support and Professor F. E. Ziegler for many helpful discussions. J.G.G. is grateful to the National Science Foundation for a Predoctoral Fellowship.

Registry No.—**1**, 1123-09-7; **2**, 1073-13-8; **3**, 6485-40-1; **4**, 89-82-7; **5**, 78-59-1; *cis*-3,5-dimethylcyclohexanone, 7214-52-0; *trans*-3,5-dimethylcyclohexanone, 7214-49-5; 4,4-dimethylcyclohexanone, 4255-62-3; *cis*-2-methyl-5-(1-methylethenyl)cyclohexanone, 3792-53-8; *trans*-2-methyl-5-(1-methylethenyl)cyclohexanone, 5948-04-9; *cis*-5-methyl-2-(1-methylethyl)cyclohexanone, 491-07-6; *trans*-5-methyl-2-(1-methylethyl)cyclohexanone, 89-80-5; 3,3,5-trimethylcyclohexanone, 873-94-9; lithium bronze, 19453-81-7; 2,2-dimethyl-5-isopropenylcyclohexanone, 54497-33-5.

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(1) (a) Review: D. Caine, *Org. React.*, **23**, 1 (1976). (b) Calculated from ref 1a, p 75, taking the density of liquid ammonia as 0.68 g/mL. (c) Cf. ref 1a, Table II.
(2) (a) V. I. Mel'nikova and K. K. Pivnitskii, *J. Org. Chem. USSR (Engl. Transl.)*, **6**, 2635 (1970); (b) *ibid.*, **8**, 2138 (1972); (c) *ibid.*, **10**, 1024 (1974).
(3) $Li{\cdot}4NH_3$ reportedly (ref 2b) may be kept in a closed container at 20 °C for 2–3 weeks, but exposure to air (especially in a dispersed form) or heat can initiate exothermic decomposition. An attempt to transfer the reagent using a glass syringe proved troublesome and hazardous, as the material coated the walls of the syringe and sparked and sputtered at the tip of the needle. The reagent may, with appropriate precautions, be transferred through polyethylene tubing using positive, inert gas pressure.
(4) E. C. Horning, M. O. Denekas, and R. E. Field, "Organic Syntheses", Collect. Vol. 3, Wiley, New York, 1955, p 317.
(5) G. Opitz and H. Holtmann, *Justus Liebigs Ann. Chem.*, **684**, 79 (1965).
(6) If desired, the excess NH_3 can be allowed to evaporate to give the reagent at room temperature. As the refluxing ammonia served to moderate the reaction temperature, we kept the dry ice condenser filled during the addition of the substrate; if the addition is commenced with the flask at room temperature, the NH_3 liberated as the reaction proceeds can cause a dramatic pressure surge, sufficient to blow out stoppers, etc.

Bicyclo[2.2.1]heptane-2,5-dione: Its Preparation and Reaction with Nucleophiles

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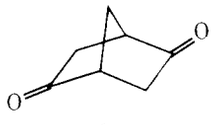
We have been exploring multigram syntheses of bicyclo[2.2.1]heptane-2,5-dione, a ketone[3,4,5] with potentially interesting stereochemistry.

Dione 1 from Diene 2 by Hydroboration–Oxidation. Bicyclo[2.2.1]hepta-2,5-diene (**2**) has been subjected to hydroboration–oxidation.[6–8] However, the literature does not identify the chief diol obtained. From studies of simpler model systems, one can infer that attachment of B should be exo,exo at positions 2 and 5, with retention of configuration upon alkaline hydrogen peroxide oxidation. We have shown that the hydroboration–oxidation must, in fact, proceed as expected, and that the predominant diol is indeed *exo,exo*-bicyclo[2.2.1]heptane-2,5-diol (**3**). We have shown that other diols are also formed: depending upon the experimental conditions, *exo,exo*-bicyclo[2.2.1]heptane-2,6-diol (**4**), and yet another diol have been detected in the reaction mixtures. It appears, however, that diol **3** predominates by about 10:1 over diol **4** in terms of isolated yields, and that the unknown third diol is obtained in still smaller amounts.

Hydroboration–oxidation[9] of **2** in our laboratory has provided 50–60% isolated yields of the diol **3**, along with about 5% of the diol **4**, and other byproducts in minor amounts. All our attempts to prepare the dione **1** directly by oxidation of the organoboron compounds resulted in very poor yields of low purity product. Our efforts at Jones oxidation of the diol to the dione proceeded in yields up to about 41%. Thus the process of converting diene **2** to dione **1** was achieved in yields of 21–25%.

Dione 1 from Diene 2 by Formylation–Oxidation. Because of difficulties with hydroboration and oxidation in obtaining dione **1**, we explored an alternative route: formylation of the diene **2** to diformate ester **5** and oxidation of that to the dione **1**. There is precedent[10] in the formylation of bicyclo[2.2.1]hept-2-ene to an exo ester. While our diformate ester appears to be previously undescribed, we have assigned it the 2,5-exo,exo configuration by analogy since it yields the dione **1**. The diformate ester was obtained in yields of 80%. Chromate oxidation in acetone resulted in 45% yields of the dione, this being 36% overall isolated yields from the diene.

Derivatives Obtained from Aryl Grignard Reagents and Dione 1. In accordance with expectations, we observed exo aryl products from the reaction of aryl Grignard reagents with the dione **1**.[11] That the attack was exo, at least in the case of phenyl Grignard reagent, was shown by the conversion of the endo,endo-diol **7a** into an acetonide **8**. Since only an endo,endo diol would be expected to give ring closure in this fashion, we have assigned endo configurations to **7a** and the other diols.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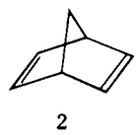
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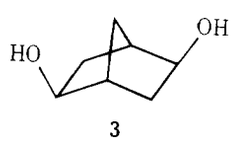
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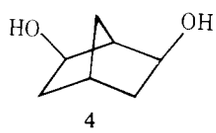
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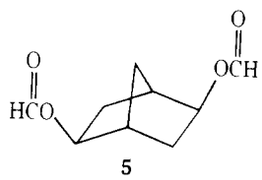
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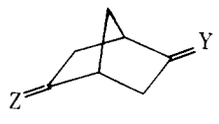
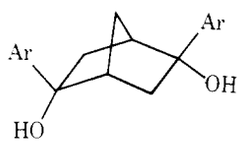
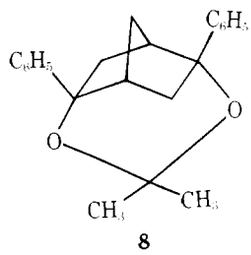

6a, Y = OCH_2CH_2O; Z = O
b, Y = Z = OCH_2CH_2O
c, Y = OCH_2CH_2O; Z = $NNHCONH_2$
d, Y = Z = $NNHC_6H_3(NO_2)_2$


7a, Ar = phenyl
b, Ar = *p*-tolyl
c, Ar = *o*-tolyl
d, Ar = 1-naphthyl


8

Derivatives of Bicyclo[2.2.1]heptane-2,5-dione. The mono(ethylene ketal), **6a**, the bis(ethylene ketal), **6b**, the semicarbazone of the mono(ethylene ketal), **6c**, and the bis(2,4-dinitrophenylhydrazone), **6d**, were prepared.

Experimental Section

Melting points were determined on a calibrated A. H. Thomas-Hoover melting point apparatus in capillary tubes. Elemental analyses were performed by M-H-W Laboratories of Garden City, Mich., or Chemalytics, Inc., of Tempe, Ariz. Infrared spectra were obtained on a Perkin-Elmer Model 457 spectrophotometer and proton magnetic resonance spectra on Varian Models A-60 and EM-390 spectrometers. GC/MS data were obtained from a Hewlett-Packard 5710A GC coupled with a 5980A MS interfaced with a 5934A data system.

Hydroboration–Oxidation of Diene 2. Several procedures were tried successfully, including (1) generation of the diborane ex situ from $NaBH_4$ and BF_3–etherate in diglyme; (2) generation in situ from the same reactants in THF with the etherate being added to the other reactants; (3) generation in situ as in (2) but with the etherate and

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diene being added intermittently; (4) generation in situ in the THF solvent with an added crown compound ("18-crown-6") to enhance solubility of the $NaBH_4$ in the THF. The third procedure was judged to be the most convenient.

The crude organic products were treated with ethyl ether whereupon white crystals appeared. The diol so obtained, in yields up to about 50%, proved to be suitable for subsequent oxidation. Further crops were obtained from some samples by trituration of residual semisolids with ether, $CHCl_3$, or ethyl acetate.

Diols from Hydroboration–Oxidation. From the complex reaction mixtures obtained by hydroboration–oxidation, two isomeric diols were isolated in reasonable purity by means of fractional crystallizations as previously mentioned. The diols were identified and characterized by the data quoted subsequently. While the major diol proved to be **3**, predominating at least 10:1 over the next most plentiful diol **4** according to isolated yields, at least one other diol was detected in minor amounts, as well as other closely related byproducts. Furthermore, the relative proportion of these products, both major and minor, varied according to the procedure employed for hydroboration, and even varied somewhat from run to run.

Gas chromatography proved to be of limited value in separating isomeric diols. On all the packed columns tested, diols **3** and **4** were incompletely resolved with retention times differing by about 3%. Furthermore, diacetate derivatives of the diols were resolved not at all on the columns we tested.

***exo,exo*-Bicyclo[2.2.1]heptane-2,5-diol (3):** mp 181–3 °C (lit.[3,4] mp 183.5–184.5 °C); diacetate bp 137.5–138.5 °C (10.4 torr), n^{22}_D 1.4640 (lit.[4] diacetate bp 139.5–140.0 °C (10.5 torr), n^{20}_D 1.4649); IR (KBr) 879 (m), 994 (s), 1035 (m), 1045 (w), and 1089 (s) inter alia (lit.[4] IR 880 (m), 993 (s), 1033 (m), 1043 (w), 1090 (s) cm^{-1}); NMR[12,13] (pyridine) δ 5.75, (s, 2 H, OH), 3.90 (m, 2 H, 2 and 5 endo), 2.40, (m, 2 H, bridgehead), 2.00 (s, 2 H, C-7), 1.58, (m, 4 H, C-3 and C-6 exo and endo). Clearly, this was not the spectrum for isomer **4** which requires two bridgehead signals, expected[5] to be at about 2.36 and 2.53 in pyridine. Retention time on 6 ft 10% SE-30 column at 185 °C was 165 s.

***exo,exo*-Bicyclo[2.2.1]heptane-2,6-diol (4):** mp 145–54 °C (lit.[14] mp 158–64 °C); IR (KBr) 993 (shoulder), 1006 (s), 1043 (s), 1089 (s), and 1097 (shoulder) inter alia (lit.[14] IR 1000 (s), 1040 (s), 1090 (s) cm^{-1}); NMR[5] (pyridine) δ 5.80 (s, 2 H, OH), 3.91, (m, 2 H, 2 and 6 endo), 2.59 (s, 1 H, C-1), 2.34 (s, 1 H, C-4), 1.88 (m, 2 H, C-7), 1.58 (m, 4 H, C-3 and C-5 exo and endo). Retention time (conditions as for 2,5-diol) was 160 s. Analysis by GC/MS of this diol (capillary column) showed it to be 98% pure, with two minor peaks of less than 1% each, hence chiefly an isomeric diol, $C_7H_{12}O_2$; on-the-fly scanning indicated the major eluting peak to be essentially homogeneous. Comparisons of literature melting point, NMR, and IR data for several other alternative isomeric diols established the identity of this one.

Jones Oxidation[15] of 3. A mixture of 6.40 g of **3** (0.05 mol) and 200 mL of acetone was stirred and cooled while 250 mL of 6 N chromic acid (50 g of CrO_3 and 80 g of concentrated H_2SO diluted to 250 mL) was added dropwise. After addition of the chromic acid, the mixture was stirred at 10–15 °C for 8 h. The clear solution was decanted from a green sludge, and the solid was washed with two 10-mL portions of acetone. The combined acetone solutions were dried (K_2CO_3). Rotary evaporation yielded 3.24 g of crude product. Sublimation of the residue at 1 torr and 80 °C gave 2.57 g of crystalline **1** (0.021 mol, 41%, mp 137–39 °C (lit.[3] mp 141.5–143 °C)).

Formylation of Diene 2. Diene **2** (20 g, 0.22 mol) and 94–97% formic acid (80 g, 1.74 mol) were refluxed 24 h. Distillation removed the excess formic acid (26–30 °C at 14–16 torr). The dark residue yielded about 10 mL of forerun; then product, **5**, was collected at 124 °C and 10 torr (32.4 g, 0.18 mol, 80%, n^{20}_D 1.4762): IR (neat) 1723 and 1170 cm^{-1}. GC analysis failed to detect any significant isomeric impurities.

Oxidation of 5. The diformate **5** was oxidized according to established methods.[10] Excess water was removed from the crude product by azeotroping the mixture with benzene. The resulting product was sublimed at 1 torr and 80 °C to yield **1** (44%, mp 124–130 °C (lit.[3] mp 141.5–143 °C)). Both the IR and NMR spectra were identical to those of known samples of **1**. NMR studies of **1** with the shift reagent $Eu(fod)_3$ allowed assignments of proton spectra: δ 2.15 (m, 6 H, C-3, C-6, and C-7), 2.86 (m, 2 H, C-1 and C-4). The α-methylene endo and exo protons moved to lowest fields and split into an A–B pattern with increasing concentrations of the shift reagent.

Derivatives of 1. Disemicarbazone. Three recrystallizations from aqueous ethanol yielded an analytical sample, mp 260–261 °C (lit.[4] 260.5–262.0 °C). Anal. Calcd for $C_9H_{14}O_2N_6$: C, 45.37; H, 5.92; N, 35.27. Found: C, 45.59; H, 5.90; N, 35.15.

Bis(2,4-dinitrophenylhydrazone), 6d. An analytical sample was prepared by three recrystallizations from ethanol (95%), mp 262.5–264.0 °C. Anal. Calcd for $C_{19}H_{16}O_8N_8$: C, 47.11; H 3.33; N, 23.13. Found: C, 46.87; H, 3.60; N, 21.15.

Mono(ethylene ketal), 6a, was prepared from a mixture of 2.48 g of **1** (0.02 mol), 1.42 g of ethylene glycol (0.02 mol), and 0.20 g of *p*-toluenesulfonic acid in 40 mL of benzene, refluxed for 20 h, and then cooled. The benzene was removed by rotary evaporation and the residue distilled at 1 torr and 94–5 °C. The product, 1.44 g, was examined by GC (6% SE-30, 6% Carbowax on Chromosorb W column, at 150 °C). It consisted of 11.5% dione, 10.0% diketal, and 78% monoketal. After separation by GC, the monoketal weighed 1.11 g, n^{25}_D 1.4875 (32.7% based on dione). Anal. Calcd for $C_9H_{12}O_3$: C, 64.27; H, 7.19. Found: C, 64.24; H, 7.24.

Semicarbazone of Mono(ethylene ketal), 6c. A sample was prepared in 80.5% yield from **6a** by the usual procedures. Thrice recrystallized from aqueous ethanol, it showed mp 202.0–204.5 °C, but reproducible results could not be obtained during combustion analyses. Nevertheless, consonant spectral data and comparisons of melting points assured us that the correct derivative was at hand.

Di(ethylene ketal), 6b. This was prepared similarly to **6a** from 1.24 g of **1** (0.01 mol), 6.2 g of ethylene glycol (0.10 mol, in excess), and 0.2 g of *p*-toluenesulfonic acid in 40 mL of benzene. The crude product was distilled at 2 torr and 101–103 °C to yield 1.26 g, n^{25}_D 1.4908 (60% based on dione). Anal. Calcd for $C_{11}H_{16}O_4$: C, 62.25; H, 7.60. Found: C, 62.69; H, 7.51.

Derivatives Obtained from Aryl Grignard Reagents and 1. *exo,exo*-2,5-Diphenylbicyclo[2.2.1]heptane-*endo,endo*-2,5-diol, 7a. As obtained by standard methods, the crude product was treated with ether, yielding white crystalline solid which was recrystallized from methanol and then ethanol. The yield was 54%, mp 121–22 °C. Anal. Calcd for $C_{19}H_{20}O_2$: C, 81.40; H, 7.19. Found: C, 81.67; H, 7.44.

***exo,exo*-2,5-Di(*p*-tolyl)bicyclo[2.2.1]heptane-*endo,endo*-2,5-diol, 7b,** was prepared by the same procedure as **7a**; the yield was 38%, mp 160–1 °C. Anal. Calcd for $C_{21}H_{24}O_2$: C, 81.78; H, 7.84. Found: C, 81.20, H, 8.20.

***exo,exo*-2,5-Di(*o*-tolyl)bicyclo[2.2.1]heptane-*endo,endo*-2,5-diol, 7c,** was prepared by the same procedure as **7a**; the yield was 14%, mp 161.5–162.5 °C (from ethanol). Anal. Calcd for $C_{21}H_{24}O_2$: C, 81.78; H, 7.84. Found: C, 81.47; H, 8.24.

***exo,exo*-2,5-Di(1-naphthyl)bicyclo-[2.2.1]heptane-*endo,endo*-2,5-diol, 7d,** was prepared from the same procedure as for **7a**, but the reaction mixture was not readily separable by fractional crystallization. A portion of the crude material was placed on a no. 1 activity alumina column. The charge was eluted with 50 mL of 20% $CHCl_3$ in hexane, 75 mL of 40% $CHCl_3$ in hexane, 50 mL of $CHCl_3$, and 50 mL of 10% methanol in $CHCl_3$. The product was detected in the second and third fractions, and purified by crystallization as before. The yield was 16%, mp 146–8 °C. Anal. Calcd for $C_{27}H_{24}O_2$: C, 85.23; H, 6.36. Found: C, 85.35; H, 6.50. No attempts were made to optimize any of these yields.

Acetonide 8 from 7a. A 0.5-g sample of the diol **7a** was dissolved in 10 mL of 2,2-dimethoxypropane and placed in a flask equipped with a Dean-Stark trap. Under gentle reflux, the 2,2-dimethoxypropane–methanol azeotrope, bp 61–2 °C, was collected. The unreacted ketal was removed and the remaining oil purified by elution from dry silica gel (once with methanol and once with $CHCl_3$). The resulting oil (yield about 35%) was found to be homogeneous to TLC (silica gel, $CHCl_3$) and also GC. The IR spectrum showed virtually no OH. Anal. Calcd for $C_{22}H_{24}O_2$: C, 82.46; H, 7.55. Found: C, 82.73; H, 7.45.

Acknowledgment. We thank Dr. Milton Lee for help in obtaining GC/MS data.

Registry No.—**1**, 27943-47-1; **1** disemicarbazone, 67711-81-3; **2**, 121-46-0; **3**, 21462-09-9; **4**, 34299-92-8; **5**, 67711-72-2; **6a**, 67594-61-0; **6b**, 67711-73-3; **6c**, 67711-74-4; **6d**, 67711-75-5; **7a**, 67711-76-6; **7b**, 67711-77-7; **7c**, 67711-78-8; **7d**, 67711-79-9; **8**, 67711-80-2; ethylene glycol, 107-21-1.

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(15) For a discussion of oxidation of this diol, including leading references and a possible explanation for our disappointing results with Sarett and two-phase chromic acid oxidations, see the appropriate sections in ref 2. Similar comments apply, of course, to the survival of the dione **1**.

Three-Carbon Annelation Reagents: 3-Bromo-2-methoxy-1-butene, an Alkyl-Substituted Methoxyallyl Bromide

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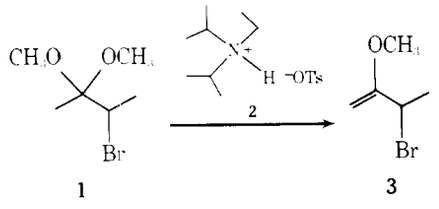
Received April 18, 1978

The utility of an electrophilic acetone synthon in the preparation of 1,4-dicarbonyl compounds and their derived cyclopentenones, furans, and pyrroles has been well demonstrated.[1,2] Our recent work on the use of 2-methoxyallyl bromide as a useful acetonyl alkylating agent has sparked our interest in the potential of various substituted derivatives, desiring to expand the scope and utility of the method. As polycyclic systems containing oxygenated methylcyclopentanes are widely found in nature, a methyl-substituted methoxyallyl bromide, 3-bromo-2-methoxy-1-butene (**3**), was chosen for the initial study. As **3** is a secondary allylic bromide, it was expected to be a less reactive alkylating agent than its parent, 2-methoxyallyl bromide.

The preparation of 3-bromo-2-methoxy-1-butene (**3**) was accomplished by the cracking of 3-bromo-2,2-dimethoxybutane (**1**) in the presence of a catalytic amount of diisopropylethylammonium tosylate (**2**) in a manner similar to that used for the preparation of 2-methoxyallyl bromide.[1] The resulting reagent contained approximately 76% of **3**, 2–5% of **1**, 3–8% of 3-bromo-2-butanone, less than 1% methanol, and little or no other "protic" impurities. In distinct contrast to our experience with 2-methoxyallyl bromide, none of the isomeric vinyl bromide was observed. Further purification by fractional distillation, though possible, was unnecessary for this work.



1 3

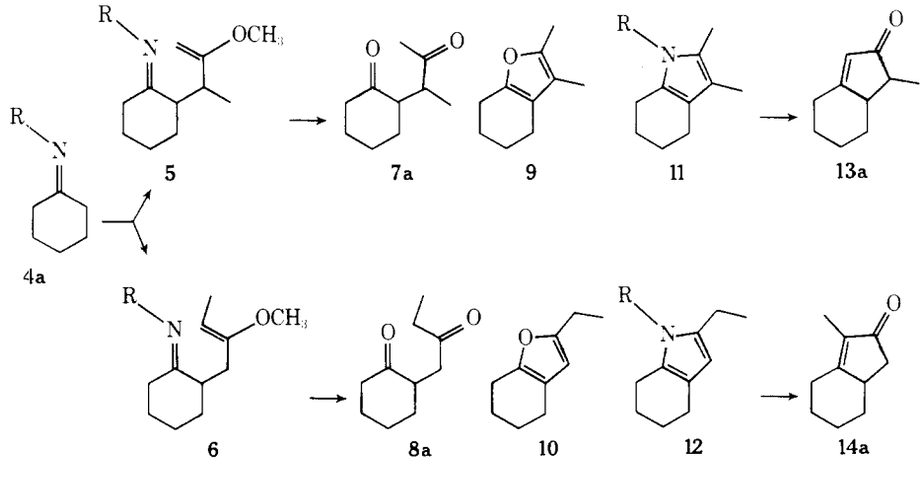
Imines of cycloalkanones were cleanly monoalkylated under standard (LDA/THF) conditions.[3,4] Imine **4a** gives a 4:1 mixture of imines **5** and **6**. The hydrolysis of the imine and enol ether functionalities requires some experimental care as subtle variation of conditions results in a large variation in product distribution. Treatment of **5** and **6** with acetic acid containing a few equivalents of water resulted in exclusive formation of furans **9** and **10** in 90% isolated yield.[5] Use of 1 M HCl in aqueous THF resulted in the predominant formation of pyrroles **11** and **12** in 80% overall yield.[6] The use of 1.5 M acetic acid in 50% aqueous THF proved optimum for hydrolysis to the diketones, providing **7a**, **8a**, and **9** in overall yields of 34, 22, and 25%, respectively. The ease of formation of furan **9** is noteworthy if predictable. The furans **9** and **10** could be hydrolyzed to diketones **7a** and **8a** with sulfuric acid[7] in high yield, allowing a good overall yield of diketone. Aldol cyclization[8] of the mixture of **7a** and **8a** gave the corresponding cyclopentenones which, under the reaction conditions, isomerized completely to the more substituted enone **14a**.

Alkylation of the imines of cycloheptanone and *N*-methyl-4-piperidone followed by hydrolysis and cyclization gave the expected cyclopentenones in good yield. Application of this annelation to the synthesis of hydroazulenes and tecomanine[9] will be reported in due course.

The reaction of **3** with singly and doubly activated esters and nitriles proceeded for the most part without difficulty. Diethyl 2-ethylmalonate (**15a**), dimethyl 2-methylmalonate (**15b**), and methyl cyanoacetate (**18**) were alkylated with **3** under standard (NaH/THF) conditions.[10] After a facile hydrolysis of the enol ethers, the resulting products were obtained in good yield. In these cases too, an S_N2' product was observed. Carbomethoxycyclohexane (**21**) and butyronitrile (**23**) could be cleanly alkylated under standard (LDA/THF) conditions.[11] Here no S_N2' products were observed.

In contrast to these successful alkylations, neither ethyl hexanoate nor methyl propionate could, in our hands, be alkylated with **3**, the competing Claisen condensation giving the observed products. Our attempts to directly alkylate ketone enolates have uniformly failed.

It is apparent that 3-bromo-2-methoxy-1-butene is a useful addition to the arsenal of annelating reagents. Its utilization, especially via alkylation of imine anions, should provide additional entries to the large number of methylcyclopentenone systems found in synthetic targets.



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