

## A New Synthesis of Benzocyclobutenes. Thermal and Electron Impact Induced Decomposition of 3-Isochromanones

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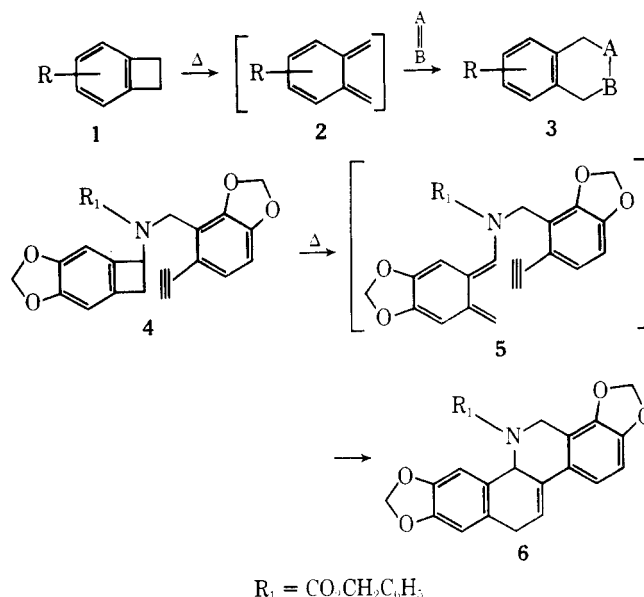
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The gas-phase pyrolysis of 3-isochromanones provides a new synthesis of benzocyclobutenes, including the parent hydrocarbon, 21, benzocyclobutenone (8), and several benzocyclobutenes with oxygenated substituents on the aryl ring, 25 and 28; fulveneallene (9) is also prepared in high yield. The relationship between the thermal and electron impact induced decomposition of the isochromanones is described.

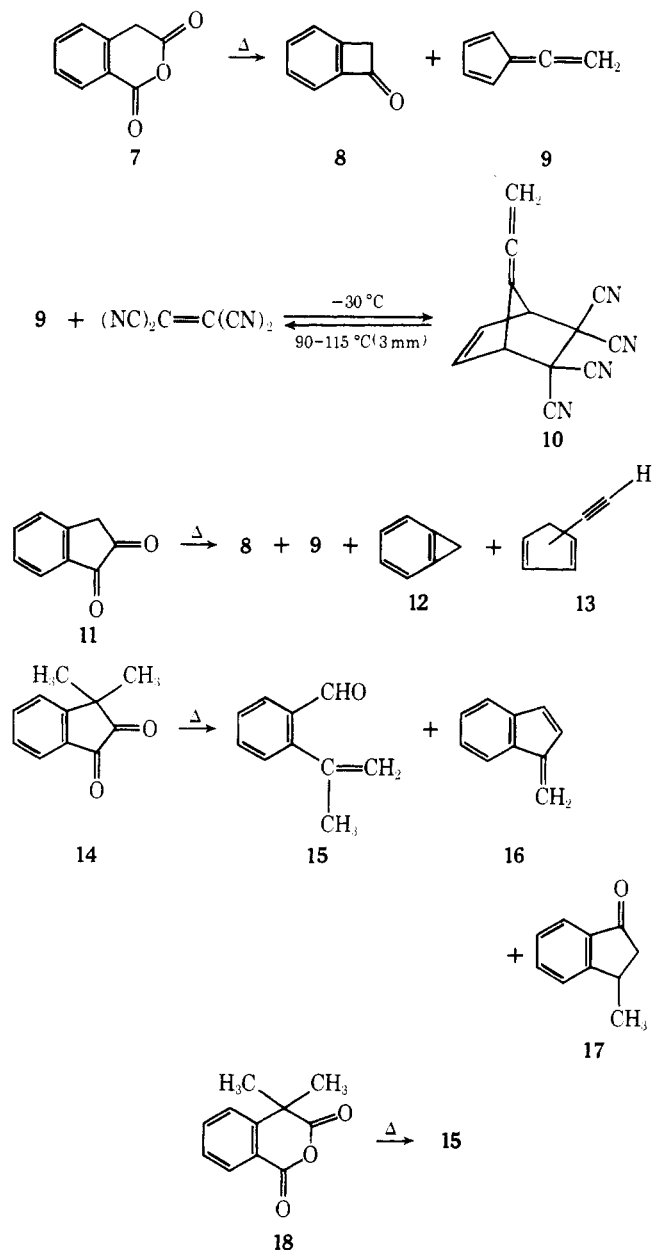
Although the development of benzocyclobutene chemistry began two decades ago,<sup>1,2</sup> and has received considerable attention since,<sup>3</sup> much interest in the chemistry of benzocyclobutenes prevails today. Theoretical calculations and physical studies of benzocyclobutenes, including their <sup>13</sup>C NMR spectra,<sup>4</sup> have been described in several recent reports.<sup>5</sup> The formation<sup>6</sup> and reactions<sup>7</sup> of numerous benzocyclobutenes are of continuing interest. 1,2-Dibromobenzocyclobutene was used as a precursor of benzocyclobutadiene in the first characterization of this elusive hydrocarbon.<sup>8</sup> Benzocyclobutenes are also useful intermediates in organic synthesis. These syntheses utilize the Diels–Alder reactivity of *o*-quinodimethanes (2) derived from benzocyclobutenes (1) by electrocyclic ring opening. Although the sequence 1 → 2 → 3 was recognized early in the development of benzocyclobutene chemistry,<sup>3</sup> it was not used synthetically until 1971 in the original synthesis of chelidonine (4 → 5 → 6).<sup>9</sup> Recent syntheses of berberines,<sup>10</sup> spirobenzylisoquinolines,<sup>11</sup> 3-arylisquinolines,<sup>12</sup> benzocarbazoles,<sup>13</sup> yohimbanes,<sup>14</sup> and tetracyclines<sup>15</sup> have also utilized the Diels–Alder reactivity of dienes (2) derived by the thermolysis of benzocyclobutenes (1).<sup>16</sup> Because of their synthetic potential, intramolecular cyclizations similar to that used in the chelidonine synthesis have been examined in more detail,<sup>17</sup> the mechanisms of intermolecular cyclizations have been discussed,<sup>18</sup> the ease of electrocyclic ring openings of benzocyclobutenes have been correlated with their <sup>13</sup>C NMR chemical shifts,<sup>19</sup> and the Diels–Alder reactions of the *o*-quinodimethane (24a) generated by ring opening of 4-methoxybenzocyclobutene (25a) have been considered in terms of frontier orbital theory.<sup>20</sup> Simultaneous with the development of new synthetic methods using benzocyclobutenes as intermediates has been the appearance of a host of new syntheses of benzocyclobutene and its derivatives. Some of these have only been applied to the synthesis of the parent benzocyclobutene,<sup>21</sup> or a specific benzocyclobutene,<sup>22</sup> while others offer promise as a more general synthesis<sup>23</sup> of various benzocyclobutenes. We wish to describe the results of the pyrolysis of 3-isochromanones, a process which provides an efficient synthesis of benzocyclobutene (21), benzocyclobutenone (8), fulveneallene (9), and several benzocyclobutenes, 25 and 28, with oxygenated substituents on the aryl ring. Furthermore, we report a relationship between the thermal and electron impact induced decomposition of the 3-isochromanones.<sup>24</sup>

**Pyrolysis of Homophthalic Anhydride (7), 4,4-Dimethylhomophthalic Anhydride (18), and 1,2-Indandione (11).** Homophthalic anhydride (7) was pyrolyzed by subliming 7 in a stream of nitrogen (22 mL/min) at 2 Torr over a heated nichrome wire. The pyrolysate, which was collected in a cold trap at -78 °C, consisted of a mixture of benzocyclobutenone (8) and fulveneallene (9); unreacted 7 solidified directly above the pyrolysis zone. When the cold trap was warmed to -25 °C at 1 mm, fulveneallene readily distilled to a second -78 °C trap. This process provided a simple means of obtaining pure



8 and 9. In all cases the material balance was excellent and little carbonization occurred. No additional products were indicated by examination of the <sup>1</sup>H NMR spectra of the pyrolysates. The yields of pyrolysis products as a function of the pyrolysis temperature are shown in Figure 1. Ketone 8 was isolated pure in greater than 40% yield when the pyrolysis temperature was 515–545 °C. At 570 °C 9 was isolated pure in 71% yield. Thus the pyrolysis of homophthalic anhydride offers a convenient, one-step preparation of either 8<sup>25</sup> or 9.<sup>26</sup> Fulveneallene was also converted to the known tetracyanoethylene adduct 10.<sup>25a</sup> When the neat adduct 10 was heated at 95–115 °C at 3 mm, 9 was regenerated and could be collected in a -78 °C cold trap. The overall process 9 → 10 → 9 proceeded in a 75% yield. Thus the unstable fulveneallene was stored in the form of the stable, solid adduct 10, and was then easily regenerated later. This observation should facilitate the further study of this hydrocarbon.<sup>27</sup>

The thermal decomposition of homophthalic anhydride was very similar to that reported by Hedaya and Kent<sup>25a</sup> for 1,2-indandione (11), where 8 and 9 were also the major products. However, these authors found that benzocyclopropene (12) and ethynylcyclopentadiene (13) were produced as minor products. These products could not be detected in the <sup>1</sup>H NMR spectra of our pyrolysates from homophthalic anhydride. So that an exact comparison of the pyrolysis of homophthalic anhydride and 1,2-indandione could be made we pyrolyzed 11 under the same conditions used for the pyrolysis of 7. Thus, the pyrolysis of 11 at 540 °C gave 8 in a 2.5% yield and 9 in a 2.5% yield. A considerable amount (94%) of the initial 11 remained unreacted in the sample reservoir as a tarry residue. In contrast the pyrolysis of homophthalic anhydride under the same conditions gave 8 in 45% yield and 9



in 36% yield and only 19% of recovered 7. Peaks attributable to 12 and 13 were absent from the NMR spectrum of both pyrolysates. Thus under our conditions at 540 °C neither 7 nor 11 produced 12 or 13. Only at considerably higher temperatures, such as used by Hedaya and Kent,<sup>25a</sup> were the latter hydrocarbons produced. Because 7 was stable and sublimed readily whereas 11 underwent tar formation at the temperature required for its sublimation, 7 is the superior precursor to 8 and 9.

To compare further the pyrolysis of 1,2-indandiones with analogous homophthalic anhydrides, we examined the pyrolysis of 4,4-dimethylhomophthalic anhydride (18). Brown and Butcher<sup>28</sup> have reported that the pyrolysis of 3,3-dimethyl-1,2-indandione (14) gave *o*-(2-propenyl)benzaldehyde (15) as the major product and lesser amounts of benzofulvene (16) and 3-methyl-1-indanone (17); 2,2-dimethylbenzocyclobutenone was not found. Pyrolysis of anhydride 18 also gave 15 as the major product in 65% yield. Furthermore, the gas chromatogram of our crude pyrolysate was qualitatively similar to that reported for the crude pyrolysate of 14 except that no peaks corresponding to 16 or 17 were observed in our chromatogram. Thus, in these two comparisons, 1,2-indandiones and the analogous homophthalic anhydrides behaved in a similar manner upon pyrolysis. We did not examine the

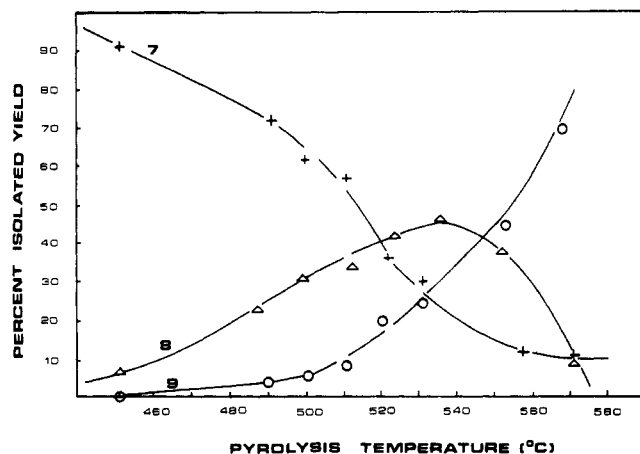
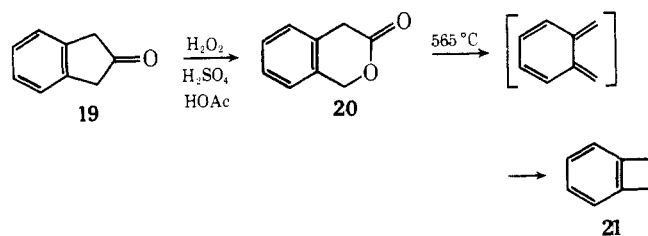


Figure 1. Pyrolysis of homophthalic anhydride (7).

mechanisms of these pyrolyses because reasonable ones have been proposed.<sup>25a,27,28</sup> Crow and Paddon-Row have suggested a common mechanism for the decomposition of 7 and 11.<sup>27</sup> We propose that 14 and 18 also decompose by the same pathway. Brown and Butcher have suggested a likely mechanism for the decomposition of 14.<sup>28</sup>

**Synthesis of Benzocyclobutene (21) from 3-Isochromanone (20).** 3-Isochromanone (20) was pyrolyzed by passing 20 vapor in a stream of nitrogen (20 mL/min) at 2 Torr over a heated, coiled nichrome wire; the crude pyrolysate was collected in a cold trap at  $-78^\circ\text{C}$  and was then vacuum distilled. The variation in the yield of distillate as a function of pyrolysis temperature is shown in Figure 2. At pyrolysis temperatures up to ca. 600 °C benzocyclobutene (21) was the sole component of the distillate (analysis by GC and <sup>1</sup>H NMR). At temperatures above ca. 600 °C the distillate had a light yellow color and traces of two additional volatile products were evident from the gas chromatogram. One of the minor products showed the same GC retention time as styrene, a known thermal decomposition product of benzocyclobutene,<sup>29</sup> but no further attempts were made to identify these minor products. An optimal 85% yield of pure benzocyclobutene was obtained at pyrolysis temperatures of 565–575 °C. 3-Isochromanone (20) was prepared in 70–80% yield by the Baeyer-Villiger oxidation of 2-indanone (19).<sup>30</sup> Thus this two-step sequence provides a simple and efficient synthesis of benzocyclobutene (21) from commercially available 2-



indanone (19)<sup>31</sup> in an overall yield of 60–65%. The good yield and brevity of the synthesis are advantages over other syntheses of benzocyclobutene.<sup>3,21</sup>

**Pyrolysis of 3-Isochromanones with Oxygenated Substituents on the Aryl Ring.** The pyrolyses of 6-methoxy-3-isochromanone (23a), 6,7-dimethoxy-3-isochromanone (23b), and 6,7-methylenedioxy-3-isochromanone (23c) gave 4-methoxybenzocyclobutene (25a) (70% yield), 4,5-dimethoxybenzocyclobutene (25b) (40% yield), and 4,5-methylenedioxybenzocyclobutene (25c) (90% yield), respectively. The optimum pyrolysis temperature for these isochromanones was found to be ca. 500 °C. 6,7-Dimethoxy-3-isochromanone (23b) was prepared in 80% yield by the reac-

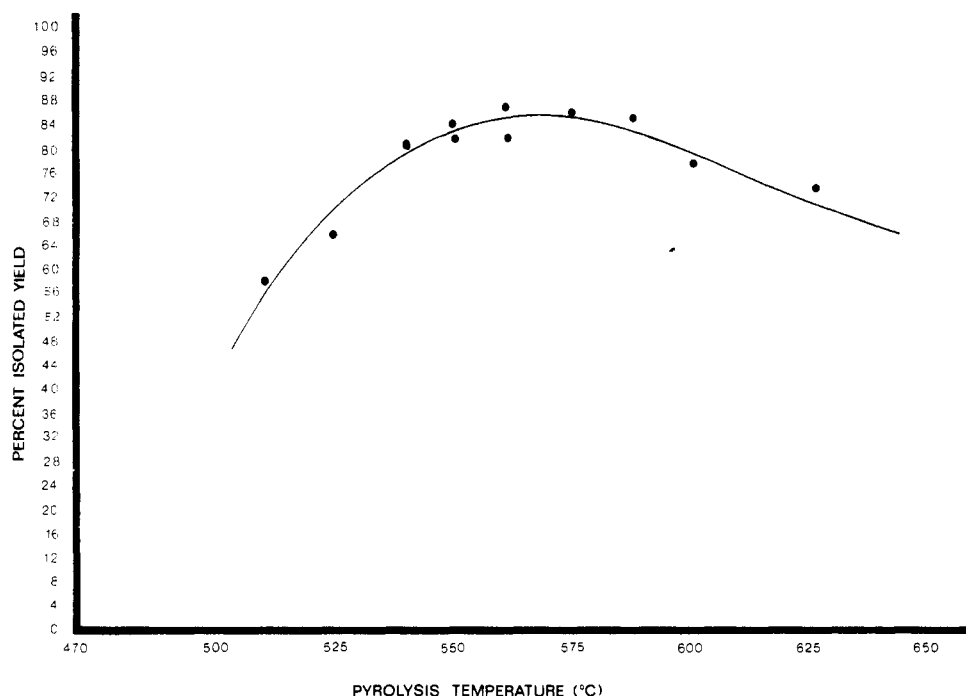
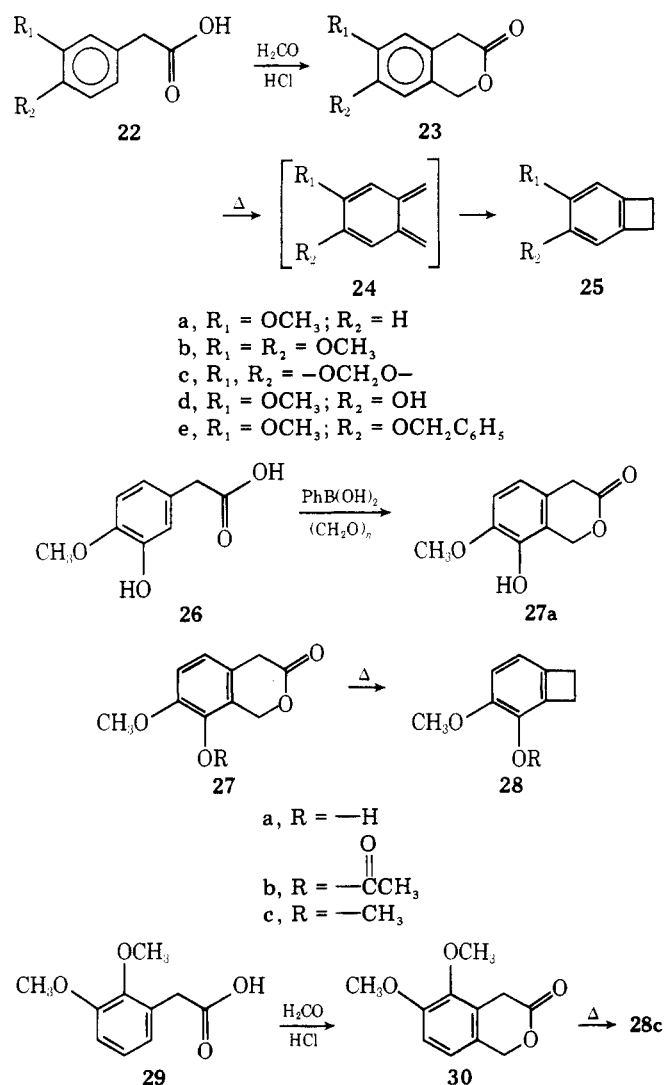


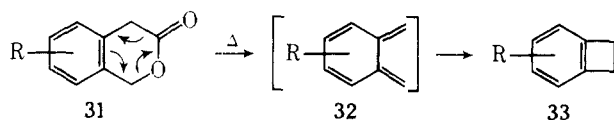
Figure 2. Pyrolysis of 3-isochromanone (20).

tion of commercially available 3,4-dimethoxyphenylacetic acid (22b) with formalin and hydrochloric acid in acetic acid.<sup>32</sup> Thus 4,5-dimethoxybenzocyclobutene (25b) is available in two synthetic steps with a 32% overall yield by this sequence. The only other reported synthesis of 25b is a seven-step sequence proceeding in ca. 20% overall yield.<sup>16,19</sup> Isochromanones 23a and 23c were similarly prepared from the known phenylacetic acids, 22a and 22c, respectively. 4-Methoxybenzocyclobutene (25a) has been prepared previously by a six-step sequence from *p*-anisaldehyde<sup>16</sup> and from 4-nitrobenzocyclobutene.<sup>20</sup> Our work constitutes the first synthesis of 4,5-methylenedioxybenzocyclobutene (25c). Pyrolysis of 23d gave only a 10% yield of impure 4-hydroxy-5-methoxybenzocyclobutene (25d) and a considerable amount of tar. The benzyl ether 23e gave dibenzyl as the only volatile pyrolysisate; the reaction again produced a large amount of tar. Thus the method appears to be unsuitable for the direct preparation of benzyloxy substituted or phenolic benzocyclobutenes. The 7,8-disubstituted isochromanones, 27a and 27c, were prepared from 3-hydroxy-4-methoxyphenylacetic acid by the procedure of Nagata et al.;<sup>33</sup> 27b was prepared from 27a. Pyrolysis of 7-methoxy-8-hydroxy-3-isochromanone (27a) gave none of the desired benzocyclobutene 28a, pyrolysis of the acetate 27b gave a 21% yield of 3-acetoxy-4-methoxybenzocyclobutene (28b), and pyrolysis of 7,8-dimethoxy-3-isochromanone (27c) gave a 10% yield of 3,4-dimethoxybenzocyclobutene (28c). 3,4-Dimethoxybenzocyclobutene was also obtained from 5,6-dimethoxy-3-isochromanone (30) in 21% yield. These reactions were accompanied by considerable tar formation. Thus as a method for the preparation of benzocyclobutenes with oxygenated substituents on the aryl ring, the pyrolysis of isochromanones is limited to methoxy and methylenedioxy substituents in the 4 and/or 5 positions of the benzocyclobutene ring system. Because this method for the preparation of 25a, 25b, and 25c is direct, it is advantageous over other known syntheses of these materials which involve multistep procedures.<sup>16,19,20</sup> This method complements other recent benzocyclobutene syntheses<sup>21-23</sup> which do not lend themselves as easily to the preparation of benzocyclobutenes with an oxygenated aryl ring. Such benzocyclobutenes are of increasing importance as intermediates in the synthesis of natural products.<sup>16</sup>

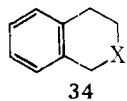


**Thermal vs. Electron Impact Induced Decomposition of 3-Isochromanones.** The relationship between the ions formed in electron impact mass spectrometry and the prod-

ucts of the pyrolysis of organic compounds has been of interest for some time.<sup>34</sup> Numerous examples have been reported in which the loss of a small neutral molecule (e.g., CO<sub>2</sub>, C<sub>2</sub>H<sub>4</sub>, H<sub>2</sub>CO, etc.) via a retro-Diels-Alder reaction was observed in the mass spectrum and also upon thermolysis of a compound. We have observed a qualitative similarity between the thermal and electron impact induced decomposition of the 3-isochromanones and homophthalic anhydrides described in this paper. The thermal formation of benzocyclobutenes from 3-isochromanones most likely occurs by a retro-Diels-Alder reaction with CO<sub>2</sub> expulsion followed by an electrocyclic ring closure (31 → 32 → 33). Analogously, all of the isochroman-



ones except the 6-methoxy-7-benzyloxy (23e) and the 7-methoxy-8-acetoxy (27b) derivatives showed a prominent M<sup>+</sup> - 44 ion in their mass spectra, arising from the loss of CO<sub>2</sub> by a retro-Diels-Alder reaction of the molecular ion. This relationship was best observed by comparing the yield obtained in the thermal reactions with the intensity of the M<sup>+</sup> - 44 ion, expressed as % Σ<sub>50</sub> (see Table II). 6-Methoxy-7-benzyloxy-3-isochromanone (23e) showed no M<sup>+</sup> - 44 ion in its mass spectrum and produced none of the expected benzocyclobutene (25e) upon pyrolysis. Both the thermal reaction and the mass spectral fragmentation occurred at the benzyl group in that the mass spectrum of 23e showed a large *m/e* 91 (C<sub>7</sub>H<sub>7</sub><sup>+</sup>) and pyrolysis gave dibenzyl as the only volatile product. The acetate (27b) also had no M<sup>+</sup> - 44 ion in its mass spectrum (the base peak corresponded to ketene loss) but did produce a low yield of the benzocyclobutene (28b) upon pyrolysis. Increasing the number of methoxy groups on the aromatic ring decreased both the yield of benzocyclobutene and the intensity of the M<sup>+</sup> - 44 ion. When the methoxy groups were adjacent to the lactone ring a further decrease in yield and M<sup>+</sup> - 44 ion intensity were observed. The phenolic isochromanones 23d and 27a were anomalous in that both had intense M<sup>+</sup> - 44 ions in their mass spectra but they gave little or none of the benzocyclobutenes 25d and 28a upon pyrolysis. With the exception of the phenolic isochromanones, the intensity of the M<sup>+</sup> - 44 ion in the mass spectrum served as a rough guide to the yield of benzocyclobutene which could be expected upon pyrolysis. Loudon has similarly compared the mass spectrum and gas-phase pyrolysis of several compounds, 34, structurally similar to the isochromanones 31 described here.<sup>35</sup> He has shown that the high-temperature thermolysis of 34 led to products analogous to the fragment ions observed in the mass spectra of these compounds. A retro-Diels-Alder reaction with loss of CH<sub>2</sub>=X was observed in all cases but was especially prominent in both the mass spectrum and thermolysis of isochroman (34b). Thus, 80% of 34b decomposed thermally to benzocyclobutene.



- a, X = CH<sub>2</sub>  
 b, X = O  
 c, X = S  
 d, X = NH

We also examined the mass spectra of the isochromanones for the presence of metastable peaks corresponding to the loss of CO<sub>2</sub>. The isochromanones 23a, 23d, 23e, and 27b showed no metastable peak for CO<sub>2</sub> loss whereas isochromanones 20, 23c, 27a, 27c, and 30 showed a weak metastable peak; only 23b showed a strong metastable peak. Thus the presence or absence of a metastable peak for CO<sub>2</sub> loss had no relationship to the yields of benzocyclobutenes obtained upon pyrolysis.

## Experimental Section

**General.** Melting points were obtained on a Thomas-Hoover capillary melting point apparatus and are uncorrected. Nuclear magnetic resonance (NMR) spectra were obtained using a Varian Anaspect EM360 spectrometer in CDCl<sub>3</sub> with tetramethylsilane as internal standard. Low-resolution mass spectra were obtained at 70 eV using a Hitachi Perkin-Elmer RMU-6E mass spectrometer; only ions with a relative intensity greater than 10% are reported. Elemental analyses were performed at the University of Idaho with a Perkin-Elmer 240 analyzer. Infrared (IR) spectra were obtained with a Perkin-Elmer 621 spectrometer. Analytical thin layer chromatography (TLC) employed precoated sheets of silica gel (F-254, 0.25 mm thick) on aluminum (E. Merck, Darmstadt, Germany).

**6,7-Methylenedioxy-3-isochromanone (23c).** A mixture of 2-phenyl-4-(4,5-methylenedioxybenzyl)-5-oxazolone<sup>36</sup> (25 g, 85.5 mmol) in 10% sodium hydroxide (250 mL) was refluxed until no more ammonia was given off (8 h). To the cooled solution, 40% sodium hydroxide (15 mL) was added while maintaining the temperature below 15 °C and the solution was then allowed to stand at room temperature for 8 h. The mixture was then acidified with dilute hydrochloric acid (90 mL) and extracted with chloroform (3 × 100 mL); the extracts were dried (MgSO<sub>4</sub>) and the solvent was evaporated to yield a mixture of benzoic acid and 3,4-methylenedioxyphenylacetic acid (22c) (22.5 g). A solution of the acids (10 g), 37% formalin (25 mL), concentrated hydrochloric acid (25 mL), and glacial acetic acid (75 mL) was heated on a steam bath for 1 h. The cooled solution was poured into water (750 mL) and extracted with chloroform (3 × 100 mL). The extracts were washed with 5% sodium bicarbonate (2 × 250 mL) and dried (MgSO<sub>4</sub>), and the solvent was evaporated to yield a dark oil. This oil was sublimed at 0.25 mm with mild heating, and the sublimate was then recrystallized from 95% ethanol to yield white crystals of 3,4-methylenedioxy-3-isochromanone (23c, 1.85 g, 25%); mp 130.5–132 °C (lit.<sup>37</sup> mp 137 °C); IR (KBr) 1750, 1485, 1475, 1246, 1233, 1138, 1022, and 915 cm<sup>-1</sup>; NMR δ 3.63 (s, 2 H), 5.23 (s, 2 H), 6.02 (s, 2 H), and 6.75 (s, 2 H); mass spectrum *m/e* (rel intensity) 192 (95), 163 (15), 149 (18), 148 (100), 147 (43), 135 (15), 91 (10), 90 (13), 89 (23), 77 (15), 74 (11), 63 (13), 51 (20), and 50 (15).

Anal. Calcd for C<sub>10</sub>H<sub>8</sub>O<sub>4</sub>: C, 62.50; H, 4.17. Found: C, 62.24; H, 4.23.

**6-Methoxy-3-isochromanone (23a).** A solution of 3-methoxyphenylacetic acid<sup>38</sup> (22a, 10 g, 66.3 mmol), glacial acetic acid (45 mL), 37% formalin (15 mL), and concentrated hydrochloric acid (3 mL) was stirred at room temperature for 5 days. The solution was poured into water (250 mL) and extracted with chloroform (3 × 75 mL). The extracts were washed with 5% sodium bicarbonate and dried (MgSO<sub>4</sub>) and the solvent was evaporated to give an oil (8.2 g). Vacuum distillation gave 23a,<sup>39</sup> bp 125–145 °C (0.04 mm), as a white solid (5.1 g, 43%), which was recrystallized from 95% ethanol: mp 74–78 °C; IR (KBr) 2960, 2900, 1737, 1618, 1592, 1503, 1382, 1265, 1245, 1142, 1125, 1024, 954, 878, 815, and 694 cm<sup>-1</sup>; NMR δ 3.61 (s, 2 H), 3.74 (s, 3 H), 5.20 (s, 2 H), and 6.54–7.34 (m, 3 H); mass spectrum *m/e* (rel intensity) 178 (90), 149 (25), 135 (15), 134 (100), 122 (15), 121 (15), 91 (41), 78 (12), 77 (17), 65 (15), 63 (15), 62 (45), 61 (15), 51 (21), 50 (10), 45 (100), and 44 (50).

Anal. Calcd for C<sub>10</sub>H<sub>10</sub>O<sub>3</sub>: C, 67.40; H, 5.62. Found: C, 67.32; H, 5.72.

**5,6-Dimethoxy-3-isochromanone (30).** A solution of 2,3-dimethoxyphenylacetic acid (29,<sup>40</sup> 3.04 g, 11.5 mmol), glacial acetic acid (15 mL), 37% formalin (5 mL), and concentrated hydrochloric acid (5 mL) was stirred at room temperature for 21 h. The solution was poured into water (75 mL) and extracted with chloroform (3 × 25 mL). The extracts were washed with 5% sodium bicarbonate (2 × 50 mL), dried (MgSO<sub>4</sub>), and evaporated to leave an oil. Vacuum distillation yielded a white solid, bp 118–121 °C (0.025 mm) (1.028 g, 43%), which was recrystallized from 95% ethanol to yield white crystals of 30: mp 59.5–62 °C; IR (KBr) 2940, 2830, 1735, 1495, 1465, 1388, 1287, 1215, 1154, 1090, 1003, 965, 805, and 690 cm<sup>-1</sup>; NMR δ 3.69 (s, 2 H), 3.80 (s, 3 H), 3.83 (s, 3 H), 5.20 (s, 2 H), and 6.87 (s, 2 H); mass spectrum *m/e* (rel intensity) 208 (100), 164 (25), 149 (64), 121 (28), 104 (15), 91 (20), 78 (16), 77 (22), 65 (15), 63 (15), and 50 (19).

Anal. Calcd for C<sub>11</sub>H<sub>12</sub>O<sub>4</sub>: C, 63.46; H, 5.77. Found: C, 63.51; H, 5.84.

**6-Methoxy-7-benzyloxy-3-isochromanone (23e).** A solution of 3-methoxy-4-benzyloxyphenylacetic acid (22e,<sup>41</sup> 4.8 g, 17.6 mmol), glacial acetic acid (60 mL), 37% formalin (15 mL), and concentrated hydrochloric acid (3 mL) was stirred at room temperature for 44 h. The solution was poured into water (250 mL) and extracted with chloroform (3 × 75 mL). The extracts were washed with 5% sodium bicarbonate (2 × 100 mL), dried (MgSO<sub>4</sub>), and evaporated to yield a white solid (4.6 g). Recrystallization from 95% ethanol gave white

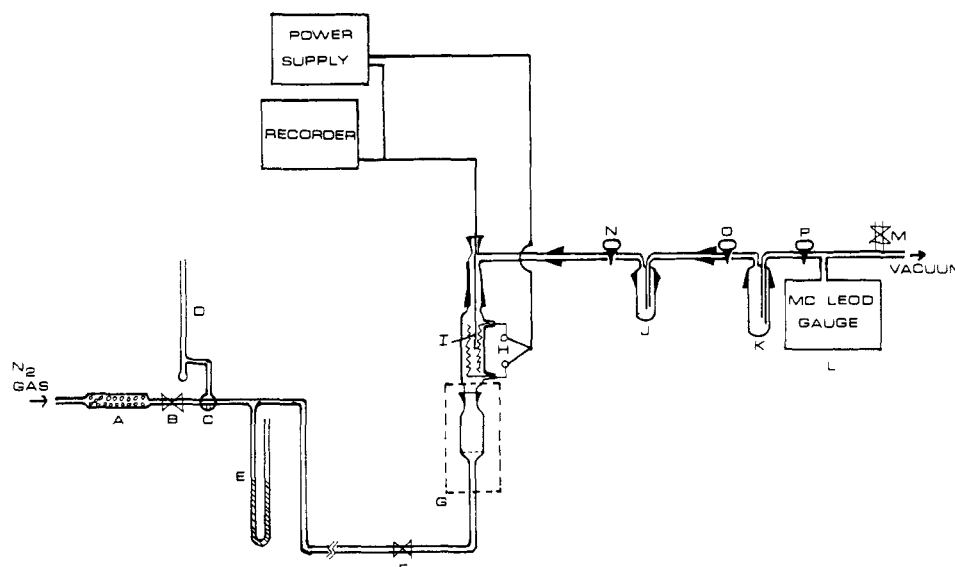


Figure 3. Pyrolysis apparatus.

crystals of **23e** (1.68 g), second crop (0.35 g), overall yield 90%: mp 137–138.5 °C; IR (KBr) 1740, 1512, 1447, 1370, 1342, 1302, 1244, 1223, 1112, 1015, 870, 744, and 698  $\text{cm}^{-1}$ ; NMR  $\delta$  3.60 (s, 2 H), 3.87 (s, 3 H), 5.11 (s, 2 H), 5.13 (s, 2 H), 6.73 (s, 2 H), 7.36 (s, 5 H); mass spectrum  $m/e$  (rel intensity) 284 (12), 91 (100), and 65 (11).

Anal. Calcd for  $\text{C}_{17}\text{H}_{16}\text{O}_4$ : C, 71.83; H, 5.63. Found: C, 72.08; H, 5.77.

**6-Methoxy-7-hydroxy-3-isochromanone (23d)**. A mixture of 6-methoxy-7-benzyloxy-3-isochromanone (**23e**, 637 mg, 2.2 mmol), 10% Pd on carbon (300 mg), 95% ethanol (50 mL), and tetrahydro-

Table I. Physical Properties of Pyrolysis Products

Registry no.	Compd	Mp, °C	IR, $\text{cm}^{-1}$	NMR, $\delta$	MS, $m/e$ (rel intensity)
694-87-1	Benzocyclobutene ( <b>21</b> ) <sup>3</sup>	Oil	(neat) 3065, 2965, 2930, 2830, 1459, 1420, 1278, 1207, 1192, 1000	2.94 (s, 4 H), 6.77– 7.24 (m, 4 H)	104 (100), 103 (45), 78 (35)
53995-96-3	4,5-Dimethoxybenzo- cyclobutene ( <b>25b</b> ) <sup>19</sup>	103–104	(KBr) 2920, 2840, 1487, 1468, 1305, 1208, 1180, 1168, 1066, 970	2.96 (s, 4 H), 3.72 (s, 6 H), 6.54 (s, 2 H)	164 (100), 149 (23), 121 (40), 78 (20), 77 (24)
56437-04-8	4-Methoxybenzocyclo- butene ( <b>25a</b> ) <sup>19,20</sup>	Oil	(neat) 2920, 2826, 1600, 1588, 1473, 1271, 1248, 1165, 1075, 1025	2.80 (s, 4 H), 3.43 (s, 3 H), 6.27–6.80 (m, 3 H)	134 (100), 104 (15), 103 (12), 91 (47), 54 (15)
61099-23-8	4,5-Methylenedioxy- benzocyclobutene ( <b>25c</b> ) <sup>a</sup>	62–63	(KBr) 2880, 2830, 1445, 1296, 1126, 1033, 936	2.91 (s, 4 H), 5.73 (s, 2 H), 6.50 (s, 2 H)	148 (51), 147 (37), 91 (55), 90 (42), 89 (100), 65 (19), 64 (30), 63 (70)
62726-48-1	3,4-Dimethoxybenzo- cyclobutene ( <b>28c</b> ) <sup>a</sup>	49–51	(KBr) 1575, 1475, 1425, 1245, 1200, 1165, 1060, 800	3.97–3.48 (m, 4 H), 3.80 (s, 3 H), 3.98 (s, 3 H), 6.44–7.90 (m, 2 H)	164 (85), 149 (100), 121 (43), 104 (14), 91 (29), 78 (35)
62726-49-2	4-Hydroxy-5-methoxy- benzocyclobutene ( <b>25d</b> ) <sup>b</sup>	Oil	(neat) 3400, 2905, 1590, (1480, 1310, 1195, 1135, 1055, 860, 825	3.07 (s, 4 H), 3.84 (s, 3 H), 5.98 (broad s, 1 H), 6.58–6.71 (m, 2 H)	150 (100), 135 (36), 107 (36)
103-29-7	Bibenzyl <sup>38</sup>	49–51 (lit. <sup>38</sup> 52.5)	(KBr) 3040, 3010, 2900, 2840, 1590, 1485, 1440, 1055, 1020, 685	2.77 (s, 4 H), 7.03 (s, 10 H)	182 (100), 92 (27), 91 (82), 77 (15), 63 (11)
62726-50-5	3-Acetoxy-4-methoxy- benzocyclobutene ( <b>28b</b> ) <sup>a</sup>	Oil	(neat) 2920, 1752, 1475, 1362, 1328, 1257, 1205, 1165, 1067, 1020	2.29 (s, 3 H), 3.07 (s, 4 H), 3.78 (s, 3 H) 6.80 (s, 2 H)	192 (25), 150 (100), 135 (41), 107 (18), 77 (14)
3469-06-5	Benzocyclobutenone ( <b>8</b> ) <sup>25</sup>	Oil	(neat) 1780, 1757, 1580, 1463, 1410, 1348, 1280, 1192, 1092, 1080, 955, 755	3.81 (s, 2 H), 7.07– 7.68 (m, 4 H)	118 (99), 90 (100), 89 (92), 63 (13), 62 (34), 61 (15), 39 (19)
23417-79-0	<i>o</i> -Isopropenylbenzal- dehyde ( <b>15</b> ) <sup>28</sup>	Oil	(neat) 3078, 2843, 2746, 1990, 1598, 1267, 1196, 906, 828, 769, 639	2.16 (m, 3 H), 4.90 (m, 1 H), 5.36 (m, 1 H), 7.1–7.5 (m, 3 H), 7.7– 8.0 (m, 1 H), 10.1 (s, 1 H)	146 (8), 129 (12), 128 (100), 127 (15), 102 (12)
27041-32-3	Fulveneallene ( <b>9</b> ) <sup>c,26</sup>	Oil	(vapor) 3130, 3090, 1978, 1962, 1958, 1949, 1930, 1922, 1496, 1482, 1388, 1082, 1072, 898, 891, 883, 853, 842, 758	5.25 (s, 2 H), 6.40 (s, 4 H)	

<sup>a</sup> Satisfactory analytical data for this compound were submitted for review. <sup>b</sup> Anal. Calcd for  $\text{C}_9\text{H}_{10}\text{O}_2$ : C, 72.00; H, 6.67. Found: C, 71.39; H, 7.36. <sup>c</sup> 5-Ethenylidene-1,3-cyclopentadiene.

Table II. Pyrolysis of Isochromanones

Registry no.	Compd pyrolyzed	Mass spectrum of compd pyrolyzed		Pyrolysis chamber, H, temp, °C	Sublimation chamber, G, temp, °C	Product	% isolated yield
		% $\Sigma_{50}$ ( $M^+ - 44$ )	$M^*$ ( $M^+ \rightarrow M^+ - 44$ )				
4385-35-7	3-Isochromanone (20) <sup>30</sup>	28	Weak	575	125	Benzocyclobutene (21)	88 (see Figure 2)
16135-41-4	6,7-Dimethoxy-3-isochromanone (23b) <sup>32</sup>	20	Strong	490	165	4,5-Dimethoxybenzocyclobutene (25b)	40
43088-72-8	6-Methoxy-3-isochromanone (23a) <sup>39</sup>	15	Absent	505	150	4-Methoxybenzocyclobutene (25a)	70
34140-20-0	6,7-Methylenedioxy-3-isochromanone (23c) <sup>37</sup>	21	Weak	505	150	4,5-Methylenedioxybenzocyclobutene (25c)	90
62726-51-6	5,6-Dimethoxy-3-isochromanone (30)	5	Weak	505	140	3,4-Dimethoxybenzocyclobutene (28c)	21
62726-52-7	6-Methoxy-7-hydroxy-3-isochromanone (23d)	22	Absent	480	180	4-Hydroxy-5-methoxybenzocyclobutene (25d)	10
62726-53-8	6-Methoxy-7-benzoyloxy-3-isochromanone (23e)	0	Absent	450	190	Bibenzyl	26
56201-87-7	7-Methoxy-8-hydroxy-3-isochromanone (27a) <sup>33</sup>	16	Weak	505	140		
4697-59-0	7,8-Dimethoxy-3-isochromanone (27c) <sup>33</sup>	7	Weak	505	140	3,4-Dimethoxybenzocyclobutene (28c)	10
62726-54-9	7-Methoxy-8-acetoxy-3-isochromanone (27b)		Absent	505	150	3-Acetoxy-4-methoxybenzocyclobutene (28b)	21
703-59-3	Homophthalic anhydride (7) <sup>38</sup>	26	Absent	530	150	Benzocyclobutenone (8) Fulveneallene (9)	43 23 (see Figure 1)
31952-55-3	4,4-Dimethylhomophthalic anhydride (18) <sup>44</sup>	14	Absent	560	130	<i>o</i> -Isopropenylbenzaldehyde (15)	65

furan (50 mL) was hydrogenated at atmospheric pressure until the theoretical amount of hydrogen (50 mL) had been absorbed. The solvent was evaporated leaving a black solid. Vacuum sublimation (150 °C, 0.04 mm) yielded a light yellow solid which was recrystallized from 95% ethanol to give white crystals of **23d** (310 mg, 71%): mp 174–177 °C; IR (KBr) 3300, 1715, 1505, 1355, 1275, 1235, 1105, 1025, 1005, and 940  $\text{cm}^{-1}$ ; NMR  $\delta$  3.60 (s, 2 H), 3.90 (s, 3 H), 5.17 (s, 2 H), 5.67 (broad s, 1 H), 6.63 (s, 1 H), and 6.74 (s, 1 H); mass spectrum  $m/e$  (rel intensity) 194 (100), 151 (13), 150 (89), 137 (17), 135 (32), 107 (42), 77 (14), 67 (14), and 51 (12).

Anal. Calcd for  $\text{C}_{10}\text{H}_{10}\text{O}_4$ : C, 61.86; H, 5.16. Found: C, 61.72; H, 5.10.

**7-Methoxy-8-acetoxy-3-isochromanone (27b)**. A solution of 7-methoxy-8-hydroxy-3-isochromanone (**27a**,<sup>33</sup> 362 mg, 1.86 mmol), acetic anhydride (1 mL), and pyridine (2 mL) was stirred for 5 h. The solution was cautiously diluted with ice water (10 mL) and made acidic with dilute hydrochloric acid. Extraction of the solution with chloroform (2  $\times$  40 mL) and evaporation of the solvent yielded a white solid. Recrystallization from 95% ethanol gave **27b** as white crystals (368 mg, 83%): mp 133–135 °C; IR (KBr) 1720, 1490, 1435, 1360, 1275, 1235, 1180, 1145, 1085, 1025, 1000, 915, and 790  $\text{cm}^{-1}$ ; NMR  $\delta$  2.37 (s, 3 H), 3.69 (s, 2 H), 3.82 (s, 3 H), 5.22 (s, 2 H), and 6.92–7.08 (m, 2 H); mass spectrum  $m/e$  (rel intensity) 236 (17), 195 (13), 194 (100), 150 (50), and 135 (20).

Anal. Calcd for  $\text{C}_{12}\text{H}_{12}\text{O}_5$ : C, 61.02; H, 5.09. Found: C, 60.83; H, 5.09.

**Pyrolysis Apparatus**. A diagram of the pyrolysis apparatus is shown in Figure 3. Nitrogen gas was dried by passage through a tower A filled with molecular sieves. The flow rate of the nitrogen carrier gas from the cylinder was controlled by means of needle valve B and was measured with three-way stopcock C open to bubble flowmeter

D. After obtaining the desired flow rate, stopcock C was turned to isolate bubble flowmeter D and to allow the carrier gas to enter the pyrolysis system. A Hewlett-Packard Model 5080-6710 gas chromatography flow controller valve F was adjusted so as to maintain the pressure gauge E at atmospheric pressure. Reactant sublimation chamber G contained a porous glass disk upon which the reactant was placed and was heated by an oil bath. The pyrolysis chamber H contained a multiple strand coiled nichrome wire. The wire was prepared by first close winding BS gauge 26 nichrome wire on a  $\frac{3}{32}$  in.  $\times$  36 cm steel bar. Two turns of the coil were pulled out every 5 cm and a loop twisted in the stretched-out portion. In this way the wire was shaped into seven 5-cm coils, each separated by a twisted loop with hooks at each end. These strands of coil were stretched by hanging each loop from a glass hook inside the pyrolysis chamber H and by hanging the two ends to leads extending through the glass wall. The resistance of the installed coil was 54 ohm.<sup>42</sup> The pyrolysis temperature was determined with a chromel–alumel thermocouple I placed in the center of the pyrolysis chamber H and connected to a –0.68 to 36.19 mV strip chart recorder. The temperature of the pyrolysis chamber H was controlled by an electronic power supply using the thermocouple as a sensor. The pyrolysate was collected in cold trap J and could be trap to trap distilled to cold trap K. The pressure of the system was regulated with needle valve M and measured with a McLeod gauge L.

**Pyrolysis of 3-Isochromanone (20)**. Using the apparatus described in the previous section, sublimation chamber G was charged with **20**<sup>30</sup> (1 g, 7.45 mmol), stopcock C was opened to the bubble flowmeter D, and the nitrogen flow rate was adjusted with valve B to 20 mL/min. The pressure of the system was then reduced to the minimum obtainable, stopcock C was then closed to the flowmeter and opened to the system, and valve F was adjusted to maintain the pressure gauge E at atmospheric pressure. The vacuum of the system

was 2.1 mm measured at the McLeod gauge L. The pyrolysis chamber H was heated to 570 °C and then sublimation chamber G was heated with an oil bath to ca. 130 °C. The pyrolysate was collected in cold trap J. When all of the isochromanone **20** had disappeared from sublimation chamber G the power to the pyrolysis chamber was turned off, stopcock N was closed, stopcock C was opened to the flowmeter, and the pressure was reduced to the minimum obtainable, ca. 1 mm. Stopcock P was then closed and the pyrolysate was distilled to cold trap K by warming cold trap J to 25 °C to yield pure benzocyclobutene (**21**, 588 mg, 85%). The properties of the benzocyclobutene thus obtained are shown in Table I. Figure 2 shows the relationship between the yield of pyrolysate and the pyrolysis temperature. The different points were obtained by using the above procedure and changing only the pyrolysis temperature.

**Pyrolysis of Substituted 3-Isochromanones, 23, 27, and 30.** The apparatus and procedure used were the same as those used for the pyrolysis of 3-isochromanone (**20**) with the following exceptions. The pressure of the system was maintained at 3 mm with needle valve M; the pyrolysis and oil bath temperatures were adjusted for each isochromanone (see Table II); the glass tubing between pyrolysis chamber H and cold trap J was heated with heat tape to ca. 200 °C; the pyrolysate was removed from cold trap J and washed with base to remove any unreacted starting material in every case except **23d** and **27a**; the pyrolysate was then recrystallized and/or distilled to yield pure products. The pyrolysis temperatures used and the results of these pyrolyses are summarized in Table II and properties of the purified pyrolysis products are shown in Table I.

**Pyrolysis of Homophthalic Anhydride (7).** The apparatus and procedure used were the same as those used for the pyrolysis of **20**. The sublimation chamber G was filled with **7**<sup>38</sup> (2.88 g, 17.75 mmol). The pressure of the system was maintained at 2.3 mm with needle valve M; the flow rate was 21 mL/min. The pyrolysis chamber and sublimation chamber were heated to 530 and 133–156 °C, respectively. When the pyrolysis was complete stopcock N was closed and the pressure reduced to 1 mm. The more volatile fulveneallene (**9**) was distilled to cold trap K by warming cold trap J to –25 °C. Benzocyclobutenone (**8**, 0.98 g, 46.7%) was obtained as a colorless oil in trap J, and fulveneallene (0.38 g, 23.6%) was obtained as a yellow liquid in trap K. Unpyrolyzed but sublimed **7** (0.83 g, 28.8%) was recovered from the arm between pyrolysis chamber H and cold trap J. No visible tar was formed during the reaction. The percent yields of **7**, **8**, and **9** as a function of the pyrolysis temperature are shown in Figure 1; the different points were obtained by using the above procedure and changing only the pyrolysis temperature. The properties of **8** and **9** are shown in Table I. Fulveneallene was converted to its tetracyanoethylene adduct (**10**) using the literature procedure.<sup>26b</sup> After five recrystallizations from acetone–water, adduct **10** was obtained as colorless crystals in 49% yield: mp 116–124 °C dec (lit. mp<sup>26b</sup> 115 °C decomp); IR (KBr) 3097, 3080, 3035, 3000, 2252, 2002, 1957, 1780, 1442, 1316, 1233, 1187, 1158, 1105, 1087, 1016, 940, 910, 899, 833, 749, and 740 cm<sup>-1</sup>; NMR (acetone-*d*<sub>6</sub>) δ 4.80 (t, 2H), 5.40 (s, 2H), 6.90 (t, 2H);<sup>43</sup> mass spectrum *m/e* (rel intensity) 128 (96), 90 (100), 89 (100), 76 (61), 64 (22), 63 (39), 62 (20), 51 (11), 50 (15), 39 (13), and 38 (24).

Adduct **10** was reconverted to fulveneallene by heating the adduct in vacuo. Thus to a 5-mL round-bottom flask equipped with a 2 × 10 cm cold trap which was in turn connected to a vacuum pump was added 1.6 g of unpurified TCNE adduct **10**. The pressure of the entire apparatus was then reduced to 3 mm while cooling the cold trap with dry ice–acetone. Heating the flask at 90–115 °C for 2 h resulted in the condensation of 540 mg of regenerated **9** on the cold finger. The overall process **9** → **10** → **9** proceeded in 75% yield.

**Pyrolysis of 4,4-Dimethylhomophthalic Anhydride (18).** The pyrolysis was carried out with the same apparatus and in the same manner as the pyrolysis of the homophthalic anhydride (**11**). Thus **18**<sup>44</sup> (3.1 g, 16.3 mmol) was pyrolyzed at 560 °C with a flow rate of 20 mL/min and a vacuum of 4.5 mm. The sublimation chamber was heated at 82–130 °C. When the pyrolysis was complete the pyrolysate on the side arm leading to trap J was removed by washing with small amounts of acetone and combined with the pyrolysate in trap J. The solvent was evaporated and the solid was washed with petroleum ether (25 mL) and filtered to give unpyrolyzed **18** (0.59 g). The washings were evaporated to yield crude *o*-isopropenylbenzaldehyde (**15**, 1.25 g, 65%). The temperature programmed gas chromatogram (12 ft × 0.125 in. column packed with 20% QF-1 on 80/100 mesh Chromosorb W/AW DMCS; column temperature 115–145 °C, programmed at 10 °C/min) of crude **15** was similar to that reported for the pyrolysate of 3,3-dimethylindan-1,2-dione (**14**) except that peaks comparable to those reported for benzofulvene (**16**) and 3-methylindan-1-one (**17**)

were absent. Pure **15** could be obtained by distillation (bp 42–44 °C, 0.25 mm). The spectral properties (see Table I) were identical with the literature values.<sup>28</sup>

**Pyrolysis of 1,2-Indandione (11).** The pyrolysis of **11** (3.0 g, 20.5 mmol) was carried out as described for 3-isochromanone. The pyrolysis chamber and sublimation chamber were heated to 540 and 91–97 °C, respectively. The nitrogen flow rate was 20 mL/min and the vacuum was 2.1 mm. After pyrolysis for 4.5 h, 2.82 g of unsublimed tar remained in the sublimation chamber. Trap J contained 110 mg of a yellow oil, which was a mixture of **8** (63 mg, 2.5%) and **9** (48 mg, 2.5%) as determined by integration of the NMR spectrum of the mixture and comparison of the spectrum with those of pure **8** and **9**.

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**Registry No.**—**10**, 27820-25-3; **11**, 16214-27-0; **22a**, 1798-09-0; **22c**, 2861-28-1; **22e**, 29973-91-9; **29**, 90-53-9; 2-phenyl-4-(4,5-methylenedioxybenzal)-5-oxazolone, 6412-89-1; benzoic acid, 65-85-0.

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## Selective Reductions. 23. Asymmetric Reduction of Representative Ketones with Diisopinocampheylborane of High Optical Purity

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Diisopinocampheylborane of high optical purity, in tetrahydrofuran, diglyme, ethyl ether, methylene chloride, and *n*-pentane, was used to reduce a representative group of ketones, RCOCH<sub>3</sub> (R = Et, *i*-Pr, *t*-Bu, Ph). Asymmetric induction in the alcohol products in the range of 9 to 37% was observed. In contrast to earlier studies in which the reagent evidently contained small amounts of sodium borohydride and other minor constituents, the present results are consistent and reproducible. It was demonstrated that small quantities of sodium borohydride in the reagent can considerably diminish the optical purities of the product alcohols.

The asymmetric reduction of representative ketones, RCOCH<sub>3</sub> (R = Et, *i*-Pr, *t*-Bu, Ph), with optically active (–)-diisopinocampheylborane (from (+)- $\alpha$ -pinene) (IPC<sub>2</sub>BH) was first reported in 1961.<sup>2</sup> The products obtained exhibited significant asymmetric induction (11 to 30%).

In a later study we attempted to carry out a related reduction of these ketones with (+)-IPC<sub>2</sub>BH (from (–)- $\alpha$ -pinene).<sup>3</sup> Here also we realized optically active products with optical purities in the range of 9.5 to 12.8%. Unfortunately, there appeared a serious disagreement in the absolute configuration of the product from pinacolone, as well as major differences in the magnitudes of the rotations realized (Table I).

At that time, the IPC<sub>2</sub>BH was a relatively crude product synthesized from  $\alpha$ -pinene by hydroboration in diglyme with sodium borohydride (used in ~10% excess) and boron trifluoride etherate.<sup>4</sup> We felt that the discrepancy might be the result of minor components present in the crude product but deferred further study until such a time as we could develop an improved synthesis of IPC<sub>2</sub>BH.

Recently, Varma and Caspi examined the reduction of these and other ketones and aldehydes by IPC<sub>2</sub>BH.<sup>5</sup> They utilized borane-THF for the synthesis of their reagent.<sup>4</sup> They realized still different results (Table I). These authors also proposed a model to predict the absolute configuration of the major isomer produced.

We have recently developed an improved synthesis of

IPC<sub>2</sub>BH based on hydroboration of  $\alpha$ -pinene with borane-THF, a procedure which makes available IPC<sub>2</sub>BH in very high purity.<sup>6</sup> This new reagent achieves the asymmetric hydroboration of *cis*-2-butene to give after oxidation 2-butanol in an optical purity as high as 98.4%.<sup>6</sup> Consequently, we decided to utilize this reagent for the asymmetric reduction of the series of four ketones in the hope of resolving the conflicting results of the three earlier studies.

We have recently established that high-purity IPC<sub>2</sub>BH can also be synthesized in THF and other solvents<sup>7</sup> by utilizing the readily available hydroborating agent, borane-methyl sulfide.<sup>8</sup> Accordingly, we extended the study to (–)-IPC<sub>2</sub>BH prepared in this manner in several solvents.

### Results and Discussion

(–)-IPC<sub>2</sub>BH was prepared in THF at 0 °C (72 h) using a 15% excess of (+)- $\alpha$ -pinene, following the published procedure.<sup>6</sup> In all experiments the ketone was added to the suspension of the reagent in THF at 0 °C.

The reduction of 2-butanone required about 9 h at –30 °C but was complete within 1 h at 0 °C. The reductions of 3-methyl-2-butanone and acetophenone were complete within 2 h at 0 °C. However, the reduction of pinacolone was much more sluggish, the reaction being incomplete after 11 h at 0 °C with a further 12 h at 25 °C necessary to achieve near completion.