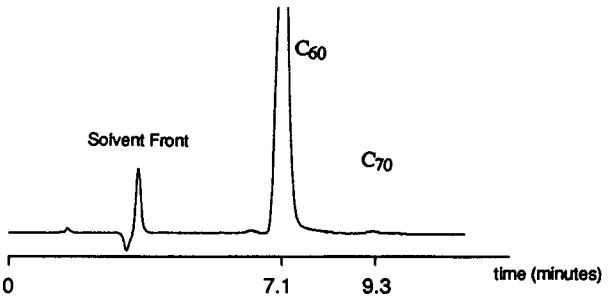

Figure 2. Reversed-phase analysis of the C_{60} fraction. Conditions: 20-μL injection of C_{60} fraction in toluene, 8-mm × 10-cm Novapak C_{18}, 60% 2-propanol/40% toluene mobile phase (1 mL/min), UV/vis detection at 590 nm.

a minimal effect on the separation. We are unable to identify the mechanism by which these compounds are separated, but we feel that hydrophobic interactions are involved rather than size filtration.

The purification protocol described above is largely free of the difficulties involved in other techniques for the isolation of the fullerenes and should increase the supply of pure C_{60} and C_{70} available for research. The use of pure toluene as the eluent leads to several substantial advantages: much smaller volumes of eluting solvent, much higher column loading, and ready recovery and reuse of the solvent. The speed and convenience of HPLC, including the option of complete automation increases the value of the method. We believe that a fully automated system, built around the components used here, will allow for the daily isolation of gram quantities of C_{60} as well as hundreds of milligrams of C_{70}.

Experimental Section

Preparation of Crude Fullerene Extract. A reactor similar to that of Krätschmer et al.[16,19] was used to pass an AC discharge between graphite electrodes in a 200-mTorr He atmosphere. The resulting fullerene-rich soot (10.5 g) was stirred with toluene (750 mL), suction-filtered (Whatman no. 1 filter paper), and evaporated to dryness, leaving 0.77 g of a dark solid. This solid was sonicated for 5 min with toluene (50 mL) and then suction filtered through a medium-porosity glass frit. The filtrate was evaporated to leave 0.46 g of fullerenes. This was suspended in 50 mL of toluene and filtered through a 0.2-μm nylon filter. The filtrate was diluted by 10% with toluene before injection.

Chromatographic Procedures. Toluene and 2-propanol were filtered through 0.2-μm nylon membrane filters. All separations and analyses were carried out on Waters 600E HPLC/GPC systems using UV/vis detection. The strong absorption of the fullerenes often leads to detector saturation, so during high concentration preparative runs the detector was set at 600 nm for the lowest available sensitivity. During C_{18} reversed-phase analysis of the collected fractions the detector was set to 590 nm, where the ratio of extinction coefficients is known to be 1:1.2 (C_{60}/C_{70}).[20]

GPC Separations. Waters Ultrastyragel (500-Å pore size) GPC columns, either 7.8 mm × 30 cm or 19 mm × 30 cm, were used for separations. Fractions were collected manually. Large injections (>2.0 mL) were accomplished by placing the concentrated extract in a solvent reservoir and pumping the desired volume onto the column and then switching to 100% toluene for elution.

Retention times on a single 19 mm × 30 cm GPC column (5 mL/min of toluene mobile phase) were 16.4 min (C_{60}) and 17.5 min (C_{70}), with the higher fullerenes eluting as a shoulder on the tail of the C_{70} peak. Typical 5-mL injections produced 10–15 mg of C_{60} (92–95% pure), 7–10 mg of an overlapping fraction (ca. 1:1 C_{60}/C_{70}), and 6–10 mg of C_{70} (24% C_{60}, 76% C_{70}, and several percent of higher molecular weight fullerenes). The amount of material in each fraction depends on manual fraction cutting technique, leading to large variations between runs. Fraction cutting times are not optimized.

Higher purity samples were obtained by reinjection and peak-shaving. For example, reinjection of 12 mg of the C_{60} fraction onto a 19-mm × 30-cm Ultrastyragel column produced 5.5 mg of 99.5% pure C_{60}; reinjection of 9 mg of the C_{70} fraction produced 4.5 mg of 95% pure C_{70}. The remainder of each sample was recovered as a C_{60}/C_{70} mixture. With two 7.8- × 30-cm columns connected in series (500-Å and 100-Å Ultrastyragel) using 1 mL/min of toluene as mobile phase, the retention times were 27 min (C_{60}) and 29 min (C_{70}).

HPLC Analyses. Samples were analyzed on Waters Novapak C_{18} reversed-phase, 8-mm × 10-cm Radial-Pak cartridges in a RCM 8 × 10 cartridge holder. Authentic C_{60} and C_{70} samples purified by chromatography on alumina were used as standards (Figure 2). Elution with 60% 2-propanol–40% toluene (1 mL/min) and detection at 590 nm gave retention times of 7.1 min (C_{60}) and 9.3 min (C_{70}).[21]

Acknowledgment. We acknowledge Mr. Michael Davis of Waters Corporation for suggesting the 500-Å Ultrastyragel column, and we thank Mr. Davis, Allen Anderson, and Michael Woodman of Waters for valuable assistance. We also thank the research group of Professor Peter Eklund of the University of Kentucky Department of Physics and the Center for Applied Energy Research (CAER) for fullerene-containing soot and alumina-purified standards. Financial support was provided by the University of Kentucky, CAER, and the U.S. Department of Energy (DE-FG05-85ER13432 to J.P.S.).

Registry No. C_{60}, 99685-96-8; C_{70}, 115383-22-7.

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Ring Expansions of Simple Cyclic Conjugated Cyclopropyl Ketones by the Nozaki Method Are Not Regiospecific

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Since cyclic conjugated cyclopropyl ketones (**1**) have significant synthetic utility,[1] it is surprising that a general method has not been developed for the ring enlargement of these compounds that maintains the conjugation of the functional groups. On the contrary, reported homologations of **1** give predominantly or exclusively the corresponding nonconjugated ring-expanded ketones. For example, ring expansion of nortricyclanone (**2**) by the three-step Tiffeneau–Demjanov procedure provides a mixture of **3** and **4** in a ratio of 90:10, respectively.[2] Similar treatment of 8,9-didehydro-2-adamantanone (**5**) gives only **6**.[3]

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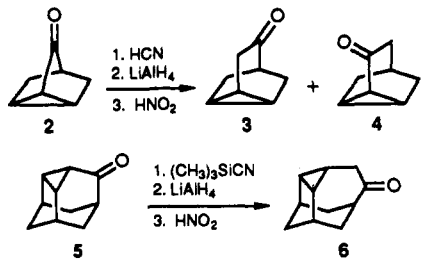
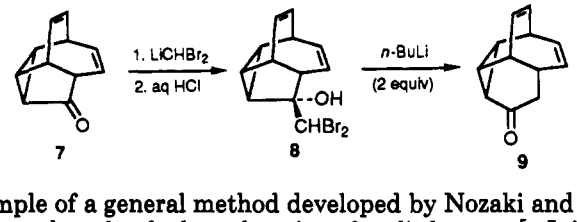
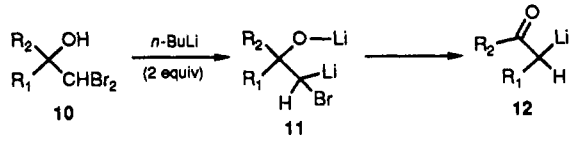


2 3 4 5 6

Considering these results, it is interesting that Vedejs and Shepherd have reported that reaction of **7** with (dibromomethyl)lithium, followed by treatment of the resulting alcohol **8** with 2 equiv of *n*-butyllithium, provides only the conjugated ketone **9**.[4] This procedure is an example of a general method developed by Nozaki and his co-workers for the homologation of cyclic ketones.[5] Initial attack of the nucleophilic (dibromomethyl)lithium occurs from the less hindered face of the carbonyl group. Subsequent treatment of the resulting dibromomethyl alcohol **10** with excess *n*-butyllithium is believed to give the β-oxido lithium–carbenoid intermediate **11**. The loss of



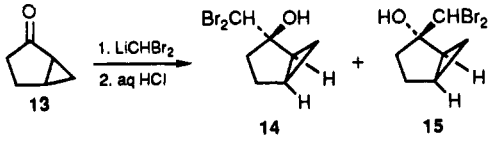
7 8 9



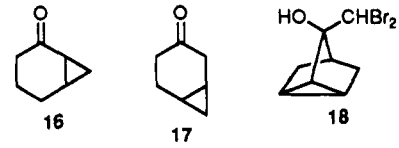
10 11 12

bromide from the carbenoid center of **11** triggers a pinacolone-type rearrangement to provide **12**.[5,6] In order to determine the generality of the observation of Vedejs and Shepherd, we have investigated the ring expansions of some *simple* cyclic conjugated cyclopropyl ketones by the Nozaki procedure.

Treatment of bicyclo[3.1.0]hexan-2-one[7] (**13**) with (dibromomethyl)lithium in tetrahydrofuran at −78 °C provides a mixture of **14** and **15** in a ratio of 90:10 and in an overall yield of 56%. The stereochemistries assigned to the substituents in **14** and **15** follow from the established preference of nucleophiles to attack the face of the carbonyl carbon in **13** that is anti to the one-carbon bridge.[8] Attempts to separate **14** and **15** by various chromatographic methods were unsuccessful. Consequently, the mixture of **14** and **15** was treated with 2.2 equiv of *n*-butyllithium in tetrahydrofuran at −100 °C. Quenching the resulting reaction mixture with 1 M aqueous oxalic acid at 0 °C provides a mixture of **16**[9] and **17**[10] in a ratio of 60:40



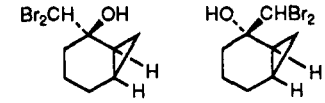
13 14 15



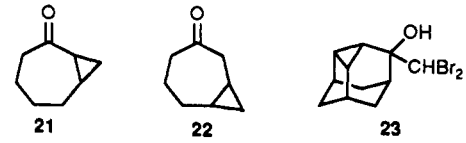
16 17 18

and in an overall yield of 68%. Although the fate of **15** cannot be determined from these results, simple mathematical analysis shows that the ring expansion of **14** gives both **16** and **17**. Thus, in the ring expansion of **13** by the Nozaki method, migration of the methylene carbon at C-3 is competitive with migration of the cyclopropyl group. In order to determine the migratory aptitudes of methine vs cyclopropyl, we prepared **18** in 74% yield by treating **2**[11] with (dibromomethyl)lithium. Reaction of **18** with excess *n*-butyllithium proceeds predominantly by migration of the cyclopropyl group to afford an 85:15 mixture of **3**[2] and **4**[8b,12] in an overall yield of 67%.

Comparable results were obtained with related ketones that contain the bicyclo[4.1.0]heptan-2-one moiety. Reaction of **16** with (dibromomethyl)lithium provides a mixture of **19** and **20** in a ratio of 60:40 and in an overall yield of 58%. Attempts to separate **19** and **20** by various chromatographic methods were unsuccessful. Treatment of this mixture of alcohols with excess *n*-butyllithium gives a mixture of ketones **21**[13] and **22**[14] in a ratio of 45:55 and in an overall yield of 84%. Similar reaction of **5**[15] with (dibromomethyl)lithium affords **23** in 81% yield. Treatment of this alcohol with excess *n*-butyllithium provides only **6**[3] in 67% yield.



19 20



21 22 23

In summary, the ring expansions of ketones **2**, **5**, **13**, and **16** clearly show that the homologations of *simple* cyclic conjugated cyclopropyl ketones by the Nozaki procedure do not maintain conjugation of the functional groups in the products. The migratory aptitudes in these examples are methylene ~ cyclopropyl > methine. These results parallel the Tiffeneau–Demjanov homologations of **2** and **5** and are consistent with the development of electrophilic character at the carbenoid center in **11** during the course of the ring expansion.[5,6]

Experimental Section

General Procedure for the Nozaki Homologation of Cyclic Ketones. A solution of lithium diisopropylamide was prepared

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by the addition of *n*-butyllithium (1.41 mL of a 1.42 M solution in hexane, 2.00 mmol) to a stirred solution of diisopropylamine (0.32 mL, 2.26 mmol, freshly distilled from calcium hydride) in anhydrous tetrahydrofuran (4.9 mL, distilled from sodium benzophenone ketyl) which was maintained at −78 °C under nitrogen. The reaction mixture was stirred at −78 °C for 15 min and then at 0 °C for 15 min before it was cooled again to −78 °C. This solution was added at a rate of approximately 0.3 mL/min via a motor-driven syringe pump to a stirred solution of the ketone (1.00 mmol) and methylene bromide (0.28 mL, 4.00 mmol, freshly distilled from phosphorus pentoxide) in anhydrous tetrahydrofuran (2.0 mL) that was maintained at −78 °C under nitrogen. After the addition was complete, the resulting dark solution was stirred for 1 h at −78 °C, and then it was poured into a mixture of ice (10 g) and ether (20 mL). After the ice had melted, the resulting solution was stirred, and 10% aqueous hydrochloric acid was added slowly until the aqueous layer was slightly acidic (pH = 6). The layers were separated and the aqueous layer was extracted with ether (20 mL). The organic layer and the ether extract were combined, washed with brine (10 mL), and dried over anhydrous magnesium sulfate. Evaporation of the solvent at reduced pressure afforded a black oil which was column chromatographed on silica gel. Elution with ether gave an orange oil which was Kugelrohr distilled to provide the corresponding dibromomethyl alcohol as a clear colorless oil.

n-Butyllithium (1.47 mL of a 1.5 M solution in hexane, 2.20 mmol) was cooled to −100 °C and then added at a rate of approximately 0.07 mL/min via a motor-driven syringe pump to a vigorously stirred (mechanical stirrer) solution of the dibromomethyl alcohol (1.00 mmol) in anhydrous tetrahydrofuran (4.4 mL) which was maintained at −100 °C under nitrogen. After the addition was complete, the resulting reaction mixture was stirred for 1 h at −100 °C, and then it was allowed to slowly warm to 0 °C. It was stirred at this temperature for 5 min, before it was treated with 1 M aqueous oxalic acid (2.20 mL). The resulting solution was stirred at 0 °C for 5 min, and then it was poured into a mixture of water (10 mL) and ether (10 mL). After this mixture was shaken vigorously, the layers were separated, and the aqueous layer was extracted with ether (10 mL). The organic layer and the ether extract were combined, washed with brine (10 mL), and dried over anhydrous magnesium sulfate. Evaporation of the solvent at reduced pressure provided a yellow oil. The ratio of the conjugated and nonconjugated cyclopropyl ketones present was determined by quantitative ^{13}C NMR spectroscopy. Control experiments established that the reaction products were stable both to the quenching procedure and to the conditions of the workup procedure.

Homologation of Bicyclo[3.1.0]hexan-2-one (13). Treatment of **13** (184 mg, 1.91 mmol) with (dibromomethyl)lithium according to the general procedure gave 292 mg (56% yield) of a mixture of 2-*exo*-(dibromomethyl)bicyclo[3.1.0]hexan-2-*endo*-ol [**14**, ^{13}C NMR δ 85.3 (C-2), 56.6 ($CHBr_2$), 32.3 (C-3), 26.4 (C-4), 24.3 (C-1), 17.8 (C-5), 6.9 (C-6)] and 2-*endo*-(dibromomethyl)bicyclo-[3.1.0]hexan-2-*exo*-ol [**15**, ^{13}C NMR δ 85.5 (C-2), 55.2 ($CHBr_2$), 33.5 (C-3), 25.9 (C-4), 25.7 (C-1), 17.5 (C-5), 7.0 (C-6)] as a clear colorless oil after Kugelrohr distillation (60–70 °C, 0.05 mm). Analysis of this material by quantitative ^{13}C NMR spectroscopy showed that **14** and **15** were present in a ratio of 90:10, respectively.

Reaction of this mixture of **14** and **15** (250 mg, 0.91 mmol) with *n*-butyllithium according to the general procedure afforded a yellow oil. Analysis of this material by ^{13}C NMR spectroscopy showed that **16** and **17** were present in a ratio of 60:40. Kugelrohr distillation (50–65 °C, 0.9 mm) of this material provided 69 mg (68% yield) of this mixture of **16** and **17**.

Homologation of Nortricyclanone (2). Treatment of **2** (800 mg, 7.39 mmol) with (dibromomethyl)lithium according to the general procedure gave 1.541 g (74% yield) of 3-(dibromomethyl)nortricyclan-3-ol (**18**) as a clear colorless oil after Kugelrohr distillation (55–60 °C, 0.04 mm): ^{13}C NMR δ 87.6 (C-3), 53.7 ($CHBr_2$), 39.4 (C-4), 32.6 (t), 31.1 (t), 20.2 (C-2), 14.1 (d), 13.2 (d); ^1H NMR δ 5.90 (s, 1 H, $CHBr_2$), 3.20–2.80 (m, 1 H, OH), 2.40–0.80 (complex m, 8 H).

Reaction of **18** (212 mg, 0.75 mmol) with *n*-butyllithium according to the general procedure afforded a yellow oil. Analysis of this material by ^{13}C NMR spectroscopy showed that **3** and **4** were present in a ratio of 85:15. Kugelrohr distillation (75 °C, 0.25 mm) of this material provided 61 mg (67% yield) of this mixture of **3** and **4**.

Homologation of Bicyclo[4.1.0]heptan-2-one (16). Treatment of **16** (530 mg, 4.82 mmol) with (dibromomethyl)lithium according to the general procedure gave 805 mg (58% yield) of a mixture of 2-*exo*-(dibromomethyl)bicyclo[4.1.0]heptan-2-*endo*-ol [**19**, ^{13}C NMR δ 73.3 (C-2), 60.2 ($CHBr_2$), 31.1 (C-3), 22.2 (C-5), 19.8 (C-1), 18.6 (C-4), 11.3 (C-6), 11.2 (C-7)] and 2-*endo*-(dibromomethyl)bicyclo[4.1.0]heptan-2-*exo*-ol [**20**, ^{13}C NMR δ 72.8 (C-2), 60.6 ($CHBr_2$), 32.1 (C-3), 22.2 (C-5), 18.9 (C-1), 15.1 (C-4), 12.3 (C-6), 5.2 (C-7)] as a clear colorless oil after Kugelrohr distillation (70–80 °C, 1.5 mm). The ^1H NMR spectrum of the mixture contained singlets for the dibromomethyl substituents of **19** and **20** at δ 5.73 and 5.76, respectively. Integration of these resonances showed that **19** and **20** were present in a ratio of 60:40.

Reaction of this mixture of **19** and **20** (250 mg, 0.87 mmol) with *n*-butyllithium according to the general procedure afforded a yellow oil. Analysis of this material by ^{13}C NMR spectroscopy showed that **21** and **22** were present in a ratio of 45:55. Kugelrohr distillation (55–70 °C, 0.9 mm) of this material provided 91 mg (84% yield) of this mixture of **21** and **22**.

Homologation of 8,9-Didehydroadamantan-2-one (5). Treatment of a mechanically stirred solution of **5** (296 mg, 2.00 mmol) and methylene bromide (0.56 mL, 7.98 mmol) in anhydrous diethyl ether (4.0 mL, distilled from sodium benzophenone ketyl) that was maintained at −100 °C under nitrogen with lithium diisopropylamide according to the general procedure gave 726 mg of a brown oil. Column chromatography of this material on 60–200-mesh silica gel with methylene chloride as eluent provided 519 mg (81% yield) of 2-(dibromomethyl)-8,9-didehydroadamantan-2-ol (**23**) as a white solid: mp 97–97.5 °C; ^{13}C NMR δ 72.0 (C-2), 61.0 ($CHBr_2$), 53.7 (C-6), 36.0 (C-3), 31.1 (t), 30.5 (d), 30.3 (d), 29.6 (t), 29.4 (C-1), 27.8 (d), 27.1 (d); ^1H NMR δ 6.24 (s, 1 H, $CHBr_2$), 2.36 (s, 1 H, OH), 2.40–1.30 (complex m, 12 H).

Reaction of **23** (483 mg, 1.5 mmol) with *n*-butyllithium according to the general procedure afforded 290 mg of a yellow oil. Analysis of this material by ^{13}C NMR spectroscopy showed that only **6** was present. Column chromatography of this material on TLC-mesh silica gel with 1:1 methylene chloride and petroleum ether gave 163 mg (67% yield) of **6**.

Acknowledgment. This work was supported by a grant from the University of Delaware Research Foundation.

Registry No. **3**, 10039-11-9; **4**, 39163-38-7; **5**, 10497-56-0; **14**, 138899-07-7; **15**, 138899-08-8; **16**, 5771-58-4; **17**, 60582-64-1; **18**, 138923-69-0; **19**, 138899-09-9; **20**, 138899-10-2; **21**, 16335-43-6; **22**, 90243-81-5; **23**, 138899-11-3; bicyclo[3.1.0]hexan-2-one, 4160-49-0; (dibromomethyl)lithium, 37555-63-8.

A Novel and Highly β-Selective Epoxidation of Δ⁵-Unsaturated Steroids with Permanganate Ion

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There has been considerable interest in recent years in the synthesis of 5β,6β-epoxides of Δ⁵-unsaturated steroids[1-3] particularly since this functionality is present in a number of biologically active steroids such as withaferin A,[4] withanolide B,[5] and jabarasalactone.[6] Due to the

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