Synthesis of cedranoid sesquiterpenes. II. Functionalization at carbon 12[1]

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Dimethyl 6,6-dimethyl-7-oxotricyclo[3.2.1.0^{2,8}]octane-1,8-dicarboxylate (**6**) undergoes homoconjugate addition with lithium diphenylcuprate to give dimethyl 3-hydroxy-4,4-dimethyl-*exo*-8-phenyl-*cis*-bicyclo[3.3.0]oct-2-ene-1,2-dicarboxylate (**12***a*), which on monodecarboxymethylation, ozonolysis, and esterification with diazomethane gives dimethyl 6,6-dimethyl-7-oxo-*cis*-bicyclo-[3.3.0]octane-1,*exo*-2-dicarboxylate (**15**). Reaction of **6** with diethylaluminum cyanide gives dimethyl *exo*-8-cyano-3-hydroxy-4,4-dimethyl-*cis*-bicyclo[3.3.0]oct-2-ene-1,2-dicarboxylate (**16**), which on hydrolysis and esterification with diazomethane also gives **15**. Sensitized photolysis of dimethyl 5-oxo-6,6-dimethylbicyclo[2.2.2]octa-2,7-diene-2,3-dicarboxylate (**19**) gives dimethyl 4,4-dimethyl-3-oxotricyclo[3.2.1.0^{2,8}]oct-6-ene-1,8-dicarboxylate (**20**), which on reduction with lithium in ammonia gives dimethyl 6,6-dimethyl-7-oxobicyclo[3.3.0]oct-3-ene-1,*exo*-2-dicarboxylate (**31**); conversion of **31** to its 2-ene isomer **32** followed by catalytic hydrogenation gives **15** and its *endo*-2 epimer **33**.

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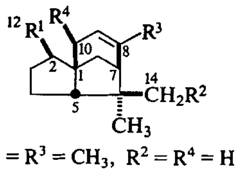
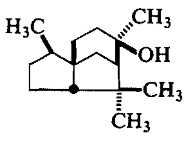
Le diméthyl-6,6 oxo-7 tricyclo[3.2.1.0^{2,8}] octanedicarboxylate-1,8 de méthyle (**6**) subit une addition homoconjuguée du diphénylcuprate de lithium pour donner l'hydroxy-3 diméthyl-4,4 phényl-8-*exo* bicyclo[3.3.0] octène-2 dicarboxylate-1,2-*cis* de méthyle (**12***a*) qui par monodécarboxyméthylation, ozonolyse et estérification par le diazométhane conduit au diméthyl-6,6 oxo-7 bicyclo[3.2.0] octanedicarboxylate-1,2-*exo* de méthyle (**15**). La réaction de **6** avec du cyanure de diéthylaluminium fournit le cyano-8-*exo* hydroxy-3 diméthyl-4,4 bicyclo[3.3.0] octène-2 dicarboxylate-1,2-*cis* de méthyle (**16**) qui, par hydrolyse et estérification par le diazométhane, conduit aussi à **15**. La photolyse sensibilisée de l'oxo-5 diméthyl-6,6 bicyclo[2.2.2] octadiène-2,7 dicarboxylate-2,3 de méthyle (**19**) fournit le diméthyl-4,4 oxo-3 tricyclo[3.2.1.0^{2,8}] octène-6 dicarboxylate-1,8 de méthyle (**20**) qui, par réduction par le lithium dans l'ammoniac, conduit au diméthyl-6,6 oxo-7 bicyclo[3.3.0] octène-3 dicarboxylate-1,2-*exo* de méthyle (**31**); la conversion de **31** dans son isomère ène-2 (**32**), suivie par une hydrogénation catalytique, conduit à **15** et à son épimère 2-*endo* (**33**).

[Traduit par le journal]

The cedranoid sesquiterpenes are a group of naturally occurring compounds and their congeners that have the tricyclo[5.3.1.0^{1,5}]undecane skeleton, of which the simplest members are α-cedrene (**1**) and cedrol (**2**) (2).[2] A variety of more highly oxygenated compounds have also been isolated, such as laccishellolic acid (**3**) (4) and shellolic acid (**4**) (5).



1 $R^1 = R^3 = CH_3$, $R^2 = R^4 = H$
3 $R^1 = R^3 = CO_2H$, $R^2 = H$
$R^4 = OH$
4 $R^1 = R^3 = CO_2H$, $R^2 = R^4 = OH$



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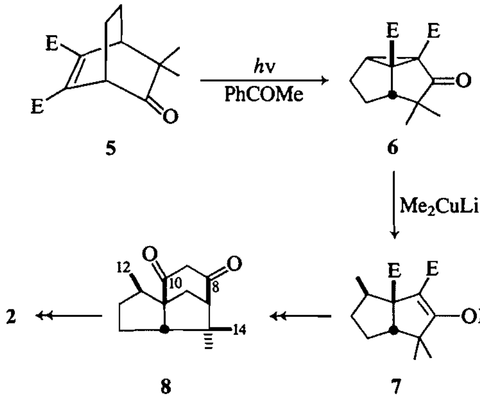
Several total syntheses of compounds **1** and **2** have been achieved (6, 7), but none of compounds **3** and **4**. We have recently designed a new synthesis of (±)-cedrol (**2**) that it was hoped could subsequently be elaborated to provide syntheses of the more highly oxygenated cedranoid sesquiterpenes, including **3** and **4** (1, 8). This synthesis (Scheme 1) has as key steps the photochemical oxa-di-π-rearrangement of the bicyclo[2.2.2]octenone **5** to the tricyclo[3.2.1.0^{2,8}]octanone **6** and reaction of lithium dimethylcuprate with the latter to give the homoconjugate addition product **7** [cf. ref. 9]. The bicyclo[3.3.0]octanone **7** was converted in five steps to the β-diketone **8**, which had earlier been prepared by Stork and Clarke by a different route and transformed into cedrol (**2**) (6). The desired elaboration of this approach requires the incorporation of oxygenated functions at C-12 and C-14 in **8** and appropriate manipulations of the ketonic functions at C-8 and C-10. We report now on progress



SCHEME 1 (E = CO$_2$Me)

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[1] For a preliminary account of part of this work, see ref. 1.

[2] At least four systems of numbering of the cedrene skeleton have been used; that in **1** is in accord with the IUPAC rules (3).

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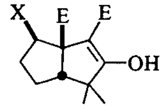
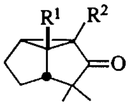
towards the attainment of the first of these objectives.

With the intention of introducing a latent carboxylic acid group in place of the C-12 methyl group of **8**, we first attempted to effect the homoconjugate addition of a vinyl group to **6** by treatment with lithium divinylcuprate reagents. However, the use of a large variety of reagents and conditions that had previously been used for the conjugate addition of a vinyl group to α,β-unsaturated carbonyl compounds (see Experimental) failed to effect homoconjugate addition.[3] Nor could such addition be effected with lithium diisobutylhex-1-enylmethylalanate (12) or with the potassium or thallous derivatives of diethyl malonate (9, 13). Attempted homoconjugate addition of an allyl group with allytrimethylsilane and titanium tetrachloride (14) led instead to homoconjugate addition of chloride ion to give **9**, which showed the typical strong ir bands at 6.06 and 6.21 μm of the enolized β-keto ester system of homoconjugate addition products from **6**. We subsequently found that the same product is formed in the presence of titanium tetrachloride alone. The failure to add an allyl group indicates that, while the ethylenic bond of allyltrimethylsilane may be relatively nucleophilic (15), chloride ion is a much better nucleophile under the conditions used. It is possible that in the case of conjugate addition to α,β-unsaturated ketones (14), conjugate addition of chloride also occurs, but is reversible.



9 $X = Cl$, $E = CO_2Me$
10 $X = Br$, $E = CO_2Me$



11a $R^1 = (C_6H_5C{\equiv}C)_2\overset{|}{C}OH$, $R^2 = CO_2Me$
11b $R^1 = CO_2Me$, $R^2 = (C_6H_5C{\equiv}C)_2\overset{|}{C}OH$

The recent report (16*a*; see, however, ref. 16*b*) of the homoconjugate addition of Grignard reagents to spiroactivated cyclopropane rings (9) led us to investigate the reaction of **6** with phenylethynylmagnesium bromide in ether. At 2°C a voluminous white precipitate formed immediately and work-up gave two products in approximately equal amounts. When the reaction was conducted at −75°C for 9 hours and then at 2°C for 11 hours, one of these products was formed almost exclusively. This was shown to be a homoconjugate addition product by strong bands in its ir spectrum at 6.06 and 6.19 μm (*vide supra*) and identified as the hydrogen bromide adduct **10**. It was prepared independently by treatment of **6** with hydrogen bromide in dichloromethane. While the other product was not fully characterized, it is tentatively assigned structure **11***a* or **11***b* on the basis of the of the following spectroscopic data and mechanistic considerations. Its ir spectrum with a single band in the carbonyl-stretching region at 5.79 μm suggested that opening of the cyclopropane ring had not occurred; this spectrum also showed a band at 3.07 μm attributable to a strongly hydrogen-bonded hydroxyl group. Its ^{1}H nmr spectrum showed that only one methyl ester group remained (δ 3.67 ppm (s, 3H)) and that two phenyl groups had been incorporated into the molecule. We suggest that the keto and C-1 ester groups or the two ester groups of **6** act as a powerful bidentate ligand and that the precipitate is a magnesium bromide complex of **6** or **10**, either of which could lead to **10** on work-up. As in the precipitation of magnesium bromide from Grignard reagents by dioxane (17), bis(phenylethynyl)magnesium remains in solution and reacts with uncomplexed **6** at 2°C, but not at −75°C. Weight is lent to these suppositions by the observation that treatment of **6** with a solution of bis(phenylethynyl)magnesium, prepared by the addition of dioxane to a solution of phenylethynylmagnesium bromide, at 4°C gives exclusively **11***a* (or **11***b*).

Eventually success was achieved in the introduction of a carboxylic acid function into **6** by the route shown in Scheme 2. Reaction with lithium diphenylcuprate led to homoconjugate addition of a phenyl group to give **12**, whose ir spectrum showed strong bands at 6.09 and 6.25 μm. Life was still not without its complications, however, since the ^{1}H nmr spectrum of this product showed that it was a ~2:1 mixture of the methyl and ethyl esters **12***a* and **12***b* (see Experimental). The ethyl ester **12***b* is considered to be formed by exchange of ethoxide for methoxide in the C-2 ester group of **12***a*; the ethoxide ion most probably has its origin in a slow reaction of phenyllithium with ether, for the phenyllithium was obtained commercially as a solution in ether and benzene (30:70).[4] It is of interest that although reaction of **6** with lithium dimethylcuprate gives, together with the homoconjugate product, small amounts of two stereoisomeric bicyclo[3.2.1]octan-3-ones formed by reduction (8), there

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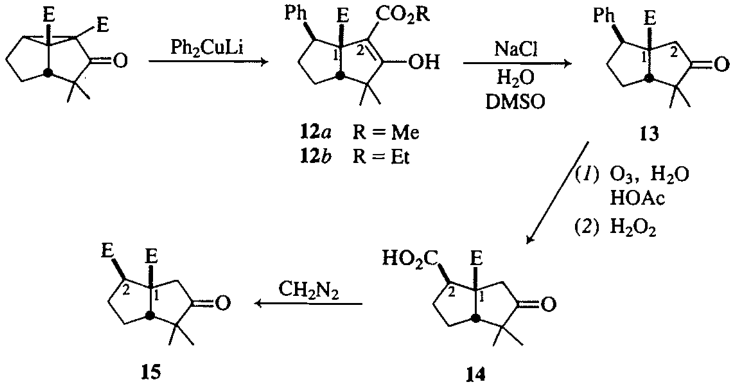
[3] In the course of other work (10) it has recently been observed that lithium divinylcuprate reagents fail to effect conjugate addition of a vinyl group to cholest-4-en-3-one, although this compound undergoes conjugate addition with lithium dimethyl- and diethylcuprate (11).

[4] Compare the slow reaction of *n*-butyllithium with tetrahydrofuran to give butane, ethylene, and the lithium enolate of acetaldehyde (18).



SCHEME 2 (E = CO_2Me)

was no evidence for the formation of reduction products in the case of its reaction with lithium diphenylcuprate; this was unexpected since the two cuprates have similar reactivities towards α,β-unsaturated ketones (19). Attempts to separate **12***a* and **12***b* were unsuccessful and the mixture was therefore subjected to monodecarboalkoxylation with sodium chloride in aqueous dimethyl sulfoxide (20) to give the single product **13**. This showed in its ir spectrum a single band in the carbonyl-stretching region at 5.80 μm as expected. Its ^1H nmr spectrum showed two one-proton doublets (J = 19 Hz) at δ 2.46 and 3.60 ppm, characteristic of the C-2 protons in this system (cf. the corresponding decarbomethoxylation product from **7**: δ 2.09 (d, 1H) and 3.35 ppm (d, 1H) (J = 20 Hz)); the signal of the methyl ester protons appears at δ 3.21 ppm as a result of shielding of these protons by the phenyl group. This shielding is in accord with the *exo* configuration assigned at C-8 in **12** and **13**, which is also based on analogy with the configuration established at this carbon in **7** (8). Ozonolysis of **13** in aqueous acetic acid followed by oxidative work-up (cf. ref. 21) gave the carboxylic acid **14**, which was characterized as the diester 15. The ir spectrum of this had a single peak in the carbonyl-stretching region at 5.78 μm, and its ^1H nmr spectrum included two three-proton singlets at δ 3.67 and 3.71 ppm and two one-proton doublets at δ 2.34 and 3.62 ppm (J = 19 Hz). The *exo* configuration of **14** and **15** at C-2 follows from their formation from **13** and is corroborated by the synthesis of the C-2 epimer of **15** (*vide infra*).

A second route from **6** to **15** is shown in Scheme 3; this process involved homoconjugate addition to **6** and proceeded more expeditiously and in better yield than by the route of Scheme 2. Reaction of **6** with diethylaluminum cyanide in toluene gave the nitrile **16** (cf. ref. 22). The introduction of a nitrile group into the product was signalled by a band at 4.46 μm in its ir spectrum and a singlet at δ 120.0 ppm in its sford ^{13}C nmr spectrum. The presence of the enolized β-keto ester was vouchsafed by strong bands at 6.01 and 6.17 μm in their spectrum of the product and a one-proton singlet at δ 10.52 ppm in its ^1H nmr spectrum. Attempts to convert **16** directly to **15** led to complex mixtures of products, and this transformation was therefore carried out in two steps. Decarboxylation as before gave **17** and treatment of this with boiling methanol containing sulfuric acid (cf. ref. 23) gave **15** as the major product, identical with the product obtained by the route in Scheme 2. A minor product was also formed in this reaction and is assigned structure **18** on the basis of its origin and its spectra. Its ir spectrum showed bands at 5.62 (m) and 5.79 (s) μm assigned to the carbonyl-stretching vibrations of the five-membered cyclic imide and five-membered cyclic ketonic groups together with an N—H stretching band at 3.02 μm. Its ^1H nmr spectrum showed two one-proton doublets at δ 2.38 and 3.22 ppm (J = 19 Hz) indicating that the bicyclo[3.3.0]-octan-3-one system was intact, and a broad one-proton singlet at δ 8.69 ppm (absent after D_2O treatment) confirming the presence of an NH group; this spectrum also revealed the absence of methoxyl protons. The conversion of **17** to **15** and **18** most probably occurs by the pathways shown in Scheme 4 (cf. ref. 24).

A third approach to **15** was undertaken in an entirely different fashion.[5] Irradiation of the dienone **19**, the precursor of **5** (8), with acetophenone as photosensitizer gave one major and two minor products (Scheme 5). The major product was identified by its spectra and further transformations (*vide infra*) as the di-π-methane rearrangement product **20**. Its ir spectrum showed a single band in the carbonyl-stretching region at 5.77 μm. Its ^1H

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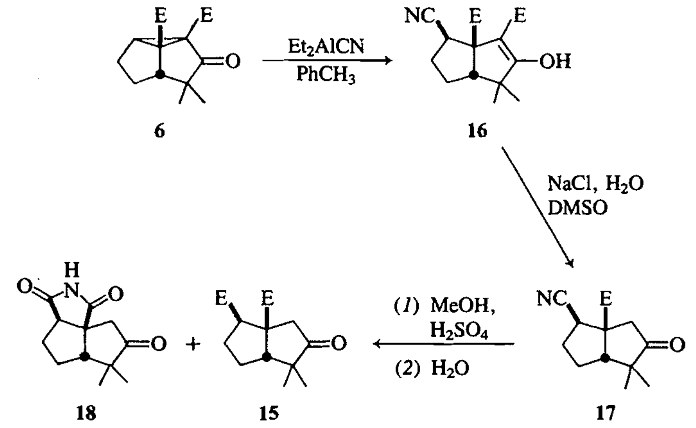
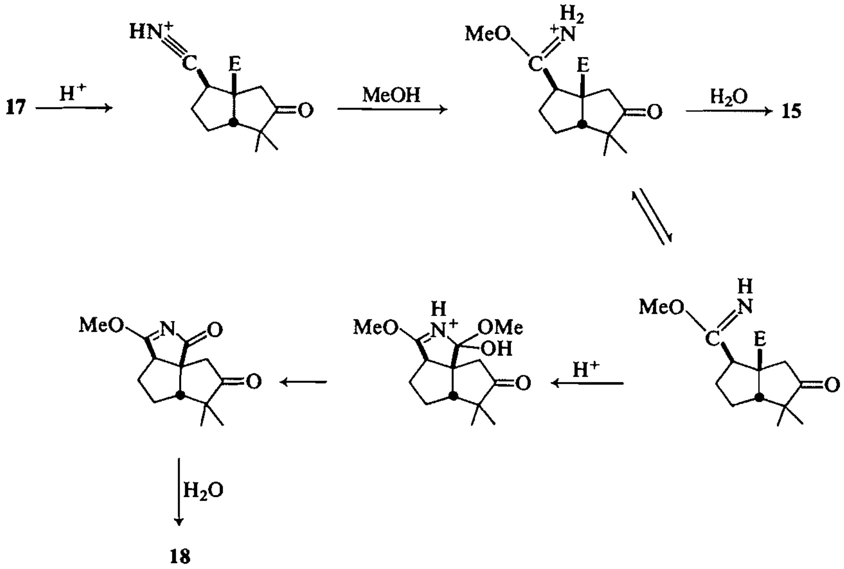
[5] We thank Miss Shirley Stiver for suggesting this route.

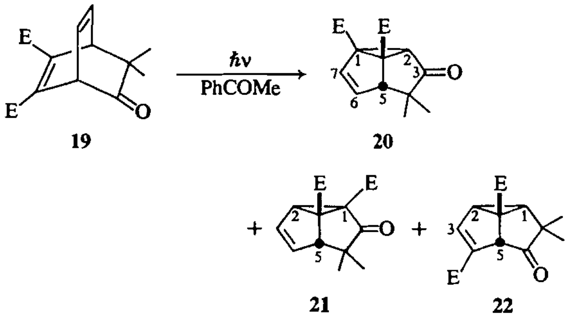


SCHEME 3 ($E = CO_2Me$)

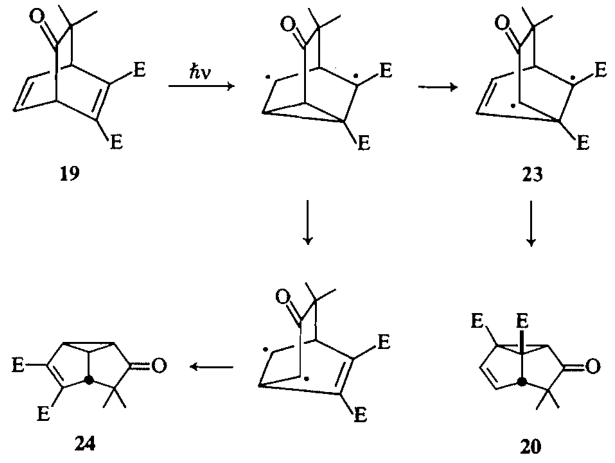


SCHEME 4 ($E = CO_2Me$)

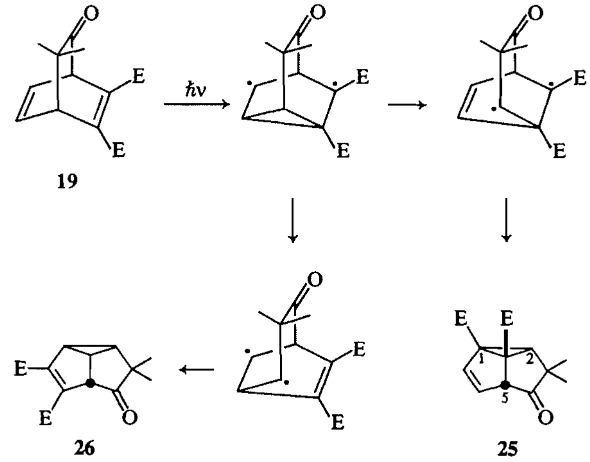
nmr spectrum (in deuteriochloroform) showed two two-proton multiplets at δ 3.5–3.7 and 5.7–6.0 ppm; the former is assigned to the C-2 and C-5 protons, and the latter to the olefinic protons. In benzene–deuteriochloroform the higher field multiplet was resolved into a one-proton singlet at δ 3.62 ppm, assigned to the C-2 proton, and a one-proton doublet at δ 3.38 ppm (J = 2.5 Hz), assigned to the C-5 proton; the lower field multiplet was resolved into a one-proton doublet at δ 5.74 ppm (J = 5.5 Hz), assigned to C-7 and a one-proton doublet of doublets at δ 5.51 ppm (J = 5.5, 2.5 Hz), assigned to C-6. The observed coupling constants are in excellent agreement with those observed for a C-3 methylene analogue of **20** (25). One of the minor products is considered to arise by an oxa-di-π-methane rearrangement in analogous fashion to the formation of **6** and to have structure **21**. Its ir and ^1H nmr spectra were similar to those of **20**, the latter spectrum (in deuteriochloroform) showing two two-proton multiplets at δ 3.4–3.7 ppm and



SCHEME 5 ($E = CO_2Me$)



SCHEME 6 (E = CO_2Me)



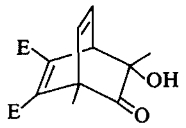
SCHEME 7 (E = CO_2Me)

5.6–5.95 ppm.[6] We shall return subsequently to the proposed structure **22** of the other minor product.

Compound **19** is capable of giving four different di-π-methane rearrangement products, **20** and **24**–**26** (Schemes 6 and 7), and two different oxa-di-π-methane rearrangement products, **21** and **28** (Schemes 8 and 9) (26).

The preference of bicyclo[2.2.2]octadienone derivatives to undergo di-π-methane rather than oxa-di-π-methane rearrangements has been observed previously, but there has been little discussion concerning its origin. The suggestion has been made that this is due to preemptive homoconjugation of the diene moiety, based on the observation that the $n \rightarrow \pi^*$ absorption band of **29** is lower in intensity than that of **30** (27). It may be noted that benzobicyclo[2.2.2]octadienone derivatives, in which the homoconjugate interaction between the aromatic π system and the olefinic double bond is expected to be reduced relative to that in bicyclo[2.2.2]octadienone derivatives without the benzene ring, undergo oxa-di-π-methane rearrangement on triplet-sensitized irradiation (28). The regioselectivity of both the di-π-methane rearrangement of **19** leading to **20** and its oxa-di-π-methane rearrangement leading to the minor product **21** may be interpreted in terms of the greater stabilization of diradicals **23** (Scheme 6) and **27** (Scheme 8) relative to the related diradicals that lead to other di-π-methane and oxa-di-π-methane rearrangement products, respectively. Similar directing influences have been proposed to account for the observed regioselectivity in di-π-methane rearrangements of 5,6-benzo-2-azabicyclo[2.2.2]-5,7-dien-3-one derivatives (29; cf. also ref. 25).

The spectra of the other minor product did not correspond with expectation for any of the other possible primary products **24**–**26** and **28**. Its ir spectrum showed bands at 5.81 (s) and 6.19 (w) μm suggestive of an α,β-unsaturated carbonyl group. Its ^1H nmr spectrum showed a one-proton doublet (J = 2.5 Hz) at δ 6.83 ppm: this proton is coupled with a proton that gives rise to a doublet of doublets at δ 2.99 ppm (J = 2.5, 7.5 Hz), which is also coupled with a proton giving rise to a doublet at δ 2.69 ppm (J = 7.5 Hz); in addition a one-proton singlet appeared at δ 4.29 ppm. On the basis of these data this product is considered to have structure **22**, with assignment of the proton signals referred to above to the C-3, C-2, C-1, and C-5 protons, respectively. This product may arise from a secondary photochemical reaction of the primary product **20** as shown in Scheme 10. A closely related thermal transformation has been reported (30).



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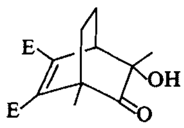

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We return now to the conversion of **20** to **15**. This was effected by the route shown in Scheme 11. Reduction with lithium in liquid ammonia and ether cleaved the C-1—C-2 bond to give **31**; the crude product was oxidized with sodium dichromate and sulfuric acid since some reduction of the ketonic group also occurred. The product was obtained as a single epimer at C-2, which is considered to be the

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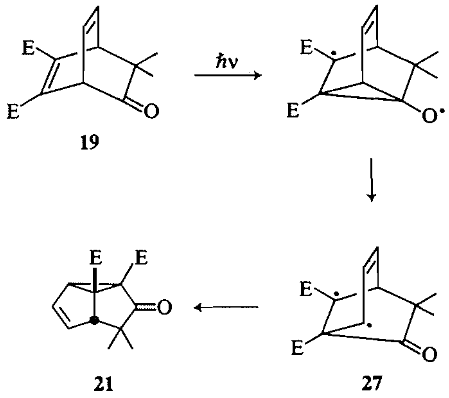
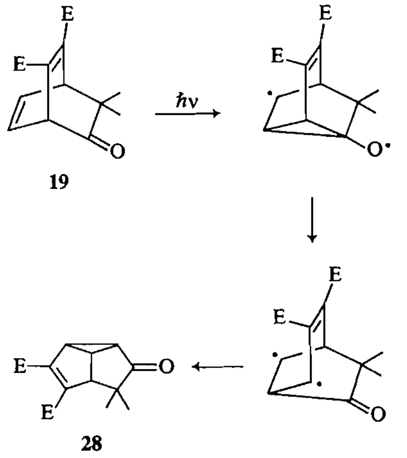
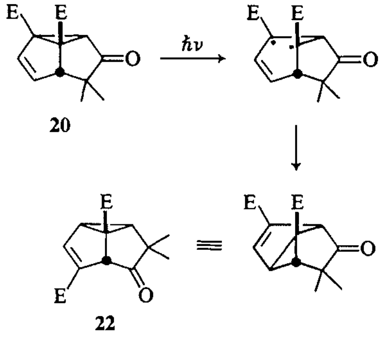
[6] This structure is preferred over structure **25** (*vide infra*), because the latter would be expected to give rise in its ^1H nmr spectrum to C-2 and C-5 proton signals with more widely separated chemical shifts, with the C-2 proton signal at higher field and the C-5 proton signal at lower field.



SCHEME 8 (E = CO_2Me)



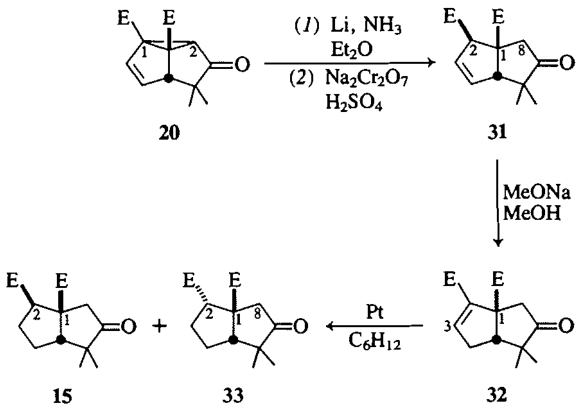
SCHEME 9 (E = CO_2Me)



SCHEME 10 (E = CO_2Me)

more stable *exo* epimer **31**. Its ir spectrum showed a carbonyl-stretching band at 5.78 μm and its ^{1}H nmr spectrum showed two one-proton doublets (J = 18.5 Hz) at δ 2.20 and 3.02 ppm, characteristic of the C-8 protons in this system, and a two-proton multiplet at δ 5.8 ppm arising from the olefinic protons. Treatment of **31** with methanolic sodium methoxide gave the isomeric α,β-unsaturated ester **32**, whose ir spectrum included a strong band at 5.83 μm and a weak band at 6.13 μm. Its ^{1}H nmr spectrum showed a one-proton triplet (J = 2 Hz) at δ 6.89 ppm, assigned to the C-3 proton. Catalytic hydrogenation of **32** over palladium/carbon in methanol at atmospheric pressure gave exclusively **15**, identical with the diester obtained by the routes in Schemes 2 and 3. Hydrogenation over platinum in cyclohexane gave mixtures of **15** and a new compound, assigned the C-2 epimeric structure **33**.[7] The reaction was exceedingly capricious and the product mixture had variable ratios of **33** and **15**, ranging up to 19:1. The ir and ^{1}H nmr spectra of the two epimers were very similar; a critical difference in the latter spectra was that in the spectrum of **33** the lower field doublet of the two one-proton doublets (J = 19 Hz) at δ 2.14 and 3.18 ppm arising from the C-8 protons exhibited a further small coupling ($J \sim 1$ Hz). This signal is assigned to the *exo* C-8 proton and the additional coupling is attributed to ^4J long range coupling with the proton at C-2. Examination of molecular models shows that the "W" relationship between the *exo* C-8 and C-2 protons required for such ^4J coupling (31) is possible only if the C-2 proton has the *exo* configuration, i.e., the ester group at C-2 has the *endo* configuration. Molecular models also show that delivery of hydrogen to **32** would be expected to occur from the less hindered *exo* face, leading to **33**. The exclusive formation of **15** in some cases and its formation in variable amounts in others may be due to epimerization of **33** by adventitious acid or base or by the catalyst itself (32).

We have thus attained our objective of functionalization of the carbon designed to become *exo* C-12 in the cedranoid sesquiterpenes by three different methods. The last method has provided in



SCHEME 11 (E = CO_2Me)

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[7] This product was not entirely freed of **15** and was obtained as a solid with a wide melting range.

addition a potential route to *endo* C-12 functionalized cedranoid sesquiterpenes, which also have been obtained from natural sources.

Experimental

Melting points were determined on a Fisher–Johns apparatus and are uncorrected. The ir spectra were taken in $CHCl_3$ solution and the ^1H and ^{13}C nmr spectra in $CDCl_3$ solution. Analytical thin layer chromatography was carried out on 0.25 mm silica gel Q6-F plates from Quantum Industries. Preparative thin layer chromatography was carried out on 20 × 20 cm plates coated with 0.5 mm, 1 mm, or 2 mm silica gel layers (Merck Kieselgel 60 PF_{254} containing gypsum). Medium pressure liquid chromatography was carried out on a Merck silica gel 60 prepacked column (Size B) operated at a pressure of ~5 psi. Solutions were dried over magnesium sulfate and concentrated on a Büchi "Rotovapor < R >" rotary evaporator under water aspirator pressure. Solvents used for work-ups and chromatography were either distilled or were of ACS Reagent Grade quality.

Attempted homoconjugate addition of an alkenyl group to dimethyl 6,6-dimethyl-7-oxotricyclo[3.2.1.0^{2,8}]octane-1,8-dicarboxylate (6)[8]

(i). With lithium divinylcuprate reagents

A solution of vinyllithium in tetrahydrofuran (THF) (1.56 *M*; 0.70 mL, 1.09 mmol) was added to a cold (−45°C), stirred slurry of cuprous iodide (109 mg, 0.57 mmol) in ether (4 mL) containing isopropyl sulfide (260 µl, 212 mg, 1.79 mmol) under argon (33). The mixture was warmed to −15°C to −20°C for 15 min, and then rapidly cooled to −75°C, producing a light grey-green solution containing some black solid. A solution of **6** (8) (99 mg, 0.37 mmol) in ether (1 mL) was added. The mixture was stirred at −75°C for 10 min and at 4°C overnight, and then 50% saturated aqueous NH_4Cl (10 mL) was added. The layers were separated, and the aqueous phase was extracted with ether (2 × 10 mL). The combined organic solutions were washed with saturated aqueous NH_4Cl (10 mL), dried, and concentrated to give a yellow oil (68 mg). No vinyl proton signals were apparent in the ^1H nmr spectrum of this material, which consisted mostly of unconsumed **6**. Attempted reaction in tetrahydrofuran produced the same result.

The following reagents (34) also failed to effect homoconjugate addition of a vinyl group to **6**: $LiCu(CH{=}CH_2)$ in ether or THF, $LiCu(CH{=}CH_2)_2$ in ether or THF/$(CH_3)_2S$, $LiCu(CH{=}CH_2)_2$ in ether/$(n\text{-}C_4H_9)_3P$, $LiCu(CH{=}CH_2)_2{\cdot}P(n\text{-}C_4H_9)_3$ in ether or THF/pentane, $LiCu[C{\equiv}CC(CH_3)_2OCH_3](CH{=}CH_2)$ in ether or THF, $LiCu[C{\equiv}CCH_2N(CH_3)_2](CH{=}CH_2)$ in triethylamine, $LiCu(CH_3)(CH{=}CH_2)$ in ether or THF, $CH_2{=}CHMgBr/CuI$ in THF, $(CH_2{=}CH)_4(CH_3)Cu_3Mg_2Br_2$ in THF.

(ii). With lithium diisobutylhex-1-enylmethylalanate

A solution of diisobutylaluminum hydride in toluene (25% by weight; 265 µL, 0.42 mmol) was added to a stirred solution of 1-hexyne (48 µL, 34 mg, 0.41 mmol) in toluene (5.0 mL) under nitrogen at room temperature. The resulting solution was warmed to 40–60°C for 45 min and then cooled to 0°C. A solution of methyllithium – lithium bromide complex in ether (1.33 *M*; 310 µL, 0.41 mmol) was added, producing a white gelatinous precipitate and a colorless solution. The mixture was stirred at 0°C for 20 min and was then allowed to warm to room temperature. A solution of **6** (100 mg, 0.38 mmol) in toluene (10 mL) was added, and the mixture was stirred at room temperature for 22 h. Ice (~15 g) was added, followed by aqueous 10% HCl (10 mL). The mixture was stirred for 1 h, the layers were separated, and the aqueous phase was extracted with ether (2 × 10 mL). The organic phases were combined, washed with saturated aqueous NaCl (10 mL), dried, and concentrated to give a yellow oil (97 mg), which was found to be **6** almost exclusively.

Reaction of 6 with titanium tetrachloride. Formation of dimethyl exo-*8-chloro-3-hydroxy-4,4-dimethyl-*cis-*bicyclo[3.3.0]oct-2-ene-1,2-dicarboxylate (9)*[8]

Titanium tetrachloride (100 µL, 0.91 mmol) was added to a stirred solution of **6** (202 mg, 0.76 mmol) in dichloromethane (4.0 mL) under nitrogen. The solution was stirred for 30 min, remaining homogeneous but gradually turning deep red. Saturated aqueous NH_4Cl (10 mL) was added, and the resulting mixture was extracted with ether (2 × 10 mL). The combined ethereal extracts were dried and concentrated to give **9** (212 mg, 0.70 mmol, 92%) as a pale yellow powder. Crystallization from pentanes gave large, white crystals, mp 102–104°C; ir λ_{max}: 5.80, 6.06, 6.21 µm; ^1H nmr δ: 1.08 (s, 3H), 1.12 (s, 3H), 1.2–2.3 (m, 4H), 2.7–3.1 (m, 1H), 3.65 (s, 3H), 3.75 (s, 3H), 4.2–4.5 (m, 1H), 11.93 (s, 1H); ms *m/e*: 304 (3), 303 (*M* + 1; 3), 302 (8). *Anal.* calcd. for $C_{14}H_{19}O_5Cl$: C 55.54, H 6.33, Cl 11.71; found: C 55.70, H 6.44, Cl 11.72.

Treatment of **6** with allyltrimethylsilane and titanium tetrachloride in dichloromethane (14) gave **9** in good yield as the only product.

*Reaction of 6 with phenylethynylmagnesium bromide. Formation of 10 and 11*a *or 11*b[8]

A solution of ethylmagnesium bromide in ether (1.75 *M*; 240 µL, 0.42 mmol) was added to a stirred solution of phenylacetylene (46 µL, 0.42 mmol) in ether (2.0 mL) under nitrogen. The clear homogeneous solution was stirred at room temperature for 30 min and then cooled to 2°C. A solution of **6** (100 mg, 0.38 mmol) in ether (1.0 mL) was added, producing a large amount of white precipitate. The mixture was stirred for 1 h at 2°C, after which aqueous 10% HCl (10 mL) was added. The resulting mixture was shaken with ether (20 mL), and the ethereal layer was washed with saturated aqueous NaCl (10 mL), dried, and concentrated to give a yellow oil (122 mg). The ^1H nmr spectrum of this oil showed it to contain phenylacetylene and a ~1:1 mixture of **10** and **11***a* or **11***b* (*vide infra*).

Reaction of 6 with hydrogen bromide. Formation of dimethyl exo-*8-bromo-3-hydroxy-4,4-dimethyl-*cis-*bicyclo[3.3.0]-oct-2-ene-1,2-dicarboxylate (10)*

Anhydrous hydrogen bromide was bubbled slowly into a cold (0°C), stirred solution of **6** (419 mg, 1.58 mmol) in dichloromethane (20 mL). After 2.5 h analytical thin layer chromatography indicated that no **6** remained. The solution was poured onto ice (~40 g). When all the ice had melted the layers were separated, and the aqueous phase was extracted with dichloromethane (2 × 10 mL). The combined organic solutions were washed with water (10 mL), saturated aqueous $NaHCO_3$ (10 mL), and saturated aqueous NaCl (10 mL). They were dried and concentrated to give a white powder (508 mg). Crystallization from pentanes – ethyl acetate (2:1 v/v) gave **10** (397 mg, 1.14 mmol, 72%) as white crystals, mp 112.5–115.5°C; ir λ_{max}: 5.80, 6.06, 6.19 µm; ^1H nmr δ: 1.12 (s, 3H), 1.16 (s, 3H), 1.3–2.5 (m, 4H), 2.75–3.15 (m, 1H), 3.74 (s, 3H), 3.83 (s, 3H), 4.25–4.60 (m, 1H), 11.02 (s, 1H); ^{13}C nmr δ: 19.9 (q), 27.4 (t), 27.9 (q), 38.1 (t), 44.3 (s), 51.3 (q), 52.0 (q), 55.1 (d), 56.6 (d), 65.3 (s), 99.4 (s), 170.8 (s), 173.7 (s), 182.4 (s); ms *m/e*: 348 (1), 346 (1). *Anal.* calcd. for $C_{14}H_{19}O_5Br$: C 48.43, H 5.52, Br 23.01; found: C 48.41, H 5.52, Br 23.01.

*Reaction of 6 with bis(phenylethynyl)magnesium. Formation of 11*a *or 11*b[8]

Dioxane (0.8 mL, 9.38 mmol) was added to a solution of phenylethynylmagnesium bromide prepared by the reaction of a

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[8] These experiments were conducted under rigorously anhydrous conditions under a positive pressure of argon or nitrogen.

solution of ethylmagnesium bromide in ether (0.81 *M*; 11.2 mL, 9.07 mmol) with a solution of phenylacetylene (1.0 mL, 9.11 mmol) in ether (20 mL) under nitrogen. After 30 min the mixture was filtered under nitrogen through a sintered glass frit. The filtrate was titrated as 0.09 *M* in bis(phenylethynyl)magnesium.

A solution of **6** (50 mg, 0.19 mmol) was added with stirring to this solution (2.5 mL, 0.23 mmol), cooled to 4°C under nitrogen. After 4 h aqueous 10% HCl (10 mL) was added, and the resulting mixture was washed with ether (20 mL). The organic layer was washed with saturated aqueous NaCl (10 mL), dried, and concentrated to give a yellow oil (65 mg). This contained only a small amount of phenylacetylene, little or no **6**, and a single major product tentatively identified as **11*a*** or **11*b***; ir λ_{max}: 3.07 (m), 5.79 µm; ^{1}H nmr δ: 0.94 (s, 3H), 1.39 (s, 3H), 3.67 (s, 3H), 6.85–7.64 (m, > 10H).

*Methyl 4,4-dimethyl-3-oxo-*exo*-8-phenyl-*cis*-bicyclo[3.3.0]octane-1-carboxylate (13)*

A solution of phenyllithium in ether–benzene (30:70 v/v) (1.9 *M*; 12.0 mL, 22.8 mmol) was added over ~20 min to a cold (5°C), stirred slurry of cuprous iodide (2.18 g, 11.4 mmol) in ether (20 mL) under argon.[8] Stirring for 1 h at 0–5°C gave a homogeneous dark green solution of lithium diphenylcuprate. A solution of **6** (1.00 g, 3.76 mmol) in ether (15 mL) was added and stirring was continued for 4 h. Aqueous 10% HCl (25 mL) was added to the cold solution, and the resulting mixture was stirred for a further 30 min and then suction-filtered. The layers of the filtrate were separated and the aqueous phase was extracted with ether (3 × 10 mL). The organic phases were combined and washed with saturated aqueous $NaHCO_3$ (10 mL), 1 *M* aqueous $Na_2S_2O_3$ (10 mL), and saturated aqueous NH_4Cl (10 mL) made slightly basic by the addition of concentrated aqueous NH_3. The organic solution was dried and concentrated to give a yellow oil (1.76 g). The ^{1}H nmr spectrum of this material included two singlets at δ 11.2 and 11.4 ppm, in a ratio of ~2:1, which are assigned to the enolic protons of **12*a*** and **12*b***, respectively. This spectrum also showed a singlet at δ 3.18 ppm, assigned to the C-1 carbomethoxy groups of both **12*a*** and **12*b***, a singlet at δ 3.78 ppm, assigned to the C-2 carbomethoxy group of **12*a***, and a quartet (*J* = 7 Hz) at δ 4.25 ppm, assigned to the carboethoxy group of **12*b***. The ir spectrum of this crude product showed strong bands at 5.83, 6.09, and 6.25 µm.

This material was stirred and heated (96°C) in dimethyl sulfoxide (8 mL) containing water (500 µL, ~27.8 mmol) and sodium chloride (413 mg, 7.1 mmol) for 6 h. The mixture was allowed to cool to room temperature and was then diluted with water (20 mL). The resulting solution was extracted with ether (4 × 10 mL). The ethereal extracts were combined, washed with water (5 × 10 mL), dried, and concentrated to leave a yellow solid (1.22 g). Crystallization from ether gave **13** (521 mg); medium pressure liquid chromatography of the mother liquors with hexanes – ethyl acetate (7:1 v/v) as eluent gave a further quantity of **13** (175 mg; total: 696 mg, 2.43 mmol, 65% from **6**). Further recrystallizations from 10% ethyl acetate – pentanes gave **13**, mp 125–127°C; ir λ_{max}: 5.80 µm; ^{1}H nmr δ: 1.02 (s, 3H), 1.08 (s, 3H), 1.2–2.5 (m, 5H), 2.46 (d, *J* = 19 Hz, 1H), 2.8–3.2 (m, 1H), 3.21 (s, 3H), 3.60 (d, *J* = 19 Hz, 1H), 7.21 (s, 5H); ^{13}C nmr δ: 18.9 (q), 27.3 (q), 29.7 (t), 31.3 (t), 46.4 (t), 49.0 (s), 51.7 (q), 57.2 (s), 57.8 (d), 59.9 (d), 127.0 (d), 127.6 (d), 128.1 (d), 139.6 (s), 175.8 (s), 219.9 (s); ms *m/e*: 286 (62). *Anal.* calcd. for $C_{18}H_{22}O_3$: C 75.50, H 7.74; found: C 75.27, H 7.77.

*Dimethyl 6,6-dimethyl-7-oxo-*cis*-bicyclo[3.3.0]octane-1,*exo*-2-dicarboxylate (15)*

Ozonized oxygen was bubbled through a solution of **13** (207 mg, 0.72 mmol) in glacial acetic acid (21.5 mL) and water (3.5 mL) for 3 h at room temperature. The solution eventually acquired a very faint blue color. It was allowed to stand at room temperature for 2 h, treated with 30% hydrogen peroxide (0.5 mL), and then allowed to stand at room temperature overnight. The solvents were removed by distillation (0.5 Torr) at room temperature, and the residue was dissolved in a mixture of ether (20 mL) and ethyl acetate (10 mL). The solution was extracted with saturated aqueous $NaHCO_3$ (3 × 10 mL). The basic extracts were combined, and made strongly acidic by the addition of concentrated H_2SO_4, and extracted with ethyl acetate (3 × 10 mL). The latter extracts were combined, washed with saturated aqueous NaCl, dried, and concentrated to give a colorless oil (130 mg). Molecular distillation (100°C/0.1 Torr) gave **14** (85 mg, 0.33 mol, ~46%) as a colorless oil containing trace impurities; ir λ_{max}: 2.7–4.0 (br), 5.73 µm; ^{1}H nmr δ: 1.02 (s, 3H), 1.08 (s, 3H), 1.6–3.0 (m, 6H), 2.35 (d, *J* = 19.5 Hz, 1H), 3.59 (d, *J* = 19.5 Hz, 1H), 3.70 (s, 3H), 10.80 (br s, 1H); ^{13}C nmr δ: 19.6 (q), 27.3 (q), 28.9 (t), 29.2 (t), 46.1 (t), 48.6 (s), 52.5 (q), 54.2 (s), 57.5 (d), 58.5 (d), 176.0 (s), 178.5 (s), 220.2 (s).

Ethereal diazomethane was added to a cold (0°C) stirred solution of crude **14** (72 mg, ~0.28 mmol) in methanol (5 mL) until the yellow color of the reagent persisted. The solution was allowed to stand at room temperature until all the diazomethane had evaporated. Concentration of this solution gave **15** (76 mg, ~0.28 mmol, ~100%). Preparative thin layer chromatography with elution with 2:1 cyclohexane – ethyl acetate (R_f 0.46), followed by sublimation (70°C/0.05 Torr), and crystallization from ethyl acetate – pentanes gave **15** as a white solid, mp 63–65°C; ir λ_{max}: 5.78 µm; ^{1}H nmr δ: 1.04 (s, 3H), 1.09 (s, 3H), 1.3–2.4 (m, 4H), 2.34 (d, *J* = 19 Hz, 1H), 2.4–3.0 (m, 2H), 3.62 (d, *J* = 19 Hz, 1H), 3.67 (s, 3H), 3.71 (s, 3H); ^{13}C nmr δ: 19.6 (q), 27.3 (q), 29.0 (t), 29.4 (t), 46.2 (t), 48.5 (s), 51.8 (s), 52.4 (q), 54.1 (s), 57.7 (d), 58.4 (d), 172.7 (s), 176.0 (s), 219.6 (s); ms *m/e*: 268 (13). *Anal.* calcd. for $C_{14}H_{20}O_5$: C 62.67, H 7.51; found: C 62.85, H 7.59.

*Dimethyl *exo*-8-cyano-3-hydroxy-4,4-dimethyl-*cis*-bicyclo[3.3.0]oct-2-ene-1,2-dicarboxylate (16)*[8]

A solution of diethylaluminum cyanide in toluene (1.57 *M*; 4.8 mL, 7.54 mmol) was added by means of a syringe equipped with a wide bore needle to **6** (995 mg, 3.74 mmol) in a round-bottomed flask equipped with a magnetic stirring bar, septum, and nitrogen inlet. The resulting solution was stirred at room temperature for exactly 2 h. It was then poured cautiously into a mixture of aqueous 10% HCl (50 mL) and ice (50 g). The resulting mixture was stirred for 1 h and extracted with ether (3 × 20 mL). The combined organic extracts were washed with saturated aqueous NaCl (10 mL), dried, and concentrated to give a white powder. Crystallization from ethyl acetate gave **16** (609 mg, 2.08 mmol, 56%). Further recrystallization gave white crystals, mp 135–137.5°C; ir λ_{max}: 4.46 (w), 6.01, 6.17 µm; ^{1}H nmr δ: 1.12 (s, 3H), 1.17 (s, 3H), 1.30–3.05 (m, 6H), 3.79 (s, 3H), 3.83 (s, 3H), 10.52 (s, 1H); ^{13}C nmr δ: 19.7 (q), 28.2 (q), 29.1 (t), 32.6 (t), 40.1 (d), 44.4 (s), 51.4 (q), 52.5 (q), 58.6 (d), 61.8 (s), 100.2 (s), 120.0 (s), 169.7 (s), 173.9 (s), 181.0 (s); ms *m/e*: 294 (*M* + 1; 7), 293 (9). *Anal.* calcd. for $C_{15}H_{19}O_5N$: C 61.42, H 6.53, N 4.78; found: C 61.32, H 6.49, N 4.69.

*Methyl *exo*-8-cyano-4,4-dimethyl-3-oxo-*cis*-bicyclo[3.3.0]octane-1-carboxylate (17)*

A mixture of **16** (303 mg, 1.03 mmol) and NaCl (86 mg, 1.47 mmol) in dimethyl sulfoxide containing water (175 µL, 9.72 mmol) was stirred and heated (94°C) under nitrogen for 5 h. After cooling, the mixture was extracted with ether (30 mL), and the extract was washed with water (4 × 10 mL). The ethereal solution was dried and concentrated. The residual oil was molecularly distilled (107°C/0.025 Torr) to give **17** (166 mg, 0.71 mmol, 69%) as a colorless, viscous oil; ir λ_{max}: 4.46 (w), 5.85 µm; ^{1}H nmr δ: 1.06 (s, 6H), 1.25–2.35 (m, 4H), 2.25 (d, *J* = 19.5 Hz, 1H), 2.55–3.1 (m, 2H), 3.62 (d, *J* = 19.5 Hz, 1H), 3.91 (s, 3H);

^{13}C nmr δ; 19.3 (q), 26.9 (q), 29.7 (t), 32.1 (t), 42.0 (d), 45.0 (t), 48.6 (s), 53.2 (q), 55.5 (s), 57.6 (d), 119.1 (s), 174.2 (s), 217.6 (s); ms *m/e*: 235 (16). *Anal.* calcd. for $C_{13}H_{17}O_3N$: C 66.36, H 7.28, N 5.95; found: C 66.18, H 7.19, N 5.97.

*Reaction of **17** with methanol and concentrated sulfuric acid. Formation of **15** and **18***

A mixture of **17** (197 mg, 0.84 mmol), methanol (16 mL), and concentrated H_2SO_4 (5.4 mL) was stirred and heated (90°C) for 26 h under nitrogen. After the mixture had cooled to room temperature, water (20 mL) was added and the methanol was removed by distillation at reduced pressure (15 Torr). The residue was extracted with ether (5 × 10 mL). The combined ethereal extracts were washed with saturated aqueous $NaHCO_3$ (10 mL) and saturated aqueous NaCl (10 mL), dried, and concentrated to give a colorless oil (136 mg). Repeated extraction of the aqueous phases with ether gave an additional quantity of crude product (31 mg). Crystallization from a mixture of toluene and pentanes gave crude **18** (19 mg, 0.09 mmol, 11%). Further crystallization gave pure **18**, mp 153.5–154.5°C; ir λ_{max}: 3.02 (m), 5.62 (m), 5.79, 7.46 (m), 8.61 (m) μm; ^{1}H nmr δ: 1.06 (s, 3H), 1.29 (s, 3H), 1.6–2.3 (m, 4H), 2.38 (d, J = 19 Hz, 1H), 2.5–3.1 (m, 2H), 3.22 (d, J = 19 Hz, 1H), 8.69 (br s, 1H); ms *m/e*: 221 (45). *Mol. Wt.* calcd. for $C_{12}H_{15}O_3N$: 221.1052; found (ms): 221.1048.

Concentration of the original mother liquor followed by molecular distillation (90°C/0.05 Torr) gave **15** (92 mg, 0.34 mmol, 41%), mp 63–65°C, whose spectra were identical with those of the sample of **15** prepared from **13** (*vide supra*).

*Sensitized photolysis of **19**. Formation of dimethyl 4,4-dimethyl-3-oxotricyclo[3.2.1.0^{2,8}]oct-6-ene-1,8-dicarboxylate (**20**), **21**, and **22***

A solution of **19** (1.10 g, 4.17 mmol) in acetophenone (freshly distilled; 110 mL) was degassed with nitrogen for 3 h. The solution was then irradiated in a Rayonet–Srinivasan–Griffin Photochemical Reactor equipped with eleven low pressure 350 nm RPR lamps for 34 h. The solvent was removed by distillation at 0.25 Torr. The oily residue was chromatographed (medium pressure liquid chromatography with hexanes – ethyl acetate (5:1 v/v) as eluent; fraction size ~ 10 mL) to give:

fraction	24	**21** (20 mg, 0.08 mmol, 2%)
	25	**20** and **21**
	26–30	**20** (540 mg, 2.05 mmol, 49%)
	31–33	**20** and **22**
	34–37	**22** (52 mg, 0.20 mmol, 5%)

Samples of compounds **20–22** for analysis were recrystallized from ethyl acetate – hexanes.

Compound **20**, mp 84–85°C; ir λ_{max}: 5.77 μm; ^{1}H nmr δ: 0.95 (s, 3H), 1.27 (s, 3H), 3.5–3.7 (m, 2H), 3.80 (s, 6H), 5.7–6.0 (m, 2H); δ ($C_6H_6/CDCl_3$): 0.78 (s, 3H), 1.12 (s, 3H), 3.38 (d, J = 2.5 Hz, 1H), 3.48 and 3.50 (two s, 6H), 3.62 (s, 1H), 5.51 (dd, J = 5.5, 2.5 Hz, 1H), 5.74 (d, J = 5.5 Hz, 1H); ^{13}C nmr δ: 17.9 (q), 25.4 (q), 47.7 (d), 52.6 (q), 52.8 (q), 53.7 (s), 56.4 (s), 58.0 (d), 62.6 (s), 127.4 (d), 136.5 (d), 167.1 (s), 168.3 (s), 209.0 (s); ms *m/e*: 264 (5). *Anal.* calcd. for $C_{14}H_{16}O_5$: C 63.63, H 6.10; found: C 63.50, H 6.25.

Compound **21**, mp 71–72.5°C; ir λ_{max}: 5.76 μm; ^{1}H nmr δ: 0.97 (s, 3H), 1.35 (s, 3H), 3.4–3.7 (m, 2H), 3.73 (s, 3H), 3.76 (s, 3H), 5.6–5.95 (m, 2H); ^{13}C nmr δ: 17.7 (q), 24.8 (q), 46.5 (d), 52.5 (q), 52.9 (q), 56.0 (s), 56.3 (d), 56.5 (s), 64.4 (s), 127.0 (d), 136.7 (d), 165.7 (s), 169.0 (s), 206.1 (s); ms *m/e*: 264 (7). *Anal.* calcd. for $C_{14}H_{16}O_5$: C 63.63, H 6.10; found: C 63.49, H 6.13.

Compound **22**, mp 88.5–89.5°C; ir λ_{max}: 5.75, 5.81, 6.19 (w) μm; ^{1}H nmr δ: 1.21 (s, 3H), 1.23 (s, 3H), 2.69 (d, J = 7.5 Hz, 1H), 2.99 (dd, J = 7.5, 2.5 Hz, 1H), 3.74 (s, 3H), 3.76 (s, 3H), 4.29 (s, 1H), 6.83 (d, J = 2.5 Hz, 1H); ^{13}C nmr δ: 25.8 (q), 29.2 (q), 43.7 (d), 46.1 (d), 48.4 (s), 50.1 (s), 51.8 (q), 52.1 (q), 57.4 (d), 134.0 (s), 141.7 (d), 161.9 (s), 170.8 (s), 210.0 (s); ms *m/e*: 264 (1). *Anal.* calcd. for $C_{14}H_{16}O_5$: C 63.63, H 6.10; found: C 63.57, H 6.13.

*Dimethyl 6,6-dimethyl-7-oxo-*cis*-bicyclo[3.3.0]oct-3-ene-1,*exo*-2-dicarboxylate (**31**)*[8]

Lithium wire (37 mg, 5.33 mmol) was added to a stirred solution of **20** (282 mg, 1.07 mmol) in ether (5 mL) and liquid ammonia (10 mL) under nitrogen. After ~40 min, all the lithium appeared to have reacted, and after a further 20 min, solid ammonium chloride was added. The ammonia was allowed to evaporate at room temperature, after which water (10 mL) was added. The phases were separated and the aqueous layer was extracted with ether (3 × 10 mL). The combined ethereal solutions were washed with saturated aqueous NaCl, dried, and concentrated to leave a colorless oil (217 mg). This was dissolved in benzene (5 mL), and the solution was stirred for 6 h with 10 mL of a solution of sodium dichromate dihydrate (1.2 g, 4.03 mmol) in acetic acid (5 mL), concentrated H_2SO_4 (6 mL), and water (19 mL). The phases were separated and the aqueous phase was extracted with ether (3 × 10 mL). The combined organic solutions were washed with water (10 mL), saturated aqueous $NaHCO_3$ (2 × 10 mL), and saturated aqueous NaCl (10 mL), dried, and concentrated to give **31** (92 mg, 0.35 mmol, 33%) as a colorless oil, which crystallized on standing. Recrystallization from ethyl acetate – hexanes gave white crystals, mp 72–73°C; ir λ_{max}: 5.78 μm; ^{1}H nmr δ: 1.06 (s, 3H), 1.09 (s, 3H), 2.20 (d, J = 18.5 Hz, 1H), 3.02 (d, J = 18.5 Hz, 1H), 3.3–3.5 (m, 1H), 3.69 (s, 3H), 3.81 (s, 3H), 4.3–4.5 (m, 1H), 5.6–6.0 (m, 2H); ^{13}C nmr δ: 22.1 (q), 26.3 (q), 41.5 (t), 47.9 (s), 52.0 (q), 52.9 (q), 55.2 (s), 58.4 (d), 65.2 (d), 128.4 (d), 131.4 (d), 171.6 (s), 175.7 (s), 218.7 (s); ms *m/e*: 266 (5). *Anal.* calcd. for $C_{14}H_{18}O_5$: C 63.15, H 6.81; found: C 62.96, H 6.85.

*Dimethyl 6,6-dimethyl-7-oxo-*cis*-bicyclo[3.3.0]oct-2-ene-1,2-dicarboxylate (**32**)*[8]

Compound **31** (68 mg, 0.26 mmol) ws stirred at room temperature under nitrogen for 1 h in a solution prepared by the reaction of sodium (15 mg, 0.65 mg atom) with methanol (2 mL). The resulting solution was poured into water (10 mL), and the mixture was extracted with ether (3 × 10 mL). The ethereal extracts were combined, washed with saturated aqueous NaCl (10 mL), dried, and concentrated to give **32** (56 mg, 0.21 mmol, 81%) as a colorless oil, which crystallized on standing. Purification by preparative thin layer chromatography with elution with cyclohexane – ethyl acetate (2:1 v/v) gave **32** (R_f 0.41), which crystallized from ethyl acetate – pentanes (~ 1:10 v/v) to give white needles, mp 84–85°C; ir λ_{max}: 5.78, 5.83, 6.13 (w) μm; ^{1}H nmr δ: 1.06 (s, 3H), 1.11 (s, 3H), 2.39 (d, J = 20 Hz, 1H), 2.4–3.2 (m, 2H), 3.56 (d, J = 20 Hz, 1H), 3.77 (s, 3H), 6.89 (t, J = 2 Hz, 1H); ^{13}C nmr δ: 20.6 (q), 26.6 (q), 34.5 (t), 42.9 (t), 48.8 (s), 51.8 (q), 52.9 (q), 57.0 (d), 58.1 (s), 138.8 (s), 145.2 (d), 163.9 (s), 174.5 (s), 219.3 (s); ms *m/e*: 266 (6). *Anal.* calcd. for $C_{14}H_{18}O_5$: C 63.14, H 6.81; found: C 62.86, H 6.83.

*Catalytic hydrogenation of **32**. Formation of dimethyl 6,6-dimethyl-7-oxo-*cis*-bicyclo[3.3.0]octane-1-*endo*-2-dicarboxylate (**33**) and **15***

Compound **32** (17 mg, 0.06 mmol) was hydrogenated at atmospheric pressure over platinum (22 mg) in cyclohexane (3 mL) for 3 h at room temperature. The catalyst was filtered off and the filtrate was concentrated to give a colorless oil (9 mg) which solidified on standing. Sublimation (< 90°C/0.1 Torr) gave **33** (8 mg, 0.03 mmol, 50%) as a white solid, which was crystallized from pentanes – ethyl acetate;[7] ir λ_{max}: 5.78 μm; ^{1}H nmr δ: 1.03 (s, 3H), 1.06 (s, 3H), 1.5–2.2 (m, 4H), 2.14 (d, J = 19 Hz, 1H), 2.4–3.0 (m, 2H), 3.18 (dd, J = 19, ~ 1 Hz, 1H), 3.69 (s, 3H), 3.82 (s, 3H); ms *m/e*: 268 (16).

Similar hydrogenation of **32** (12 mg) over 10% palladium/carbon (5.5 mg) in methanol (4 mL) gave a product (11 mg) whose ^{1}H nmr spectrum showed it to be **15**; the presence of **33** could not be detected.

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