Thermal reaction of diastereomeric benzocyclobutenols. Evidence for reversible opening of 1,2-dihydrobenzocyclobutenols to hydroxy-*o*-xylylenes

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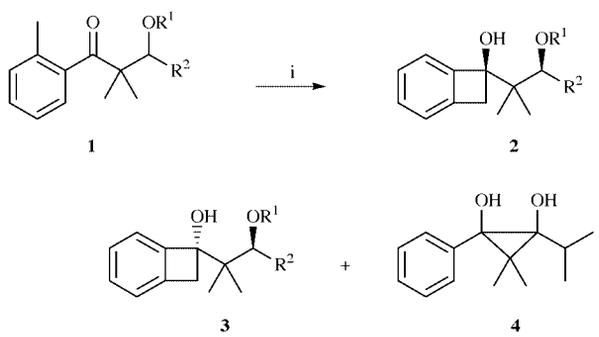
Thermolysis of 1,2-dihydrobenzocyclobutenols **2a,b** or **3a**–**c** without solvent at 120 °C gave a 1 : 1 mixture of **2a**–**c** and **3a**–**c** together with 3-hydroxy-2,2-dimethyl-1-(*o*-methylphenyl)alkan-1-ones **1a**–**c** and *o*-methylisobutyrophenone **5**. Thermolysis of **2a** or **3a** under the same conditions but at 150 °C gave only **5**. Thermolysis of **2c** or **3c** in benzene-d_6 at 120 °C resulted in clean interconversion between **2c** and **3c**. Thermolysis of 1,2-dihydrobenzocyclobutenols **2d**–**f** or **3d**–**f** without solvent at 150 °C gave a mixture of **2d**–**f** and **3d**–**f** together with 3-acetoxy-2,2-dimethyl-1-(*o*-methylphenyl)alkan-1-ones **1d**–**f** and benzyl ketones **9a**–**c**.

It is well known that benzocyclobutenes undergo an electrocyclic ring opening of the four-membered ring to generate *o*-xylylenes. The *o*-xylylenes are so reactive that they react with various dienophiles to give [4 + 2] cycloadducts[1] or undergo dimerization.[2] The inter- and intramolecular cycloaddition reactions of *o*-xylylenes have been used in the synthesis of polycyclic ring systems.[3] Thermolysis of benzocyclobutenols affords hydroxy-*o*-xylylenes,[4] the geometry of which has been investigated by the analysis of the adduct with maleic anhydride or *N*-phenylmaleimide.[4a] The benzocyclobutenol preferentially opens to produce the (*E*)-dienol. Although the reaction of (*E*)-dienols in the presence of dienophiles has been widely studied,[5] there are few reports on recyclization of dienols generated from benzocyclobutenols. Sammes and co-workers reported that heating optically active 1-methyl-1,2-dihydrobenzocyclobutenol at 110 °C readily gave 2-methylacetophenone because the intermediary (*E*)-dienol underwent proton transfer faster than recyclizationtoproduceracemic1-methyl-1,2-dihydrobenzocyclobutenol.[4a] We report here the thermal interconversion of diastereomeric 1,2-dihydrobenzocyclobutenols **2** and **3**, which are prepared by photocyclization of 3-hydroxy- and 3-acetoxy-2,2-dimethyl-1-(*o*-methylphenyl)alkan-1-ones **1**.



a R^1 = H, R^2 = Pr^i **b** R^1 = H, R^2 = Et **c** R^1 = H, R^2 = Me
d R^1 = Ac, R^2 = Pr^i **e** R^1 = Ac, R^2 = Et **f** R^1 = Ac, R^2 = Me

Scheme 1 *Condition*: i, hν.

Results and discussion

Irradiation of the hydroxy ketone **1a** in methanol with Pyrex-filtered light gave two diastereomeric 1,2-dihydrobenzocyclobutenols **2a** and **3a** together with *trans*- and *cis*-cyclopropane-1,2-diols **4** (Scheme 1).[6] The 1,2-dihydrobenzocyclobutenols **2a** and **3a** could be isolated by column chromatography on silica. The configuration of **2a** was determined by X-ray crystallographic analysis to be (3*S**,1′*S**), so that **3a** had the (3*S**,1′*R**) configuration. The ^{1}H NMR spectrum of **2a** showed peaks due to two methylene protons of the four-membered ring as an AB quartet at δ 2.96 and 3.60 and two methyl singlets on C-2 at δ 0.78 and 1.13, whereas that of **3a** showed two methylene protons at δ 3.03 and 3.55 and two methyl singlets at δ 0.71 and 1.25. The two methylene signals of **2a** were further apart than those of **3a** and the two methyl singlets of **2a** were closer than those of **3a**. Irradiation of hydroxy ketones **1b,c** under the same conditions also gave two diastereomeric 1,2-dihydrobenzocyclobutenols **2b,c** and **3b,c**, the configurations of which could be assigned by comparison of their ^{1}H NMR spectra to those of **2a** and **3a**. Irradiation of acetoxy ketones **1d**–**f** under the same conditions also gave two diastereomeric benzocyclobutenols **2d**–**f** and **3d**–**f** in 95% yield. The configurations of these compounds were determined by the X-ray crystallographic analyses of **3d**, **2e**[7] and **2f**. Results of the photochemical reaction of hydroxy and acetoxy ketones **1a**–**f** are given in Table 1.

When the (3*S**,1′*S**)-1,2-dihydrobenzocyclobutenol **2a** was heated at 120 °C in a sealed glass tube and the progress of the reaction was monitored by ^{1}H NMR, the gradual disappearance of **2a** was observed together with the gradual formation of the (3*S**,1′*R**)-1,2-dihydrobenzocyclobutenol **3a** as well as with the formation of small amounts of the hydroxy ketone **1a** and *o*-methylisobutyrophenone **5** (Scheme 2). After 20 h, a thermal equilibrium between **2a** and **3a** was established, where the **2a** : **3a** ratio was 1 : 1. The yields of the mixture of **2a** and **3a**, the hydroxy ketone **1a** and *o*-methylisobutyrophenone **5** were 93, 2 and 5%, respectively. Heating the (3*S**,1′*R**)-1,2-dihydrobenzocyclobutenol **3a** under the same conditions for 20 h also gave the 1 : 1 mixture of **2a** and **3a** together with small amounts of **1a** and **5**. However, when **2a** or **3a** was heated under the same conditions but at 150 °C for 10 h, only 2-methylisobutyrophenone **5** was obtained. At 150 °C, the 1,2-dihydrobenzocyclobutenols **2a** and **3a** were converted completely into

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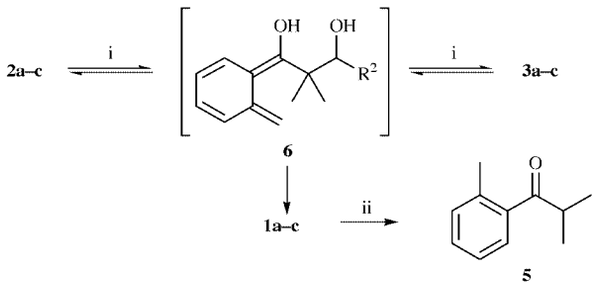


Scheme 2 *Conditions*: i, 120 °C; ii, 150 °C.

the hydroxy ketone **1a** which further underwent retro-aldol cleavage to give **5**. The 1,2-dihydrobenzocyclobutenols **2b** and **3b** also underwent thermal interconversion at 120 °C. However, since the 1,2-dihydrobenzocyclobutenol **2c** has a melting point of 136 °C, it remained unchanged on heating at 120 °C without solvent. On the other hand, when a dilute benzene-d_6 solution of **2c** in an NMR tube was heated at 120 °C, the conversion into the diastereomeric isomer **3c** occurred cleanly without formation of either the hydroxy ketone **1c** or 2-methylisobutyrophenone **5**, though a long time was required to reach a thermal equilibrium between **2c** and **3c**. The compound **3c**, having a melting point below 120 °C, was converted into **2c** on heating at 120 °C without solvent. In this case, a large amount of the hydroxy ketone **1c** was formed after heating for 20 h. However, **3c** was converted cleanly into a 1:1 mixture of **2c** and **3c** on heating in benzene-d_6 at 120 °C. The acetoxy-substituted 1,2-dihydrobenzocyclobutenols **2d–f** and **3d–f** were also interconverted into each other on heating at 150 °C without solvent, together with the formation of **1d–f** and benzyl ketones **9a–c**. After 20 h, a thermal equilibrium between **2d–f** and **3d–f** was established. Results of the thermal reaction of **2** and **3** are given in Table 2.

As already mentioned, the 1,2-dihydrobenzocyclobutenol undergoes selective thermal opening of the cyclobutene ring to form the (*E*)-dienol. The thermal interconversion of the diastereomeric 1,2-dihydrobenzocyclobutenols **2** and **3** probably proceeds *via* the (*E*)-dienol intermediate **6** because the (*E*)-dienol species is sufficiently long-lived to be able to cyclize to give epimers.[8] As shown in Table 2, the major reaction of the diastereomeric 1,2-dihydrobenzocyclobutenols **2** and **3** was the interconversion of diastereomers. Since the (*E*)-dienols formed from **2** and **3** are very congested because of the orientation of the bulky quarternary alkyl group, the possibility that β-hydroxy- and β-acetoxy ketones **1a–f** are formed from the (*Z*)-dienol cannot be ruled out. However, since the thermolysis of a dilute benzene-d_6 solution of **2c** or **3c** cleanly gave a 1:1 mixture of **2c** and **3c**, the 1,2-dihydrobenzocyclobutenols **2** and **3** would open selectively to the (*E*)-dienol because the (*Z*)-dienol is very short-lived and undergoes a rapid 1,5-sigmatropic hydrogen shift to give the ketone **1**.[9] The resulting (*E*)-dienol undergoes recyclization to give 1,2-dihydrobenzocyclobutenols **2** and **3** along with intermolecular hydrogen transfers to give hydroxy and acetoxy ketones **1**.[10] The lower yields of hydroxy ketones **1a**,**b** compared with **1c** in the thermolysis of **3a–c** without solvent at 120 °C may be due to a bulkier substituent in **3a**,**b** than in **3c**. The bulky substituent may prevent the approach of the initially formed (*E*)-dienols. The (*E*)-dienols formed from 1,2-dihydrobenzocyclobutenols having a relatively small substituent react with various dienophiles to give cycloadducts.[5] However, when the 1,2-dihydrobenzocyclobutenol **2a** or **3a** was heated at 120 °C in the presence of dimethyl acetylenedicarboxylate or maleic anhydride, no adduct of the (*E*)-dienol **6** ($R^2 = Pr^i$) with the dienophile could be detected but the interconversion between **2a** and **3a** was observed, perhaps due to steric congestion of **6** ($R^2 = Pr^i$) preventing the access of the dienophile.

The **2a–c**:**3a–c** ratios in the photochemical reaction of **1a–c** increased with increasing size of R^2, whereas these ratios were 1:1 in the thermal reactions of **2a–c** and **3a–c** regardless of the size of R^2 (Table 1 and 2). It is well known that benzocyclobutenols are prepared from the (*E*)-dienols generated by the irradiation of *o*-tolyl ketones.[11] The photochemically generated (*E*)-dienols from **1a–c** in methanol must be solvated by meth-

Table 1 Photochemical reaction of *o*-tolyl ketones **1a–f**

Ketone **1**	Irradiation time/h[a]	Conversion (%)[b]	Yield (%)[c] (**2** + **3**)[d]	Yield (%)[c] **4**	**2**:**3** Ratio[e]
a	2	66	17	43	4:1
b	4	74	47	—	3:2
c	5	50	37	—	4:3
d	15	97	95	—	3:2
e	15	100	95	—	6:5
f	15	94	95	—	1:1

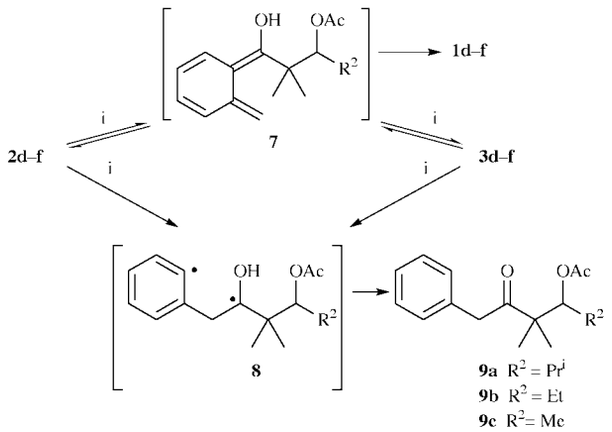
[a] A solution of the ketone (600 mg) in methanol (160 cm^3) was irradiated with a 100 W high-pressure mercury lamp through a Pyrex filter. Ketones **1a–c** were irradiated under ice-cooling. Ketones **1d–f** were irradiated at room temperature. [b] Based on the amount of consumed starting material. [c] Isolated yield based on converted starting material. [d] Sum yield of **2** and **3**. These compounds could be isolated by repeated chromatography. [e] Determined by ^{1}H NMR on the fractions of the mixture after chromatography.

Table 2 Thermal reaction of benzocyclobutenols **2a–f** and **3a–f**

Benzocyclobutenol	Solvent	Temp/°C	Time/h	Yield (%)[a] **1**	(**2** + **3**)	**5**	**9**	**2**:**3** Ratio[b]
2a	None	120	20	2	93	5	—	1:1
3a	None	120	20	5	84	3	—	1:1
2a	None	150	10	—	—	88	—	—
3a	None	150	10	—	—	88	—	—
2b	None	120	20	7	71	—	—	1:1
3b	None	120	20	6	71	—	—	1:1
2c	C_6D_6	120	80	—	100	—	—	1:1
3c	None	120	20	63	16	6	—	1:1
3c	C_6D_6	120	80	—	100	—	—	1:1
2d	None	150	20	20	72	—	8	7:4
3d	None	150	20	9	68	—	11	7:4
2e	None	150	20	7	62	—	11	3:2
3e	None	150	20	18	60	—	11	3:2
2f	None	150	20	11	66	—	2	2:3
3f	None	150	20	20	66	—	7	2:3

[a] Isolated yield. [b] Estimated by ^{1}H NMR on the fractions after chromatography.

anol. The solvated (*E*)-dienols may cyclize to **2** and **3** in a ratio that depends on the size of R^2.[12] The **2d–f**:**3d–f** ratios in the thermal reaction of **2d–f** or **3d–f** were also different from those in the photochemical reaction of **1d–f**. In both thermal and photochemical reactions, the **2d–f**:**3d–f** ratios increased with increasing size of R^2. Finally, the benzyl ketone **9** may be formed by a process involving homolytic cleavage between the aryl carbon and C-1 followed by hydrogen transfer (Scheme 3).[13]



Scheme 3 *Condition*: i, 150 °C.

Experimental

Mps are uncorrected and bps are oven temperatures in Kugelrohr distillation. IR spectra were recorded on a Hitachi 270-50 spectrometer for solutions in CCl_4. ^1H NMR spectra were obtained with a Bruker AC 200, a Bruker AC 300-P or a Bruker AM 400 spectrometer with $CDCl_3$ as a solvent. Tetramethylsilane was used as an internal standard and *J* values are given in Hz. ^{13}C NMR spectra were measured on a Bruker AC 200 or a Bruker AC 300-P spectrometer with $CDCl_3$ as a solvent. An Ushio 100 W high-pressure mercury lamp was used as an irradiation source. Starting compounds **1a**–**c** were prepared by the condensation of *o*-methylisobutyrophenone with the aldehyde according to previously described methods.[14] Compounds **1d**–**f** were prepared by refluxing **1a**–**c** in acetic anhydride in the presence of a catalytic amount of hydrochloric acid.

General procedure for the photolysis of 1a–f

A solution of **1** (600 mg) in methanol (160 cm^3) was irradiated with a 100 W high-pressure mercury lamp through a Pyrex filter under argon for 2–15 h (see Table 1). The solvent was removed under reduced pressure, and the residue was chromatographed on silica gel [hexane–ethyl acetate (6:1 to 22:1)] to give 1,2-dihydrobenzocyclobutenols **2** and **3** and the cyclopropane-1,2-diol **4**. The physical properties of **4** have already been described in a previous paper.[6]

(3*S,1′*S**)-2-(1′-Hydroxy-1′,2′-dihydrobenzocyclobuten-1′-yl)-2,4-dimethylpentan-3-ol 2a.** Mp 67–68 °C (from hexane) (Found: C, 77.1; H, 9.3. $C_{15}H_{22}O_2$ requires C, 76.9; H, 9.5%); ν_{max}/cm^{-1} 3400br (OH); δ_H (300 MHz) 0.78 (3 H, s) and 1.13 (3 H, s) (1-H_3 and 2-Me), 0.99 (3 H, d, *J* 7) and 1.08 (3 H, d, *J* 7) (CH*Me*$_2$), 2.00 (1 H, m, C*H*Me$_2$), 2.96 (1 H) and 3.60 (1 H) (AB-pair, *J* 15, 2′-H_2), 2.97 (1 H, br s) and 3.90 (2 H, m) (2 × OH and 3-H) and 7.1–7.3 (4 H, m, ArH); δ_C (50 MHz) 16.3 (q), 16.9 (q), 21.7 (q) and 23.4 (q) (4 × Me), 29.3 (d, C-4), 42.4 (s, C-2), 43.7 (t, C-2′), 80.8 (d, C-3), 89.1 (s, C-1′), 121.9 (d), 123.5 (d), 127.1 (d), 129.2 (d), 142.5 (s) and 148.7 (s) (ArC).

(3*S,1′*R**)-2-(1′-Hydroxy-1′,2′-dihydrobenzocyclobuten-1′-yl)-2,4-dimethylpentan-3-ol 3a.** Mp 74–75 °C (from hexane) (Found: C, 77.1; H, 9.3. $C_{15}H_{22}O_2$ requires C, 76.9; H, 9.5%); ν_{max}/cm^{-1} 3450br (OH); δ_H (300 MHz) 0.71 (3 H, s) and 1.25 (3 H, s) (1-H_3 and 2-Me), 0.99 (3 H, d, *J* 7) and 1.06 (3 H, d, *J* 7) (CH*Me*$_2$), 2.00 (1 H, m, C*H*Me$_2$), 3.03 (1 H) and 3.55 (1 H) (AB-pair, *J* 15, 2′-H_2), 3.01 (1 H, br s, OH), 3.78 (1 H, m, 3-H), 4.10 (1 H, br s, OH) and 7.1–7.3 (4 H, m, ArH); δ_C (50 MHz) 16.4 (q), 17.3 (q), 21.4 (q) and 23.2 (q) (4 × Me), 29.5 (d, C-4), 42.5 (s, C-2), 43.1 (t, C-2′), 80.3 (d, C-3), 89.6 (s, C-1′), 121.9 (d), 123.5 (d), 127.1 (d), 129.2 (d), 142.5 (s) and 148.3 (s) (ArC).

(3*S,1′*S**)-2-(1′-Hydroxy-1′,2′-dihydrobenzocyclobuten-1′-yl)-2-methylpentan-3-ol 2b.** Mp 96–97 °C (from hexane) (Found: C, 76.4; H, 9.2. $C_{14}H_{20}O_2$ requires C, 76.3; H, 9.2%); ν_{max}/cm^{-1} 3300br (OH); δ_H (200 MHz) 0.75 (3 H, s) and 0.92 (3 H, s) (1-H_3 and 2-Me), 0.99 (3 H, t, *J* 7, 5- H_3), 1.3–1.6 (2 H, m, 4-H_2), 2.88 (1 H) and 3.53 (1 H) (AB-pair, *J* 15, 2′-H_2), 3.74 (1 H, m, 3-H), 3.14 (1 H, br s) and 4.02 (1 H, br s) (2 × OH) and 7.1–7.3 (4 H, m, ArH); δ_C (50 MHz) 11.3 (q), 16.8 (q) and 21.8 (q) (3 × Me), 24.6 (t, C-4), 41.3 (s, C-2), 43.5 (t, C-2′), 80.1 (d, C-3), 88.0 (s, C-1′), 121.9 (d), 123.2 (d), 126.8 (d), 128.9 (d), 142.4 (s) and 148.6 (s) (ArC).

(3*S,1′*R**)-2-(1′-Hydroxy-1′,2′-dihydrobenzocyclobuten-1′-yl)-2-methylpentan-3-ol 3b.** Mp 104–105 °C (from hexane) (Found: C, 76.4; H, 9.2. $C_{14}H_{20}O_2$ requires C, 76.3; H, 9.2%); ν_{max}/cm^{-1} 3300br (OH); δ_H (200 MHz) 0.69 (3 H, s) and 1.14 (3 H, s) (1-H_3 and 2-Me), 1.05 (3 H, t, *J* 7, 5-H_3), 1.4–1.8 (2 H, m, 4-H_2), 3.03 (1 H) and 3.57 (1 H) (AB-pair, *J* 15, 2′-H_2), 3.65 (1 H, m, 3-H), 4.27 (1 H, br s) and 5.11 (1 H, br s) (2 × OH) and 7.1–7.3 (4 H, m, ArH); δ_C (50 MHz) 11.1 (q), 16.6 (q) and 21.6 (q) (3 × Me), 24.8 (t, C-4), 41.7 (s, C-2), 42.9 (t, C-2′), 79.3 (d, C-3), 88.8 (s, C-1′), 121.9 (d), 123.5 (d), 127.1 (d), 129.1 (d), 142.4 (s) and 148.4 (s) (ArC).

(2*S,1′*S**)-3-(1′-Hydroxy-1′,2′-dihydrobenzocyclobuten-1′-yl)-3-methylbutan-2-ol 2c.** Mp 136–137 °C (from hexane) (Found: C, 75.5; H, 8.7. $C_{13}H_{18}O_2$ requires C, 75.7; H, 8.8%); ν_{max}/cm^{-1} 3400br (OH); δ_H (300 MHz) 0.74 (3 H, s) and 1.05 (3 H, s) (4-H_3 and 3-Me), 1.22 (3 H, d, *J* 7, 1-H_3), 2.98 (1 H) and 3.63 (1 H) (AB-pair, *J* 15, 2′-H_2), 3.69 (1 H, br s) and 3.55 (1H, br s) (2 × OH), 4.19 (1 H, q, *J* 7, 2-H) and 7.1–7.3 (4 H, m, ArH); δ_C (75 MHz) 15.5 (q), 18.4 (q) and 22.0 (q) (3 × Me), 41.4 (s, C-3), 43.9 (t, C-2′), 73.9 (d, C-2), 88.4 (s, C-1′), 121.9 (d), 123.5 (d), 127.1 (d), 129.3 (d), 142.4 (s) and 148.5 (s) (ArC).

(2*S,1′*R**)-3-(1′-Hydroxy-1′,2′-dihydrobenzocyclobuten-1′-yl)-3-methylbutan-2-ol 3c.** Mp 84–85 °C (from hexane) (Found: C, 75.5; H, 8.7. $C_{13}H_{18}O_2$ requires C, 75.7; H, 8.8%); ν_{max}/cm^{-1} 3450br (OH); δ_H (300 MHz) 0.62 (3 H, s) and 1.15 (3 H, s) (4-H_3 and 3-Me), 1.16 (3 H, d, *J* 7, 1-H_3), 3.02 (1 H) and 3.55 (1 H) (AB-pair, *J* 15, 2′-H_2), 3.85 (1 H, br s) and 4.20 (1 H, br s) (2 × OH), 4.07 (1 H, q, *J* 7) and 7.1–7.3 (4 H, m, ArH); δ_C (50 MHz) 15.5 (q), 18.4 (q) and 21.7 (q) (3 × Me), 41.5 (s, C-3), 42.8 (t, C-2′), 73.2 (d, C-2), 88.8 (s, C-1′), 121.8 (d), 123.5 (d), 127.1 (d), 129.2 (d), 142.4 (s) and 148.3 (s) (ArC).

(3*S,1′*S**)-3-Acetoxy-2-(1′-hydroxy-1′,2′-dihydrobenzocyclobuten-1′-yl)-2,4-dimethylpentane 2d.** Mp 72–73 °C (from hexane) (Found: C, 74.0; H, 8.9. $C_{17}H_{24}O_3$ requires C, 73.9; H, 8.8%); ν_{max}/cm^{-1} 3500br (OH) and 1720 (C=O); δ_H (200 MHz) 0.90 (3 H, s) and 1.22 (3 H, s) (1-H_3 and 2-Me), 0.96 (3 H, d, *J* 7) and 1.01 (3 H, d, *J* 7) (CH*Me*$_2$), 2.12 (3 H, s, COMe), 2.0–2.2 (1 H, m, C*H*Me$_2$), 3.31 (1 H, br s, OH), 2.83 (1 H) and 3.59 (1 H) (AB-pair, *J* 15, 2′-H_2), 5.18 (1 H, d, *J* 3, 3-H) and 7.1–7.3 (4 H, m, ArH); δ_C (50 MHz) 17.7 (q), 18.1 (q), 21.1 (q), 21.3 (q) and 23.3 (q) (5 × Me), 28.7 (d, C-4), 43.2 (s, C-2), 43.4 (t, C-2′), 79.9 (d, C-3), 86.1 (s, C-1′), 122.1 (d), 123.3 (d), 127.0 (d), 129.1 (d), 143.0 (s) and 148.2 (s) (ArC) and 172.0 (s, C=O).

(3*S,1′*R**)-3-Acetoxy-2-(1′-hydroxy-1′,2′-dihydrobenzocyclobuten-1′-yl)-2,4-dimethylpentane 3d.** Mp 67–68 °C (from hexane) (Found: C, 74.1; H, 8.8. $C_{17}H_{24}O_3$ requires C, 73.9; H,

8.8%); ν_{max}/cm^{-1} 3500br (OH) and 1750 (C=O); δ_H (200 MHz) 0.90 (3 H, s) and 1.14 (3 H, s) (1-H_3 and 2-Me), 0.97 (3 H, d, *J* 7) and 0.98 (3 H, d, *J* 7) (CH*Me*$_2$), 2.14 (3 H, s, COMe), 2.1–2.3 (1 H, m, C*H*Me$_2$), 2.67 (1 H, br s, OH), 2.99 (1 H) and 3.66 (1 H) (AB-pair, *J* 15, 2′-H_2), 5.14 (1 H, d, *J* 2, 3-H) and 7.1–7.3 (4 H, m, ArH); δ_C (50 MHz) 17.4 (q), 20.3 (q), 20.6 (q), 21.2 (q) and 23.2 (q) (5 × Me), 29.2 (d, C-4), 43.1 (s, C-2), 43.8 (t, C-2′), 81.0 (d, C-3), 86.9 (s, C-1′), 121.8 (d), 123.4 (d), 127.0 (d), 129.1 (d), 142.4 (s) and 148.7 (s) (ArC) and 172.0 (s, C=O).

(3*S,1′*R**)-3-Acetoxy-2-(1′-hydroxy-1′,2′-dihydrobenzocyclobuten-1′-yl)-2-methylpentane 2e.** Mp 83–84 °C (from hexane) (Found: C, 73.3; H, 8.6. $C_{16}H_{22}O_3$ requires C, 73.3; H, 8.5%); ν_{max}/cm^{-1} 3500br (OH) and 1720 (C=O); δ_H (200 MHz) 0.82 (3 H, s) and 1.19 (3 H, s) (1-H_3 and 2-Me), 0.91 (3 H, t, *J* 7, 5-H_3), 1.66 (2 H, m, 4-H_2), 2.11 (3 H, s, COMe), 2.83 (1 H) and 3.58 (1 H) (AB-pair, *J* 15, 2′-H_2), 3.55 (1H, br s, OH), 5.17 (1 H, dd, *J* 3 and 10, 3-H) and 7.1–7.3 (4 H, m, ArH); δ_C (50 MHz) 10.8 (q), 17.7 (q), 21.1 (q) and 21.3 (q) (4 × Me), 22.8 (t, C-4), 42.5 (s, C-2), 43.1 (t, C-2′), 79.2 (d, C-3), 85.6 (s, C-1′), 122.1 (d), 123.2 (d), 126.9 (d), 129.0 (d), 142.8 (s) and 148.1 (s) (ArC) and 172.1 (s, C=O).

(3*S,1′*S**)-3-Acetoxy-2-(1′-hydroxy-1′,2′-dihydrobenzocyclobuten-1′-yl)-2-methylpentane 3e.** Mp 72–73 °C (from hexane) (Found: C, 73.4; H, 8.5. $C_{16}H_{22}O_3$ requires C, 73.3; H, 8.5%); ν_{max}/cm^{-1} 3500br (OH) and 1750 (C=O); δ_H (200 MHz) 0.85 (3 H, s) and 1.08 (3 H, s) (1-H_3 and 2-Me), 0.88 (3 H, t, *J* 7, 5-H_3), 1.67 (2 H, m, 4-H_2), 2.11 (3 H, s, COMe), 2.79 (1 H, br s, OH), 2.96 (1 H) and 3.63 (1 H) (AB-pair, *J* 15, 2′-H_2), 5.21 (1 H, dd, *J* 1 and 3, 3-H) and 7.1–7.3 (4 H, m, ArH); δ_C (50 MHz) 10.9 (q), 19.7 (q), 20.3 (q) and 21.2 (q) (4 × Me), 23.7 (t, C-4), 42.5 (s, C-2), 44.2 (t, C-2′), 79.9 (d, C-3), 86.5 (s, C-1′), 122.0 (d), 123.4 (d), 127.0 (d), 129.2 (d), 142.7 (s) and 148.8 (s) (ArC) and 171.2 (s, C=O).

(2*S,1′*S**)-2-Acetoxy-3-(1′-hydroxy-1′,2′-dihydrobenzocyclobuten-1′-yl)-3-methylbutane 2f.** Mp 79–80 °C (from hexane) (Found: C, 72.7; H, 8.2. $C_{15}H_{22}O_3$ requires C, 72.6; H, 8.1%); ν_{max}/cm^{-1} 3630 (OH) and 1750 (C=O); δ_H (200 MHz) 0.89 (3 H, s) and 1.13 (3 H, s) (4-H_3 and 3-Me), 1.25 (3 H, d, *J* 7, 1-H_3), 2.04 (3 H, s, COMe), 2.88 (1 H) and 3.66 (1 H) (AB-pair, *J* 15, 2′-H_2), 3.07 (1 H, br s, OH), 5.34 (1 H, q, *J* 7, 2-H) and 7.1–7.3 (4 H, m, ArH); δ_C (50 MHz) 15.6 (q), 17.2 (q), 21.0 (q) and 21.6 (q) (4 × Me), 42.2 (s, C-3), 43.7 (t, C-2′), 74.0 (d, C-2), 85.8 (s, C-1′), 122.0 (d), 123.4 (d), 127.1 (d), 129.2 (d), 142.9 (s) and 148.6 (s) (ArC) and 171.0 (s, C=O).

(2*S,1′*R**)-3-Acetoxy-3-(1′-hydroxy-1′,2′-dihydrobenzocyclobuten-1′-yl)-3-methylbutane 3f.** Bp 96–98 °C at 0.3 mmHg (Found: C, 72.6; H, 8.2. $C_{15}H_{22}O_3$ requires C, 72.6; H, 8.1%); ν_{max}/cm^{-1} 3470br (OH) and 1740 (C=O); δ_H (200 MHz) 0.87 (3 H, s) and 1.10 (3 H, s) (4-H_3 and 3-Me), 1.25 (3 H, d, *J* 7, 1-H_3), 2.06 (3 H, s, COMe), 2.74 (1 H, br s, OH), 2.95 (1 H) and 3.64 (1 H) (AB-pair, *J* 15, 2′-H_2), 5.22 (1 H, q, *J* 7, 2-H) and 7.1–7.3 (4 H, m, ArH); δ_C (50 MHz) 16.0 (q), 19.4 (2q) and 21.4 (q) (4 × Me), 41.8 (s, C-3), 44.1 (t, C-2′), 75.2 (d, C-2), 86.2 (s, C-1′), 122.0 (d), 123.3 (d), 126.9 (d), 129.1 (d), 142.5 (s) and 148.6 (s) (ArC) and 170.3 (s, C=O).

Pyrolysis of 1′,2′-dihydrobenzocyclobutenols 2a–f and 3a–f

1′,2′-Dihydrobenzocyclobutenol **2a–c** or **3a–c** (100 mg) was sealed in an 8 mm diameter Pyrex tube under argon. The tube was heated at 120 °C for 20 h. The ^{1}H NMR analysis of the mixture revealed that interconversion occurred between **2a–c** and **3a–c**. The mixture was chromatographed on silica gel and eluted with a mixture of hexane and ethyl acetate (4:1 to 6:1) to give two isomeric 1,2-dihydrobenzocyclobutenols **2a–c** and **3a–c**, hydroxy ketone **1a–c** and *o*-methylisobutyrophenone **5**. The same treatment of 1,2-dihydrobenzocyclobutenol **2d–f** or **3d–f** (100 mg) but at 150 °C for 20 h gave acetoxy ketone **1d–f**, 1,2-dihydrobenzocyclobutenol **2d–f** and **3d–f** and 4-acetoxy-3,3-dimethyl-1-phenylbutan-2-one **9a–c**. 1,2-Dihydrobenzocyclobutenol **2c** or **3c** (*ca.* 10 mg) in benzene-d_6 (*ca.* 0.5 cm^3) was placed in a 5 mm diameter NMR tube and degassed by freeze–pump–thaw cycles. The tube was heated at 120 °C for 80 h. The ^{1}H NMR spectrum of the mixture showed only peaks due to a 1:1 mixture of **2c** and **3c**.

4-Acetoxy-3,3,5-trimethyl-1-phenylhexan-2-one 9a. Bp 97–98 °C at 0.4 mmHg (Found: C, 73.6; H, 8.8. $C_{17}H_{24}O_3$ requires C, 73.9; H, 8.8%); ν_{max}/cm^{-1} 1740 (ester C=O) and 1720 (C=O); δ_H (300 MHz) 0.86 (3 H, d, *J* 7) and 0.89 (3 H, d, *J* 7) (6-H_3 and 5-Me), 1.13 (3 H, s) and 1.22 (3 H, s) (3-Me_2), 1.90 (1 H, d × sept, *J* 6 and 7, 5-H), 2.09 (3 H, s, COMe), 3.81 (1 H) and 3.88 (1 H) (AB-pair, *J* 16, 1-H_2), 5.20 (1 H, d, *J* 6, 4-H) and 7.2–7.4 (5 H, m, ArH); δ_C (75 MHz) 18.5 (q), 20.1 (q), 20.8 (q), 21.5 (q) and 22.7 (q) (5 × Me), 29.6 (d, C-5), 44.5 (t, C-1), 52.3 (s, C-3), 80.7 (d, C-4), 126.7 (d), 128.4 (d), 129.6 (d) and 134.3 (s) (ArC), 170.7 (s, OC=O) and 210.4 (s, C=O).

4-Acetoxy-3,3-dimethyl-1-phenylhexan-2-one 9b. Bp 86–88 °C at 0.3 mmHg (Found: C, 73.2; H, 8.5. $C_{16}H_{22}O_3$ requires C, 73.3; H, 8.5%); ν_{max}/cm^{-1} 1740 (ester C=O) and 1720 (C=O); δ_H (200 MHz) 0.86 (3 H, t, *J* 7, 6-H_3), 1.16 (3 H, s) and 1.19 (3 H, s) (3-Me_2), 1.4–1.5 (2 H, m, 5-H_2), 2.07 (3 H, s, COMe), 3.82 (2 H, s, 1-H_2), 5.25 (1 H, dd, *J* 5 and 8, 4-H) and 7.2–7.3 (4 H, m, ArH); δ_C (50 MHz) 10.8 (q), 20.3 (q), 21.2 (q) and 23.5 (q) (4 × Me), 20.8 (t, C-5), 44.5 (t, C-1), 52.1 (s, C-3), 78.4 (d, C-4), 126.7 (d), 128.4 (d), 129.6 (d) and 134.4 (s) (ArC), 170.7 (s, ester C=O) and 210.1 (s).

4-Acetoxy-3,3-dimethyl-1-phenylpentan-2-one 9c. Bp 96–98 °C at 0.4 mmHg (Found: C, 72.7; H, 8.2. $C_{15}H_{22}O_3$ requires C, 72.6; H, 8.1%); ν_{max}/cm^{-1} 1740 (ester C=O) and 1720 (C=O); δ_H (200 MHz) 1.16 (3 H, d, *J* 7, 5-H_3), 1.17 (3 H, s) and 1.19 (3 H, s) (3-Me_2), 1.97 (3 H, s, COMe), 3.79 (2 H, s, 1-H_2), 5.26 (1 H, q, *J* 7, 4-H) and 7.1–7.3 (5 H, m, ArH); δ_C (50 MHz) 14.9 (q), 19.6 (q), 20.8 (q) and 21.0 (q) (4 × Me), 44.2 (t, C-1), 51.4 (s, C-3), 74.0 (d, C-4), 126.6 (d), 128.3 (d), 129.5 (d) and 134.2 (s) (ArC), 170.1 (s, ester C=O) and 210.1 (s, C=O).

Pyrolysis of 2a and 3a in the presence of dienophile

A solution of 100 mg of **2a** or **3a** and 2 equiv. of dimethyl acetylenedicarboxylate or maleic anhydride in 1 cm^3 of benzene was sealed in a glass tube. The tube was degassed by freeze–pump–thaw cycles and heated at 120 °C for 20 h. The solvent was removed and the residue was fractionated by chromatography on silica gel using a 4:1 mixture of hexane and ethyl acetate. The ^{1}H NMR spectrum of each of the fractions revealed that **2a** and **3a** were interconverted, while no adduct of the dienol arising from **2a** or **3a** with dienophile was detected.

Crystallographic analysis of 2a, 2f and 3d

Data were collected on a MAC Science DIP3000 diffractometer with Mo-Kα radiation (λ = 0.71073 Å) at 298 K and the structure was solved by direct methods. Crystal data for **2a**: $C_{15}H_{22}O_2$, *M* = 234.37, orthorhombic, *a* = 7.8840(5), *b* = 12.514(1), *c* = 14.297(1) Å, *V* = 1410.6(2) Å^3, *Z* = 4, space group $P2_12_12_1$, μ = 0.067 mm^{-1}. The crystal used had dimensions of 0.5 × 0.5 × 0.4 mm. The final cycle of full-matrix least-squares refinement was based on 1747 observed reflections [$I > 3\sigma(I)$] and 242 variable parameters with $R(R_w)$ = 0.049 (0.062). Crystal data for **2f**: $C_{15}H_{22}O_3$, *M* = 248.32, monoclinic, *a* = 11.308(2), *b* = 9.460(1), *c* = 13.187(1) Å, *V* = 1402.4 (3) Å^3, *Z* = 4, space group $P2_1/n$, μ = 0.075 mm^{-1}. The crystal used had dimensions of 0.3 × 0.3 × 0.28 mm. The final cycle of full-matrix least-squares refinement was based on 1920 observed

reflections [$I > 3\sigma(I)$] and 243 variable parameters with $R(R_w) = 0.053$ (0.067). Crystal data for **3d**: $C_{17}H_{24}O_3$, $M =$ 276.38, monoclinic, $a = 10.106(1)$, $b = 25.218(2)$, $c = 12.298(2)$ Å, $V = 3134.2(2)$ Å^3, $Z = 8$, space group $P2_1/n$, $\mu = 0.074$ mm^{-1}. The crystal used had dimensions of $0.15 \times 0.15 \times 0.15$ mm. The final cycle of full-matrix least-squares refinement was based on 2941 observed reflections [$I > 3\sigma(I)$] and 415 variable parameters with $R(R_w) = 0.054$ (0.071).

CCDC reference number 207/396. See http://www.rsc.org/suppdata/p1/a9/a908326j for crystallographic files in .cif format.

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