

Cyclodehydrogenation of 3-Isopropenyl- and 3-(1-Phenylvinyl)-tropolones to 8*H*-Cyclohepta[*b*]furan-8-one Derivatives

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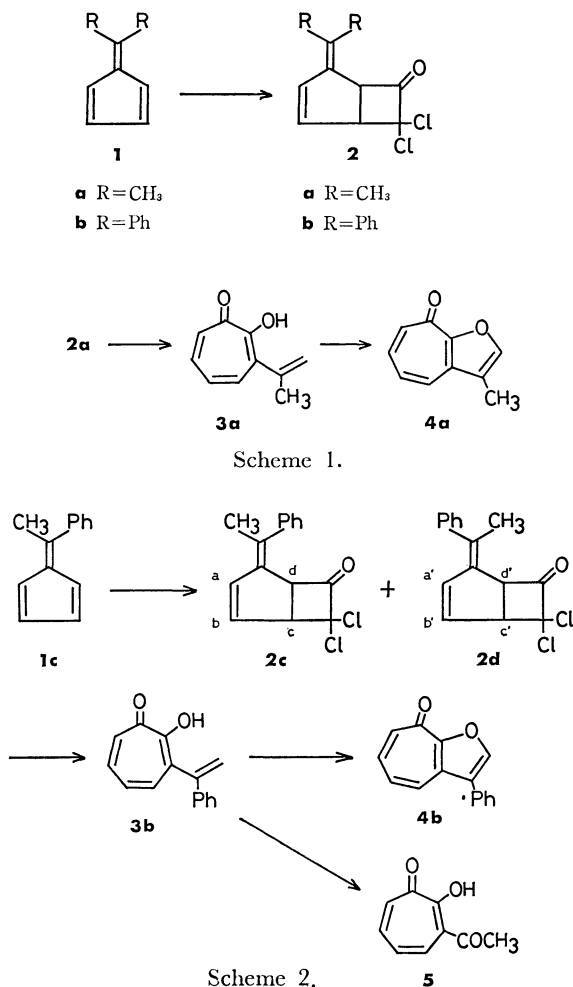
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3-(1-Phenylvinyl)tropolone (**3b**) was prepared by the hydrolysis of cycloadducts of 6-methyl-6-phenylfulvene with dichloroketene. 3-Isopropenyltropolone and **3b** were treated with 2,3-dichloro-5,6-dicyano-*p*-benzoquinone or performic acid to give 3-methyl- and 3-phenyl-8*H*-cyclohepta[*b*]furan-8-one, respectively. Reaction of **3b** with hydrazoic acid afforded an unexpected 3-acetyltropolone.

Several heterocycle-condensed troponoid skeletons have been found in natural products, but not troponoid condensed with furan ring. Kitahara and Funamizu¹⁾ reported the formation of a furotropone, 2-methyl-8*H*-cyclohepta[*b*]furan-8-one, by peroxy acid oxidation of 3-propenyltropolone. Takase²⁾ also obtained the same compound by treatment of 3-acetyltropolone with sulfuric acid. Papers have appeared concerning the synthesis of furotropone derivatives, prepared from tropone derivatives^{3,4)} and from furan derivatives.^{5,6)}

In this communication, we wish to report the synthesis of 3-methyl- and 3-phenyl-8*H*-cyclohepta[*b*]furan-8-one (**4a** and **4b**) by 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ) or performic acid treatment of the corresponding 3-($\Delta^{\alpha,\beta}$ -alkenyl)tropolones (**3a** and **3b**).



Results and Discussion

Synthesis of 3-(1-Phenylvinyl)tropolone (**3b**).

Tropolones having an $\Delta^{\alpha,\beta}$ -alkenyl group at C-3 position are of interest as synthetic precursors, being obtained by hydrolysis of cycloadducts of 6-alkyl-substituted fulvenes with dichloroketene,⁷⁾ which is an advantageous method of preparation.

Most cycloaddition reactions of fulvenes result in a 1,4-monoadduct. The formation of 1,2-monoadduct is little known except for the addition of benzonitrile oxide⁸⁾ and diazomethane⁹⁾ to 6,6-dimethylfulvene. 1,2-Cycloaddition reactions of dichloroketene to 6,6-dimethyl- (**1a**)⁷⁾ and 6,6-diphenylfulvene (**1b**)¹⁰⁾ were reported. The cycloadduct (**2a**) from dimethylfulvene was hydrolyzed to afford 3-isopropenyltropolone (**3a**),⁷⁾ a useful intermediate for the synthesis of 3-acetyltropolone.¹¹⁾ The structure of the cycloadducts (**2b**) from diphenylfulvene was also established by detailed PMR spectral investigation.

We obtained the cycloadducts from the reaction of 6-methyl-6-phenylfulvene (**1c**)¹²⁾ with dichloroketene. The reaction of **1c** with dichloroketene (generated *in situ*) afforded an oily substance. The IR spectrum shows a strong carbonyl absorption at 1800 cm⁻¹, which is very similar to that of **2a** and **2b** and is reasonable for a saturated four-membered ring.¹³⁾ The PMR spectrum (Fig. 1) shows the oily substance to consist of two isomeric substances which may be produced by the presence of unequivalent methyl and phenyl groups at the C-6 position of the fulvene (**1c**). The two products were assigned to (*Z*)- and (*E*)-7,7-dichloro-4-(α -methylbenzylidene)bicyclo[3.2.0]hept-2-en-6-one (**2c** and **2d**), respectively, in comparison with the spectra of **2a** and **2b**. The assignments fit perfectly the structures (**2c**): δ /ppm: 2.21 (s, 3H, CH₃), 4.0–4.2 (m, 1H, H-c), 4.86 (d, 1H, J_{dc} =7.9 Hz, H-d), 5.8–6.1 (m, 1H, H-b), 6.47 (dd, 1H, J_{ab} =

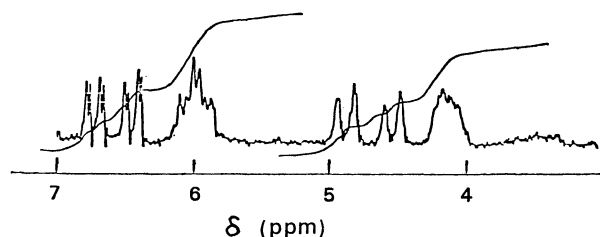


Fig. 1. PMR spectrum of mixture of cycloadducts (**2c** and **2d**).

6.0 Hz, $J_{ac}=1.8$ Hz H-a), 7.2–7.5 (m, 5H, Ph) and (**2d**): δ /ppm: 2.21 (s, 3H, CH₃), 4.0–4.2 (m, 1H, H-c'), 4.52 (d, 1H, $J_{a'c'}=7.0$ Hz, H-d'), 5.8–6.1 (m, 1H, H-b'), 6.72 (dd, 1H, $J_{a'b'}=6.0$ Hz, $J_{a'c'}=1.8$ Hz, H-a'), 7.2–7.5 (m, 6H, Ph). The spectrum (Fig. 1) also shows the formation of equimolar **2c** and **2d** isomers. However, the separation of the isomers was not achieved by distillation, column and TLC chromatography, and gas chromatography.

Hydrolysis of a mixture of the adducts (**2c** and **2d**) afforded 3-(1-phenylvinyl)tropolone (**3b**). The PMR spectrum of **3b** shows peaks at δ 5.34 (s, 1H), 5.81 (s, 1H), 6.70–7.65 (m, 4H), and 7.28 ppm (s, 5H), supporting the structure. The elemental analysis also gave a satisfactory result.

Cyclodehydrogenation with DDQ. Recently attempts have been made to synthesize 2H-chromenes by cyclodehydrogenation of 2-($\Delta^{\beta,\gamma}$ -alkenyl)phenols with DDQ.¹⁴ However, little is known about the cyclodehydrogenation of 2-($\Delta^{\alpha,\beta}$ -alkenyl)phenols except for the reactions of 2-(3-methyl-1-butenyl)phenol and 2-(1-phenyl-1-propenyl)phenol.¹⁵ The former gave 2,2-dimethyl-2H-chromene and the latter 2-methyl-3-phenylbenzofuran.

A solution of 3-isopropenyltropolone (**3a**) in dry benzene was refluxed for 20 h with DDQ to afford 3-methyl-8H-cyclohepta[b]furan-8-one (**4a**) in 22% yield. The UV spectrum [λ_{max}/nm (log ϵ): 227 (4.18), 273 (4.27), 340 (3.57)] is very similar to that of 2-methyl isomer.² The IR spectrum of **4a** shows absorptions at 1639 (C=O) and 1090 cm⁻¹ (C–O–C). These results indicate the formation of **4a**.

Reaction of 3-(1-phenylvinyl)tropolone (**3b**) with DDQ gave 3-phenyl-8H-cyclohepta[b]furan-8-one (**4b**) in 51% yield. The UV spectrum of **4b** is also very similar to that of **4a** and its 2-methyl isomer. The IR spectrum shows absorptions at 1638 (C=O) and 1102 cm⁻¹ (C–O–C).

Oxidative Cyclization with Performic Acid. Nozoe and Hayashi¹⁶ found that **3a** gives **4a** by peroxy acid oxidation, but their results have not been published.

We have carried out the same reaction of **3a** with performic acid and obtained **4a** (51%). 3-(1-Phenylvinyl)tropolone (**3b**) also reacted with performic acid to afford **4b** (62%). On the other hand, **3a** was not oxidized with alkaline hydrogen peroxide, **3a** being recovered (91%).

Treatment of 3b with Hydrazoic Acid. In a previous paper,¹¹ it was reported that the reaction of **3a** with sodium azide in sulfuric acid gives 3-acetyltropolone (**5**). Phenyl derivatives (**3b**) was similarly treated with sodium azide in concentrated sulfuric acid to give 3-acetyltropolone (**5**) in 44% yield, the desired 3-benzoyltropolone not being obtained.

Experimental

The melting points were measured on a Yanagimoto MP-S2 melting point measuring apparatus and are uncorrected. The IR spectra were taken on a JASCO IRA-1 spectrophotometer, UV spectra on a Hitachi EPS-3T spectrophotometer, and PMR spectra on a Hitachi R-24 spectrometer (60 MHz).

6-Methyl-6-phenylfulvene (1c). 6-Methyl-6-phenylfulvene (**1c**) was prepared by the method of Thiele.¹² Bp 143.5 °C/18 Torr (lit.¹² 130.5 °C/10.5 Torr). PMR (CDCl₃) δ : 2.50 (s, 3H, CH₃), 6.05 (m, 1H), 6.35 (m, 1H), 6.48 (s, 2H), 7.30 ppm (s, 5H, Ph).

Cycloaddition to 6-Methyl-6-phenylfulvene (1c). A solution of triethylamine (18 ml) in anhydrous hexane (83 ml) was added dropwise to a solution of **1c** (10.2 g) and dichloroacetyl chloride (7 ml) in anhydrous hexane (83 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 filtered, the filtrate evaporated off and the residue distilled under reduced pressure to give a dark red oil. Yield 6.8 g (41%). Bp 169 °C/2 Torr. This oily substance was a mixture of (Z)- and (E)-7,7-dichloro-4-(α -methylbenzylidene)bicyclo[3.2.0]hept-2-en-6-one (**2c** and **2d**).

3-(1-Phenylvinyl)tropolone (3b). A mixture (16.7 g) of the cycloadducts (**2c** and **2d**) was refluxed for 16 h in acetic acid (71.5 ml)–water (7.2 ml) containing sodium hydroxide (13.2 g). 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 chloroform from the dried extract (over sodium sulfate) gave 3-(1-phenylvinyl)tropolone (**3b**) as pale yellow scales (from hexane). Yield 1.8 g (14%). Mp 108–111 °C. IR (CHCl₃): 1620 cm⁻¹ (C=O); PMR (CDCl₃) δ : 5.34 (s, 1H, =CH–H), 5.81 (s, 1H, =CH–H), 6.70–7.65 (m, 4H), 7.28 ppm (s, 5H, Ph). Found: C, 80.38; H, 5.40%. Calcd for C₁₅H₁₂O₂: C, 80.33; H, 5.40%.

Cyclodehydrogenation with DDQ. a): A mixture of 3-isopropenyltropolone (**3a**) (162 mg, 1 mmol) and DDQ (454 mg, 2 mmol) was refluxed for 6 h in dry benzene (20 ml). The reaction mixture was filtered, concentrated, chromatographed on a Wakogel B-10 plate (30 × 30 cm²) with ethyl acetate, and recrystallized from hexane to afford 3-methyl-8H-cyclohepta[b]furan-8-one (**4a**) as pale orange prisms. Yield 15 mg (9.4%). Mp 95–96 °C. IR (CHCl₃): 1639, 1580, 1090 cm⁻¹; UV (MeOH) λ_{max}/nm (log ϵ): 227 (4.18), 273 (4.27), 340 (3.57); PMR (CDCl₃) δ : 2.24 (s, 3H, CH₃), 6.8–7.5 (m, 4H), 7.63 ppm (m, 1H, H-2). Found: C, 74.99; H, 5.01%. Calcd for C₁₀H₈O₂: C, 74.99; H, 5.03%.

b): Prolonged reaction (20 h) of **3a** (162 mg, 1 mmol) and DDQ (454 mg, 2 mmol) in dry benzene (20 ml) gave **4a** (35 mg, 22%) after the work-up mentioned above.

c): A mixture of 3-(1-phenylvinyl)tropolone (**3b**) (224 mg, 1 mmol) and DDQ (454 mg, 2 mmol) was refluxed for 20 h in dry benzene (20 ml). The reaction mixture was worked up in a similar way to that for a) and recrystallized from cyclohexane to give 3-phenyl-8H-cyclohepta[b]furan-8-one (**4b**) as pale yellow needles. Yield 114 mg (51%). Mp 146–148 °C. IR (CHCl₃): 1638, 1580, 1102 cm⁻¹; UV (MeOH) λ_{max}/nm (log ϵ): 232 (4.35), 282 (4.20), 338^{sh} (3.67), 356^{sh} (3.45); PMR (CDCl₃) δ : 6.7–7.6 (m, 4H), 7.38 (s, 5H, Ph), 7.89 ppm (s, 1H, H-2). Found: C, 81.21; H, 4.47%. Calcd for C₁₅H₁₀O₂: C, 81.06; H, 4.54%.

Cyclization with Performic Acid. a): **3a** (420 mg, 2.6 mmol) was added to a performic acid solution, prepared from 85% formic acid (5 ml) and 30% hydrogen peroxide (1 ml), and heated on a water bath for 2 h. The reaction mixture was heated again with 6 M sodium hydroxide solution, neutralized with 3 M hydrochloric acid, and extracted with chloroform. The chloroform extract was dried over sodium sulfate and evaporated to dryness. The residue was recrystallized from hexane to afford **4a** (212 mg, 51%).

b): **3b** (448 mg, 2 mmol) was heated in performic acid, prepared in the same way as for *a*), for 2 h and worked up as mentioned above. Crude product was recrystallized from cyclohexane to afford **4b** (227 mg, 62%).

Treatment of 3b with Hydrazoic Acid. Sodium azide (200 mg) was added to a stirred mixture of **3b** (360 mg), concentrated sulfuric acid (1 ml), and chloroform (2 ml). The mixture was stirred at 50 °C for 3 h. After removal of chloroform layer, the acid layer was diluted with water (4 ml) and then left overnight. The crystals deposited were collected and recrystallized from methanol to afford 3-acetyltropolone (**5**)¹¹ as pale yellow needles. Yield 120 mg (44%). Mp 131–132 °C.

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