

A Convenient Synthesis of 4- and 5-Acetyltropolone

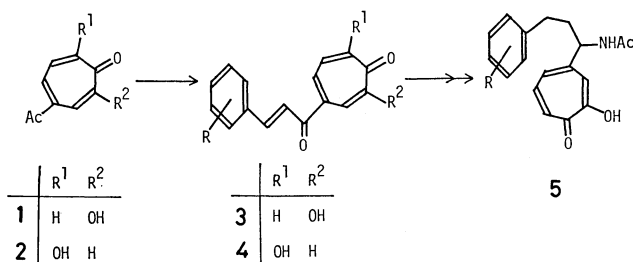
Hiroshi YAMAMOTO,* Atsushi HARA, Ayashi NOGUCHI, Heizan KAWAMOTO, Saburo INOKAWA, and Tetsuo NOZOE†

Department of Chemistry, Faculty of Science, Okayama University, Tsushima, Okayama 700

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4-Acetyltropolone is derived from hinokitiol (β -thujaplicin) in four steps, with an overall yield of 60%, via readily available 8-azidohinokitiol. γ -Thujaplicin almost quantitatively forms its difluoroboron complex, which, upon bromination, provides an 85% yield of the 8-bromo- γ -thujaplicin difluoroboron complex. This bromo compound readily gives γ -dolabrin (87% with triethylamine) and 8-azido- γ -thujaplicin (88% with sodium azide), from which 5-acetyltropolone is derived in an 80% yield by ozonolysis or in a 40% yield with sulfuric acid. The considerable differences in the reactivities observed between these 4- and 5-substituted tropolones are discussed. The pK_a values of 4- and 5-acetyltropolone and 4- and 5-(3,4,5-trimethoxycinnamoyl)tropolones are also reported.

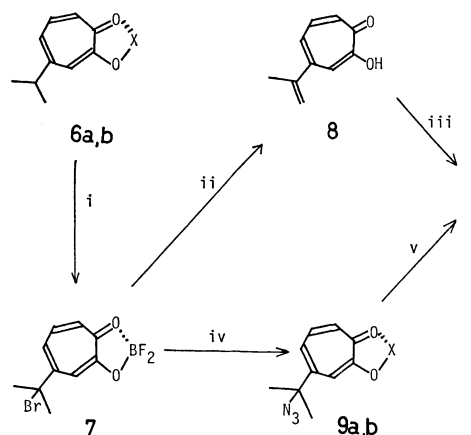
The tropolone nucleus is well known to be susceptible to many electrophilic substitution reactions, but does not undergo the Friedel-Crafts-type alkylation or acylation.¹⁻⁴⁾ Several examples of direct carbon-carbon bond formation on the tropolone nucleus by various methods under basic conditions (*e.g.*, the Reimer-Tiemann reaction, hydroxymethylation, and the Mannich reaction) have been reported. These reactions, however, have drawbacks either with respect to the preparative yield or the regioselective control.¹⁻⁵⁾ Organometallic reagents, such as Grignard or lithium reagents, give rise to the alkyl- or aryl-substitution products only at the 2-position of the tropolone nucleus.¹⁾ Therefore, one of the present authors (T.N.) and his co-workers utilized naturally occurring β -dolabrin⁶⁾ (**8**) or 3-carboxy-4-carboxymethyltropolone derived from natural purpurogallin¹⁻³⁾ as the starting material in preparing tropolones bearing a *C*-substituent at the 4-position.⁷⁾ For example, **8** was oxidatively converted^{6b)} into 4-acetyltropolone (**1**), which subsequently afforded a wide variety of the cinnamoyltropolones (**3**) and their derivatives (**5**) for the attempted synthesis of colchicine analogs,^{1,8)} although the detailed experimental results have remained unpublished⁷⁾ (Scheme 1). 5-Acetyltropolone (**2**) was also derived from **8** by a multi-step conversion in a 10–15% overall yield and likewise afforded the 5-cinnamoyltropolones⁹⁾ (**4**).



Scheme 1.

Renewed interest in the pharmacology of colchicine, particularly concerning the binding sites of the microtubulins in the muscle and nerve cells,⁸⁾ led us to reinvestigate our old synthetic scheme involving **3** or **4** as an intermediate. However, the extremely limited supply of the natural β -dolabrin necessitated

a search for an alternative, efficient method of preparing two acetyltropolones, **1** and **2**. Although two practically valuable methods have been reported recently for the preparation of **8** starting from tropone-tricarbonyliron⁴⁾ or quinone monoacetals,^{8a)} the conversion of hinokitiol¹⁾ (**6a**) and γ -thujaplicin¹⁰⁾ (**10a**) into **1** and **2** appeared to be more preparative value, since these isopropyltropolones are easily available from an isopropylcyclopentadiene-dichloroketene adduct by applying the Stevens method.^{11,12)} We wish to describe herein the effective synthesis of two acetyltropolones **1** and **2** as the initial part of a reinvestigation of the synthesis of various 4- and 5-substituted tropolones including colchicine analogs.



Scheme 2. a: X = H, b: X = BF₂. Reagents: i, Ref. 13; ii, *n*-Bu₄N⁺Br⁻-0.5 M NaOH-CH₂Cl₂; iii, Ref. 6b, 16; iv, NaN₃; v, H₂SO₄.

Seto *et al.*¹³⁾ reported an efficient conversion of **6a** into the bromo compound (**7**), which in turn was dehydrobrominated to afford a 30% yield of **8** (Scheme 2). Since the above elimination reaction with potassium *t*-butoxide in *t*-butyl alcohol failed to produce **8** in our experiment, we examined the conversion of **7** to **8** using various other bases, such as triethylamine in chloroform, 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in DMF, or 0.5 mol dm⁻³ sodium hydroxide-dichloromethane with tetrabutylammonium bromide as a phase-transfer catalyst. Among these, only the last procedure afforded a 20–25% yield of **8**; the major products under these conditions were an intractable, polymerized substance and 8-hydroxyhinoki-

† 811, 2-5-1, Kamiyoga, Setagaya-ku, Tokyo 158.

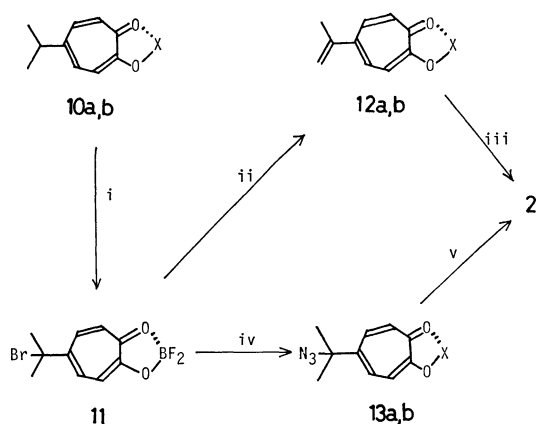
TABLE 1. IONIZATION CONSTANTS AND UV SPECTRA^{a)}

Compd	Species ^{c)}	Ionization in water (25 °C)			Spectroscopy ^{b)} in water			
		p <i>K</i> _a	Concn/M	A.w.l. ^{d)}	λ _{max} /nm	log ε	pH	
1	0				251, 318, 382	4.50, 3.75, 3.76	1.0	
	—	6.23±0.06	3.09×10 ⁻⁵	436	267, 344, 436	4.33, 4.02, 3.77	9.1	
2	0				226, 257, 342	4.57, 4.39, 4.34	1.0	
	—	4.97±0.05	1.43×10 ⁻⁵	389	237, 270, 389	4.59, 4.00, 4.66	9.1	
3^{e)}	0				255, 342	4.41, 4.31	MeOH ^{f)}	
	0				254, 340, 370	4.34, 4.14, 4.15	1.0	
	—	6.08±0.07	1.19×10 ⁻⁵	348	222, 262, 275, 348, 425	4.27, 4.16, 4.14, 4.34, 3.60	9.1	
	0				228, 259, 358	4.47, 4.23, 4.32	1.0	
4^{e)}	—	4.85±0.06	1.19×10 ⁻⁵	425	230, 240, 272, 388, 425	4.50, 4.43, 4.03, 4.33, 4.51	9.1	

a) Measured with a Hitachi EPS 3T Recording Spectrophotometer. b) Inflections in italics. c) Neutral species (0) and monoanion (—). d) Analytical wavelength in nm (*cf.* Ref. 19). e) R=3,4,5-(MeO)₃ (*cf.* Refs. 1, 7, 9). f) From Ref. 7c.

tiol.¹⁴⁾ Because of the fluctuation in the yield and the difficulties in optimizing the conditions of the above reaction, we sought for a more reliable alternative route to 4-acetyltropolone (**1**).

Thus, the treatment of **7** with 1.3 equivalent sodium azide in DMF produced an 85% yield of the boron complex (**9b**), which in turn was directly transformed into **1** (82%) with concd sulfuric acid, apparently by means of a Schmidt reaction¹⁵⁾ (Scheme 2). The structure of the hitherto unreported intermediate, **9b**, was based on the elementary analysis and the spectroscopic data (see Experimental section). The mild alkaline hydrolysis of **9b** readily afforded crystalline 8-azidohinokitiol (**9a**; 88% yield), which had been postulated by Doi¹⁶⁾ as an intermediate during the conversion of **8** into **1** with hydrazoic acid. The free tropolone (**9a**) indeed produced **1** in an 80% yield when similarly subjected to the Schmidt reaction. The overall yield of **1** from **6a** (*via* **9b**) was *ca.* 60%, which far exceeds that obtained through the formerly employed route *via* **8** (10–15%).^{6b,16)}

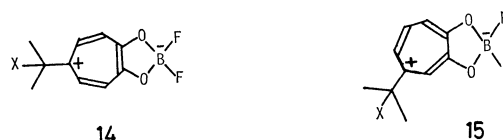


Scheme 3. a: X=H, b: X=BF₂. Reagents: i, BE₃·OEt₂; ii, Et₃N; iii, O₃-Me₂S; iv, NaN₃; v, H₂SO₄.

This convenient synthetic method of preparing **1** led us to examine an analogous approach in preparing 5-acetyltropolone (**2**) (Scheme 3). Thus, γ -thujaplicin (**10a**) was almost quantitatively converted into its

difluoroboron complex (**10b**), and then into the 8-bromo derivative (**11**) in an 85% yield, by employing a slight modification of the procedure described above. Compound **11** was found to undergo surprisingly facile dehydrobromination with triethylamine in chloroform at 15 °C to furnish γ -dolabrin (**12a**) in an 85% overall yield after the hydrolysis of the intermediate boron complex (**12b**). This was in striking contrast with the results for its β -isomer (**7**), which gave mostly a polymerized product and 8-hydroxyhinokitiol. Since **12a** had been prepared⁹⁾ either from the octyl ester of 5-carboxytropolone (7% overall) or β -dolabrin (**8**) by a three-step conversion (15%), the above method is obviously of some value for preparing **12a**.

Although 5-acetyltropolone (**2**) was obtained from **12a** through oxidative cleavage (60–70% overall yield with HCO₃H, NaOH, and HIO₄),⁹⁾ the ozonolysis of **12a** at –70 °C was found to provide **2** more conveniently in an 80–85% yield. Alternatively, a similar application of the Schmidt reaction on either 8-azido- γ -thujaplicin (**13a**) or its difluoroboron complex (**13b**), both of which are readily available from **11**, as in the case of the β -isomer, produced only a moderate yield (40%) of 5-acetyltropolone (**2**), together with a minor amount of 5-aminotropolone.¹⁷⁾ This result was again different from that for the β -isomer (**9a,b**), which produced **1** exclusively. 5-Acetyltropolone (**2**) was thus found to be synthesized from γ -thujaplicin (**10a**) more satisfactorily through γ -dolabrin (**12a**) in an overall yield of 70%.



Scheme 4. X=Br, N₃.

Considerable differences in various reactivities were observed between the 4- and 5-positions in the tropolone nucleus. The extremely facile dehydrobromination in **11** and the increased migratory aptitude of tropolone ring in **13** to produce a considerable amount of 5-aminotropolone could be explained in terms of

a very limited contribution of a polar resonance form **14** to the actual ground state of the 5-substituted tropolones (**11** and **13**) compared with that of **15** to the 4-substituted tropolones **7** and **9b** (Scheme 4). On the other hand, the presence of an appreciable cationic charge at Position 4, as is shown in **15**, would suppress the elimination reaction in **7** and promote the polymerization of the side-chain of the β -dolabrin difluoroboron complex formed. Formula **15** is also compatible with the suppressed migratory aptitude of the tropolone nucleus in the Schmidt reaction of **9**. However, a closer mechanistic study with regard to these interesting differences is currently in progress.

A significant positional difference was also observed in the pK_a values of 4- and 5-acetyltropolone and the readily obtainable 4- and 5-(3,4,5-trimethoxycinnamoyl)tropolones [**3,4**; R=3,4,5-(MeO₃)]; these hitherto unreported values are recorded in Table 1, along with their UV-spectral values in aqueous buffers. The pK_a value of **2** fits this relation:

$$pK_a = 6.42 - 3.10\sigma$$

if the σ_p constant for phenol is used (predicted: 4.8).¹⁸ These values, therefore, appear to be in conformity with the generally observed feature that Positions 4 and 5 in tropolones are approximately to be equated with Positions 3 and 4 in phenols.

The 4- and 5-acetyltropolone (**1** and **2**), thus synthesized easily from the readily available starting materials, **6a** and **10a**, are considered to be valuable intermediates in synthesizing various 4- and 5-substituted troponoids, including colchicine analogs, which are under investigation.

Experimental

The ¹H-NMR spectra were measured in CDCl₃ with a Hitachi High-resolution NMR Spectrometer, R-20A (60 MHz) at 30 °C. The chemical shifts are reported as δ values in ppm relative to TMS (δ 0.0) as the internal standard. The IR spectra were taken with a Nihon-Bunko IR-S spectrometer. The microanalysis was carried out in this department using a Yanagimoto CHN Corder, MT-2. Substances stated to be identical were compared by means of their IR and ¹H-NMR spectra, TLC (silica gel), HPLC (Hitachi gel #3011, with 0.1% AcOH/MeOH as a solvent), and paper chromatography (developed in 7:3 *n*-BuOH/5 M (1 M=1 mol dm⁻³) AcOH or 2:1 *n*-PrOH/1% aq ammonia).

Difluoro(3-isopropyl-7-oxo-1,3,5-cycloheptatrienyloxy)borane (*Hinokitiol Difluoroborane*; **6b**).

The procedure of Seto *et al.*¹³ was followed, but on a much larger scale, using an overhead mechanical stirrer, a three-necked flask fitted with a dropping funnel, and a condenser. Thus, 18.0 g (0.11 mol) of **6a** and 15.6 g (0.11 mol) of freshly distilled boron trifluoride etherate gave 22.2 g (96%) of the difluoroborane (**6b**) after recrystallization from chloroform-benzene (*ca.* (4:7); mp 171–172 °C (lit.¹³ 178–179 °C). Further purification by silica-gel chromatography with 5% AcOEt/C₆H₆ and recrystallization did not raise the melting point. NMR 1.37 (6H, d, *J*=7.0), 3.20 (1H, sept, *J*=7.0), and 7.35–8.1 (4H, m).

[3-(1-Bromo-1-methylethyl)-7-oxo-1,3,5-cycloheptatrienyloxy]difluoroborane (*8-Bromohinokitiol Difluoroborane*; **7**). This material was also prepared according to the procedure of

Seto *et al.*,¹³ but on a larger scale and with a slight modification. Thus, 15.0 g (0.094 mol) of freshly distilled bromine was slowly added to a refluxing solution of 15.0 g (0.071 mol) of **6b** dissolved in 150 ml of dry chloroform under a tungsten light with mechanical stirring. The mixture was refluxed for 6 h with stirring, with protection against moisture being provided by a CaCl₂ tube. The precipitate was filtered off and washed with chloroform, giving 18.3 g (89%) of **7**; mp 176–180 °C dec (from CHCl₃) (lit.¹³ 188–189 °C). NMR (DMSO-*d*₆/CDCl₃, 1:2) 2.30 (6H, s) and 7.8–8.4 (4H, m).

4-Isopropenyl-2-hydroxy-2,4,6-cycloheptatrien-1-one (β -Dolabrin; **8**).

A suspension of 0.29 g (1.0 mmol) of **7** in 20 ml of dichloromethane was added at 40 °C to a stirred mixture of 20 ml of 0.5 mol dm⁻³ NaOH and 5 ml of CH₂Cl₂ containing 70 mg (0.21 mmol) of tetrabutylammonium bromide over a period of 50 min; then the mixture was stirred under N₂ at 40–45 °C for 12 h. After separation, the aq layer was washed with CH₂Cl₂, carefully brought to pH 3 at 5 °C with 6 mol dm⁻³ HCl, and extracted with CH₂Cl₂. The dried (over Na₂SO₄) extracts were evaporated *in vacuo*, and the residue was flash-distilled at 85 °C (bath)/7 Torr (1 Torr $\approx$ 133.322 Pa), giving 40 mg (25%) of **8** as a pale yellow liquid which slowly solidified on standing and which was identical with an authentic specimen. No appreciable amount of **8** was obtained when other bases were used *e.g.*, triethylamine in chloroform (50 °C, 6 h; 60% recovery, 15% of 8-hydroxyhinokitiol), *t*-BuOK/*t*-BuOH¹³ (10–20 °C, 1.5 h; 30% recovery of **7**, 10% of 8-hydroxyhinokitiol, and 5% of **8**), DBU/DMF (0 °C, 1.5 h; 40% of **7**, 10% of 8-hydroxyhinokitiol). In all cases, the residue was an intractable gummy substance, apparently a polymerized product.

[3-(1-Azido-1-methylethyl)-7-oxo-1,3,5-cycloheptatrienyloxy]difluoroborane (*8-Azidohinokitiol Difluoroborane*; **9b**).

A solution of 4.11 g (14.1 mmol) of **7** and 1.18 g (18.2 mmol) of sodium azide in 40 ml of dry DMF was stirred under N₂ at 15 °C for 15 h. The solvent was then removed *in vacuo* (pump), and the residue, diluted with water, was extracted with benzene. The combined extracts were dried over Na₂SO₄ and evaporated *in vacuo*. The residue was purified by passing it through a short column of silica gel with 5% AcOEt-C₆H₆, thus affording 3.04 g (85%) of **9b** as colorless crystals; mp 71–73 °C (from benzene-light petroleum). NMR 1.74 (6H, s, 2CH₃-8) and 7.6–8.2 (4H, m, aromatic). IR (CHCl₃) 2150 (N₃) and 1615 cm⁻¹ (C=O). Found: C, 47.25; H, 4.11; N, 16.49%. Calcd for C₁₀H₁₀N₃O₂BF₂: C, 47.47; H, 3.98; N, 16.61%.

4-(1-Azido-1-methylethyl)-2-hydroxy-2,4,6-cycloheptatrien-1-one (*8-Azidohinokitiol*; **9a**).

A mixture of 46 mg of **9b**, 2 ml of *t*-butyl alcohol, and 2 ml of 1 mol dm⁻³ KOH was stirred at 20 °C for 5 h. The alcohol was then removed *in vacuo*, and the remaining aq layer was taken to pH 4 with 2 mol dm⁻³ HCl at 5 °C and extracted with CH₂Cl₂. The combined organic layers were dried over Na₂SO₄ and evaporated *in vacuo*, giving 33 mg (88%) of **9a** as colorless prisms (from ether-light petroleum); mp 45–46 °C. NMR 1.68 (6H, s, 2CH₃-8), 7.2–7.45 (3H, m, H-5,6,7), 7.56 (1H, bs, H-3), and 8.0 (1H, bm, HO-2, D₂O exchangeable). IR (CHCl₃) 3450 (OH), 2150 (N₃), and 1610 cm⁻¹ (C=O). Found: C, 58.65; H, 5.62; N, 20.15%. Calcd for C₁₀H₁₁N₃O₂: C, 58.53; H, 5.40; N, 20.48%.

4-Acetyl-2-hydroxy-2,4,6-cycloheptatrien-1-one (*4-Acetyltropolone*; **1**).

Three milliliters of concd sulfuric acid were added dropwise to a solution of 3.84 g (15.2 mmol) of **9b** in 6 ml of chloroform at 0 °C; the mixture was then stirred at 0 °C for 15 min and at 20 °C for 2 h. After the CHCl₃ layer

had then been removed, the acid layer was diluted with 15 ml of cold water, brought to pH 3 by adding solid NaHCO_3 , and extracted with CHCl_3 . The combined extracts were dried over Na_2SO_4 and evaporated *in vacuo*, giving 2.04 g (82%) of **1** as yellow crystals; mp 125–127 °C (from 70% aq ethanol). The product was identical with an authentic specimen⁹) (mp 129 °C). 8-Azidohinokitiol (**9a**) produced **1** in 80% and 64% yields when similarly treated with concd sulfuric acid and polyphosphoric acid (at 55 °C) respectively.

Di fluoro(4-isopropyl-7-oxo-1,3,5-cycloheptatrienyloxy)borane (γ -Thujaplicin Difluoroborane; **10b**). The procedure for the β -isomer was followed. Thus, 5.3 g (31 mmol) of trifluoroboron etherate, dissolved in 10 ml of dry ether, was added dropwise to a solution of 4.59 g (28 mmol) of **10a** in 80 ml of dry ether–benzene (1:1) at 5 °C over a period of 1 h with stirring under the protection of a CaCl_2 tube. After being stirred at 5 °C for 4 h, the mixture was concentrated *in vacuo*, and the residue was recrystallized from benzene/light petroleum to give 5.05 g of **10b** as white needles; mp 104–105 °C. The filtrate was concentrated *in vacuo*, and the residue was chromatographed over silica gel with 5% ether–benzene, thus affording 0.50 g more of **10b**; mp 103 °C (from the same mixed solvent); thus, the combined yield of **10b** was 5.55 g (94%). NMR 1.35 (6H, d, $J=6.5$, 2CH_3 -8), 2.13 (1H, sept, $J=6.5$, H-8), 7.75 (2H, d, $J=11$, H-2,6), and 8.00 (2H, d, $J=11$, H-3,5). Found (for material dried at 40 °C/15 Torr): C, 56.43; H, 5.11%. Calcd for $\text{C}_{10}\text{H}_{11}\text{O}_2\text{BF}_2$: C, 56.60; H, 5.18%.

[4-(1-Bromo-1-methylethyl)-7-oxo-1,3,5-cycloheptatrienyloxy]difluoroborane (8-Bromo- γ -thujaplicin Difluoroborane; **11**). To a stirred suspension of 6.78 g (32 mmol) of **10b** in 250 ml of dry CCl_4 was added dropwise 5.2 g (32.5 mmol) of bromine dissolved in 20 ml of dry CCl_4 at 20 °C over a period of 90 min under a tungsten light and a slow stream of N_2 ; the mixture was subsequently stirred at room temperature for 4 h. The precipitate was filtered off and washed with CCl_4 , thus giving 7.82 g (85%) of **11** as colorless crystals; mp 116–119 °C. Recrystallization from benzene–light petroleum raised the melting point to 119–120 °C. A lesser yield of **11** was obtained when chloroform was used as the solvent or when the reaction mixture was refluxed. NMR 2.28 (6H, s, 2CH_3 -8), 7.81 (2H, d, $J=12$, H-2,6), and 8.51 (2H, d, $J=12$, H-3,5). Found: C, 41.01; H, 3.25%. Calcd for $\text{C}_{10}\text{H}_9\text{O}_2\text{BrBF}_2$: C, 41.24; H, 3.42%.

Di fluoro(4-isopropenyl-7-oxo-1,3,5-cycloheptatrienyloxy)borane (γ -Dolabrin Difluoroborane; **12b**). To a solution of 200 mg (0.69 mmol) of **11** in 3 ml of dry CH_2Cl_2 was added 73 mg (1.37 mmol) of triethylamine under N_2 at 0 °C. The mixture was stirred at 15 °C for 7 h, and then a 3-ml portion of cold water was added. After separation, the aq layer was extracted with CH_2Cl_2 . The combined organic layers were dried over Na_2SO_4 and evaporated *in vacuo*, thus giving 130 mg (90%) of **12b** as colorless needles; mp 148–149 °C (from benzene–light petroleum). NMR 2.26 (3H, bs, CH_3 -8), 5.40 (2H, bs, $\text{CH}_2=\text{C}$ -8), 7.84 (2H, d, $J=12$, H-2,6), and 8.17 (2H, d, $J=12$, H-3,5). Found: C, 57.51; H, 4.48%. Calcd. for $\text{C}_{10}\text{H}_9\text{O}_2\text{BF}_2$: C, 57.17; H, 4.76%.

5-Isopropenyl-2-hydroxy-2,4,6-cycloheptatrien-1-one (γ -Dolabrin; **12a**). A mixture of 4.40 g (15 mmol) of **11** and 3.50 g (35 mmol) of triethylamine in 60 ml of dry CHCl_3 was stirred under N_2 at 20 °C for 3 h and then concentrated *in vacuo*. The residue was stirred with a mixture of 50 ml of *t*-butyl alcohol and 260 ml of 1.3 mol dm^{-3} KOH at 20 °C for 30 min. The alcohol was removed *in vacuo*, and the residue was carefully taken to pH 3 with 2 mol dm^{-3}

HCl at 5 °C. The precipitate was filtered off and washed with water, thus giving 1.88 g of **12a** as pale yellow crystals; mp 98–100 °C (lit.⁹) 100–101 °C). From the filtrate, 0.25 g more of **12a** was obtained after extraction with CHCl_3 , sublimation at 80 °C/0.01 Torr, and recrystallization from cyclohexane; thus, the total yield of **12a** from **11** was 2.13 g (87%). NMR 2.15 (3H, bs, CH_3 -8), 5.20 and 5.28 (1H, each, m, $\text{CH}_2=\text{C}$ -8), 7.33 (2H, d, $J=11$, H-3,7), 7.49 (2H, d, $J=11$, H-4,6), and 7.80 (1H, bs, HO-2, D_2O exchangeable). The product was identical with an authentic specimen.⁹)

[4-(1-Azido-1-methylethyl)-7-oxo-1,3,5-cycloheptatrienyloxy]difluoroborane (**13b**) and 8-Azido- γ -thujaplicin (**13a**). A mixture of 20 mg (0.069 mmol) of **11** and 6 mg (0.092 mmol) of sodium azide in 0.5 ml of dry DMF was stirred under N_2 at 50 °C for 1.5 h. The solvent was then evaporated at 20 °C/0.3 Torr. The residue was dissolved in benzene, washed with water, dried over Na_2SO_4 , and evaporated *in vacuo*, thus giving 10 mg (57%) of **13b** as pale yellow needles; mp 81–83 °C (from ether–light petroleum). NMR 1.75 (6H, s, 2CH_3 -8), 7.86 (2H, d, $J=12$, H-2,6), and 8.32 (2H, d, $J=12$, H-3,5). IR (CHCl_3) 2150 (N_3) and 1615 cm^{-1} (C=O). Found: C, 47.25; H, 4.16; N, 16.32%. Calcd for $\text{C}_{10}\text{H}_{10}\text{N}_3\text{O}_2\text{BF}_2$: C, 47.47; H, 3.98; N, 16.61%.

When the reaction was carried out using 116 mg of **11** at 20 °C for 16 h, 89 mg (88%) of a ca. 2:1 mixture of **13b** and **13a** (see below) were produced as an amber liquid.

A mixture of 17 mg (0.066 mmol) of **13b**, 1 ml of 1 mol dm^{-3} KOH, and 1 ml of *t*-BuOH was stirred under N_2 at 20 °C for 3 h. The alcohol was then removed *in vacuo*, and the remaining aq solution was taken to pH 4 with 2 mol dm^{-3} HCl and extracted with CHCl_3 , thus giving 11 mg (80%) of **13a** as a pale amber oil. NMR 1.58 (6H, s, 2CH_3 -8), 7.30 (2H, d, $J=12$, H-3,7), 7.64 (2H, d, $J=12$, H-4,6), and 7.7 (1H, bm, OH). IR (CHCl_3) 3450 (OH), 2150 (N_3), and 1610 cm^{-1} (C=O).

5-Acetyl-2-hydroxy-2,4,6-cycloheptatrien-1-one (5-Acetyltropolone; **2**).

A): Into a stirred solution of 0.50 g (3.9 mmol) of **12a** in 50 ml of dry CH_2Cl_2 was passed 42 mg (8.5 mmol) of ozone at –70 °C over a period of 1 h; then 0.6 ml of dimethyl sulfide was added. The mixture was gradually warmed, and the stirring was continued at 15 °C for 3 h. The solvent was evaporated *in vacuo*, and the residue, diluted with brine, was extracted with CHCl_3 , thus giving 0.43 g (85%) of **2** as pale yellow crystals after recrystallization from CHCl_3 –ethanol (with carbon); mp 179–181 °C (lit.⁹) 182–183 °C). NMR 2.63 (3H, s, Ac), 6.1 (1H, bs, OH, D_2O exchangeable), 7.37 (2H, d, $J=12$, H-3,7), and 8.11 (2H, d, $J=12$, H-4,6). The product was identical with an authentic specimen.⁹)

B): To a cold solution of 36 mg of crude **13b** in 1.5 ml of CHCl_3 was added 1.5 ml of concd sulfuric acid at 0 °C. The mixture was stirred at 20 °C for 1 h, after which the organic layer was separated. The aq layer was diluted with 4 ml of cold water, taken to pH 3 with NaHCO_3 , and extracted with CHCl_3 , thus giving 10 mg (40%) of **2** as pale yellow crystals; mp 175–178 °C (from CHCl_3 –EtOH). The above aq layer (after CHCl_3 extraction at pH 3) was found to contain 5-aminotropolone (by HPLC and paper chromatography), which was subsequently isolated and identified as the picrate: yellow crystals, mp 220–225 °C dec (lit.¹⁷) 225–226 °C dec). Almost the same result was obtained by using **13a** as the starting material or by employing polyphosphoric acid as the reaction medium.

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