

S_N' Reactions on Some Cyclopentene Derivatives employing Simple Nucleophiles and Organocuprate Reagents

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The cyclopentenyl bromides (1) and (9) react with thiophenoxide ion in S_N' *syn*-fashion with very high selectivity. The bromide (4) reacts with the same nucleophile to give the products of S_N2 and S_N2' *syn*-reactions. The lactones (1), (4), (15), and (16) react with lithium dibutylcuprate in the S_N' *anti*-fashion predominantly, while the esters (9) and (11) react *via* the S_N' *syn*-mode preferentially. Mechanisms are presented to explain the substitution patterns observed for the cuprate reactions.

THE initial experiments designed to investigate the preferred stereochemistry for the S_N2' reaction involved the reaction of piperidine with selected cyclohexenyl benzoates.¹ However, the high selectivity in favour of *syn*-displacements observed in this work should not be regarded as typical for this class of reaction. The cyclohexenyl system appears biased towards an S_N' *syn*-displacement process, perhaps because this mode of reaction minimizes the motion of non-participating atoms and groups.²

Recent results have shown that an S_N' displacement † can display predominantly *syn*- or *anti*-stereochemistry depending on the following factors: (a) the nucleophile involved;³ (b) the nature of the leaving group;⁴ (c) the solvent;³ and (d) the structure of the unsaturated substrate (*e.g.* cyclic or acyclic).

A cyclobutenyl halide appears to possess the same bias as the cyclohexenyl system in undergoing S_N' *syn* reactions preferentially.⁵ Apart from one isolated example,⁶ the cyclopentenyl system has not been studied but it has been suggested on theoretical grounds that the S_N' *anti*-reaction might be preferred.²

Cyclohexenyl epoxides,⁷ esters,⁸ and ethers⁹ have been reacted with alkylcuprate reagents and, in contrast to the reactions involving 'simple' nucleophiles, the S_N' *anti*-pathway is highly favoured. The initial formation of a copper(III) intermediate by an S_N2 process followed by S_Ni' delivery of the alkyl group accounts for the observed stereochemical outcome of this coupling:¹⁰ cyclohexenyl carbamates are exceptional in reacting with lithium dimethylcuprate in S_N' *syn*-fashion exclusively.¹¹

We have examined reactions of the cyclopentenyl halides (1), (4), (9), and (11), the acyloxy-compounds (14) and (16), and the cyclopentenyl epoxide (17) with amines, thiolate ion, and lithium dibutylcuprate.¹²

RESULTS AND DISCUSSION †

Reactions involving Amines and Thiophenolate Ion.—The bromolactone (1) reacted with thiophenoxide ion in

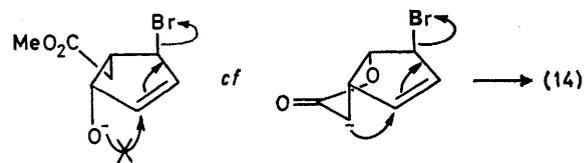
† S_N' will refer to nucleophilic substitutions of unknown kinetic order involving an allylic shift of the double bond; S_Ni' will refer to intramolecular nucleophilic substitutions involving an allylic shift of the double bond.

tetrahydrofuran (thf) to give the products (5), (18), and (20) derived from S_N' *syn* (83%), S_N' *anti* (4%), and S_N2 (3%) reactions, respectively. With diethylamine only the product (6), derived from (1) by an S_N' *syn*-process, was obtained (93% yield). Morpholine behaved in a similar manner with the lactone (1) giving the aminolactone (7) (70%) together with the aminoamide (22) (25%). Clearly the S_N' *syn*-reaction predominates in these cases.

An S_Ni' *anti*-reaction is observed on treatment of the lactone (1) with potassium *t*-butoxide, and the strained tricyclic lactone (14) is produced. Significantly, when a mixture of the bromolactones (1) and (4) was treated with *t*-butoxide, the lactone (14) was formed from both isomers at approximately the same rate, indicating that the S_Ni' reaction involving the lactone (1) is as facile as the S_N2 reaction involving the lactone (4).

Thiophenoxide ion reacted with the bromolactone (4) to give equal quantities of the thiophenoxy lactones (2) and (18) (93%). The S_N2 displacement competes with the S_N' *syn*-reaction in this case. Reaction of the 6-bromolactone (4) with methoxide ion did not afford a significant amount of the epoxyester (17) [in contrast to the same reaction involving the 8-bromolactone (1)¹³] suggesting that it is not easy to perform an S_Ni' *anti*-displacement on a five-membered ring system when the entering moiety is an oxyanion homoallylic to the leaving group (Scheme 1),

The bromobicyclo[3.2.0]heptene (9) gave only the



SCHEME 1

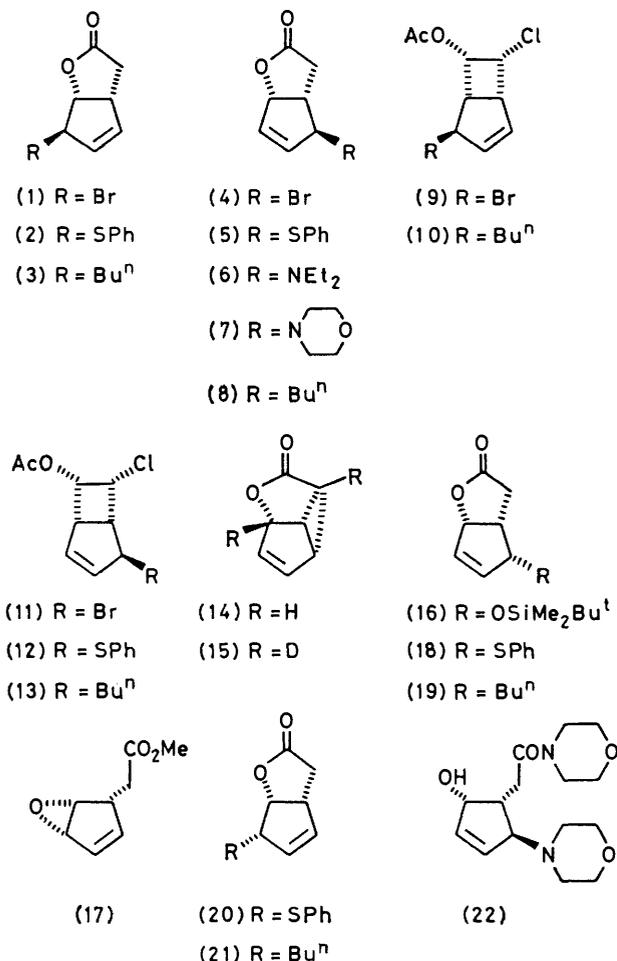
thiophenoxyester (12) (100%) on reaction with thiophenoxide ion.

In summary, the bromo-compounds (1), (4), and (9) undergo S_N' *syn*-reactions with thiolate ion and in the

‡ Reactions described herein were performed on racemates; only one enantiomer is depicted in the diagrams.

case of (1) with amines also. The geometries of the bicyclic molecules (1), (4), and (9) presumably disfavour the S_N' *anti*-reaction. An S_N' *anti*-reaction involving a carbanion derived from the lactone (1) has been observed while an analogous S_N' *anti*-reaction involving an oxyanion seemed less favoured.

Reactions involving Cuprate Reagents.—Lithium dibutylcuprate reacted with the bromolactone (1) to give the butyl-lactones (19) (S_N' *anti*), (21) (S_N2), and (8) (S_N' *syn*) in the ratio 20 : 1 : 2 (54% yield). The relative amounts of the three components was assessed by g.l.c. The major component (19) was identified by n.m.r.



spectroscopy (H-1 and H-6 appear as broadened doublets) and the minor components were identified by comparison of the g.l.c. retention times with those of authentic samples. The modest yield from this reaction is attributable to further modification of the lactone (19) [and probably the lactone (8) also] under the reaction conditions (see below).

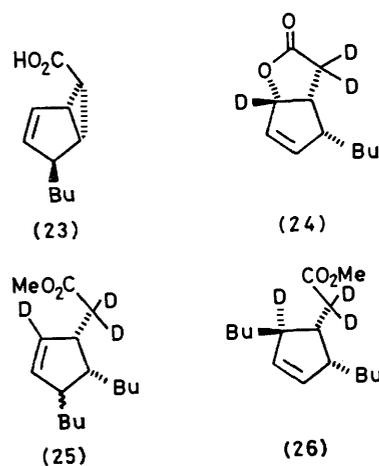
The 6-bromolactone (4) reacted in a complementary fashion with lithium dibutylcuprate furnishing the 8-*endo*-butyl-lactone (21) contaminated with the 6-*endo*- (19) and the 8-*exo*-butyl-lactone (3). G.l.c. analytical data indicated that the ratio of (21) (S_N' *anti*), (19)

(S_N2), and (3) (S_N' *syn*) was 75 : 20 : 5. For the lactone (21) H-1 appeared as a high-field triplet.

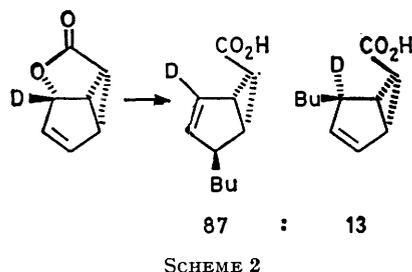
Thus with the lactones (1) and (4) lithium dibutylcuprate predominantly reacted in S_N' *anti*-fashion.

The epoxyester (17) reacted with thiophenoxide ion in the expected fashion to give only the lactone (2) (66%), resulted from an initial S_N2 reaction. Reaction of (17) with lithium dibutylcuprate gave a three-component mixture containing the lactones (8) (S_N' *anti*), (19) (S_N' *syn*), and (3) (S_N2) in the ratio 15 : 1 : 4 (60%). The major component was identical to an authentic sample of the 6-*exo*-butyl-lactone (8) prepared by oxidation of the corresponding lactol.¹⁴ Lithium alkylcyanocuprates have been recommended for alkylation of allyl halides with concomitant double-bond migration.¹⁵ Reaction of the epoxide (17) with lithium butylcyanocuprate gave an increased amount of the S_N' *syn*-product (19) at the expense of the S_N2 product (3) [ratio (8) : (19) : (3) was 15 : 3 : 2 by g.l.c.] but the overall yield of the butyl-lactones was low.

Reaction of the tricyclic lactone (14) with the butylcuprate reagent gave the carboxylic acid (23) (75%).



Preparation and subsequent reaction of the partially deuterated analogue (15) indicated that this reaction took place predominantly *via* the S_N' *anti*-pathway (Scheme 2).¹⁶



Finally, two 6-*endo*-substituted-2-oxabicyclo[3.3.0]oct-7-en-3-ones were subjected to the cuprate reaction. The silyloxylactone (16) has been reported to react with an alkenylcuprate reagent solely by the S_N2 pathway¹⁷ but on treatment with lithium dibutylcuprate followed by

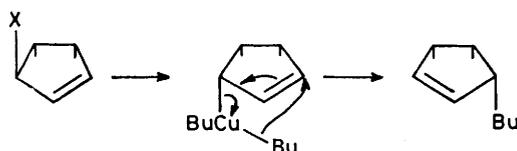
aqueous HF the product (3), derived from an initial S_N' *anti*-reaction, was formed in favour of the product (8), resulting from an initial S_N2 reaction [ratio (3) : (8) was 3 : 2]. The deuteriolactone (24) was obtained (90% pure only) by reaction of the appropriate labelled

We¹² and others¹⁰ have suggested that the product derived from the S_N' *anti*-process is produced by the initial formation of a copper(III) intermediate (Scheme 3) similar to that postulated for the reaction of a simple alkyl halide with a cuprate reagent.¹⁸ The extra length

TABLE 1
Reaction of some cyclopentene derivatives with nucleophiles and a cuprate reagent

Ratio of products derived from reaction of the substrate with thiolate ion-amine				Substrate	Ratio of products derived from reaction of the substrate with lithium dibutylcuprate (LiCuBu ₂)		
Reagent	S_N2	S_N' <i>syn</i>	S_N' <i>anti</i>		S_N2	S_N' <i>syn</i>	S_N' <i>anti</i>
Thiophenoxide	3	93	4	(1)	5	9	86
Morpholine		100		(4)	20	5	75
Diethylamine		100		(17)	18	5	77
Thiophenoxide	50	50		(15)	13		87
Thiophenoxide	100			(16)	42		58
				(24)	56		44
Thiophenoxide		100		(9)		100	
				(11)		100	

bromolactone with lithium dibutylcuprate. Reaction of the lactone (24) with a further quantity of the butylcuprate reagent gave the products (25) and (26) (in the



SCHEME 3

ratio 9 : 11) resulting from S_N' (*syn* and/or *anti*) and S_N2 reactions, respectively.

In short, reaction of the compounds (1), (4), (15), (16), and (17) with lithium dibutylcuprate gave mixtures of compounds in which the product derived from an S_N'

of the copper-carbon bond appears to allow this intermediate to be formed in cases where S_N2 attack by a 'normal' nucleophilic species is not observed. S_N' Alkylation from the copper(III) intermediate completes the overall S_N' *anti*-process.

We reasoned that for the bromochloroheptanes (9) and (11) the acetate group and the chlorine atom should prohibit the initial S_N2 reaction and formation of the copper(III) intermediate, and that a different substitution pattern might result. Indeed the bromochloroacetate (9) reacted smoothly with lithium dibutylcuprate to give the butyl compound (13) (95%); similarly a 1 : 1 mixture of the esters (9) and (11) gave equimolar amounts of the isomers (13) and (10) (96%).¹⁴ Thus the bromochlorobicycloheptanes (9) and (11) react with lithium dibutylcuprate *specifically* in the S_N' *syn*-mode.

TABLE 2

Some details from the n.m.r. spectra of the compounds (1)–(8), (16), and (18)–(21)

Compound	Nature (and position) of substituent on the ring	Chemical shift (δ) [and major coupling constants (Hz)] of selected protons			
		H-1	H-5	H-6	H-8
(1)	Br(8- <i>exo</i>)	5.14 (5)	3.72 ^a		4.96 (<1)
(2)	SPh(8- <i>exo</i>)	5.02 (6)	3.45 ^a		4.37 (<1)
(3)	Bu ⁿ (8- <i>exo</i>)	4.76 (6)	3.50 ^a		(b)
(20)	SPh(8- <i>endo</i>)	5.18 (6,6)	3.50 ^a		4.38 (6)
(21)	Bu ⁿ (8- <i>endo</i>)	4.86 (6,6)	3.37 ^a		2.83 (6)
(4)	Br(6- <i>exo</i>)	5.66 (7)	3.47 (10,7)	4.87 (<1)	
(5)	SPh(6- <i>exo</i>)	5.20 (7)	3.04 (10,7)	4.02 (<1)	
(6)	NEt ₂ (6- <i>exo</i>)	5.54 (6)	b	3.87 (<1)	
(7)	Morpholino(6- <i>exo</i>)	5.52 (6)	3.28 ^a	3.70 (<1)	
(8)	Bu ⁿ (6- <i>exo</i>)	5.53 (6)	b		
(16)	OSiMe ₂ Bu ^t (6- <i>endo</i>)	5.25 (7)	3.30 (10,7,7,7)	4.85 (7)	
(18)	SPh(6- <i>endo</i>)	5.34 (7)	3.40 (10,7,7,7)	4.45 (7)	
(19)	Bu ⁿ (6- <i>endo</i>)	5.34 (7)	3.27 (9,9,7,6)	2.80 (6)	

^a Complex multiplet. ^b Signal hidden in complex multiplet.

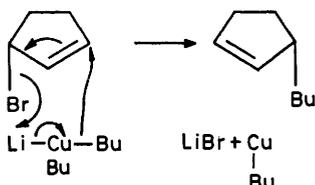
anti-reaction predominated over that from an S_N' *syn*-process by $\geq 4 : 1$. In the case of the compounds (15), (16), and (17) an S_N2 reaction would appear to be sterically unhindered, yet the product derived from the S_N' process is formed preferentially.

We propose that the latter reactions proceed *via* a transition state that does not involve a copper(III) intermediate (Scheme 4).

The contrasting behaviour of cuprate reagents *vis-à-vis* other nucleophiles on reaction with cyclopentene

derivatives possessing a good leaving group at the allylic position is illustrated in Table 1.

Assignment of Structure.—The structures of the compounds (1)—(13), (16), and (18)—(21) were elucidated by inspection of the n.m.r. spectra. The relevant signals from the spectra of compounds (1)—(8) and (16)—(21) are presented in Table 2. From these the following facts emerge: (a) 8-*exo*-substituted-2-oxabicyclo[3.3.0]octan-3-ones have the signal due to (i) H-1 as a broad doublet at high field, (ii) H-5 as a multiplet at low field, and (iii) H-8 as a broad singlet; (b) 8-*endo*-substituted-2-oxabicyclo[3.3.0]octan-3-ones have the signal due to (i) H-1 as a triplet at high field, (ii) H-5 as a multiplet at



SCHEME 4

low field, and (iii) H-8 as a slightly broadened doublet; (c) 6-*exo*-substituted-2-oxabicyclo[3.3.0]octan-3-ones have the signal due to (i) H-1 as a broad doublet at low field, (ii) H-5 as a multiplet at high field, and (iii) H-6 as a broad singlet; (d) 6-*endo*-substituted-2-oxabicyclo[3.3.0]octan-3-ones have the signal due to (i) H-1 as a broad doublet at low field, (ii) H-5 as a multiplet at high field, and (iii) H-6 as a broad doublet. High field and low field refer to the same series of compounds to take into account the anisotropic effects due to the substituent.

The structures of the compounds (9)—(13) were deduced by observation of the small coupling between H-4 and H-5 ($J \leq 2$ Hz), and by double-irradiation techniques.

EXPERIMENTAL

M.p.s were determined by the capillary tube method. The Buchi Kugelrohr (bulb-to-bulb) system was used for distillations and the b.p.s reported are oven temperatures at distillation. I.r. spectra were recorded on a Perkin-Elmer 257 spectrometer for neat films. N.m.r. spectra were recorded on a Varian EM 360 or a Perkin-Elmer R-32 spectrometer (CCl_4 or CDCl_3 solvent). Column chromatography was performed using silica gel M.F.C.; t.l.c. was accomplished using silica gel G (Merck). Anhydrous magnesium sulphate was used as a drying agent for solutions in organic solvents. Light petroleum refers to the fraction boiling at 60–80 °C. The starting materials (1),¹⁹ (4),¹⁹ (9),¹⁴ (11),¹⁴ (16),¹⁷ and (17)¹⁹ were prepared as described previously.

General Procedures.—(a) *Reactions involving thiophenoxide ion.* (i) To the substrate in anhydrous thf was added sodium thiophenoxide (1.2 equiv.) with stirring. After 15 h at room temperature, the mixture was evaporated to dryness and the residue was chromatographed over silica using ethyl acetate in light petroleum.

(ii) As for (i) except that after the reaction period, chloroform was added. Extraction with water, back-extraction of the aqueous phases with chloroform, combin-

ation of the organic extracts gave, after drying and evaporation, a residue which was chromatographed as described above.

(b) *Reactions involving lithium di-*n*-butylcuprate.* (i) Cuprous bromide–dimethyl sulphide complex²⁰ (1.1 equiv.) was dissolved in ether–dimethyl sulphide (ratio 2:1, minimum quantity) under argon at –78 °C. *n*-Butyllithium (2.2 equiv. of a 1.6M solution in hexane) was added with stirring. After 15 min the substrate, dissolved in ether, was added dropwise with stirring. After a given time, saturated aqueous ammonium chloride solution was added. The ether layer was separated and washed with 1M sulphuric acid, saturated aqueous sodium hydrogen carbonate and water. The aqueous washes were combined and back-extracted with ether. The combined ethereal phases were dried and evaporated to leave a residue, which was chromatographed over silica using chloroform or ethyl acetate in light petroleum.

(ii) As for (i) except that the saturated aqueous sodium hydrogencarbonate wash was omitted.

Reaction of 8-*exo*-Bromo-2-oxabicyclo[3.3.0]oct-6-en-3-one (1) with Sodium Thiophenoxide.—Using general procedure (a) (i) was obtained 6-*exo*-thiophenoxy-2-oxabicyclo[3.3.0]oct-7-en-3-one (5) (83%); ν_{max} 1775, 1172 cm^{-1} ; δ 7.26 (5 H, m, Ph), 6.0 (1 H, dd, J 6 and 2 Hz, H-7 or H-8), 5.85 (1 H, dt, J 6 and 1.5 Hz, H-8 or H-7), 5.20 (1 H, dt, J 7 and 1.5 Hz, H-1), 4.02 (1 H, br s, H-6), 3.04 (1 H, m, H-5), 2.70 (1 H, dd, J 16 and 10 Hz, H-4-*exo*), and 2.22 (1 H, dd, J 16 and 6 Hz, H-4-*endo*) (Found: M^+ , 232.055 8. $\text{C}_{13}\text{H}_{12}\text{O}_2\text{S}$ requires M , 232.055 7) 6-*endo*-thiophenoxy-2-oxabicyclo[3.3.0]oct-7-en-3-one (18) (4%); ν_{max} 1775 cm^{-1} ; δ 7.29 (5 H, m, Ph), 6.00 (2 H, m, H-7 and H-8), 5.34 (1 H, d, J 7 Hz, H-1), 4.45 (1 H, d, J 7 Hz, H-6), 3.40 (1 H, m, H-5), 2.86 (1 H, dd, J 17 and 6 Hz, H-4-*endo*), and 2.45 (1 H, dd, J 17 and 10 Hz, H-4-*exo*) (Found: M^+ , 232.055 8. $\text{C}_{13}\text{H}_{12}\text{O}_2\text{S}$ requires M 232.055 7), and 8-*endo*-thiophenoxy-2-oxabicyclo[3.3.0]oct-6-en-3-one (20) (3%), m.p. 79 °C; ν_{max} 1760 cm^{-1} ; δ 7.3 (5 H, m, Ph), 5.75 (2 H, m, H-6 and H-7), 5.18 (1 H, t, J 6 Hz, H-1), 4.38 (1 H, dd, J 6 and 1 Hz, H-8), 3.50 (1 H, m, H-5), 2.77 (1 H, dd, J 18 and 9 Hz, H-4-*exo*), and 2.37 (1 H, dd, J 18 and 4 Hz, H-4-*endo*) (Found: M^+ , 232.055 8. $\text{C}_{13}\text{H}_{12}\text{O}_2\text{S}$ requires M , 232.055 7).

Reaction of 8-*exo*-Bromo-2-oxabicyclo[3.3.0]oct-6-en-3-one with Lithium Di-*n*-butylcuprate.—Using general procedure (b) (i) and a reaction time of 2.5 h, a crude product was obtained (54%) containing 6-*endo*- (19), 8-*endo*- (21), and 6-*exo*-butyl-2-oxabicyclo[3.3.0]octen-3-one (8) in the ratio 20:1:2 (g.l.c. analysis employing a 3% OV-225 column at 120 °C, rising to 220 °C at 4 °C min^{-1}). The lactone (19) was purified by chromatography over silica, b.p. 110 °C at 0.5 mmHg; ν_{max} 1775 cm^{-1} ; δ 5.90 (1 H, dt, J 8.5 and 1 Hz, H-7 or H-8), 5.77 (1 H, dt, J 8.5 and 2 Hz, H-8 or H-7), 5.34 (1 H, dt, J 7 and 1 Hz, H-1), 3.27 (1 H, dddd, J 9, 9, 7, and 6 Hz, H-5), 2.80 (1 H, dm, J 6 Hz, H-6), 2.32 (2 H, m, 2 \times H-4), 1.37 (6 H, m, 3 \times CH_2), and 0.92 (3 H, t, Me) (Found: M^+ , 180.114 4. $\text{C}_{11}\text{H}_{16}\text{O}_2$ requires M , 180.114 9).

6-*exo*-Diethylamino-2-oxabicyclo[3.3.0]oct-7-en-3-one (6).—The lactone (1) (0.2 g) in thf (20 ml) containing diethylamine (0.7 g) was refluxed for 20 h, and the solution was then evaporated. Chloroform (50 ml) was added and the solution was extracted with water (3 \times 20 ml). The combined aqueous extracts were washed with chloroform and the organic fractions were dried and evaporated to

afford the *amine* (6) (0.18 g); ν_{\max} 1 775 cm^{-1} ; δ 6.04 (2 H, m, H-7 and H-8), 5.54 (1 H, dt, J 6 and 1 Hz, H-1), 3.87 (1 H, m, H-6), 3.04—2.0 (7 H, m, 2 \times H-4, H-5, and 2 \times CH₂), and 1.04 (6 H, t, J 7 Hz, 2 \times CH₃) (Found: M^+ , 195.125 8. C₁₁H₁₇NO₂ requires M , 195.125 8).

6-*exo-Morpholino-2-oxabicyclo*[3.3.0]*oct-7-en-3-one* (7).—A solution of the lactone (1) (0.2 g) in morpholine (5 ml) was stirred at room temperature for 30 min. Water and chloroform were added and the separated organic phase was washed with a saturated aqueous solution of sodium chloride, dried, and evaporated to give a semi-solid residue which was chromatographed over silica to give the *amine* (7) (70%), m.p. 98 °C; ν_{\max} 1 770 cm^{-1} ; δ 6.12 (2 H, m, H-7 and H-8), 5.52 (1 H, br d, J 6 Hz, H-1) 3.70 (5 H, m, H-6 and CH₂OCH₂), 3.28 (1 H, m, H-5), and 2.8 (6 H, m, 2 \times H-4 and CH₂NCH₂) (Found: C, 62.9; H, 7.3; N, 6.7. C₁₁H₁₅NO₃ requires C, 63.1; H, 7.2; N, 6.7%), and the *amide* (22) (25%); ν_{\max} 1 625 cm^{-1} (Found: M^+ , 296.173 4. C₁₅H₂₄N₂O₄ requires M^+ , 296.173 5). The amino-lactone (7) prepared in this way was identical (spectroscopically and chromatographically) to a sample prepared by oxidation of the corresponding lactol.¹⁴

Reaction of 6-exo-Bromo-2-oxabicyclo[3.3.0]*oct-7-en-3-one* (4) with *Sodium Thiophenoxide*.—Using general procedure (a) (i) was obtained a 1:1 mixture (93%) of 6-*endo-thiophenoxy-2-oxabicyclo*[3.3.0]*oct-7-en-3-one* (18), identical with the sample prepared as described above, and 8-*exo-thiophenoxy-2-oxabicyclo*[3.3.0]*oct-6-en-3-one* (2); ν_{\max} 1 775 cm^{-1} ; δ 7.33 (5 H, m, Ph), 5.88 (1 H, m, H-6 or H-7), 5.73 (1 H, d, J 6 Hz, H-6 or H-7), 5.02 (1 H, d, J 6 Hz, H-1), 4.37 (1 H, s, H-8), 3.45 (1 H, m, H-5), 2.73 (1 H, dd, J 18 and 10 Hz, H-4-*exo*), and 2.35 (1 H, dd, J 18 and 2 Hz, H-4-*endo*) (Found: M^+ , 232.055 1. C₁₃H₁₂O₂S requires M , 232.055 7).

Reaction of 6-exo-Bromo-2-oxabicyclo[3.3.0]*oct-7-en-3-one* (4) with *Lithium Di-n-butylcuprate*.—Using procedure (b) (i) and a reaction time of 4 h a crude product (50%) was obtained containing 8-*endo-* (21), 6-*endo-* (19), and 8-*exo-butyl-lactone* (3) in the ratio 75:20:5 (g.l.c. analysis). Chromatography over silica provided pure *lactone* (21), b.p. 115 °C at 0.8 mmHg; ν_{\max} 1 780 cm^{-1} ; δ 5.53 (2 H, m, H-6 and H-7), 4.86 (1 H, t, J 6 Hz, H-1), 3.37 (1 H, m, H-5), 2.83 (1 H, dm, J 6 Hz, H-8), 2.55—2.30 (2 H, m, 2 \times H-4), 1.7—1.1 (6 H, m, 3 \times CH₂), and 0.93 (3 H, br t, Me) (Found: M^+ , 180.114 9. C₁₁H₁₆O₂ requires M , 180.114 9).

Reaction of Methyl cis-3,4-Epoxy-cyclopent-2-en-1-ylacetate (17) with *Sodium Thiophenoxide*.—Using procedure (a) (ii) the 8-*exo-thiophenoxy-lactone* (2) (66%) was obtained, identical (n.m.r., t.l.c.) to the sample described above.

Reaction of Methyl cis-3,4-Epoxy-cyclopent-2-en-1-ylacetate (17) with *Lithium Di-n-butylcuprate*.—Using procedure (b) (i) and a reaction time of 3.5 h a crude product (60%) was obtained containing 6-*exo-* (8), 6-*endo-* (19), and 8-*exo-butyl-lactone* (3) in the ratio 15:1:4 (g.l.c. analysis). The major component was purified by chromatography over silica to give the *lactone* (8); ν_{\max} 1 770 cm^{-1} ; δ 5.95 (1 H, dd, J 6 and 1.5 Hz, H-7 or H-8), 5.76 (1 H, dt, J 6 and 1.5 Hz, H-8 or H-7), 5.33 (1 H, dm, J 6 Hz, H-1), 2.8—2.2 (4 H, m, H-5, H-6, and 2 \times H-4), 1.34 (6 H, m, 3 \times CH₂), and 0.90 (3 H, br t, Me) (Found: M^+ , 180.114 9. C₁₁H₁₆O₂ requires M , 180.114 9); identical with a sample obtained on oxidation of the corresponding lactol with Jones reagent.¹⁴

Cuprous cyanide (1.1 equiv.) and *n*-butyl-lithium (1.1 equiv. of a 1.6M solution in hexane) in ether were stirred

for 30 min at -78 °C. The epoxide (17) in ether was added dropwise. After 3 h the reaction was worked-up as described in general procedure (b) (ii) (with omission of the acid wash) to give a crude product containing the lactones (8), (19), and (3) in the ratio 15:3:2 (g.l.c. analysis).

Reaction of 6-endo-(t-Butyldimethylsilyloxy)-2-oxabicyclo[3.3.0]*oct-7-en-3-one* (16) with *Lithium Di-n-butylcuprate*.—Using procedure (b) (ii), a reaction time of 6 h, and allowing the reaction temperature to rise to -20 °C over this period, a crude product was obtained which was treated with acetonitrile containing aqueous HF. Work-up in the usual manner gave an oil (90%) consisting of the lactones (3) and (8) in the ratio 3:2. The analytical data on a purified sample of the lactone (3) were as follows: ν_{\max} 1 780 cm^{-1} ; δ 5.80 (1 H, m, H-6 or H-7), 5.54 (1 H, dm, J 6 Hz, H-6 or H-7), 4.76 (1 H, d, J 6 Hz, H-1), 3.5 (1 H, m, H-5), 3.0—2.6 (2 H, m, H-8 and H-4-*exo*), 2.38 (1 H, dd, J 18 and 2 Hz, H-4-*endo*), 1.34 (6 H, m, 3 \times CH₂), and 0.90 (3 H, br t, Me) (Found: M^+ , 180.114 9. C₁₁H₁₆O₂ requires M , 180.114 9).

Reaction of 6-endo-Butyl-1,4,4-trideuterio-2-oxabicyclo[3.3.0]*oct-7-en-3-one* (24) with *Lithium Di-n-butylcuprate*.—The lactone (24) (90% pure) was treated as described in procedure (b) (ii) allowing the reaction temperature to rise to 0 °C over 5 h. The oil obtained was chromatographed over silica to give a product (66%) which was treated with ethereal diazomethane to give a crude product which was purified to give a mixture of the esters (25) and (26) in the ratio 9:11. The ratio was ascertained by ¹H n.m.r. through inspection of the integration over the vinyl and methyl ester regions.

The same reaction performed on the undeuteriated butyl-lactone (19) gave a product, homogeneous by t.l.c., which gave the following data: Found M^+ , 252.208 8. C₁₆H₂₈O₂ requires M , 252.208 8.

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