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THE SYNTHESIS OF BICYCLO[2.2.2]OCTAN-2-ONES BY SEQUENTIAL MICHAEL REACTIONS

KENNETH BRUCE WHITE and WILLIAM REUSCH
Department of Chemistry, Michigan State University, East Lansing, MI 48824, U.S.A.

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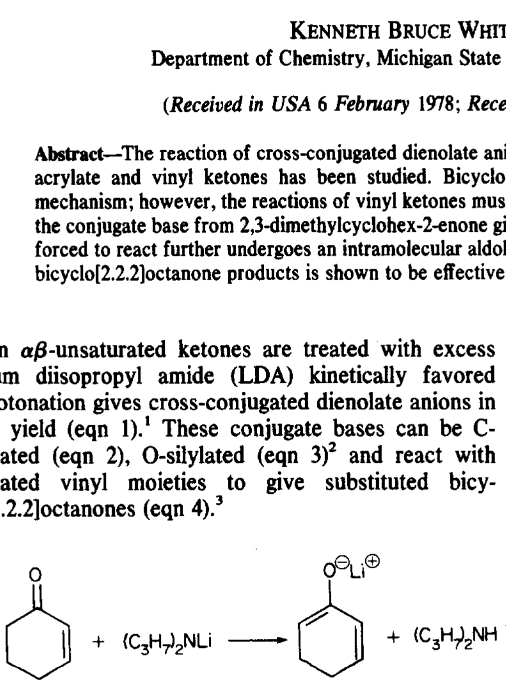
Abstract—The reaction of cross-conjugated dienolate anions derived from substituted cyclohexenones with methyl acrylate and vinyl ketones has been studied. Bicyclo[2.2.2]octan-2-ones are formed by a sequential Michael mechanism; however, the reactions of vinyl ketones must be conducted under amine-free conditions. Unexpecedly, the conjugate base from 2,3-dimethylcyclohex-2-enone gives only a single Michael adduct with vinyl ketones, and if forced to react further undergoes an intramolecular aldol condensation. An alternative Diels–Alder approach to the bicyclo[2.2.2]octanone products is shown to be effective.

When $\alpha\beta$-unsaturated ketones are treated with excess lithium diisopropyl amide (LDA) kinetically favored deprotonation gives cross-conjugated dienolate anions in good yield (eqn 1).[1] These conjugate bases can be C-alkylated (eqn 2), O-silylated (eqn 3)[2] and react with activated vinyl moieties to give substituted bicyclo[2.2.2]octanones (eqn 4).[3]

(1)



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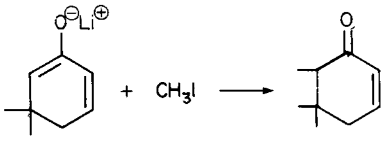
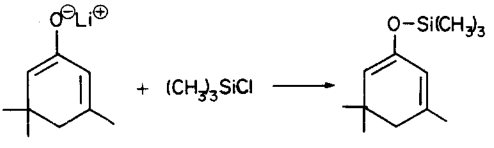


(3)



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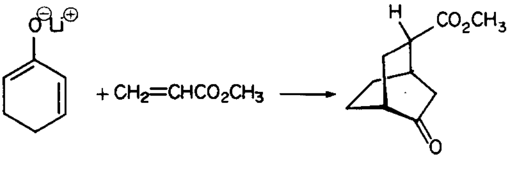
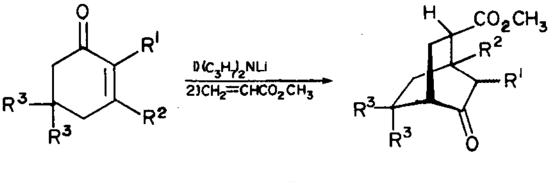


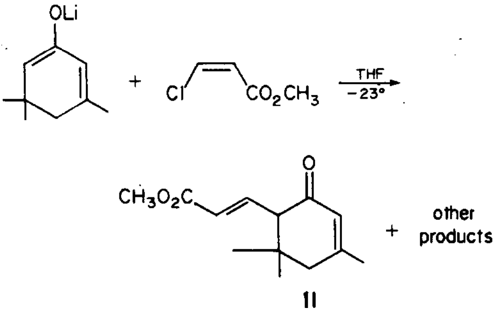
Since the latter reaction class seemed ideally suited to the synthesis of natural products having a bicyclooctane skeleton (e.g. seychellene[4]), we have further explored the scope and mechanism of these transformations. For example, conjugate bases generated from mmole quantities of enones **1–5** reacted quickly with methyl acrylate at −20° to −40° to give the corresponding bicyclo[2.2.2]octanones **6** through **10** in excellent yields.



1 $R^1=R^2=R^3=H$ **6**
2 $R^1=CH_3$; $R^2=R^3=H$ **7**
3 $R^2=CH_3$; $R^1=R^3=H$ **8**
4 $R^2=R^3=CH_3$; $R^1=H$ **9**
5 $R^1=R^2=CH_3$; $R^3=H$ **10**

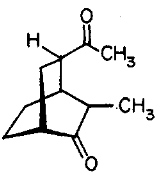
Although these reactions conceivably proceed by either a [4+2] cyclo-addition or sequential Michael reactions, the very mild conditions under which they occur suggests the latter pathway is followed.[3a] Since Michael reactions in which β-chlorovinyl esters and ketones serve as enolate anion acceptors are known to proceed by an addition-elimination sequence,[5] we anticipated that reactions of our dienolate anions with methyl β-chloroacrylate would be diverted from a sequential Michael course. Indeed, when the cross-conjugated dienolate anion from isophorone was treated with *cis*-β-chloroacrylate methyl ester at −25°, no adduct having a bicyclo-octane skeleton was obtained. The only substance identified from the highly colored product mixture was the vinylogous keto ester **11**. This result is consistent with the sequential Michael mechanism; however, we do not know enough about the dienophilic properties of the chloroacrylate ester to rule out the alternative Diels–Alder mechanism in reaction 4.

(5)



11

In contrast to the efficient transformations noted above for acrylate esters, vinyl ketones such as 1-buten-3-one and 1-penten-3-one were found to give only poor yields of analogous bicyclooctane adducts under similar conditions. Since vinyl ketones are normally more reactive than acrylate esters, we attributed this behavior to the intervention of 1,4-amine addition to vinyl ketone. In order to improve these reactions, it would, therefore, be necessary to remove the amine produced in the initial dienolate anion formation (eqn 1). An effective means of accomplishing this was to evaporate the conjugate base solution to dryness under reduced pressure. The resulting colorless salt was then dissolved in fresh THF and allowed to react with the vinyl ketone in the usual manner. By this simple procedure very good yields of bicyclo[2.2.2]octanediones **12** through **14** were obtained from enones **2** through **4** on reaction with methyl vinyl ketone. Compound **12** proved to be a mixture of epimers at C-3.



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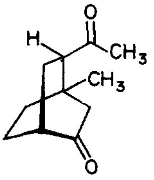

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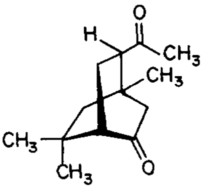
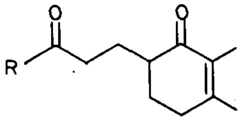


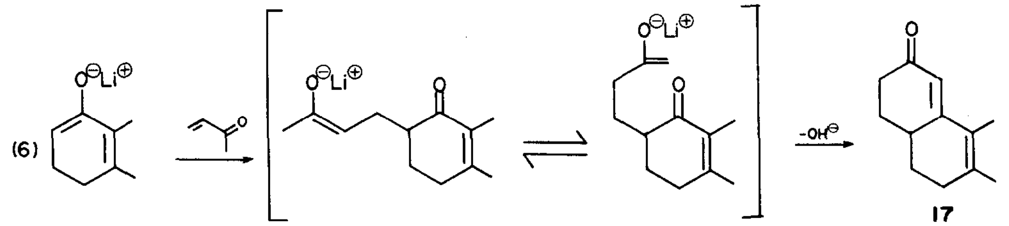
14

The corresponding reaction of the amine-free conjugate base from 2,3-dimethylcyclohex-2-enone (**5**) with either methyl vinyl ketone or ethyl vinyl ketone did not proceed to the bicyclic product. Instead, the corresponding single Michael adducts **15** and **16** were isloated in excellent yield, even after extended reaction (25°, 24 hr).



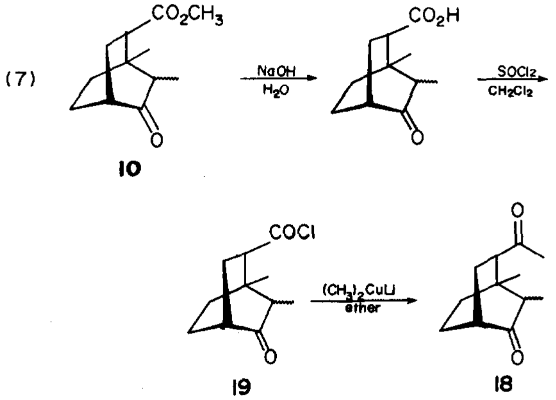
15 $R = CH_3$
16 $R = C_2H_5$

Under forcing conditions (reflux, 14 days) the reaction with methyl vinyl ketone gave dienone **17**, which could also be prepared by vigorous treatment of **15** with potassium t-butoxide in THF-t-butanol solution.



17

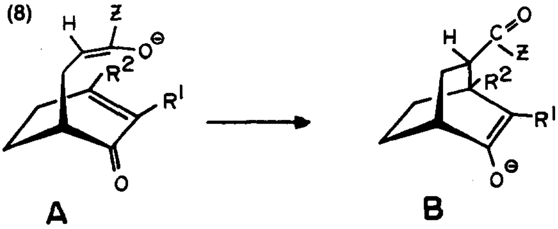
In order to establish whether the double Michael adduct **18**, corresponding to **15**, is stable under the reaction conditions that yield **17**, we synthesized **18** from acrylate adduct **10**. Thus, hydrolysis of 10 followed by treatment of the resulting ketoacid with thionyl chloride gave the acid chloride **19**, which was then treated with dimethylcopperlithium (eqn 7). A similar sequence of reactions in which the isophorone-acrylate adduct **9** was converted to **14**, not only confirmed the nature of these transformations, but also provided evidence for a uniform *endo* stereoselectivity[3a] in all these reactions. This stereochemistry corresponds to that predicted by a bidentate anion-cation intermediate in which the two carbonyl functions are held near each other by a mutual interaction with the cation.[11]



10 19 18

In an important and dramatic experiment **18**, on treatment with potassium t-butoxide at 25° for 2 days, was completely converted to the Robinson annelation product **17**. Similar treatment of **14** gave only slight epimerization to the *exo* isomer, over 90% of the diketone being recovered unchanged.

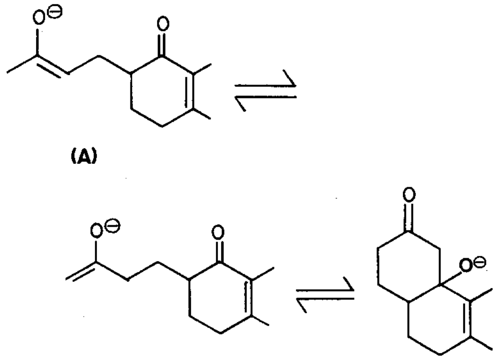
The variability of the enolate reactions described above can be rationalized in terms of steric and electronic factors influencing the second Michael addition (eqn 8).



A B

Since ester enolate bases are less stable and more reactive than ketone enolate anions (esters are over 10,000 times weaker as Brønsted acids than are ketones), there is a thermodynamic driving froce favoring cyclization (A→B) of the intermediate formed from acrylate ester addition ($Z = OCH_3$ in eqn 8). Vinyl ketone reactions, on the other hand, proceed through a series of ketone enolate anions among which this driving force is missing. In the absence of strong steric hindrance the cyclization should still be favored because of the increase in bond energy that normally accompanies the conversion of π-bonds to σ-bonds. Indeed, this is observed for all cases in which at least one of the R substituents (R^1 or R^2) is a hydrogen atom. However, when both R^1 and R^2 are methyl, we suggest that nonbonded repulsions destabilize the bicyclic product (B) relative to the monocylic precursor and the latter (A) predominates. The second Me group may also provide an additional stabilizing effect in enone A.

In the presence of a weak proton donor such as t-butanol the initially formed enolate anion A equilibrates with other enolate species (eqn 9) and eventually an intramolecular aldol condensation leads to the Robinson annelation product.

(9)

(A)

As an alternative to the sequential Michael synthesis of bicyclo[2.2.2]octanones, we have also examined some Diels–Alder reactions of trialkylsilyloxy cyclohexadienes **20** and **21**, prepared by O-silylation of the corresponding cross-conjugated dienolate anion (eqn 10). Shortly after we began this study Rubottom and Krueger published their illuminating account of such reactions,[6] and we have, therefore, limited our effort to completing the work described here.

Diels–Alder reactions of **20** and **21** with acrolein, acrylonitrile and methyl vinyl ketone were effected in high yield (> 90%) in refluxing toluene solution (12–24 hr). The reaction of methyl acrylate with **21** proceeded in slightly lower yield (*ca.* 80%). Since the sequential Michael procedure becomes less efficient for large scale preparations (> 100 mmoles), the Diels–Alder synthesis will clearly be the method of choice for many preparations.

The regioselectivity and stereoselectivity of the Diels–Alder reaction of **20** with acrolein was confirmed by the conversion of adduct **22** to known diketone **18**, as shown in eqn (12). With the exception of the acrylonitrile adduct, the endo adduct appears to predominate in the Diels–Alder reactions of **20** and **21**. Analysis of the adducts from **21** by PMR indicates that the cyano derivative (Z = CN) is formed as a 50 : 50 mixture of epimers. The *exo* isomer of the carbonyl adducts (Z = CHO or COMe) is a minor component (*ca.* 20%).

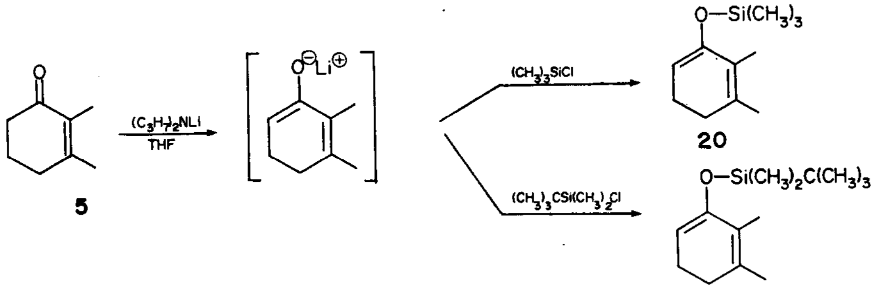
EXPERIMENTAL

IR spectra were recorded on a Perkin–Elmer 237B grating spectrophotometer. PMR spectra were taken in $CDCl_3$ soln with a Varian T-60 spectrometer, and are calibrated in parts per million (δ) downfield from TMS as an internal standard. UV spectra were recorded on a Unicam SP-800 spectrophotometer. Mass spectra were obtained with a Hitachi RMU 6 mass spectrometer.

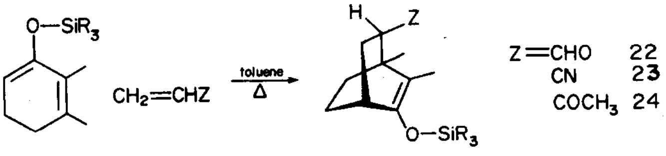
M.p were taken on either a Hoover–Thomas apparatus (capillary tubes) or on a hot-stage microscope and are uncorrected.

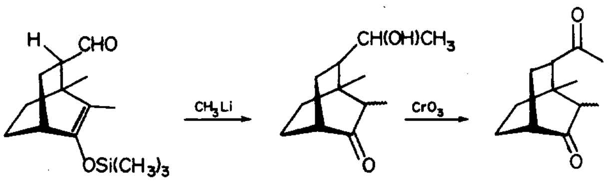
All reactions in which LDA[7] is used to generate enolate anions are conducted under dry argon. In working up these reactions they are quenched by the addition of water, extracted with ether and combined ether extracts washed in turn with INHCl (three times), water and brine.

Microanalyses of C and H were performed by Spang Microanalytical Laboratories, Ann Arbor, Michigan, and in all cases were within 0.2% of the calculated values.

(10)


5 20 21

(11)


(12)


22 25 18

The preparation of ketoesters **6** through **10** is illustrated by the following synthesis of *methyl* endo - 5 - *oxo* - *bicyclo*[2.2.2]*octane* - 2 - *carboxylate* (**6**):

To a stirred solution of LDA (121 mmoles) in 250 ml of a 4 : 1 THF/hexane mixture at − 23° was added 10 g of cyclohex - 2 - enone (105 mmoles) in dripwise fashion. This soln was stirred at − 23° for 1 hr, at which time 11.3 g of methyl acrylate (132 mmoles) was added over a 15 min period. After 2 hr at − 23° the mixture was worked-up as described in the introduction. Removal of the extraction solvent yielded 17.8 g (90%) of crude **6**, which was homogeneous by glpc (4% QF-1) and tlc (silica gel). A short path distillation afforded pure **6**, b.p. 100–104° (0.65–0.75 mm); IR (neat) 1735, 1725 cm^{-1}; PMR (CCl_4) δ 3.69 (s, 3H), 2.8–1.8 (m, 11H); mass spectrum (70 eV) *m/e* (rel. intensity) 182 (30) P, 96 (100).

A 2,4-dinitrophenylhydrazone derivative of **6**, m.p. 139–140°, analysed as $C_{16}H_{18}N_4O_6$.

Methyl endo - 5 - *oxo* - 6 - *methylbicyclo*[2.2.2]*octane* - 2 - *carboxylate* **7** was prepared in 81% yield from 2.0 mmoles of 2 - methylcyclohex - 2 - enone.[8] Properties:IR ($CDCl_3$) 1730, 1250, 1150 cm^{-1}; PMR ($CDCl_3$) δ 3.65 (s, 3H), 2.8–0.90 (m, 13H); mass spectrum (70 eV) *m/e* (rel. intensity) 196 (20)P, 110 (100); analysis $C_{11}H_{16}O_3$.

Methyl endo - 5 - *oxo* - 1 - *methylbicyclo*[2.2.2]*octane* - 2 - *carboxylate* **8** was prepared in 98% yield from 5.0 mmoles of 3-methylcyclohex - 2 - enone. Properties: IR ($CDCl_3$) 1725 and 1175 cm^{-1}; PMR ($CDCl_3$) δ 3.6 (s, 3H), 2.9–1.3 (m, 10H), 0.95 (s, 3H); mass spectrum (70 eV) *m/e* (rel. intensity) 196 (11)P, 110 (100); analysis $C_{11}H_{16}O_3$.

Methyl endo - 5 - *oxo* - 1,8,8'- *trimethylbicyclo*[2.2.2]*octane* - 2 - *carboxylate* (**9**) was prepared in 98% yield from 1.5 mmoles of isophorone. Properties: m.p. 53.5 to 54.5° (lit.[9] 54.5–55.5°); IR and PMR spectra identical to those reported by Nozaki *et al.*[9] for **9** prepared by the Diels–Alder reaction of methyl acrylate with the cross-conjugated dienamine derivative of isophorone.

Methyl endo - 5 - *oxo* - 1,6 - *dimethylbicyclo*[2.2.2]*octane* - 2 - *carboxylate* **10** was prepared in 91% yield from 2.0 mmoles of 2,3 - dimethylcyclohexenone.[10] Properties: IR (CCl_4) 1730, 1190, 1160 cm^{-1}; PMR (CCl_4) δ 3.6(s, 3H), 2.9–1.3 (m, 9H), 1.1 (s, 3H), 0.9 (d, 3H); mass spectrum (70 eV) *m/e* (rel. intensity) 210 (5)P, 124 (100); analysis $C_{12}H_{18}O_3$.

6 - (2' - *Carbomethoxyvinyl*) - 3,5,5 - *trimethylcyclohex* - 2 - *en* - *one* (**11**). To a stirred soln of 2.4 mmoles of LDA in 80 ml of THF, at − 23° under an argon atmosphere, was added dropwise a soln of 0.30 ml (2.0 mmoles) of isophorone in 5 ml of THF. The resulting mixture was stirred for 1 hr, following which a soln of 0.264 g (2.2 mmoles) of *cis*-β-chloromethyl acrylate* in 5 ml of THF was added dropwise over a 5 min period. This mixture was stirred for 2 hr at − 23°, and worked-up in the usual fashion. Removal of the solvent gave 0.404 g of a reddish oil. Analysis by glpc showed a mixture of isophorone and keto-ester **11** (ratio 1 : 1). An analytical sample of **11** obtained by preparative glpc showed the following properties: λ max (95% EtOH) 242 nm (ε = 13,400); ($CDCl_3$) 1725, 1670 cm^{-1} (both broad and strong); PMR ($CDCl_3$) δ 6.3–6.1 (m, 3H), 3.6(s, 3H), 2.4–1.2 (m, 6H), 1.05(s, 3H), 0.95 (s, 3H); mass spectrum (70 eV) *m/e* (rel. intensity) 222 (3)P, 190 (27), 175 (100) (Found: C, 70.33; H, 8.25 Calc. for $C_{13}H_{18}O_3$: C, 70.24; H, 8.16%).

endo 5-*Acetyl*-3-*methylbicyclo*[2.2.2]*octan*-2-*one* (**12**)

To a stirred soln of 2.2 mmoles of LDA in 40 ml of THF at − 78° was added a soln of 0.22 g (2.0 mmoles) of 2-methylcyclohexenone in 5 ml of THF. After stirring for 1 hr at − 78°, the reaction was warmed to 25° and the solvent and amine were removed under vacuum, being careful to avoid exposure to air. The resulting solid was dissolved in 80 ml of THF and this soln was cooled to − 78°. To this soln was added 0.18 ml (2.2 mmoles) of methyl vinyl ketone in 10 ml of THF over a 10 min period. The resulting mixture was stirred 12 hr at 25°, and worked-up in the usual manner. Removal of the solvent gave 0.308 g (81%) of crude dione **12** as a pale yellow oil. Glpc analysis (4% QF-1, 160°) showed this to be a mixture of epimers and starting material (9 : 1). An analytical sample obtained by preparative glpc (4% QF-1 190°) exhibited the following properties: IR (CCL_4) 1730 cm^{-1}; PMR (CCl) δ 2.8–2.2 (m, 3H), 2.15 (s, 3H), 2.0–1.0 (m, 10H); mass spectrum (70 eV) *m/e* (rel. intensity) 181 (6)P + 1, 180 (44)P, 110 (100). (Found: C, 73.12; H, 8.97 Calc. for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95%).

endo 5 - *Acetyl* - 4 - *methylbicyclo*[2.2.2]*octan* - 2 - *one* (**13**) and endo 5 - acetyl - 4,7,7 - trimethylbicyclo[2.2.2]octan - 2 - *one* (**14**) were synthesized in over 70% yield from 3 - methylcyclohex - 2 - enone and isophorone respectively by equivalent experimental procedures. These products exhibited the following characteristic properties: Compound **13**: IR (CCl_4) 1735 cm^{-1} (broad, strong); PMR (CCl_4) δ 2.8–2.2 (m, 3H), 2.1(s, 3H), 2.0–1.2 (m, 7H), 0.95 (s, 3H); mass spectrum (70 eV) *m/e* (rel. intensity) 180 (49)P, 110 (100); analysis $C_{11}H_{16}O_2$. Compound **14**: m.p. 51–53°; IR (CCl_4) 1725 cm^{-1}; PMR ($CDCl_3$) δ 2.8–2.25 (m, 2H), 2.15 (s, 3H), 1.95–1.30 (m, 7H), 1.15 (s, 3H), 1.0 (s, 3H), 0.9 (s, 3H); mass spectrum (70 eV) *m/e* (rel. intensity) 208 (15)P, 193 (18), 138 (28), 123 (100); analysis $C_{13}H_{20}O_2$.

3' - *Oxo* - 6 - *butyl* - 2,3 - *dimethylcyclohex* - 2 - *enone* (**15**). To a stirred solon of 22 mmoles of LDA in 200 ml of THF, at − 78° was added a soln of 2.48 g (20 mmoles) of 2,3 - dimethylcyclohexenone in 50 ml of THF. The mixture was warmed to 25°, and the solvent and amine were removed under vacuum, being careful to avoid exposure to the air. The resulting solid was dissolved in 400 ml of THF and the soln was cooled to −78°. To this soln was added 1.80 ml (22 mmoles) of freshly distilled methyl vinyl ketone in 100 ml of THF over a 10 min period. The resulting mixture was stirred 12 hr at room temp., and worked-up in the usual manner. Removal of the solvent yielded 2.8 g of a yellow oil, which on distillation (100°, 5 microns) afforded 2.41 g (60%) of dione **15** as a colorless oil which exhibited the following properties: λ max (95% EtOH) 245 nm (ε = 8200); IR (CCl_4) 1715, 1660 cm^{-1}; PMR (CCl_4) δ 2.7–2.2 (m, 6H), 2.1 (s, 3H), 1.85 (bs, 4H), 1.70 (bs, 4H), 1.3–1.0 (m, 1H); mass spectrum (70 eV) *m/e* (rel. intensity) 194 (3)P, 137 (41), 124 (19), 96 (100). (Found: C, 74.19; H, 9.20 Calc. for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34%).

9,10 - *Dimethylbicyclo*[4.4.0]*deca* - 2,9 - *diene* - 3 - *one* (**17**). To a stirred soln of 0.56 g (5 mmoles) of t-BuOK and 5 ml of t-BuOH in 80 ml of THF at 25° was added a solon of 0.388 g (2 mmoles) of dione **15** in 5 ml of THF. The mixture was stirred and worked-up in the usual fashion. Removal of the solvent afforded 0.323 g (91%) of **17** as an oil. An analytical sample obtained by preparative glpc (4% QF-1) exhibited the following properties: λ_{max} (EtOH) 291 nm (ε = 19,600); IR ($CHCl_3$) 1650 (broad and strong), 1620 cm^{-1}; PMR (CCl_4) δ 5.5 (bs, 1H), 2.4–2.0 (m, 7H), 1.8 (m, 8H); mass spectrum (70 eV) *m/e* (rel. intensity) 177 (7)P + 1, 176 (56)P, 133 (30), 105 (100). (Found: C, 81.77; H, 9.00 Calc. for $C_{12}H_{16}O$: C, 81.77; H, 9.00%).

5 - endo - *Chloroformyl* - 3,4 - *dimethylbicyclo* - [2.2.2]*octan* - 2 - *one* (**19**). Hydrolysis of 1.71 g (8.14 mmoles) of **10** was effected by 10% NaOH at 25°. Ether extraction of the acidified hydrolysis mixture gave 1.30 g (82%) of the corresponding ketoacid. Recrystallization of this ketoacid from hexane/EtOHc gave colorless crystals, m.p. 113–115°; IR ($CDCl_3$) 3300–3000, 1720 cm^{-1}; PMR ($CDCl_3$) δ 8.0 (bs, 1H), 2.9–1.5 (m, 8H), 1.2–1.0 (m, 7H); mass spectrum (70 eV) *m/e* (rel. intensity), 196 (9)P, 124 (100).

To a soln of this ketoacid (1.58 g, 8.5 mmoles) and 5.g of LiCl in 150 ml $CHCl_3$ was added 25 ml $SOCl_2$. After the mixture was stirred for 4 days at 25° it was filtered and concentrated under reduced pressure. The resulting oil was repeatedly stirred under vacuum until a constant weight of crude **19** was obtained (1.69 g, 89%). This product appeared to be homogeneous by glpc analysis (4% QF-1, 190°), and a sample purified by preparative glpc showed the following properties: IR ($CDCl_3$) 1795 and 1725 cm^{-1}; PMR ($CDCl_3$) δ 3.1–1.3 (m, 9H), 1.1 (s, 3H), 1.0 (overlapping doublets, 3H); mass spectrum (70 eV) *m/e* (rel. intensity) 216 (1)P + 2, 214 (2)P, 178 (46), 124 (37), 79 (100).

5 - endo - *Acetyl* - 3,4 - *dimethylbicyclo* - [2.2.2]*octan* - 2 - *one* (**18**). To a stirred solon of 11.76 g (60 mmoles) of cuprous iodide in 400 ml ether at − 78° (argon atmosphere) was added 120 ml (70.5 mmoles) of a soln of 1.7 M MeLi in ether. The resulting mixture was stirred for 20 min, following which a solon of 4.28 g (20 mmoles) of **19** in 50 ml ether was added. After stirring this mixture for 4 hr, it was quenched by adding 2 ml AcOH. Water

and ether were added and the aqueous phase was extracted 3 times with ether. The combined ether extracts were washed 3 times with a buffered ammonium hydroxide soln (pH 9), once each with water and sat. Na_2SO_4aqs and finally dried over $MgSO_4$. Removal of the solvent afforded 2.00 g (52%) of **18** as an oil which was homogeneous by glpc (4% QF-1, 160°). An analytical sample obtained by preparative glpc (4% QF-1, 190°) exhibited the following properties: IR (CCl_4) 1720 cm^{-1}; PMR (CCl_4) δ 2.8–2.1 (m, 2H), 2.05 (s, 3H), 2.0–1.1 (m, 7H), 0.90 (s, 3H), 0.85 (d, 3H); mass spectrum (70 eV) *m/e* (rel. intensity)194 (20)P, 124 (100). (Found: C, 74; H, 9.21 Calc. for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34%).

Conversion of ketoester **9** *to diketone* **14**. Hydrolysis of 2.98 g (13.2 mmoles) of **9** by NaOHaq gave 2.26 g (82%) of a crystalline ketoacid, m.p. 148–150°.

To a soln of this ketoacid (2.0 g, 8.8 mmoles) and 10 g LiCl in 200 ml $CHCl_3$ was added 20 ml $SOCl_2$. After the mixture was stirred for 3 days at 25°, it was filtered and concentrated under reduced pressure. This resulted in the crystallization of 1.78 g (89%) of crude **19**. Recrystallization from $CHCl_3$ gave a colorless solid, m.p. 63–65°; IR ($CDCl_3$) 1795 and 1725 cm^{-1}; PMR ($CDCl_3$) δ 2.5–1.2 (m, 8H), 1.10 (s, 3H), 1.05 (s, 3H), 0.90 (s, 3H); mass spectrum (70 eV) *m/e* (rel. intensity) 230 (4)P + 2, 228 (8)P, 165 (20), 138 (28), 123 (100).

A soln of 0.45 g (2 mmoles) of the previous acid chloride in 5 ml ether was added dropwise to a stirred soln of 6 mmoles of dimethylcopper lithium in 80 ml ether at −78°. After 4 hr at −78°, the reaction was quenched by the addition of AcOH (1 ml). Water and ether were added and the aqueous phase was extracted 3 times with ether. The combined ether extracts were washed with ammonium hydroxide buffer (pH 9), water and brine. Removal of the solvent from the dried extracts yielded 1.70 g (85%) of an oil which proved to be identical with authentic **14** in all respects.

Treatment of dione **14** *with base*. To a stirred soln of 0.56 g (5 mmoles) of BuOK and 5 ml of t-BuOH in 80 ml of THF at 25° was added a soln of 0.194 g (1 mmole) of **14** in 5 ml THF. After stirring at 25° for 2 days, the mixture was worked-up in the usual manner. Removal of the solvent gave 0.139 g (77%) of an oil which showed two products, dione **14** and the epimer of dione **14** (ratio 9 : 1). An analytical sample of the major product obtained by preparative glpc (4% QF-1, 190°) exhibited identical spectral and gas chromatographic properties as **14** prepared earlier.

Treatment of dione **18** *with base*. To a stirred soln of 0.56 g (5 mmoles) of t-BuOK and 5 ml of t-BuOH in 80 ml of THF at 25° was added a soln of 0.776 g (4 mmoles) of **18** in 5 ml THF. After stirring at 25° for 2 days, the mixture was worked-up in the usual manner. Removal of the solvent afforded 0.437 g (62%) of an oil. An analytical sample collected by preparative glpc exhibited identical spectral and gas chromatographic properties as 17.

1,2-Dimethyl-3-trimethylsilyloxycyclohexa-1,3-diene (**20**). To a stirred soln of 55.5 mmoles of LDA in 300 ml THF at −78° was added dropwise a soln of 6.2 g (50 mmoles) 2,3-dimethylcyclohexenone in 100 ml THF. Shortly thereafter 5 ml HMPA was added, the mixture was warmed to 0° and a soln of 12.6 ml (100 mmoles) trimethylchlorosilane in 100 ml THF was added over a 10 min period. The mixture was stirred for 18 hr at 25°, and worked-up in the usual manner. Removal of the solvent gave a clear oil, which on purification by vacuum distillation (104°, 7 mm), yielded 8.58 g (87%) of **20** as a clear oil. IR (neat) 1640, 1620 cm^{-1}; PMR (CCl_4) δ 4.75 (bs, 1H), 2.05 (m, 4H), 1.7 (m, 6H), 0.20 (s, 9H); mass spectrum (70 eV) *m/e* (rel. intensity) 198 (5)P + 2, 197 (18)P + 1, 196 (59)P, 73 (100). (Found: C, 67.17; H, 10.07. Calc. for $C_{11}H_{20}OSi$: C, 67.28; H, 10.26%).

3-t-Butyldimethylsilyloxy-1,2-dimethylcyclohexa-1,3-diene (**21**). To a stirred soln of 55.5 mmoles LDA in 300 ml THF at −78° was added dropwise a soln of 6.2 g (50 mmoles) 2,3-dimethylcyclohexenone in 100 ml THF. Shortly thereafter 5 ml HMPA was added, the mixture was warmed to 0° and a soln of 10.5 g (70 mmoles) t-butyldimethylchlorosilane in 100 ml THF was added over a 10 min period. The mixture was stirred for 18 hr at 25°, and worked-up in the usual manner. Removal of the solvent gave a clear oil, which on purification by vacuum distillation (123°, 6 mm), yielded 10.0 g (88%) of **21** as a clear oil: IR (neat) 1645, 1620 cm^{-1}; PMR (CCl_4) δ 4.6 (bs, 1H), 2.1–1.6 (m, 10H), 0.95 (s, 9H), 0.20 (s, 6H); mass spectrum (70 eV) *m/e* (rel. intensity 238 (5)P, 236 (5), 75 (100). (Found: C, 70.47; H, 10.84. Calc. for $C_{14}H_{26}OSi$: C, 70.52; H, 10.99%).

Diels–Adler reactions of dienes **20** and **21** have been conducted with acrolein, acrylonitrite, methyl vinyl ketone and methyl acrylate. The following procedure is typical.

3,4-Dimethyl-5-formyl-2-trimethylsilyloxybicyclo[2.2.2]*oct-2-ene* (**22**). To a stirred soln of 1.98 g (10 mmoles) of **20** in 200 ml toluene containing 10 mg hydroquinone was added 1.35 ml (20 mmoles) acrolein. This mixture was refluxed for 24 hr under an argon atmosphere. Removal of the solvent afforded 2.30 g (92%) of **22**, as an oil which was homogeneous by glpc (4% QF-1, 100°). An analytical sample obtained by preparative glpc (4% QF-1, 190°) exhibited the following properties: IR (neat) 1680, 1635 cm^{-1}; PMR ($CDCl_3$) 9.15 (d, 1H), 2.5–0.9 (m, 14H), 0.1 (s, 9H); mass spectrum (70 eV) *m/e* (rel. intensity) 252 (6)P, 196 (100). (Found: C, 66.41; H, 9.61. Calc. for $C_{14}H_{24}O_2Si$: C, 66.61; H, 9.58%).

5-Cyano-3,4-dimethylsilyloxybicyclo[2.2.2]*oct-2-ene* (**23**) was prepared in 95% yield from **20** and acrylonitrile. Properties: IR ($CHCl_3$) 2230, 1670 cm^{-1}; PMR ($CDCl_3$) δ 2.5–1.0 (m, 14H), 0.2 (two close singlets, 9H); mass spectrum (70 eV) *m/e* (rel. intensity) 249 (13)P, 196 (100); analysis (C and H) $C_{11}H_{23}OSiN$.

5-Acetyl-3,4-dimethyl-2-trimethylsilyloxybicyclo[2.2.2]*oct-2-ene* (**24**) was prepared in 97% yield from **20** and methyl vinyl ketone. Properties: IR (neat) 1725, 1680 cm^{-1}; PMR ($CDCl_3$) δ 2.5–1.3 (m, 14H), 1.1 (s, 3H), 0.2 (bs, 9H); mass spectrum (70 eV) *m/e* (rel. intensity) 266 (12)P, 196 (100); analysis (C and H) $C_{15}H_{26}O_2Si$.

Conversion of **22** *to* **18**. A soln of **22** (2.66 g, 10 mmoles) in dry ether (100 ml) was treated with MeLi (30 mmoles), added as a 1.6 M ether soln under an argon atmosphere. After 4 days at 25°, the mixture was worked-up, and yielded 1.59 g (81%) of an oily hydroxy ketone. This material appeared to be homogeneous by glpc analysis (4% QF-1, 160°), and exhibited properties consistent with the expected product: IR ($CHCl_3$) 3600, 3430, 1720 cm^{-1}; PMR ($CDCl_3$) ~1 : 1 ratio of Me protons to non-Me protons; mass spectrum (70 eV) *m/e* (rel. intensity) 196 (8)P.

The crude hydroxy ketone product (0.364 g, 2 mmoles) was oxidized by pyridinium chlorochromate (5 mmoles) in methylene chloride soln. The crude organic extracts were filtered through a layer of Florisil, washed in turn with alkaline acetyl acetone, water and brine, and finally dried over $MgSO_4$. Removal of the solvent yielded 0.30 g (83%) of an oil, which proved to be identical in all respects with authentic **18**.

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