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

By **Christopher B. Chapleo, Mark A. W. Finch, Stanley M. Roberts,*** and **Geoffrey T. Woolley,** Department of Chemistry, Salford University, Salford, Lancs. M5 4WT
**Roger F. Newton** * and **David W. Selby,** Chemical Research Department, Glaxo Group Research Ltd., Ware, Herts. SG12 ODJ

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 than 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 ethers [9] 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]

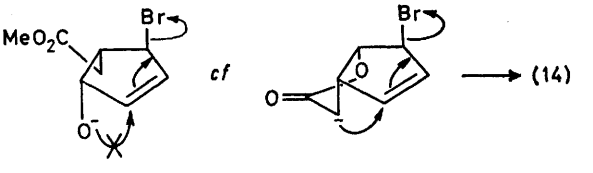
## RESULTS AND DISCUSSION ‡

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

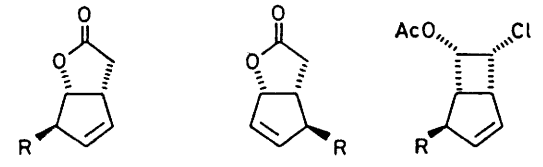
In summary, the bromo-compounds (1), (4), and (9) undergo $S_N'$ *syn*-reactions with thiolate ion and in the

† $S_N'$ 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.

‡ 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 $S_Ni'$ *anti*-reaction involving a carbanion derived from the lactone (1) has been observed while an analogous $S_Ni'$ *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.



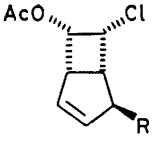
(1) R = Br
(2) R = SPh
(3) R = $Bu^n$



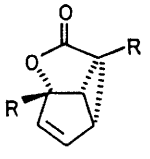
(4) R = Br
(5) R = SPh
(6) R = $NEt_2$
(7) R = N O
(8) R = $Bu^n$



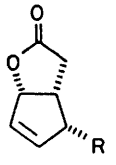
(9) R = Br
(10) R = $Bu^n$



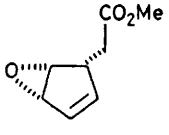
(11) R = Br
(12) R = SPh
(13) R = $Bu^n$



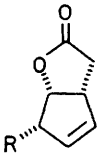
(14) R = H
(15) R = D



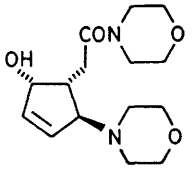
(16) R = $OSiMe_2Bu^t$
(18) R = SPh
(19) R = $Bu^n$



(17)



(20) R = SPh
(21) R = $Bu^n$



(22)

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).

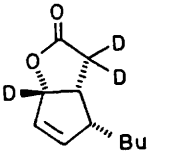
The 6-bromolactone (4) reacted in a complementary fashion with lithium dibutylcuprate furnishing the 8-*endo*-butyl-lactone (21) contaminated with the 6 *endo*-(19) and the 8-*exo*-butyl-lactone (3). G.l.c. analytical data indicated that the ratio of (21) ($S_N'$ *anti*), (19) ($S_N2$), and (3) ($S_N'$ *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.

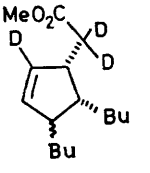
The epoxyester (17) reacted with thiophenoxide ion in the expected fashion to give only the lactone (2) (66%), resulted from an initial $S_N2$ reaction. Reaction of (17) with lithium dibutylcuprate gave a three-component mixture containing the lactones (8) ($S_N'$ *anti*), (19) ($S_N'$ *syn*), and (3) ($S_N2$) 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%).

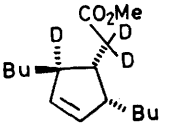
(23)



(24)

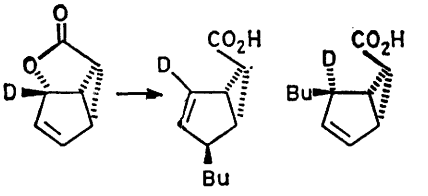


(25)



(26)

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

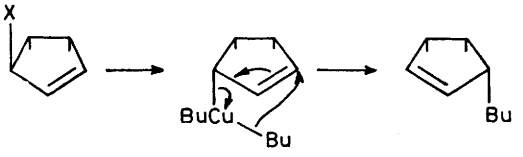


87 : 13

SCHEME 2

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 $S_N2$ pathway [17] 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 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 ratio 9 : 11) resulting from $S_N'$ (*syn* and/or *anti*) and $S_N2$ reactions, respectively.




SCHEME 3

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 $S_N'$ *anti*-reaction predominated over that from an $S_N'$ *syn*-process by $\geqslant 4 : 1$. 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 [12] and others [10] 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 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. $S_Ni'$ 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. 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

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 | $S_N2$ | $S_N'$ *syn* | $S_N'$ *anti* | | $S_N2$ | $S_N'$ *syn* | $S_N'$ *anti* |
| Thiophenoxide | 3 | 93 | 4 | | | | |
| Morpholine | | 100 | | (1) | 5 | 9 | 86 |
| Diethylamine | | 100 | | | | | |
| Thiophenoxide | 50 | 50 | | (4) | 20 | 5 | 75 |
| Thiophenoxide | 100 | | | (17) | 18 | 5 | 77 |
| | | | | (15) | 13 | | 87 |
| | | | | (16) | 42 | | 58 |
| | | | | (24) | 56 | | 44 |
| Thiophenoxide | | 100 | | (9) | | 100 | |
| | | | | (11) | | 100 | |

TABLE 2

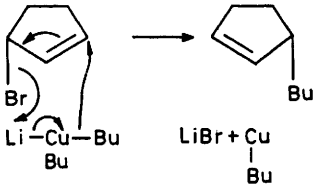
Some details from the n.m.r. spectra of the compounds (1)—(8), (16), and (18)—(21)

| 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-*exo*) | 5.14 (5) | 3.72 [a] | | 4.96 (<1) |
| (2) | SPh(8-*exo*) | 5.02 (6) | 3.45 [a] | | 4.37 (<1) |
| (3) | $Bu^n$(8-*exo*) | 4.76 (6) | 3.50 [a] | | (*b*) |
| (20) | SPh(8-*endo*) | 5.18 (6,6) | 3.50 [a] | | 4.38 (6) |
| (21) | $Bu^n$(8-*endo*) | 4.86 (6,6) | 3.37 [a] | | 2.83 (6) |
| (4) | Br(6-*exo*) | 5.66 (7) | 3.47 (10,7) | 4.87 (<1) | |
| (5) | SPh(6-*exo*) | 5.20 (7) | 3.04 (10,7) | 4.02 (<1) | |
| (6) | $NEt_2$(6-*exo*) | 5.54 (6) | *b* | 3.87 (<1) | |
| (7) | Morpholino(6-*exo*) | 5.52 (6) | 3.28 [a] | 3.70 (<1) | |
| (8) | $Bu^n$(6-*exo*) | 5.53 (6) | *b* | *b* | |
| (16) | $OSiMe_2Bu^t$(6-*endo*) | 5.25 (7) | 3.30 (10,7,7,7) | 4.85 (7) | |
| (18) | SPh(6-*endo*) | 5.34 (7) | 3.40 (10,7,7,7) | 4.45 (7) | |
| (19) | $Bu^n$(6-*endo*) | 5.34 (7) | 3.27 (9,9,7,6) | 2.80 (6) | |

[a] Complex multiplet. [b] Signal hidden in complex multiplet.

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 ($J \leqslant 2$ 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, combination 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 complex [20] (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 hydrogencarbonate 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%); $\nu_{max.}$ 1 775, 1 172 $cm^{-1}$; 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. $C_{13}H_{12}O_2S$ requires *M*, 232.055 7) 6-endo-*thiophenoxy*-2-*oxabicyclo*[3.3.0]*oct*-7-*en*-3-*one* (18) (4%); $\nu_{max.}$ 1 775 $cm^{-1}$; 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. $C_{13}H_{12}O_2S$ requires *M* 232.005 7), and 8-endo-*thiophenoxy*-2-*oxabicyclo*[3.3.0]*oct*-6-*en*-3-*one* (20) (3%), m.p. 79 °C; $\nu_{max.}$ 1 760 $cm^{-1}$; 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. $C_{13}H_{12}O_2S$ 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; $\nu_{max.}$ 1 775 $cm^{-1}$; 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 × H-4), 1.37 (6 H, m, 3 × $CH_2$), and 0.92 (3 H, t, Me) (Found: $M^+$, 180.114 4. $C_{11}H_{16}O_2$ 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 × 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); $\nu_{max.}$ 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 × H-4, H-5, and 2 × $CH_2$), and 1.04 (6 H, t, *J* 7 Hz, 2 × $CH_3$) (Found: $M^+$, 195.125 8. $C_{11}H_{17}NO_2$ 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; $\nu_{max.}$ 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 $CH_2OCH_2$), 3.28 (1 H, m, H-5), and 2.8 (6 H, m, 2 × H-4 and $CH_2NCH_2$) (Found: C, 62.9; H, 7.3; N, 6.7. $C_{11}H_{15}NO_3$ requires C, 63.1; H, 7.2; N, 6.7%), and the *amide* (22) (25%); $\nu_{max.}$ 1 625 $cm^{-1}$ (Found: $M^+$, 296.173 4. $C_{15}H_{24}N_2O_4$ 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); $\nu_{max.}$ 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. $C_{13}H_{12}O_2S$ 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; $\nu_{max.}$ 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 × H-4), 1.7—1.1 (6 H, m, 3 × $CH_2$), and 0.93 (3 H, br t, Me) (Found: $M^+$, 180.114 9. $C_{11}H_{16}O_2$ requires *M*, 180.114 9).

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

*Reaction of Methyl* cis-3,4-*Epoxycyclopent*-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); $\nu_{max.}$ 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 × H-4), 1.34 (6 H, m, 3 × $CH_2$), and 0.90 (3 H, br t, Me) (Found: $M^+$, 180.114 9. $C_{11}H_{16}O_2$ 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: $\nu_{max.}$ 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 × $CH_2$), and 0.90 (3 H, br t, Me) (Found: $M^+$, 180.114 9. $C_{11}H_{16}O_2$ 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. $C_{16}H_{28}O_2$ requires *M*, 252.208 8.

We thank Glaxo Group Research (Ware) and the S.R.C. for support (C.A.S.E. awards to M. A. W. F. and G. T. W.) and the Company for a post-doctoral Fellowship award (to C. B. C.).

[9/1728 *Received*, 29*th October*, 1979]

REFERENCES

[1] G. Stork and W. N. White, *J. Amer. Chem. Soc.*, 1953, **75**, 4119; 1956, **78**, 4609.
[2] E. Toromanoff, *Tetrahedron*, 1978, **34**, 1665.
[3] G. Stork and A. F. Kreft, *J. Amer. Chem. Soc.*, 1977, **99**, 3850, 3851; A. H. Dobbie and K. H. Overton, *J.C.S. Chem. Comm.*, 1977, 722; J. Martel, A. Blade-Font, C. Marie, M. Vivat, E. Toromanoff, and J. Buendia, *Bull. Soc. chim. France* (*II*), 1978, 131.
[4] T. Oritani and K. H. Overton, *J.C.S. Chem. Comm.*, 1978, 454; R. M. Majid and O. S. Fruchey, *J. Amer. Chem. Soc.*, 1979, **101**, 2107.
[5] W. Kirmse, F. Scheidt, and H.-J. Vater, *J. Amer. Chem. Soc.*, 1978, **100**, 3945.
[6] W. F. Johns, *J. Org. Chem.*, 1963, **28**, 161.
[7] J. Staroscik and B. Rickborn, *J. Amer. Chem. Soc.*, 1971, **93**, 3046; D. M. Wieland and C. R. Johnson, *ibid.*, 3047; J. P. Marino and J. S. Farina, *J. Org. Chem.*, 1976, **41**, 3213.
[8] H. L. Goering and V. D. Singleton, *J. Amer. Chem. Soc.*, 1976, **98**, 7854; A. Kreft, *Tetrahedron Letters*, 1977, 1035.
[9] A. Claesson and L.-I. Olsson, *J.C.S. Chem. Comm.*, 1978, 621.
[10] G. Teutsch and A. Betanger, *Tetrahedron Letters*, 1979, 2051.
[11] C. Gallina and P. G. Ciattini, *J. Amer. Chem. Soc.*, 1979, **101**, 1035.
[12] Preliminary communication; C. B. Chapleo, M. A. W. Finch, T. V. Lee, S. M. Roberts, and R. F. Newton, *J.C.S. Chem. Comm.*, 1979, 677.

[13] S. M. Ali, M. A. W. Finch, T. V. Lee, S. M. Roberts, and R. F. Newton, *J.C.S. Chem. Comm.*, 1979, 678.
[14] C. B. Chapleo, S. M. Roberts, and R. F. Newton, *J.C.S. Perkin I*, in the press.
[15] J. P. Marino and D. M. Floyd, *Tetrahedron Letters*, 1979, 675.
[16] S. M. Ali, C. B. Chapelo, R. J. Cave, M. A. W. Finch, S. M. Roberts, G. T. Woolley, and R. F. Newton, *J.C.S. Perkin I*, in the press.
[17] E. J. Corey and J. Mann, *J. Amer. Chem. Soc.*, 1973, **95**, 6832.
[18] G. A. Posner, *Org. Reactions*, 1972, **22**, 253.
[19] C. B. Chapleo, M. A. W. Finch, T. V. Lee, S. M. Roberts, and R. F. Newton, *J.C.S. Perkin I*, in the press.
[20] H. O. House, C. Y. Chu, J. M. Wilkins, and M. J. Uner, *J. Org. Chem.*, 1975, **40**, 1460.