclohexylidene-7,7-dichlorobicyclo[3.2.0]-hept-2-en-6-one (**2b**) as a pale yellow oil: bp 139—141 °C/0.45 Torr; IR (neat) 1800 cm^{-1} (C=O); NMR (CCl_4) $\delta=1.3$—1.9 (m, 6H), 2.0—2.7 (m, 4H), 3.95—4.15 (m, 1H, H-1), 4.74 (d, 1H, $J_{1,5}=6.6$ Hz, H-5), 5.92 (dd, 1H, $J_{2,3}=6.0$, $J_{1,2}=3.0$ Hz, H-2), 6.58 (dd, 1H, $J_{2,3}=6.0$, $J_{1,3}=1.8$ Hz, H-3).

*4-Cycloheptylidene-7,7-dichlorobicyclo[3.2.0]hept-2-en-6-one (**2c**).* A solution of triethylamine (46 g) in anhydrous hexane (500 ml) was added dropwise to a solution of **1c** (35 g) and dichloroacetyl chloride (34 g) in anhydrous hexane (700 ml) over a period of 3 h with stirring at room temperature. The reaction mixture was worked up, as mentioned above, to give 35 g (60%) of 4-cycloheptylidene-7,7-dichlorobicyclo[3.2.0]hept-2-en-6-one (**2c**) as a pale yellow oil: bp 151—152 °C/0.45 Torr; IR (neat) 1800 cm^{-1} (C=O); NMR (CCl_4) $\delta=1.3$—1.9 (m, 8H), 2.0—2.6 (m, 4H), 3.95—4.20 (m, 1H, H-1), 4.73 (d, 1H, $J_{1,5}=7.2$ Hz, H-5), 5.89 (dd, 1H, $J_{2,3}=6.0$, $J_{1,2}=2.4$ Hz, H-2), 6.57 (dd, 1H, $J_{2,3}=6.0$, $J_{1,3}=1.8$ Hz, H-3).

*3-(1-Cyclopentenyl)tropolone (**3a**).* A suspended solution of the cycloadduct (**2a**) (20 g) in acetic acid (99 g) and water (9 ml) containing sodium hydroxide (16 g) was refluxed for 10 h. The mixture was steam-distilled and the distillate was extracted with chloroform. The extract was washed with sodium hydrogencarbonate solution, water, and saturated sodium chloride solution. Evaporation of the solvent from the dried extract gave 4.0 g (26%) of 3-(1-cyclopentenyl)-tropolone (**3a**) as pale yellow needles (from hexane): mp 79—80 °C; IR ($CHCl_3$) 3140 (OH), 1616 cm^{-1} (C=O); NMR ($CDCl_3$) $\delta=1.7$—2.3 (m, 2H), 2.4—3.0 (m, 4H), 6.8—7.7 (m, 5H), 9.50 (br, 1H, OH). Found: C, 76.27: H, 6.45%. Calcd for $C_{12}H_{12}O_2$: C, 76.57; H, 6.43%.

*3-(1-Cyclohexenyl)tropolone (**3b**).* The cycloadduct (**2b**) (17 g) was hydrolyzed, as mentioned above, by refluxing for 10 h in acetic acid (71 g) and water (7 ml) containing sodium hydroxide (13 g) and steam-distilled to give 5.6 g (42%) of 3-(1-cyclohexenyl)tropolone (**3a**) as pale yellow needles (from hexane): mp 53—55 °C; IR ($CHCl_3$) 3140 (OH), 1615 cm^{-1} (C=O); NMR ($CDCl_3$) $\delta=1.4$—1.9 (m, 4H), 2.0—2.6 (m, 4H), 5.7—5.9 (m, 1H), 6.7—7.1 (m, 4H), 9.20 (br, 1H, OH).

Found: C, 77.21; H, 7.00%. Calcd for $C_{13}H_{14}O_2$: C, 77.20; H, 6.98%.

3-(1-Cycloheptenyl)tropolone (3c) The cycloadduct (**2c**) (35 g) was also hydrolyzed, as mentioned above, by refluxing for 10 h in acetic acid (157 g) and water (14 ml) containing sodium hydroxide (26 g) and steam-distilled to give 4.5 g (16%) of 3-(1-cycloheptenyl)tropolone (**3c**) as pale yellow needles (from hexane): mp 39—41 °C; IR ($CHCl_3$) 3120 (OH), 1614 cm^{-1} (C=O); NMR ($CDCl_3$) δ=1.5—2.0 (m, 6H), 2.1—2.6 (m, 4H), 5.65—5.95 (m, 1H, H-2'), 6.65—7.60 (m, 4H), 9.40 (br, 1H, OH). Found: C, 78.01; H, 7.27%. Calcd for $C_{14}H_{16}O_2$: C, 77.75; H, 7.46%.

Oxidation of 3-(1-Cyclopentenyl)tropolone (3a). 3-(1-Cyclopentenyl)tropolone (**3a**) (3.76 g) was added to a performic acid solution, prepared from 90% formic acid (50 ml) and 30% hydrogen peroxide (10 ml), and heated on a water bath for 2 h. The reaction mixture was alkalized with 20% sodium hydroxide solution and heated again on a water bath for 45 min. The mixture was slightly acidified with 3 M hydrochloric acid and extracted with chloroform. The extract was washed with water and dried over anhydrous sodium sulfate. After the evaporation of the solvent, the residue was chromatographed on four Wakogel B-10 plates (30×30 cm^2) with chloroform to afford two fractions. Crystals from the upper band were recrystallized from benzene to give 171 mg (4.5%) of 1,2,3,5-tetrahydrocyclohepta[*b*]cyclopenta[*d*]furan-5-one (**4a**): mp 217—218 °C; IR ($CHCl_3$) 1642 cm^{-1} (C=O); UV (CH_3OH) 227 (log ε 4.16), 286 (4.39), 313 nm (sh, 3.94); NMR ($CDCl_3$) δ=2.2—3.1 (m, 6H), 6.7—7.4 (m, 4H). Found: C, 77.24; H, 5.42%. Calcd for $C_{12}H_{10}O_2$: C, 77.40; H, 5.41%. Crystals from the lower band were also recrystallized from benzene to give 316 mg (7.7%) of 3-(2-oxocyclopentyl)tropolone (**5**): mp 97—99 °C; IR ($CHCl_3$) 3180 (OH), 1745 (C=O), 1618 cm^{-1} (C=O); NMR ($CDCl_3$) δ=1.5—2.8 (m, 6H), 3.42 (m, 1H, H-1'), 6.7—7.5 (m, 4H), 8.90 (br, 1H, OH). Found: C, 70.45; H, 5.93%. Calcd for $C_{12}H_{12}O_3$: C, 70.57; H, 5.92%.

Oxidation of 3-(1-Cyclohexenyl)tropolone (3b). 3-(1-Cyclohexenyl)tropolone (**3b**) (2.33 g) was added to a performic acid solution, prepared from 90% formic acid (25 ml) and 30% hydrogen peroxide (5 ml), and heated on a water bath for 2 h. The reaction mixture was alkalized with 20% sodium hydroxide solution and heated on a water bath for 45 min. The mixture was slightly acidified with 3 M hydrochloric acid and extracted with chloroform. The extract was washed with water and dried over anhydrous sodium sulfate. After the evaporation of the solvent, the residue was recrystallized from benzene to give 842 mg (38%) of 1,2,3,4-tetrahydro-6*H*-cyclohepta[*b*]benzofuran-6-one (**4b**): mp 174—176 °C; IR ($CHCl_3$) 1650 cm^{-1}; UV (CH_3OH) 229 (log ε 4.18), 284 (4.37), 313 nm (sh, 3.89); NMR ($CDCl_3$) δ=1.3—2.2 (m, 4H), 2.3—3.1 (m, 4H), 6.7—7.6 (m, 4H). Found: C, 77.69; H, 6.06%. Calcd for $C_{13}H_{12}O_2$: C, 77.98; H, 6.04%.

Dehydrogenation of 1,2,3,4-Tetrahydro-6H-cyclohepta[b]benzofuran-6-one (4b). A mixture of 1,2,3,4-tetrahydro-6*H*-cyclohepta[*b*]benzofuran-6-one (**4b**) (1.0 g) and 5% palladium-charcoal (2.0 g) in xylene (20 ml) was refluxed for 48 h. The catalyst was filtered off. The filtrate was chromatographed on three Wakogel B-10 plates (30×30 cm^2) with ethyl acetate. Crystals from the upper band gave 6*H*-cyclohepta[*b*]benzofura-6-one (**6**). Fraction from the lower band was a mixture of **4b** and **6**, and was rechromatographed. The fractions, corresponding to **6**, were combined and recrystallized from benzene to give 235 mg (24%) of **6**: mp 139—141 °C; IR ($CHCl_3$) 1635 cm^{-1} (C=O); UV (CH_3OH) 274 (log ε 4.40), 305 (4.18), 336 (sh, 3.89), 350 (sh, 3.78), 366 nm (sh, 3.61); NMR ($CDCl_3$) δ=6.90—8.05 (m). Found: C, 79.39; H, 4.07%. Calcd for $C_{13}H_8O_2$: C, 79.58; H, 4.11%.

Oxidation of 3-(1-Cycloheptenyl)tropolone (3c). 3-(1-Cycloheptenyl)tropolone (**3c**) (432 mg) was added to a performic acid solution, prepared from 90% formic acid (5 ml) and 30% hydrogen peroxide (1 ml), and heated on a water bath for 2 h. The reaction mixture was worked up, as mentioned above, and recrystalized from benzene to give 111 mg (26%) of 5,7,8,9,10,11-hexahydrodicyclohepta[*b,d*]furan-5-one (**4c**): mp 173—175 °C; IR ($CHCl_3$) 1648 cm^{-1} (C=O); UV (CH_3OH) 227 (log ε 4.18), 284 (4.37), 310 nm (sh, 3.91); NMR ($CDCl_3$) δ=1.6—2.2 (m, 6H), 2.4—3.1 (m, 4H), 6.7—7.4 (m, 4H). Found: C, 78.18; H, 6.79%. Calcd for $C_{14}H_{14}O_2$: C, 78.48; H, 6.59%.

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