Aust. J. Chem., 1984, **37**, 2305–21

The Reactivity of 3-Ethenyl-4-methylcyclohex-2-en-1-one and Related Compounds Towards Some Carbanionic Nucleophiles

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Abstract

The reaction of 3-ethenyl-4-methylcyclohex-2-en-1-one (4) with 2-methylcyclopentane-1,3-dione in refluxing toluene containing pyridine gave 6% of 9bξ-hydroxy-3a,6-dimethyl-3a,4,5,6,7,9b-hexahydro-1*H*-benz[*e*]indene-3,9(2*H*,8*H*)-dione (10). When the same reactants were heated at 100–110° (sealed tube) in benzene containing t-butyl alcohol and diethylamine the main product (61%) was 5′,6-dimethylspiro[bicyclo[3.2.1]octane-1,2′-cyclohexane]-3,6′,8′-trione (11); the yield of (11) was 72% when the reaction was carried out in the presence of silica gel. Attempts to effect a similar reaction of the dienone (4) with methyl 1β-t-butoxy-7aβ-methyl-5-oxo-1,2,3,3aα,4β,6,7,7a-octahydroindene-4-carboxylate (21a) gave no conjugate Michael addition product, but (21a) underwent aminolysis to the corresponding diethylamide (21b). Attempts to alkylate the t-butoxy β-keto ester (21a) under various conditions with 7-acetyloxy-7-ethenyl-8ξ-methyl-1,4-dioxaspiro[4,5]decane (41) failed. Similarly, attempts to effect alkylation of the anion of the t-butoxy keto ester (21a) with 7-ethenyl-8-methyl-1,4-dioxaspiro[4,5]dec-6-ene (43) under Lewis acid catalysis were also unsuccessful.

Introduction

We recently described the synthesis of 3-ethenyl-4-methylcyclohex-2-en-1-one (4) from 4-methylanisole,[1] or less efficiently, from 7a-methyl-2,3,7,7a-tetrahydro-1*H*-indene-1,5(6*H*)-dione via the diene acetal (44).[2] As pointed out previously,[1] the conjugated dienone (4) is a possible precursor of rings A and B in the synthesis of 10-methyl steroids if it acts as a Michael acceptor in the conjugate addition of an anionic C/D synthon. In this paper we describe conjugate Michael addition reactions of the dienone (4) with the anion from 2-methylcyclopentane-1,3-dione (5); attempts to effect similar reactions with bicyclic C/D synthons failed.

The preparation and some reactions of 1-acetyloxy-1-ethenyl-5,5-ethylenedioxy-2-methylcyclohexane (41), and of the conjugated diene acetal (43) are also described.

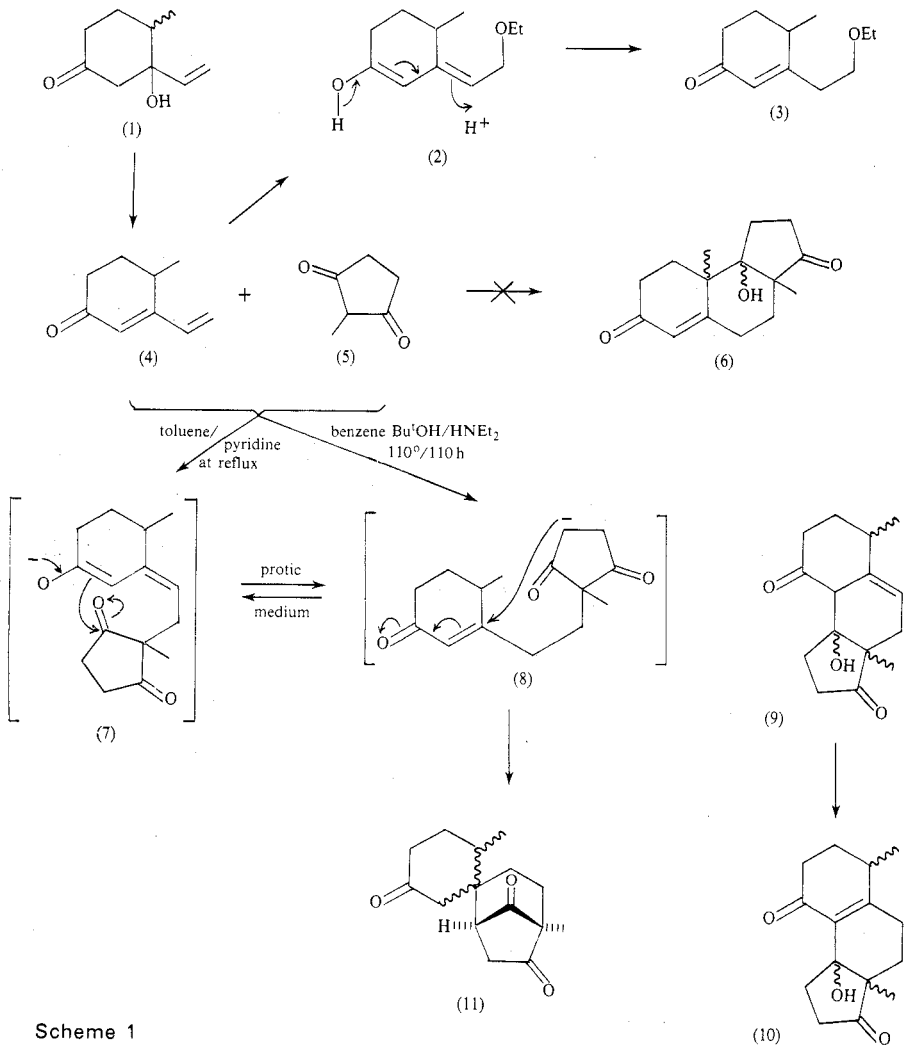
Results and Discussion

The last step in our synthesis of the conjugated dienone (4)[1] from 4-methylanisole has been improved. This originally involved treatment of the hydroxy vinyl ketone (1)

[1] Burge, G. L., Collins, D. J., and Reitze, J. D., *Aust. J. Chem.*, 1982, **35**, 1913.
[2] Brown, R. F. C., Burge, G. L., and Collins, D. J., *Aust. J. Chem.*, 1984, **37**, 2295.

0004-9425/84/112305$02.00

(Scheme 1) with 1 M sulfuric acid in ethanol; the ethoxy enone (3) was also formed, and was the major product when 8 M sulfuric acid was used. The pure dienone (4) was obtained easily (in 68% yield after flash chromatography) by treatment of (1) with 0·1 M sodium hydrogen carbonate in methanol.



Scheme 1

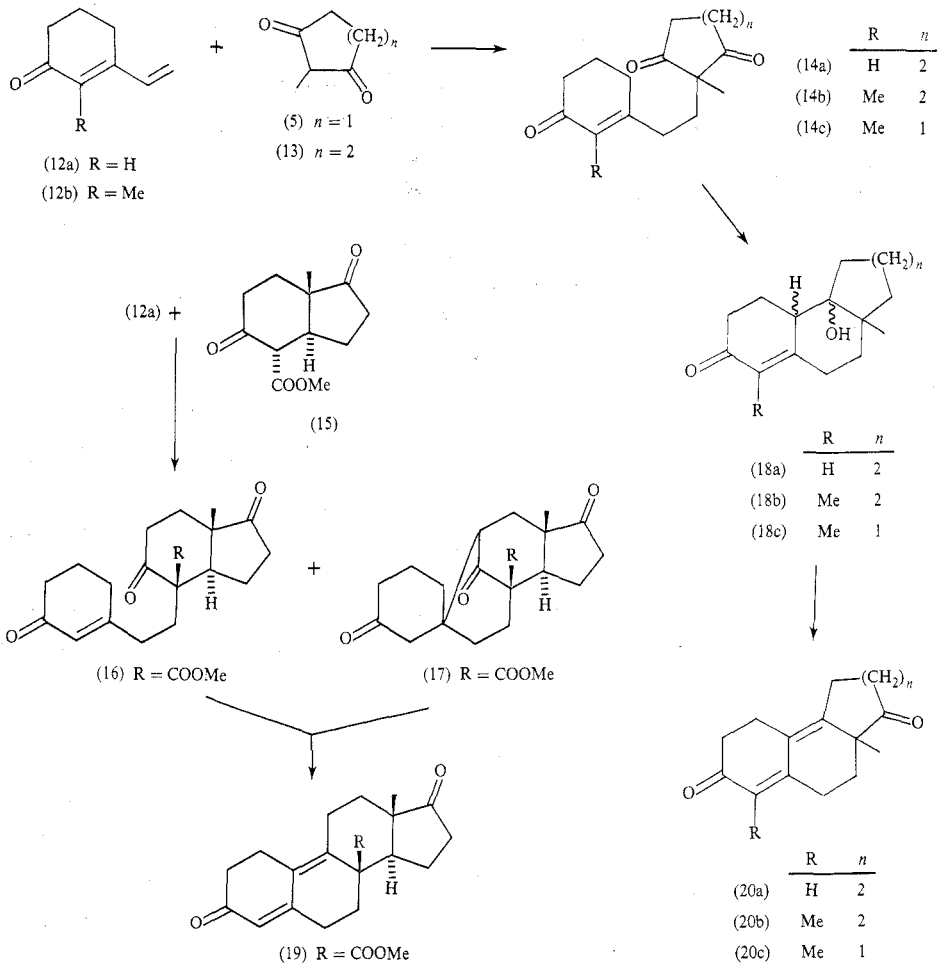
When a mixture of the dienone (4) and 2-methylcyclopentane-1,3-dione (5) in toluene containing pyridine and a trace of hydroquinone was heated under reflux for 90 h a small amount (6%) of the tricyclic hydroxy diketone (10) was isolated. This showed u.v. absorption at 244 nm (ε 8500) and i.r. absorption at 3420, 1730, 1660 and 1600 cm^{-1}. The ^1H n.m.r. spectrum showed one methyl group as a doublet (δ 1·21, J 7·0 Hz) and another as a singlet (δ 1·07), and there was no vinylic proton. These data exclude structure (6) and are consistent with structure (10) which can arise by attack of the initial enolate anion in intermediate (7) on one of the

carbonyl groups on the five-membered ring to give initially compound (9); base-catalysed isomerization would then give the α,β-unsaturated enone system in (10). The mass spectrum showed no parent molecular ion, but there was a low intensity peak at *m/z* 230 due to loss of the elements of water, a fragmentation to be expected for the allylic tertiary carbinol system of (10). Although it showed only two methyl resonances in the ^{1}H n.m.r. spectrum, compound (10) appears to be a mixture of two of the four possible diastereoisomers since there were two types of exchangeable hydroxyl protons at δ 4·5 and 4·6; the upfield signal exchanged almost immediately with deuterium oxide at room temperature but the other had undergone only 30% exchange after 2 h. When a mixture of the dienone (4) and 2-methylcyclopentane-1,3-dione (5) was heated at 100–110° in benzene containing t-butyl alcohol, diethylamine and hydroquinone for 110 h, 31% (crude yield) of the hydroxy diketone (10) was obtained, but the major product (61%) was the crystalline spiro triketone (11). This showed i.r. absorption at 1760, 1725 and 1710 cm^{-1}, only end absorption in the u.v. spectrum, and the parent molecular ion at *m/z* 248 in the mass spectrum. The ^{1}H n.m.r. spectrum showed a doublet at δ 1·22 for one methyl group and a singlet at 1·05 for the other; there was no signal for olefinic hydrogen. The ^{13}C n.m.r. spectrum showed no olefinic carbon atoms, three carbonyl resonances (208·5, 210·9, 213·9 ppm) and other signals with multiplicities fully consistent with structure (11). The formation of (11) is readily explicable by intramolecular Michael addition in the initial Michael adduct (8) (Scheme 1). An analogous product (17) was obtained by Sakai and Amemiya[3] from the reaction of 3-ethenylcyclohex-2-en-1-one (12a) with the bicyclic β-keto ester (15) (Scheme 2); this reaction gave 81% of a mixture of compounds (16) and (17), both of which were convertible into the steroid derivative (19). The 4-methyl group in the dienone (4) appears to influence the course of base-catalysed reactions with the dione (5); approach of the anion of (5) probably occurs more readily to the *cisoid* conformation of (4) to give the adduct (7) in which the central olefinic bond has the *Z* configuration. In the aprotic medium (pyridine/toluene) the opportunity for tautomerization of the enolate anion (and hence geometric isomerization of the central double bond) is restricted, and the *Z* geometry of (7) facilitates internal aldol condensation to give (9), thence (10). On the other hand, in the more polar and protic medium of benzene/t-butyl alcohol/diethylamine, the intermediate (7) can more readily tautomerize, and the equilibrium concentration of the alternative anion (8) permits internal Michael addition to give the spiro triketone (11).

No product analogous to compounds (9) or (10) has been isolated from similar reactions of the simple dienone (12a), or its 2-methyl analogue (12b), with 2-methylcyclopentane-1,3-dione (5) or its homologue (13) (Scheme 2). Depending on the conditions used Ananchenko and Torgov[4] obtained the various 'normal' products (14a), (18a) and (20a) from reactions of (12a) with the six-membered ring dione (13), and reaction of the 2-methyl dienone (12b) with (13) gave mainly the triketone (14b) which was converted into (20b) via (18b). Eschenmoser *et al.*[5] found that reaction of the 2-methyl dienone (12b) with 2-methylcyclohexane-1,3-dione (13) in benzene containing diethylamine and t-butyl alcohol in a sealed tube at 110° for 110 h gave

[3] Sakai, K., and Amemiya, S., *Chem. Pharm. Bull.*, 1970, **18**, 641.
[4] Ananchenko, S. N., and Torgov, I. V., *Izv. Akad. Nauk. SSSR, Otd. Khim. Nauk*, 1960, **9**, 1649.
[5] Eschenmoser, A., Schreiber, J., and Julia, S. A., *Helv. Chim. Acta*, 1953, **36**, 482.

42% of the hydroxy diketone (18b) by *in situ* aldol condensation of (14b). Similarly, Panouse and Sannie found[6] that conjugate Michael addition of the anion of 2-methylcyclopentane-1,3-dione (5) to the 2-methyl dienone (12b) in toluene containing pyridine gave 82% of the triketone (14c) which was separately cyclized to give 76% of the diene dione (20c).[7]

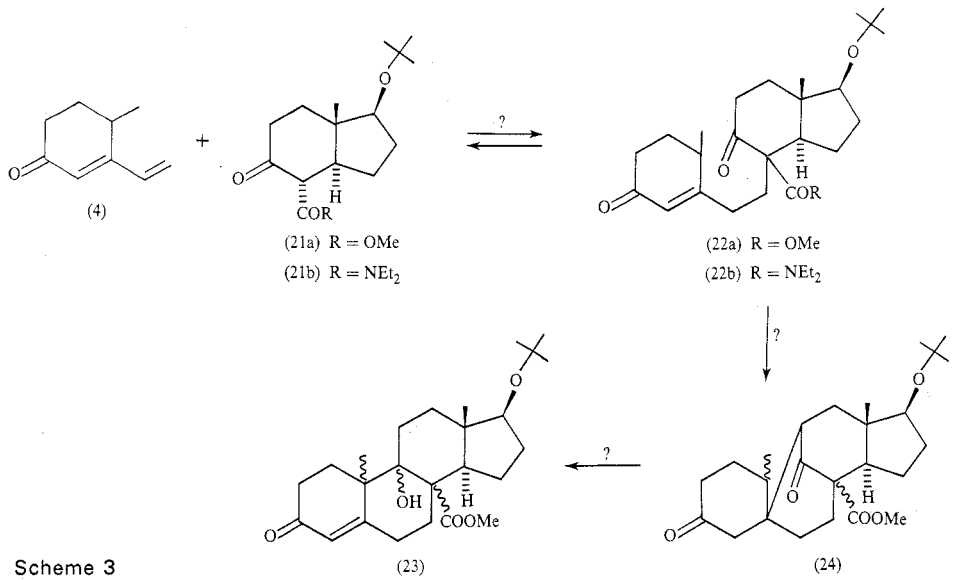


Scheme 2

Because the conformation of 3-ethenyl-4-methylcyclohex-2-en-1-one (4) is probably important in determining the outcome in its reaction with the dione (5), it was of interest to test the effect of inclusion of an adsorbent with a large surface area. When a mixture of (4) and (5) in benzene containing diethylamine, t-butyl alcohol and silica gel (230–400 mesh ASTM) was heated in a sealed tube at 100–110° for 110 h, 72% of the spiro triketone (11) was produced and none of the hydroxy diketone (10) was detected.

[6] Panouse, J. J., and Sannie, C., *Bull. Soc. Chim. Fr.*, 1956, 1429.
[7] Sannie, C., and Panouse, J. J., *Bull. Soc. Chim. Fr.*, 1965, 1435.

The preparation of (11) from (4) and (5) led us to expect that reaction of the dienone (4) with the bicyclic β-keto ester (21a)[8] might similarly give the conjugate Michael adduct (22a) and/or the corresponding cyclized spiro diketo ester (24) which should be convertible into the steroid derivative (23) (Scheme 3, cf. the conversion of (16) and (17) into (19),[3] Scheme 2). When a mixture of the dienone (4) and the t-butoxy keto ester (21a) in benzene, t-butyl alcohol and diethylamine was heated in a sealed tube at 105–110° for 110 h the major product (79%) was the bicyclic t-butoxy keto amide (21b). Interestingly, when the dienone (4) was omitted from a similar experiment, no aminolysis of the ester function occurred and (21a) was recovered. Possibly, the bicyclic amide (21b) was formed by aminolysis of a low equilibrium concentration of the Michael adduct (22a), and the reverse Michael reaction liberated the amide (21b). The use of the more hindered base diisopropylamine gave no conjugate Michael reaction product from (4) and (21a), and no aminolysis occurred.

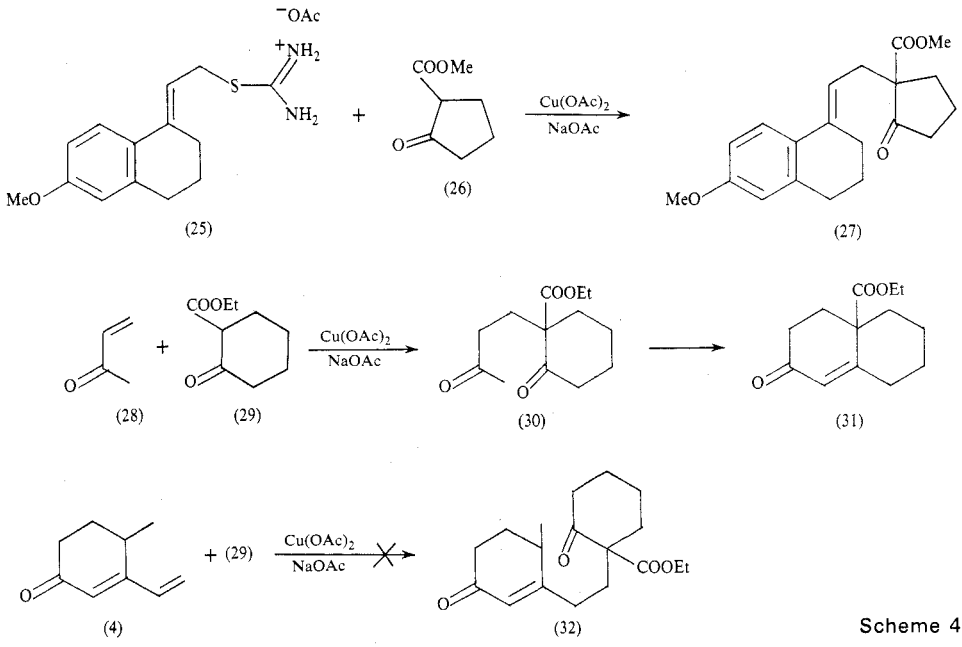


Scheme 3

The following sets of reaction conditions also failed to promote the reaction of (4) and (21a) to give (22a) and/or (24): sodium methoxide in tetrahydrofuran at room temperature for 110 h; dry pyridine in refluxing xylene for 100 h; triethylamine, or 1,5-diazabicyclo[4.3.0]non-5-ene, or 1,4-diazabicyclo[2.2.2]octane in refluxing toluene under a Dean–Stark separator for 90 h; potassium t-butoxide in tetrahydrofuran at room temperature for 5 h (cf. Sakai and Amemiya[3]), or in dimethyl sulfoxide under similar conditions; generation of the anion of the bicyclic β-keto ester (21a) with sodium hydride in either tetrahydrofuran or dimethyl sulfoxide, then addition of the dienone (4). The use of a molar equivalent of a strong base such as potassium t-butoxide resulted in rapid polymerization of the dienone (4). When catalytic amounts of a strong base (e.g. sodium methoxide in tetrahydrofuran) were used no reaction occurred at room temperature, and at 65–70° there was complete polymerization of the dienone (4), and recovery of the β-keto ester (21a) was poor.

[8] Micheli, R. A., Hajos, Z. G., Cohen, N., Parrish, D. R., Portland, L. A., Sciamanna, W., Scott, M. A., and Wehrli, P. A., *J. Org. Chem.*, 1975, **40**, 675.

Other possible procedures for promotion of the conjugate Michael addition of the β-keto ester (21a) were then investigated. Whereas the modified Torgov synthesis of oestrone is highly efficient with 2-methylcyclopentane-1,3-dione (5) as the nucleophile,[9] similar reactions with cyclic β-keto esters[10] gave very low yields; this problem was overcome by using copper enolates of β-keto esters. For example alkylation of the β-keto ester (26) with the salt (25) in the presence of one equivalent of copper acetate buffered with sodium acetate gave 66% of compound (27) (Scheme 4).[10] Copper enolates do not appear to have been used previously as nucleophiles in Michael addition reactions. In a model experiment we found that the reaction of methyl vinyl ketone (28) with ethyl 2-oxocyclohexane-1-carboxylate (29) gave 90% of the pure diketo ester (30) which was cyclized to give the enone ester (31) (Scheme 4). Standard procedures have given even higher yields of (30) and (31) (see, for example, Wynberg and Greijdanus[11]), but the mild conditions afforded by copper acetate/sodium acetate might be beneficial in some otherwise low-yielding Michael addition reactions. The conjugated dienone (4) was found to be stable to copper acetate/sodium acetate in aqueous ethanol at $<40°$, but attempts to condense the simple cyclic β-keto ester (29) with the conjugated dienone (4) by the use of this reagent mixture at 40° gave none of compound (32). At higher reaction temperatures the dienone polymerized. In view of this, the analogous reaction between the copper enolate of the bicyclic β-keto ester (21a) and the dienone (4) was not attempted.

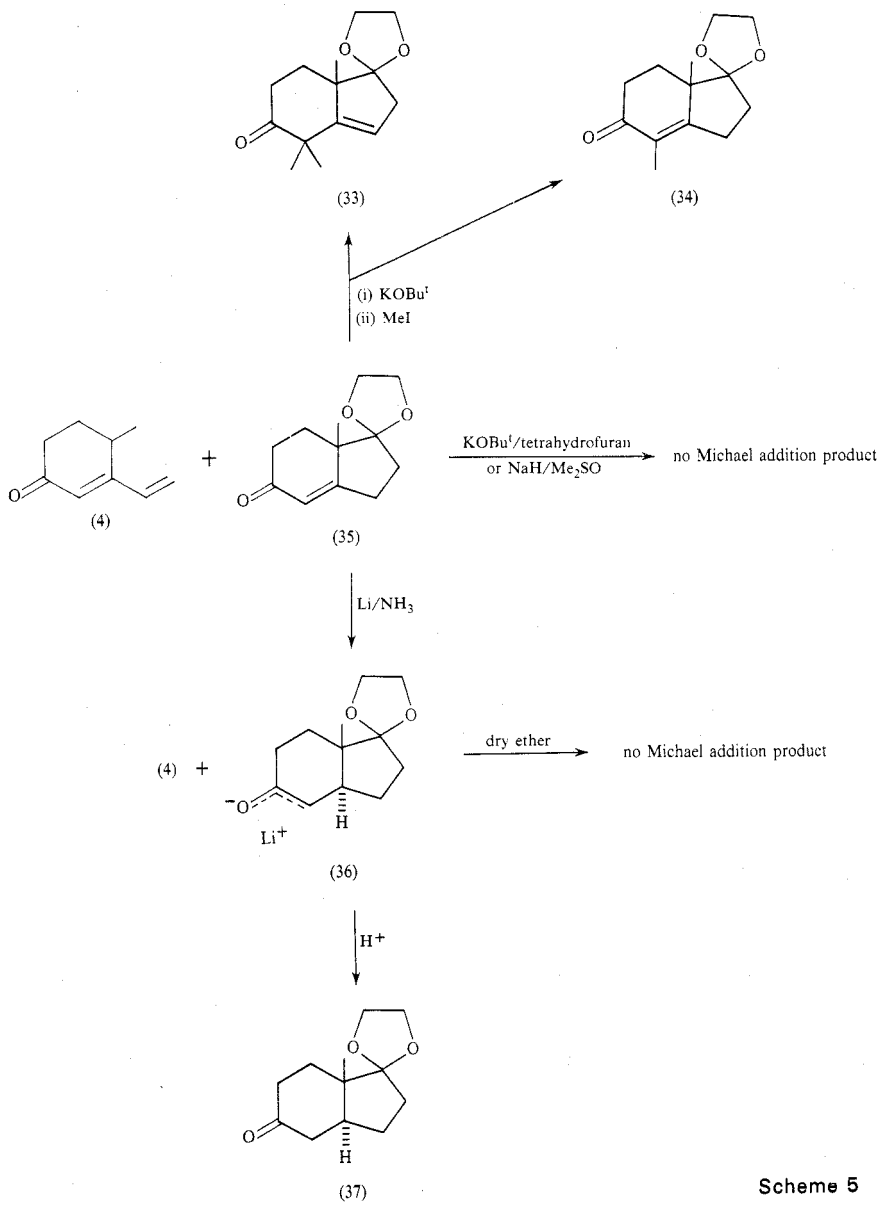


Scheme 4

Several attempts to effect the conjugate Michael addition of the potassium enolate of the bicyclic enone (35) (generated with potassium t-butoxide) with the dienone (4)

[9] Kuo, C. H., Taub, D., and Wendler, N. L., *J. Org. Chem.*, 1968, **33**, 3126.
[10] Magriotis, P. A., Murray, W. V., and Johnson, F., *Tetrahedron Lett.*, 1982, 1993.
[11] Wynberg, H., and Greijdanus, B., *J. Chem. Soc., Chem. Commun.*, 1978, 427.

resulted only in the polymerization of (4) (Scheme 5). A reaction in which the sodium enolate of (35) was generated with sodium hydride in dimethyl sulfoxide was similarly unsuccessful. Confirmation that the anion of (35) had been generated was obtained by treatment of a tetrahydrofuran solution of (35) with potassium t-butoxide, then with methyl iodide; flash chromatography of the product yielded 48% of the *gem*-dimethylated ketone (33) and 5% of the methylated enone (34) (cf. Escher *et al.*[12]). In another experiment an ether or tetrahydrofuran suspension



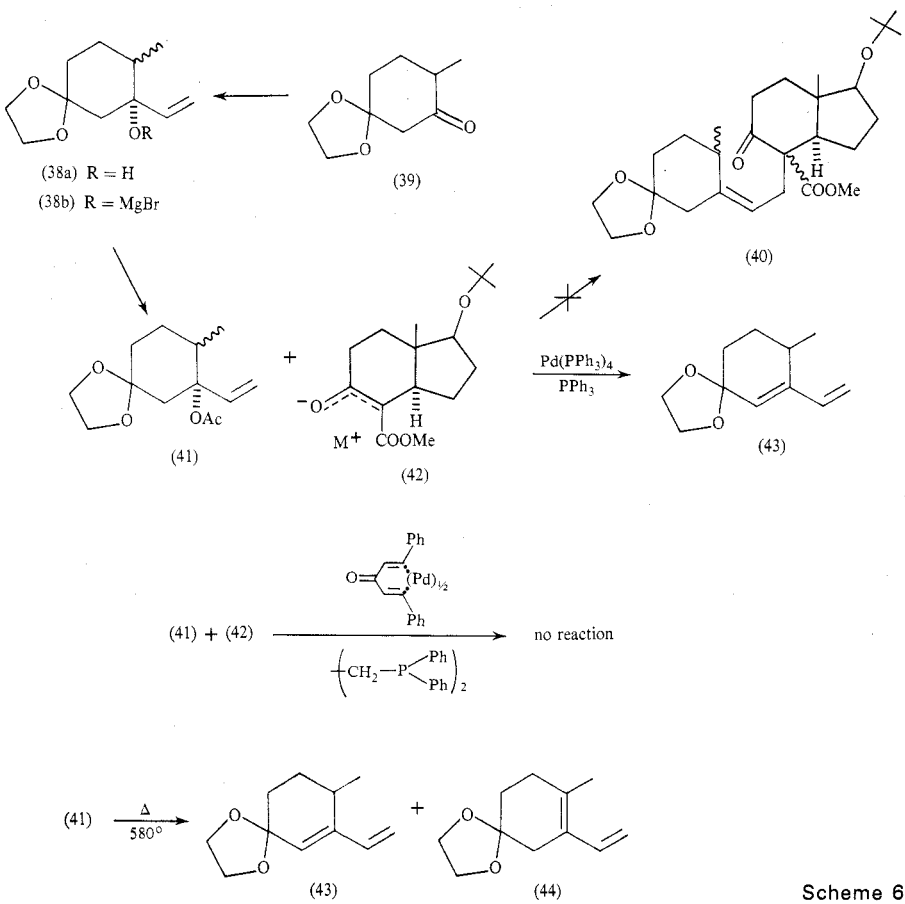
Scheme 5

[12] Escher, S., Giersch, W., and Ohloff, G., *Helv. Chim. Acta*, 1981, **64**, 943.

of the lithium enolate (36), obtained by reduction of the enone (35) with lithium in anhydrous ammonia (cf. Baudin and Pietrasanta[13]), was treated overnight at room temperature with the dienone (4); workup gave only the saturated keto acetal (37) and the dienone (4).

Attempted Alkylation of the Allylic Acetate (41)

A considerable amount of work has been done on the palladium-catalysed alkylation of β-dicarbonyl compounds with allylic ethers or esters.[14] With this in mind we required the allylic acetate (41) to attempt its reaction with the enolate (42) to give the potentially useful intermediate (40) (Scheme 6). 4-Dimethylaminopyridine is a very effective catalyst for the acetylation of some tertiary alcohols.[15-18]



Scheme 6

[13] Bauduin, G., and Pietrasanta, Y., *Tetrahedron*, 1973, **29**, 4225.
[14] Trost, B. M., *Acc. Chem. Res.*, 1980, **13**, 385.
[15] Litvinenko, L. M., and Kirichenko, A. I., *Dokl. Akad. Nauk SSSR*, 1967, **176**, 97.
[16] Höfle, G., Steglich, W., and Vorbrüggen, H., *Angew. Chem., Int. Ed. Engl.*, 1978, **17**, 569.
[17] Hassner, A., Krepski, L. R., and Alexanian, V., *Tetrahedron*, 1978, **34**, 2069.
[18] Connors, K. A., and Albert, K. S., *J. Pharm. Sci.*, 1973, **62**, 845.

However, treatment of the vinyl carbinol (38a)[1] with acetic anhydride and triethylamine containing a catalytic amount of 4-dimethylaminopyridine in dichloromethane failed to give the allylic acetate (41); even after twelve weeks at room temperature only 5% of (41) was detected (^{1}H n.m.r. and g.l.c.). Treatment of the allylic tertiary alcohol (38a) with n-butyllithium and quenching of the lithium salt with acetyl chloride afforded 48% of the acetate (41). A better yield (67%) of compound (41) was obtained by reaction of acetic anhydride containing 4-dimethylaminopyridine with the Grignard complex (38b) from reaction of the keto acetal (39)[1] with vinylmagnesium bromide. A solution of the allylic tertiary acetate (41) in tetrahydrofuran was treated with triphenylphosphine and palladium tetrakis(triphenylphosphine) (cf. Trost *et al.*[19]) and to this was added the sodium enolate (42) prepared from the β-keto ester (21a) with sodium hydride in tetrahydrofuran. After 12 h at reflux workup gave only the β-keto ester (21a) and the known[2] conjugated diene acetal* (43); there is a precedent[20] for palladium catalysis of the elimination of an allylic acetoxy group to give a diene. In a similar experiment in which the enolate (42) was added to a tetrahydrofuran solution of (41) containing bis(dibenzylideneacetone)palladium and a trace of ethane-1,2-diylbis(diphenylphosphine) (modification of Fiaud and Malleron[21]) there was no reaction after 48 h.

Flash vacuum pyrolysis of the allylic acetate (41) at 580° afforded a 7 : 3 mixture of the conjugated diene acetal (43) and its regioisomer (44). An efficient synthesis of compound (44) was described in the previous paper.[2]

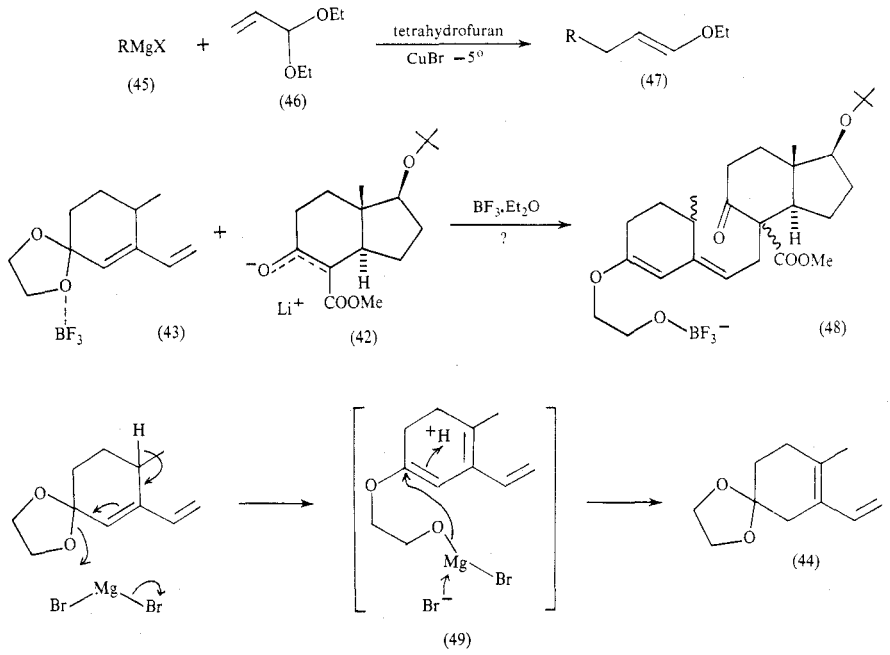
Attempted Alkylation of the Conjugated Diene Acetal (43)

Recent reports of the reactions of preformed lithium enolates of ketones with trimethyl orthoformate[22] or with acetals[23] in the presence of boron trifluoride etherate suggests that double activation (i.e. the ketone as a carbanion and an alkoxyalkane as the source of a stabilized carbocation) is a useful procedure for carbon–carbon bond formation. This, coupled with a report[24] that allylic acetals such as (46) undergo alkylation with double bond migration and elimination of an alkoxy group to give compounds (47) when treated with Grignard reagents (45) (Scheme 7), led us to attempt reaction of the conjugated diene acetal (43), activated by a Lewis acid, with the enolate (42), to give compound (48). When an ethereal solution of the bicyclic enolate (42) was added to a mixture of the conjugated diene acetal and boron trifluoride etherate in ether at −78° only the starting materials were recovered. The use of magnesium bromide as the Lewis acid gave the same result. In a similar experiment in which half of the ether was removed and replaced by dry dimethyl sulfoxide the conjugated diene acetal (43) was isomerized almost quantitatively to the diene acetal (44). The isomerization of (43) by interaction with magnesium bromide probably proceeds via the complex (49) without involvement of the enolate

* Both compounds (43) and (44) have conjugated diene systems but, for convenience, the term conjugated diene acetal is applied to compound (43) because of its direct structural relationship to the fully conjugated dienone (4).

[19] Trost, B. M., and Verhoeven, T. R., *J. Am. Chem. Soc.*, 1980, **102**, 4730.
[20] Trost, B. M., Verhoeven, T. R., and Fortunak, J. M., *Tetrahedron Lett.*, 1979, 2301.
[21] Fiaud, J. C., and Malleron, J. L., *Tetrahedron Lett.*, 1980, 4437.
[22] Suzuki, M., Yanagisawa, A., and Noyori, R., *Tetrahedron Lett.*, 1982, 3595.
[23] Pelter, A., and Al-Bayati, R., *Tetrahedron Lett.*, 1982, 5229.
[24] Normant, J. F., Commercon, A., Bourgain, M., and Villieras, J., *Tetrahedron Lett.*, 1975, 3833.

(42); when the conjugated diene acetal (43) was treated with only magnesium bromide etherate in benzene and dimethyl sulfoxide for 1 h, 90% of the isomeric diene acetal (44) was obtained.



Scheme 7

Conclusion

The 4-methyl group in the conjugated dienone (4) greatly reduces its reactivity as a Michael acceptor compared with the related conjugated dienones (12a) and (12b); when it *does* react it probably does so in the *cisoid* conformation. The formation of compound (10) in an essentially aprotic medium is indicative of this. Under protic conditions tautomerization of the initial enolate (7) gave (8) which then underwent internal Michael addition to give the spiro triketone (11). Such a reaction is potentially useful, but all attempts to effect a similar reaction of (4) with the enolate of the bicyclic keto ester (21a) failed, and this approach to synthesis of the steroid skeleton is unpromising.

Experimental

Instrumentation and general methods were as described in the previous paper.[2]

(a) 3-Ethenyl-4-methylcyclohex-2-en-1-one (4)

To a solution of 3-ethenyl-3-hydroxy-4ξ-methylcyclohexan-1-one (1)[1] (800 mg) in methanol (16 ml) was added 0·1M sodium bicarbonate solution (32 ml), and the solution was stirred at 35° for 1 h. The mixture was extracted with ether/benzene (×3), and the combined extracts were washed with saturated sodium chloride solution (×2) then dried over anhydrous sodium sulfate and evaporated to yield the crude dienone. Flash chromatography on silica gave pure 3-ethenyl-4-methylcyclohex-2-en-1-one (4) (480 mg, 68%) which was identical (i.r. and ^{1}H n.m.r. spectra) with the material obtained previously by acid catalysed dehydration of (1).[1]

(*b*) *3-(2′-Ethoxyethyl)-4-methylcyclohex-2-en-1-one* (*3*)

To a solution of 3-ethenyl-3-hydroxy-4ξ-methylcyclohexan-1-one (1) (1·0 g) in ethanol (100 ml) was added 8 M H_2SO_4 (30 ml). The solution was stirred at room temperature for 48 h, then extracted with ether/benzene (×3). The combined extracts were washed with 2% sodium bicarbonate, water (×2), then dried (Na_2SO_4) and evaporated to give a mixture of 3-ethenyl-4-methylcyclohex-2-en-1-one (4) and 3-(2′-ethoxyethyl)-4-methylcyclohex-2-en-1-one (3) (1 : 4 by ^{1}H n.m.r.). Flash column chromatography (10% ethyl acetate/light petroleum) gave the conjugated dienone (190 mg) followed by the ethoxy enone (840 mg). Bulb-to-bulb distillation (140°/1 mm) of the latter gave pure *3-(2′-ethoxyethyl)-4-methylcyclohex-2-en-1-one* (3) (Found: C, 71·7; H, 9·8; $M^{+\bullet}$, 182·131±0·002. $C_{11}H_{18}O_2$ requires C, 72·5; H, 9·9; $M^{+\bullet}$, 182·1306). λ_{max} 237 nm (ε 13000). ν_{max} (film) 1660s, 1460w, 1450w, 1410w, 1380m, 1350m, 1325w, 1300w, 1255m, 1200m, 1170w, 1105s, 1020w, 980w, 945w, 920w, 865w cm^{-1}. ^{1}H n.m.r. δ (60 MHz, $CDCl_3$) 1·20, t, *J* 7 Hz, OCH_2Me; 1·22, d, *J* 7 Hz, Me; 1·69–2·70, m, 7H; 3·53, q, *J* 7 Hz, OCH_2Me; 3·65, t, *J* 7 Hz, OCH_2; 5·90, s, $W_{h/2}$ 3 Hz, H 2. ^{13}C n.m.r. δ ($CDCl_3$) 15·1, q, $MeCH_2$; 17·8, q, Me; 30·1, t, C5*; 33·4, d, C4; 34·1, t, C6*; 35·6, t, C1′*; 66·4 and 68·1, t, 2×OCH_2; 125·7, d, C2; 167·3, s, C3; 199·6, s, C1. Mass spectrum: *m/z* 182 (M, 7%), 109 (7), 59 (100), 41 (8), 31 (75).

(*c*) *Reactions of 2-Methylcyclopentane-1,3-dione* (*5*) *with 3-Ethenyl-4-methylcyclohex-2-en-1-one* (*4*)

(i) *In toluene containing pyridine.*—A mixture of 3-ethenyl-4-methylcyclohex-2-en-1-one (4) (87 mg, 0·64 mmol), 2-methylcyclopentane-1,3-dione (5) (87 mg, 0·77 mmol), hydroquinone (1 mg), pyridine (1·5 ml) and toluene (6 ml) was refluxed for 90 h. The black mixture was cooled, diluted with water and extracted with toluene/ether. The organic phase was washed with copper sulfate solution, water, dried (Na_2SO_4) and evaporated. Preparative t.l.c. (silica gel, 40% ethyl acetate/light petroleum) gave a major band at R_F *c.* 0·2, extraction of which with dichloromethane gave *9bξ-hydroxy-3a,6-dimethyl-3a,4,5,6,7,9b-hexahydro-1*H*-benz*[e]*indene-3,9(2*H*,8*H*)-dione* (10) (10 mg, 6%) as colourless prisms, m.p. 90–92° (Found: $M^{+\bullet}$, 248·143±0·003 (at 20 eV). $C_{15}H_{20}O_3$ requires $M^{+\bullet}$, 248·1411). λ_{max} (EtOH) 244 nm (ε 8500). ν_{max} (Nujol) 3420s, (OH) 1730s (C=O), 1660s (C=O), 1600m, 1450m, 1420m, 1400m, 1370m, 1330w, 1300m, 1285m, 1270m, 1250w, 1215w, 1195w, 1190w, 1150w, 1110m, 1090w, 1060m, 1040w, 965m, 950w, 880w, 815w cm^{-1}. ^{1}H n.m.r. δ (90 MHz, $CDCl_3$) 1·07, s, Me; 1·21, d, *J* 7 Hz, Me; 1·46–2·94, m, 12H; 4·50 and 4·60, s, exch. OH (combined integral ≡ 1H). The OH at δ 4·50 was completely exchanged after 3 min, but that at 4·60 was only 90% exchanged after 24 h. Mass spectrum: *m/z* 230 (3%, M−18), 192 (44), 191 (100), 177 (14), 150 (33), 55 (10); *m/z* (20 eV) 248 (12%, M).

(ii) *In a sealed tube with diethylamine.*—A mixture of 3-ethenyl-4-methylcyclohex-2-en-1-one (4) (520 mg), 2-methylcyclopentane-1,3-dione (5) (514 mg), t-butyl alcohol (3 ml), diethylamine (0·5 ml), hydroquinone (1 mg) and benzene (8 ml) was heated in a sealed tube [which had been flushed with nitrogen and evacuated at water pump pressure (*c.* 16 mm)] at 100–110° for 110 h. The mixture was cooled, neutralized with 2 M HCl, extracted with ether/benzene, dried (Na_2SO_4) and evaporated to give a red oil which solidified on cooling. The colour was removed by trituration with light petroleum, and recrystallization from chloroform/methanol gave *5′,6-dimethylspiro[bicyclo[3.2.1]-octane-1,2′-cyclohexane]-3,6′,8′-trione* (11) (579 mg, 61%) as colourless prisms, m.p. 222–224° (sublimed to needles at 155–158°) (Found: $M^{+\bullet}$, 248·139±0·003. $C_{15}H_{20}O_3$ requires $M^{+\bullet}$, 248·1411). ν_{max} (Nujol) 1760s (C=O), 1725s (C=O), 1710s (C=O), 1465m, 1450m, 1420w, 1410w, 1380m, 1350m, 1335w, 1265w, 1240w, 1185w, 1250m, 1070m, 1060m, 980w, 920w, 810w, 720w cm^{-1}. ^{1}H n.m.r. δ (90 MHz, $CDCl_3$) 1·05, s, Me; 1·22, d, *J* 7 Hz, Me; 1·53–2·98, m, 14H. ^{13}C n.m.r. δ ($CDCl_3$) 11·8, q, Me; 14·6, q, Me; 28·0, 28·7, 36·5, 37·8, 40·8, 45·2 all t; 34·8, d, C6; 51·6, s, C2′; 52·3, d, C1′; 58·3, s, C5′; 208·5, s, C3; 210·9, s, C6′; 213·9, s, C8′. Mass spectrum: *m/z* 248 (M, 8%), 230 (14), 175 (15), 149 (10), 125 (20), 124 (100), 96 (18), 67 (17).

Flash chromatography (10% ethyl acetate/light petroleum) of the mother liquor residue gave a viscous yellow oil (10 mg) which was not identified. Further elution (20% ethyl acetate/light petroleum) gave a colourless oil (294 mg > 31%) which was shown by its ^{1}H n.m.r. and i.r. spectra to be identical with (10) described in (i) above.

(iii) *In a sealed tube with diethylamine and silica gel.*—A mixture of 3-ethenyl-4-methylcyclohex-2-en-1-one (4) (126 mg), 2-methylcyclopentane-1,3-dione (5) (100 mg), t-butyl alcohol (2 ml),

* These assignments may be interchanged.

diethylamine (0·8 ml), hydroquinone (1 mg), silica gel (0·040–0·063 mm, 230–400 mesh ASTM) (100 mg) and benzene (6 ml) was heated in a sealed tube at 110–100° for 110 h. The mixture was cooled, diluted with ether/benzene, neutralized with 2 M HCl, filtered, washed with 10% sodium chloride solution, dried (Na_2SO_4) and evaporated to give an oil which solidified on cooling. Recrystallization from chloroform/methanol gave the spiro triketone (11) (125 mg, 72%), m.p. 222–224°, identical (i.r. and ^{1}H n.m.r. spectra) with the material described in (ii) above.

(d) 1β-t-Butoxy-7aβ-methyl-5-oxo-1,2,3,3aα,4β,6,7,7a-octahydroindene-4-carboxylic Acid Methyl Ester (21a)

By use of a five-step sequence developed by Micheli *et al.*,[8] 7a-methyl-2,3,7,7a-tetrahydro-1*H*-indene-1,5(6*H*)-dione was converted into the t-butoxy keto ester (21a) which crystallized from ether/light petroleum as colourless needles, m.p. 111–113° (lit.[8] 112·5–113·5°). ν_{max} (Nujol) 1743s (ester C=O), 1710s (C=O) cm^{-1}. ^{1}H n.m.r. δ (90 MHz, $CDCl_3$) 1·00, s, 7a-Me; 1·12, s, CMe_3; 1·31–2·54, m, 9H; 3·34, d, $J_{3a,4}$ 13 Hz, H4; 3·52–3·68, m, H1; 3·70, s, COOMe. ^{13}C n.m.r. δ ($CDCl_3$) 11·0, q, 7a-Me; 28·7, q, **Me$_3$C**; 24·4, C3; 31·5, C7; 35·0, C2; 37·3, C6; 42·0, s, C7a; 46·7, d, C3a; 51·9, q, MeO; 58·9, d, C4; 72·7, s, CMe_3; 79·0, d, C1; 170·0, s, **C**OOMe; 206·0, s, C5. Mass spectrum: *m/z* 116 (M, 9%), 57 (100), 41 (31).

(e) Attempted Reactions of 3-Ethenyl-4-methylcyclohex-2-en-1-one (4) with the Bicyclic β-Keto Ester (21a)

(i) *In the presence of diethylamine (cf. Eschenmoser* et al.[5]).—To a solution of 3-ethenyl-4-methylcyclohex-2-en-1-one (240 mg, 1·7 mmol), benzene (6 ml), t-butyl alcohol (6 ml) and diethylamine (3 ml) in a thick-walled glass tube was added the bicyclic β-keto ester (21a) (500 mg, 1·7 mmol). The tube was evacuated under water pump pressure, filled with nitrogen, again evacuated and sealed. The mixture was heated at 105–110° for 110 h, cooled, poured onto 1 M HCl, washed with water, dried over anhydrous magnesium sulfate and evaporated to give a pale yellow semi-solid (510 mg). Recrystallization from ether/light petroleum gave *1β-t-butoxy*-N,N-*diethyl-7aβ-methyl-5-oxo-2,3,3aα,4β,5,6,7,7a-octahydroindene-4-carboxamide* (21b) (450 mg, 79%) as colourless prisms which sublimed to needles at 115°, and melted at 130–132° (Found: M$^{+\bullet}$, 323·246±0·002. $C_{19}H_{33}NO_3$ requires M$^{+\bullet}$, 323·2459). ν_{max} (Nujol) 1712s (C=O), 1638s (amide C=O), 1460s, 1440s, 1380s, 1360s, 1340w, 1310w, 1290w, 1280w, 1265w, 1235m, 1195s, 1150m, 1125s, 1100s, 1080s, 1070m, 1035w, 1000w, 910w, 890w, 800w, 775w cm^{-1}. ^{1}H n.m.r. δ (90 MHz, $CDCl_3$) 1·01, s, 7a-Me; 1·12, s, Me_3C; 1·12, t, *J* 7 Hz, 2×OCH_2**Me**; 1·32–2·54, m, 9H; 3·10–4·64, m, H1,4, 2×OCH_2Me. ^{13}C n.m.r. δ ($CDCl_3$) 11·3, q, 7a-Me; 13·1, 14·9, q, 2×OCH_2**Me**; 28·7, q, **Me$_3$C**; 24·6, C3; 31·5, C7; 34·6, C2; 37·5, C6; 40·6, t, OCH_2Me; 41·7, s, C7a; 42·2, t, OCH_2Me; 46·3, d, C3a; 55·2, d, C4; 72·6, s, **C**Me$_3$; 79·2, d, C1; 167·9, s, C=O amide; 207·5, s, C5. Mass spectrum: *m/z* 323 (M, 8%), 267 (15), 266 (17), 224 (16), 158 (24), 157 (100), 142 (28), 115 (27), 100 (66), 74 (36), 72 (65), 58 (33), 57 (51), 55 (12), 44 (12), 41 (21).

An identical experiment, in which the conjugated dienone (4) was omitted, failed to produce any of the amide (21b). When diisopropylamine was used as the base, only starting material was recovered.

(ii) To a stirred solution of the bicyclic β-keto ester (21a) (310 mg, 1·1 mmol) in tetrahydrofuran (6 ml) containing sodium methoxide (6 mg, 0·1 mmol) was added 3-ethenyl-4-methylcyclohex-2-en-1-one (150 mg, 1·1 mmol) in tetrahydrofuran (2 ml). The mixture was stirred at room temperature for 110 h, then poured into iced water, extracted with chloroform, washed with water, dried over anhydrous sodium sulfate and evaporated. The product was shown by ^{1}H n.m.r. and i.r. spectroscopy to be a mixture of both starting materials.

A similar experiment carried out in refluxing tetrahydrofuran for five days yielded only the β-keto ester and a yellow gum which was not identified.

(iii) To a solution of 3-ethenyl-4-methylcyclohex-2-en-1-one (200 mg, 1·5 mmol) and the bicyclic β-keto ester (21a) (410 mg, 1·5 mmol) in xylene (8 ml) was added dry pyridine (0·5 ml). The mixture was heated at 130–135° for 100 h, then poured into iced water. Workup as above yielded the bicyclic β-keto ester and a poor recovery of the dienone (10 mg).

(iv) To a solution of 3-ethenyl-4-methylcyclohex-2-en-1-one (150 mg, 1·1 mmol) and the bicyclic β-keto ester (21a) (310 mg, 1·1 mmol) in toluene (5 ml) was added triethylamine (1 ml). The mixture was refluxed under a Dean–Stark separator for 90 h, then poured into water, extracted

with ether, washed with water, dried over anhydrous sodium sulfate and evaporated. There was no reaction (i.r. and ^{1}H n.m.r. spectra).

Similar experiments, in which 1,5-diazabicyclo[4.3.0]non-5-ene and 1,4-diazabicyclo[2.2.2]octane were used as the base, were similarly unsuccessful.

(v) To a stirred solution of the bicyclic β-keto ester (21a) (245 mg, 0·87 mmol) in dry tetrahydrofuran (5 ml) under an atmosphere of nitrogen, was added potassium t-butoxide (10 mg, 0·08 mmol) in tetrahydrofuran (2 ml). The mixture was stirred at room temperature for 1 h, then treated dropwise with a solution of 3-ethenyl-4-methylcyclohex-2-en-1-one (118 mg, 0·87 mmol) in tetrahydrofuran (1 ml). The mixture was stirred at room temperature. T.l.c. (silica gel/10% ethyl acetate/light petroleum) showed no reaction after 5 h. The mixture was then refluxed and its composition checked by t.l.c. at 30 min intervals. After 3 h of refluxing only the bicyclic β-keto ester (21a) remained; the dienone (4) had polymerized.

Similar experiments in which 3-ethenyl-4-methylcyclohex-2-en-1-one in tetrahydrofuran was added dropwise into a refluxing mixture of the bicyclic β-keto ester in tetrahydrofuran containing either a 0·1 or a 1·0 molar equivalent of potassium t-butoxide resulted in polymerization of the dienone and recovery of the bicyclic β-keto ester.

Reactions in which dimethyl sulfoxide was substituted for tetrahydrofuran also failed to produce any cycloaddition adduct.

(vi) The bicyclic β-keto ester (21a) (200 mg, 0·7 mmol) in dry tetrahydrofuran (3 ml) was treated with light petroleum/washed sodium hydride (21 mg of an 80% suspension in oil, 0·7 mmol), and the mixture was stirred under an atmosphere of nitrogen for 30 min. 3-Ethenyl-4-cyclohex-2-en-1-one (95 mg, 0·7 mmol) in tetrahydrofuran (1 ml) was added dropwise during 30 min. When the mixture was heated to 40° a black gum was deposited; ^{1}H n.m.r. spectroscopy and t.l.c. indicated that this was polymeric.

(f) Reaction of the Copper Enolate of Ethyl 2-Oxocyclohexane-1-carboxylate (29) with Methyl Vinyl Ketone

Copper(II) acetate (1·18 g, 5·9 mmol) was dissolved in hot (80°) 0·1 M sodium acetate solution (10 ml). The mixture was allowed to cool to 40°, then treated with a solution of the β-keto ester (29) (1·00 g, 5·9 mmol) in ethanol (7 ml). The green mixture was stirred at 25° for 15 min, then methyl vinyl ketone (0·5 g, 7·1 mmol) was added and the mixture was stirred at room temperature for 20 h. It was then poured into ice-cold saturated ammonium chloride solution, and the product was isolated with ether. Bulb-to-bulb distillation gave pure ethyl 2-oxo-1-(3′-oxobutyl)cyclohexane-1-carboxylate (30) (1·28 g, 90%) b.p. 90–93°/0·3 mm (lit.[25] 138–140°/0·4–0·5 mm). ν_{max} (film) 1720s, C=O; 1445m, 1420m, 1360s, 1300m, 1255s, 1220s, 1195s, 1165s, 1140m, 1100m, 1080m, 1060w, 1040w, 1020w cm^{-1}. ^{1}H n.m.r. δ (60 MHz, $CDCl_3$) 1·29, t, J 7 Hz, OCH_2Me; 2·16, s, Me; 1·61–2·80, m, H 6,6; 4·27, q, J 7 Hz, OCH_2Me. ^{13}C n.m.r. δ ($CDCl_3$) 14·2, q, OCH_2Me; 22·6, 27·6, 28·5, 38·2, 38·9, 41·4, all t, C 3,4,5,6,1′,2′; 30·0, q, Me; 60·1, s, C 1; 61·5, t, OCH_2Me; 172·1, C=O ester; 207·9, s, C=O; 208·1, s, C=O. Mass spectrum: m/z 224 (M+2, 11%), 223 (21), 222 (14), 152 (13), 151 (45), 150 (90), 149 (100), 148 (44), 139 (17), 138 (19), 123 (18), 122 (27), 121 (23), 109 (18).

The diketo ester (30) (240 mg) was dissolved in benzene (10 ml) containing *p*-toluenesulfonic acid (5 mg) and heated at reflux under a Dean–Stark water separator for 2 h. Additional *p*-toluenesulfonic acid (5 mg) was added and heating was continued for a further 20 h. The cooled solution was poured onto cold 2% sodium bicarbonate solution, extracted with ether, washed with water, dried (Na_2SO_4) and evaporated to give a pale yellow oil (204 mg, 92%). Bulb-to-bulb distillation gave ethyl 2-oxo-2,3,4,4a,5,6,7,8-octahydronaphthalene-4a-carboxylate (31), b.p. 100–103°/0·2 mm (lit.[25,26] 154–156°/3·8 mm, m.p. 130–131°). ν_{max} (film) 1722s ester C=O, 1665s, α,β-unsat. C=O. ^{1}H n.m.r. δ (60 MHz, $CDCl_3$) 1·27, t J 7 Hz OCH_2Me; 1·45–2·62, m, H 6,6; 4·28, q, J 7 Hz, OCH_2Me; 6·00, s ($W_{h/2}$ 3 Hz), H 1. ^{13}C n.m.r. 14·2, q, OCH_2Me; 23·1, 26·6, 34·2, 34·7, 34·7, 38·4, C 3,4,5,6,7,8; 48·9, s, C 4a; 61·4, t, OCH_2Me; 126·6, s, C 1; 163·2, s, C 8a; 173·4, s, C=O ester; 198·8, s, C 2. Mass spectrum: m/z 222 (M, 3%), 170 (27), 151 (11), 142 (12), 125 (17), 124 (25), 123 (18), 109 (15), 95 (15), 81 (22), 58 (10), 55 (28), 43 (100).

[25] Dreiding, A. S., and Tomasewski, A. J., *J. Am. Chem. Soc.*, 1955, **77**, 411.
[26] Dauben, W. G., Tweit, R. C., and MacLean, R. L., *J. Am. Chem. Soc.*, 1955, **77**, 48.

(*g*) *Attempted Reactions of Ethyl 2-Oxocyclohexane-1-carboxylate* (*29*) *with 3-Ethenyl-4-methylcyclohex-2-en-1-one* (*4*)

Numerous attempts to condense the Cu^{II} enolate of the β-keto ester (29) (prepared as described in (*e*)) with 3-ethenyl-4-methylcyclohex-2-en-1-one in ethanol failed. Vigorous conditions such as heating the dienone with the Cu^{II} enolate in ethanol and sodium acetate solution in a sealed tube at 145° for 3 days also gave no reaction as shown by ^1H n.m.r. spectroscopy, and by g.l.c. (15% Carbowax 20M on A.W. DMCS Chromosorb W).

(*h*) *Attempted Reaction of the Anion* (*36*) *Derived by Lithium/Ammonia Reduction of 1,1-Ethylenedioxy-7a-methyl-2,3,7,7a-tetrahydro-1*H*-inden-5*(6H)*-one* (*35*), *with 3-Ethenyl-4-methylcyclohex-2-en-1-one* (*4*)

A solution of the 1-monoacetal (35) (565 mg, 2·7 mmol) in dry ether (6 ml) was added to dry liquid ammonia (120 ml) which contained lithium (38 mg, 5·4 mmol). The blue solution was stirred for 30 min then most of the ammonia was evaporated during which time the blue colour discharged. The dienone (4) (200 mg) in ether (5 ml) was added and the solution was stirred at 25° overnight. The product was extracted with ether/benzene, washed with 2 M HCl, 10% sodium chloride solution, dried over anhydrous magnesium sulfate and evaporated. Flash chromatography (10% ethyl acetate/light petroleum) gave the dienone (4) (20 mg) identified by its ^1H n.m.r. spectrum. Further elution gave a mixture (540 mg) of 1,1-ethylenedioxy-7a-methyl-2,3,3a,4,7,7a-hexahydro-1*H*-inden-5(6*H*)-one (37) and the starting enone acetal (35) in the ratio of 9 : 1 (^1H n.m.r. spectrum). The saturated keto acetal (37) showed δ 1·00 for the angular methyl group (cf.[13]), while the methyl group of the conjugated enone (35) appears at δ 1·27.[27] A polymeric gum (130 mg) was obtained when the column was eluted with methanol.

A similar experiment in which the lithium enolate was treated with magnesium bromide before the addition of the dienone (4) also failed to give any addition products.

(*i*) *Attempted Michael Addition of the Anion Derived from 1,1-Ethylenedioxy-7a-methyl-2,3,7,7a-tetrahydro-1*H*-inden-5(6*H*)-one* (*35*) *with 3-Ethenyl-4-methylcyclohex-2-en-1-one* (*4*)

A solution of the keto acetal (35) (520 mg, 2·5 mmol) in tetrahydrofuran (8 ml) was treated dropwise with a solution of potassium t-butoxide (328 mg, 2·9 mmol) in tetrahydrofuran (20 ml) containing t-butyl alcohol (1 ml). The resultant blue solution was stirred for a further 15 min then treated dropwise with a solution of the dienone (4) (340 mg, 1·0 mmol) in tetrahydrofuran containing diethylamine (trace) at −20°, 0°, 20° and 60° in four separate experiments, and the reactions were followed by t.l.c. and g.l.c. The experiments at −20° and 0° were allowed to warm to room temperature and all of the reactions were continued for at least 16 h. In each case the keto acetal was recovered and as the reaction temperature increased the amount of dienone recovered decreased.

The use of potassium 2,2-dimethylpropan-1-olate in 2,2-dimethylpropan-1-ol or sodium hydride in 1,2-dimethoxyethane to generate the anion likewise failed to give any condensation product with the dienone (4).

In a control experiment the anion generated as above from the unsaturated keto acetal (35) (520 mg, 2·5 mmol) was treated dropwise with methyl iodide (0·35 g, 2·5 mmol), and the resulting purple solution was stirred overnight. The yellow solution was treated with 0·1 M HCl (10 ml), extracted with ether/toluene, washed successively with 2% sodium bicarbonate solution, 10% sodium chloride solution, dried ($MgSO_4$) and evaporated to give a pale yellow oil. Preparative t.l.c. (alumina, 40% ethyl acetate/light petroleum) gave 1,1-ethylenedioxy-4,4,7a-trimethyl-2,4,7,7a-tetrahydro-1*H*-inden-5(6*H*)-one (33) (R_F 0·72, 285 mg, 48%). ^1H n.m.r. and i.r. spectra were the same as those previously reported.[12] ^{13}C n.m.r. δ ($CDCl_3$) 22·1, 23·9, 27·5, q, 3 Me; 27·1, t, C7; 36·6, t, C6; 40·6, t, C2; 48·2*, s, C4; 49·1*, s, C7a; 64·5, 65·2, t, OCH_2CH_2O; 119·9, s, C1 and C3; 153·9, s, C3a; 215·4, s, C1.

Preparative t.l.c. also yielded the more polar mono-methylated product, 1,1-ethylenedioxy-4,7a-dimethyl-2,3,7,7a-tetrahydro-1*H*-inden-5(6*H*)-one (34) (R_F 0·64; 30 mg, 5%). The ^1H n.m.r. and i.r. spectra were the same as those previously reported.[12] Some keto acetal (35) (R_F 0·45, 40 mg) was also recovered.

[27] Brown, R. F. C., Burge, G. L., and Collins, D. J., *Aust. J. Chem.*, 1983, **36**, 117.

(*j*) *Preparation of 1-Acetoxy-1-ethenyl-5,5-ethylenedioxy-2ξ-methylcyclohexane (41)*

(i) To a stirred solution of the allylic tertiary carbinol (38a)[1] (600 mg, 3 mmol) in dry tetrahydrofuran (10 ml) under an atmosphere of nitrogen was added dropwise n-butyllithium (2·5 ml, 1·2 M). The mixture was stirred at room temperature for 30 min, treated with acetyl chloride (0·23 ml, 3·3 mmol) in tetrahydrofuran (6 ml), then refluxed for 1 h. The mixture was cooled, poured onto ice-water, extracted with ether, washed with 10% sodium chloride solution, dried over anhydrous magnesium sulfate and evaporated to give a colourless oil (620 mg). The ^{1}H n.m.r. spectrum of this oil showed it to be a 1 : 1 mixture of starting material and the acetate (41). Flash chromatography (2% ethyl acetate/light petroleum) afforded the alcohol (285 mg) followed by the corresponding acetate (280 mg) shown to be 96% pure by g.l.c. (15% Carbowax 20M on A.W. DMCS Chromosorb W). Bulb-to-bulb distillation gave pure *1-acetoxy-1-ethenyl-5,5-ethylenedioxy-2ξ-methylcyclohexane* (41) as a colourless oil, b.p. 55–58°/0·1 mm (Found: C, 65·1, H, 8·7. $C_{13}H_{20}O_4$ requires C, 65·0; H, 8·4%). ν_{max} (film) 1738s C=O, 1440w, 1360s, 1265m, 1240s, 1200s, 1150s, 1125w, 1100w, 1060s, 1035w, 1015s, 975m, 955w, 940w, 910m, 805m cm^{-1}. ^{1}H n.m.r. δ (90 MHz, $CDCl_3$) 0·96, d, *J* 7 Hz, Me; 1·21–1·77, m, H6e,8,9,10,10; 2·04, s, OMe; 3·04, dd, *J* 15 Hz, 2 Hz, H6a; 3·88, s, OCH_2CH_2O; 4·88–5·19, m and 5·78–6·19 m, CH_2=CH. Upon irradiation of the signal at δ 3·04, the signals at 1·55 and 1·72, *J* 15 Hz (H6 equatorial) collapsed to a singlet. Separate irradiation of this doublet (centred at 1·63) caused the signals centred at 3·04 (H6 axial) to appear as a singlet. The addition of an equal weight of shift reagent (Eu(fod)$_3$) clearly revealed the doublet due to H6e which originally formed part of the multiplet at δ 1·21–1·77. ^{13}C n.m.r. δ ($CDCl_3$) 14·6, q, Me; 22·1, q, MeCO; 27·9, t, C9; 35·2, t, C10; 37·7, t, C6; 41·3, d, C8; 63·7 and 64·9, t, OCH_2CH_2O; 83·4, s, C7; 108·6, s, C5; 113·0 and 141·3, CH_2=CH; 170·9, s, C=O. Mass spectrum: *m/z* 240 (M, 5%), 181 (23), 141 (18), 99 (100), 86 (24), 55 (35), 43 (45).

(ii) *By acetolysis of the Grignard complex (38b) prepared from the keto acetal (39).*—To a stirred solution of 8-methyl-1,4-dioxaspiro[4,5]decan-7-one (39) (5·0 g, 0·029) in sodium dried ether (100 ml) at −20° was added dropwise a solution of vinylmagnesium bromide (3×10^{-2} mol) under an atmosphere of nitrogen. The reaction mixture was kept at −20° for 20 min, then allowed to warm to −5° and kept at this temperature for 3·5 h. A mixture of 4-dimethylaminopyridine (1·0 g) and acetic anhydride (20 ml), which had been stirred at room temperature for 30 min, was added to the solution under an atmosphere of nitrogen; stirring was continued for a further 14 h at room temperature. Ice-water (30 ml) was added and the mixture was extracted with ether, washed with water, dried (Na_2SO_4) and evaporated under reduced pressure to give the crude allylic acetate (5·3 g). Flash chromatography (2% ethyl acetate/light petroleum) gave first the tertiary alcohol (38a) (1·42 g), followed by the pure allylic acetate (41) (4·65 g, 67%). The spectral data were identical with those reported above.

(iii) A solution of the alcohol (38a) (250 mg) in dichloromethane (15 ml) was treated at 26° with triethylamine (1·0 ml), acetic anhydride (0·32 ml) and 4-dimethylaminopyridine (100 mg) and kept at 25° for 12 weeks. The mixture was poured onto ice-water then washed successively with 5% sodium bicarbonate solution, water (×3), dried over anhydrous magnesium sulfate and evaporated to give a colourless oil (240 mg). This was shown by ^{1}H n.m.r. spectroscopy and g.l.c. (15% Carbowax 20M on A.W. DMCS Chromosorb W) to be a 95 : 5 mixture of starting material (38a) and the acetate (41).

(*k*) *Attempted Reaction of the Bicyclic β-Keto Ester (21a) with the Allylic Acetate (41) in the Presence of Palladium Catalysts*

(i) According to the procedure of Trost and Verhoeven[19] a mixture of 1-acetoxy-1-ethenyl-5,5-ethylenedioxy-2ξ-methylcyclohexane (41) (220 mg, 0·92 mmol), triphenylphosphine (24 mg, 0·092 mmol) and tetrakis(triphenylphosphine)palladium (74 mg, 0·06 mmol) was stirred in dry tetrahydrofuran (1·0 ml) under nitrogen for 1·5 h. In a separate flask the bicyclic β-keto ester (21a) (258 mg, 0·92 mmol) was slowly added to a slurry of sodium hydride (28 mg, of an 80% suspension in oil, 0·92 mmol) in dry tetrahydrofuran (3 ml) and stirred for 20 min. The resulting clear solution of the enolate (42) was added in one portion to the first solution and the combined mixture was heated at reflux for 12 h. The mixture was cooled, diluted with ether and water, and the aqueous phase was extracted with ether (3 × 40 ml). Evaporation of the dried ($MgSO_4$) extract gave a yellow oil (430 mg). Preparative t.l.c. (silica gel, 10% ethyl acetate/light petroleum) gave the β-keto ester

(21a) (248 mg) and 1-ethenyl-3,3-ethylenedioxy-6-methylcyclohex-1-ene (43) (106 mg, 64%), as a colourless oil. This was identical (i.r. and ^{1}H n.m.r. spectra) with material prepared previously by another route.[2]

(ii) According to the procedure of Fiaud and Malleron[21] a mixture of the allylic acetate (41) (130 mg, 0·54 mmol), 1,2-bis(diphenylphosphino)ethane (diphos) (2 mg, 5·4 μmol) and bis(dibenzylideneacetone)palladium[28] (3 mg, 5·4 μmol) was stirred in dry tetrahydrofuran (3 ml) for 35 min. The anion (42) of the bicyclic β-keto ester (21a) (153 mg, 0·54 mmol) prepared as in (*e*), in tetrahydrofuran (1·8 ml) was added in one portion to the first solution and the mixture was stirred at room temperature for 48 h. T.l.c. (silica gel, 20% ethyl acetate/light petroleum) showed that no reaction had taken place during 48 h. The mixture was warmed to 60° and eventually refluxed for 48 h. After workup as in (i) t.l.c. and ^{1}H n.m.r. indicated both starting materials as the only components.

(*l*) *Pyrolysis of 1-Acetoxy-1-ethenyl-5,5-ethylenedioxy-2ξ-methylcyclohexane (41)*

The allylic acetate (41) (100 mg) was pyrolysed (580°, 0·1 mm, 60°, 20 min) to give a colourless oil which was collected on anhydrous sodium bicarbonate in the trap. The oil was extracted with ether, washed with water, dried (Na_2SO_4), and evaporated. The ^{1}H n.m.r. spectrum of the residual oil (71 mg) showed that it was a mixture of 1-ethenyl-3,3-ethylenedioxy-6-methylcyclohex-1-ene (43)[2] and 2-ethenyl-4,4-ethylenedioxy-1-methylcyclohex-1-ene (44)[2] in the ratio of 7 : 3. Attempts to separate these two isomeric dienes by preparative t.l.c. or by flash chromatography were unsuccessful.

(*m*) *Reactions of 1-Ethenyl-3,3-ethylenedioxy-6-methylcyclohex-1-ene (43) with the Bicyclic β-Keto Ester (21a)*

(i) *In the presence of boron trifluoride etherate.*—A solution of the conjugated diene acetal (43) (170 mg, 0·94 mmol) in dry ether (5 ml) at −78° was treated dropwise with freshly distilled boron trifluoride etherate (0·2 ml). The mixture was stirred for 20 min, then treated with an ethereal solution (3 ml) of the enolate salt (42) prepared by treatment of the β-keto ester (21a) (266 mg, 0·94 mmol) with sodium hydride (46 mg of a 50% suspension in oil). After 2 h the brown mixture was diluted with ether and washed with 2% sodium bicarbonate solution. Evaporation of the washed, dried (Na_2SO_4) extract gave a gum (255 mg). ^{1}H n.m.r. spectroscopy showed the presence of the β-keto ester (21a), but the diene acetal (43) appeared to have polymerized.

(ii) *In the presence of magnesium bromide.*—A solution of magnesium bromide (0·56 mmol) was prepared by the method of Bachmann *et al.*[29]

To a stirred solution of the conjugated diene acetal (43) (100 mg, 0·56 mmol) in benzene (5 ml) at 0° was added dropwise under nitrogen a solution of magnesium bromide (0·56 mmol) in ether. The reaction mixture was kept at 0° for 10 min then treated with a solution of the enolate (42) prepared from the β-keto ester (21a) (156 mg, 0·56 mmol) in benzene (5 ml) and sodium hydride (15 mg, 98% sodium hydride). The resulting mixture was stirred at 0° for 3 h, when t.l.c. and ^{1}H n.m.r. spectroscopy indicated that no reaction had occurred. The ether was distilled from the mixture which was then heated at reflux for a further 3 h. T.l.c. and ^{1}H n.m.r. analysis of a small sample showed that only the starting materials were present. The mixture was concentrated to a volume of 4 ml, dimethyl sulfoxide (4 ml) was added, and the solution was stirred for 10 min, then poured onto iced 2% sodium bicarbonate solution and extracted with ether/benzene. The washed, dried (Na_2SO_4) extract gave an oil, the ^{1}H n.m.r. spectrum of which showed it to be a mixture of the β-keto ester (21a) and the diene acetal (44) formed by isomerization of (43). Flash chromatography (10% ethyl acetate/light petroleum) gave pure 2-ethenyl-4,4-ethylenedioxy-1-methylcyclohex-1-ene (44) as a colourless oil (78 mg), identical (i.r. and ^{1}H n.m.r. spectra) with the material described previously.[2]

(*n*) *Isomerization of 1-Ethenyl-3,3-ethylenedioxy-6-methylcyclohex-1-ene (43) with Magnesium Bromide*

A solution of the conjugated diene acetal (43) (100 mg, 0·56 mmmol) in benzene (4 ml) and dimethyl sulfoxide (4 ml) was treated with a solution of magnesium bromide (0·56 mmol) in ether

[28] Takahashi, Y., Ito, T., Sakai, S., and Ishii, Y., *Chem. Commun.*, 1970, 1065.
[29] Bachmann, W. E., Horwitz, J. P., and Warzynski, R. J., *J. Am. Chem. Soc.*, 1953, **75**, 3268.

(2 ml). The ether was removed by distillation and the remaining solution was refluxed for 1 h then poured into iced 2% sodium bicarbonate solution, extracted with ether/benzene, dried (Na_2SO_4) and evaporated to give a colourless oil (92 mg). Examination of the olefinic and methyl regions of the ^1H n.m.r. spectrum showed that the product was a mixture of 2-ethenyl-4,4-ethylenedioxy-1-methylcyclohex-1-ene (44) and the starting material (43) in the ratio 9 : 1.

Acknowledgment

One of us (G.L.B.) gratefully acknowledges the receipt of a Commonwealth Postgraduate Award.

Manuscript received 28 May 1984