Tetrahedron Vol. 45, No. 2, pp. 455 to 466, 1989
Printed in Great Britain.

0040-4020/89 $3.00+.00

THE SYNTHESIS OF 2,3-DISUBSTITUTED CYCLOPENTENONES USING THE RAMBERG-BÄCKLUND REACTION IN CONJUNCTION WITH ORGANOCOPPER CHEMISTRY

GUY CASY AND RICHARD J.K. TAYLOR*

School of Chemical Sciences, University of East Anglia, Norwich, NR4 7TJ, U.K.

(*Received in USA 24 June* 1988)

Abstract

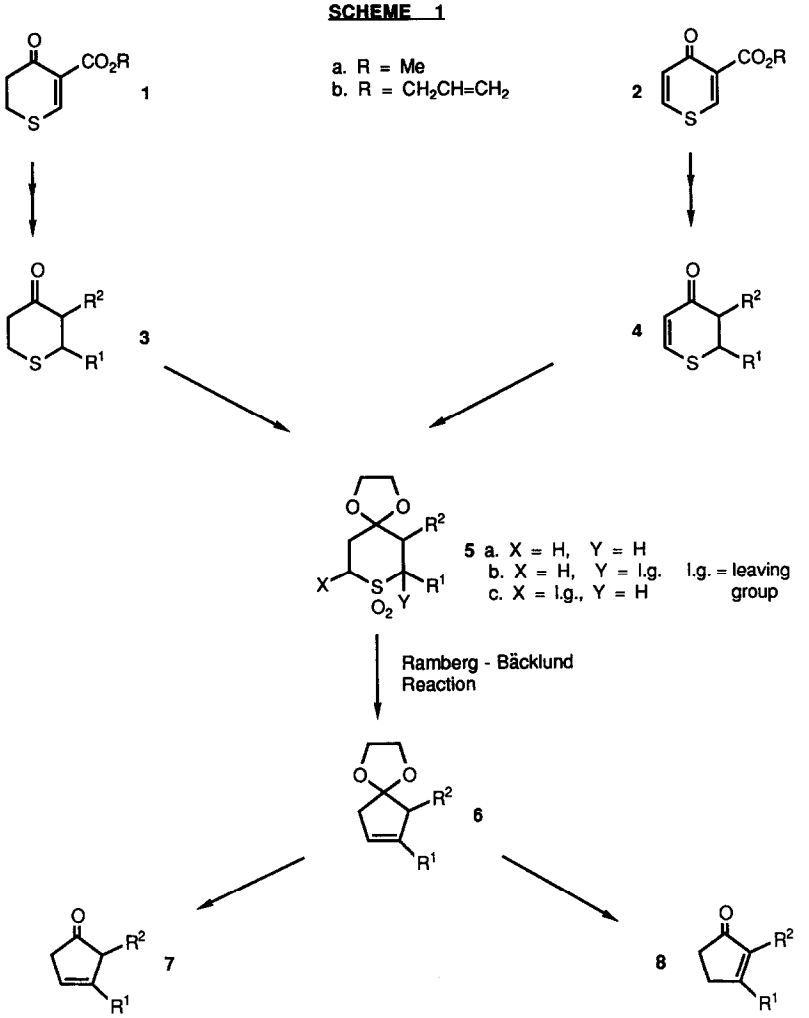
An improved synthetic procedure is described for the preparation of 2,3-dialkylated 2,3-dihydrothiin-4-ones using organocopper chemistry. The utility of these, and the corresponding saturated compounds for the synthesis of Δ^3- and Δ^2-2,3-disubstituted cyclopentenones via the Ramberg-Bäcklund reaction is discussed. The application of this methodology to a formal total synthesis of the antimicrobial natural product tetrahydrodicranenone B is described.

Substituted cyclopentenones are widespread in nature and considerable efforts have been directed towards the development of new synthetic routes for their preparation.[1,2] We required a convergent approach to 2,3-disubstituted cyclopentenones which would provide access to both Δ^3- and Δ^2-isomers.[3] The proposed synthetic routes, outlined in Scheme 1, commence from unsaturated 3-alkoxycarbonylthian-4-ones 1 and 2 and proceed by way of the dialkylated thianones 3 and 4 prepared using the organocopper conjugate addition-enolate alkylation-decarboxyalkylation sequence previously established in these laboratories.[4,5] Functional group manipulation would be used to convert 3 and 4 into sulphones 5 as potential substrates for base-induced Ramberg-Bäcklund ring contraction.[6] The resulting cyclopentenes 6 should be ideal precursors for the target cyclopentenones 7 and 8. Related approaches to cyclopentenones, recently reported by Matsuyama et al.,[7] are limited to monosubstituted derivatives and are complementary in that they rely mainly on carbanion alkylation procedures to introduce the ring substituent.

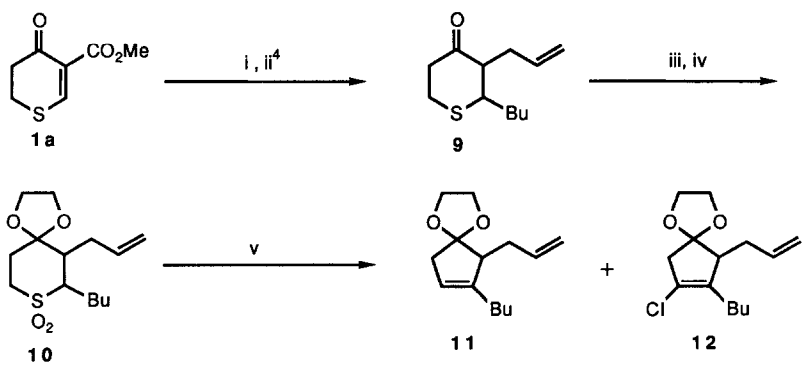
Ramberg-Bäcklund Reaction using Meyers' Conditions

The most straightforward approach appeared to involve the formation of sulphones **5a** and treatment with CCl_4/KOH/^{t}BuOH under Meyers' conditions[8] to effect α-chlorination (to **5b** + 5c) and *in situ* Ramberg-Bäcklund ring contraction. This procedure was investigated on a simple model system (Scheme 2). The requisite sulphone 10 was prepared from the known[4] sulphide 9 [available in

SCHEME 1



SCHEME 2



Reagents:

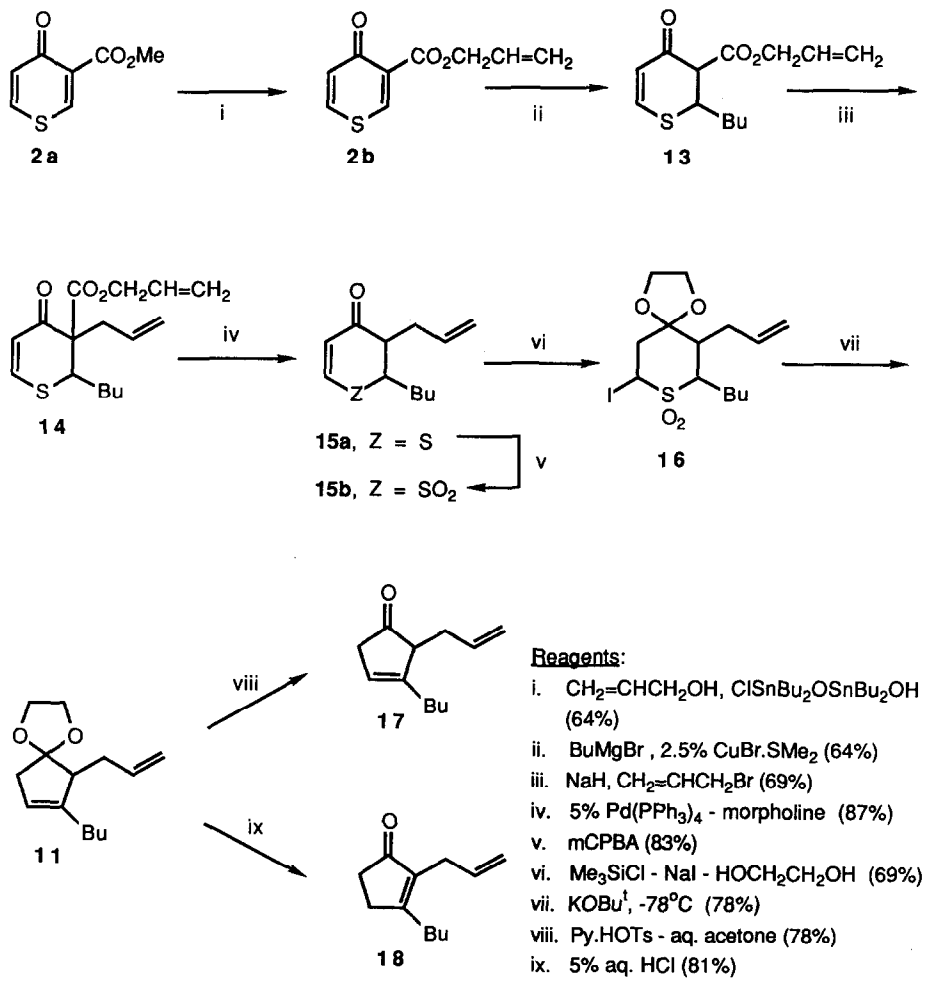
i.[4] $BuCu.SMe_2$ then $CH_2=CHCH_2Br$ (72%)
ii.[4] LiI, aq.DMF (87%)
iii. $HOCH_2CH_2OH$, H^+ (ca.100%)
iv. $NaIO_4$ (71%)
v. KOH, ^tBuOH, CCl_4 (**11**, 23%; **12**, 14%)

three steps from 2,3-dihydro-3-methoxycarbonylthiin-4-one(1a)], by treatment with ethylene glycol and p-toluenesulphonic acid followed by oxidation using sodium periodate. A solution of sulphone 10 in CCl_4-^tBuOH was treated with a large excess of KOH at 50°C, the desired cyclopentene 11 being isolated in 23% yield along with the corresponding vinyl chloride 12 (14%). The formation of vinyl chloride by-products from Ramberg-Bäcklund reactions using Meyers' conditions has been previously reported.[9] In view of the disappointing yields from this reaction we concentrated our efforts on the alternative approach described in the following section. Matsuyama et al.[7] successfully employed Meyers' variant of the Ramberg-Bäcklund reaction for the synthesis of a range of 2-substituted cyclopentenones in moderate to good yields.

Ramberg-Bäcklund Reactions on Preformed α-Halosulphones

Three component coupling sequences can also be employed to prepare 2,3-dialkylated-2,3-dihydrothiin-4-ones (4)[5] which should be ideal precursors for the required α-halosulphones (5c), the Ramberg-Bäcklund leaving group being introduced by a Michael-type process (Scheme 1). Model studies were carried out to investigate this approach as shown in Scheme 3.

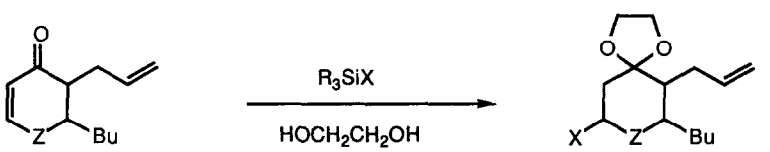
SCHEME 3



The organocopper conjugate addition-enolate alkylation-decarboxymethylation reaction of 3-methoxycarbonylthiin-4-one 2a provides a short route to 2,3-dialkylated-2,3-dihydrothiin-4-ones (4)[5] but the generality of this process is limited by the difficulties often encountered with the decarboxyalkylation reaction. This problem can be overcome by the use of allyl ester 2b, prepared from methyl ester 2a[5,10] by a distannoxane-catalysed transesterification procedure[11] as shown in Scheme 3. All attempts at transesterification using more conventional procedures[12] resulted in failure. Treatment of allyl ester 2b with butylmagnesium bromide in the presence of 2.5% $CuBr.SMe_2$ gave conjugate addition adduct 13 as a mixture of keto and enol tautomers (64%) which was alkylated using NaH/allyl bromide to produce β-keto ester 14 in 69% yield. To complete the sequence the ester group was cleanly removed to give thioenone 15a (87%) in a palladium(0)-catalysed process employing morpholine as the acceptor nucleophile.[13] We have subsequently established that the palladium-catalysed decarboxyallylation process proceeds efficiently with a range of alkylated 3-allyloxycarbonyl-2,3-dihydrothiin-4-ones and thian-4-ones[14] thereby providing a means of overcoming the problems of reproducibility encountered with the corresponding reactions involving decarboxymethylation.[4,5]

Thioenone 15a was readily oxidised to the corresponding sulphone 15b and attention was then turned to the introduction of an α-sulphonyl halide substituent in a Michael-type process. Halosilanes have been employed for halide conjugate addition to simple enones[15] and modifications to this process have been reported which allow direct access to β-halo acetals.[16,17] The latter procedures appeared particularly well-suited to the conversion of enones 15 into Ramberg-Bäcklund precursors (e.g. 16) and they were therefore investigated (Table 1).

TABLE 1



15a, Z = S
15b, Z = SO_2

16

Starting Material	Silyl halide	Solvent	Results
15a	$SiCl_4$	CH_2Cl_2	Recovered 15a
15a	Me_3SiI[a]	CH_3CN	Complex Reaction Mixture
15b	$SiCl_4$	CH_2Cl_2	Recovered 15b
15b	Me_3SiI[a]	CH_3CN	16 (X=I,Z=SO_2) (69%)[b]

[a] Prepared *in situ* from Me_3SiCl/NaI[17] [b] A minor product, believed to be the corresponding β-iodo ketone, was also isolated (7%).

Thioenone 15a failed to react with $(CH_2OH)_2/SiCl_4$[16] and gave a complex mixture of products with $(CH_2OH)_2/Me_3SiCl/NaI$.[17] The corresponding sulphone 15b, which might be expected to be a better Michael-acceptor, also failed to react with $(CH_2OH)_2/SiCl_4$ but gave the required iodo-acetal 16 (69%) on treatment with $(CH_2OH)_2/Me_3SiCl/NaI$.

With α-iodo sulphone 16 in hand, attention was turned to the Ramberg-Bäcklund reaction. Treatment of compound 16 with potassium *t*-butoxide (1.2 equivalents) in THF at -78°C effected ring-contraction to afford the protected

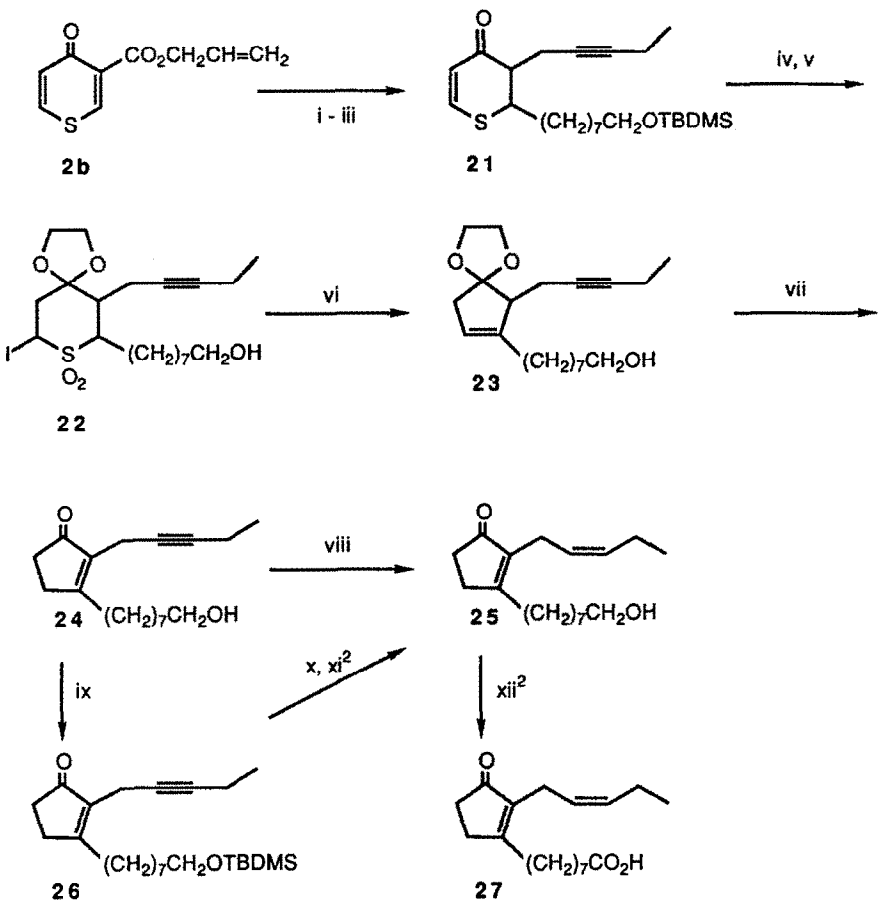
Δ^3-cyclopentenone 11 in 78% yield, identical to the sample obtained from the Meyers' route (Scheme 2), as the sole detectable product. The facile nature of this process is remarkable when contrasted to related processes.[6,7] Hydrolysis of compound 11 using pyridinium p-toluenesulphonate in aq. acetone[18] gave the disubstituted Δ^3-cyclopentenone (17) ($\nu_{max.}$ 1750 cm^{-1}) in 78% yield. Hydrolysis of 11 using dilute hydrochloric acid afforded only the Δ^2-isomer (18) ($\nu_{max.}$ 1702 cm^{-1}) in 81% yield.

Application to the Synthesis of Tetrahydrodicranenone B

The methodology established in model studies was applied to a formal total synthesis of tetrahydrodicranenone B (27), one of a group of antimicrobial natural products isolated from Japanese mosses[19] (Scheme 4).

SCHEME 4

TBDMS = $SiMe_2Bu^t$



Reagents:

i. TBDMSO$(CH_2)_8$MgBr (19), 2.5% CuBr.SMe_2 (60%)
ii. NaH, $CH_3CH_2C{\equiv}CCH_2Br$ (20) (82%)
iii. 5% $Pd(PPh_3)_4$ - morpholine (93%)
iv. mCPBA (83%)
v. Me_3SiI - $HOCH_2CH_2OH$ (65%)
vi. $KOBu^t$-78°C (65%)
vii. 5% aq. HCl (95%)
viii. H_2 - 10% Pd / C (86%: see text)
ix. TBDMSCl, DMAP (87%)
x.[2] H_2 - Pd -$BaSO_4$ (100%)
xi.[2] Aq. AcOH - THF
xii.[2] Pt, O_2 (54%)

The requisite Grignard reagent 19 was readily prepared from 8-bromooctan-1-ol[20] using standard procedures.[21,22] Copper-catalysed conjugate addition of Grignard reagent 19 to 3-allyloxycarbonylthiin-4-one (2b) followed by β-keto ester alkylation using 1-bromopent-2-yne (20)[23] and palladium-catalysed decarboxyallylation gave the dialkylated dihydrothiinone 21 in 46% overall yield. Oxidation to the corresponding sulphone followed by treatment as before with ethylene glycol and iodotrimethylsilane generated *in situ* gave the expected desilylated β-iodo acetal 22 in 32% yield. The use of preformed iodotrimethylsilane in this procedure effected clean iodide addition-acetalisation-desilylation in respectable yield (65%). Ramberg-Bäcklund ring contraction of α-iodosulphone 22 was achieved using potassium t-butoxide (2.05 eq.), cyclopentene 23 being produced in 65% yield as the sole observable product. Treatment of compound 23 with aqueous hydrochloric acid gave Δ^2-cyclopentenone 24 in high yield. Catalytic hydrogenation of compound 24 using Lindlar-type catalysts[24] gave only recovered starting material whereas the use of 10% palladium on carbon gave a mixture (86%) of the required *Z*-alkene 25 contaminated by the corresponding *E*-isomer and over-reduced analogue. This problematic reduction can be avoided by the silylation of compound 24 giving silyl ether 26, which has been reported[2] to undergo smooth, stereoselective hydrogenation, subsequent desilylation giving *Z*-alkene 25 uncontaminated by by-products (Scheme 4). Compounds 25 and 26 were spectroscopically identical to authentic samples which have been converted into tetrahydrodicranenone B (27) by Moody, Roberts and Toczek.[2] The novel chemistry outlined in Scheme 4 therefore represents a formal total synthesis of tetrahydrodicranenone B (27).

In summary, the organocopper conjugate addition-enolate alkylation reaction of 3-allyloxycarbonylthiin-4-one (2b), in conjunction with the Ramberg-Bäcklund reaction, provides an efficient route for the synthesis of Δ^3- and Δ^2-2,3-disubstituted cyclopentenones. We are currently exploring the scope and limitations of this procedure and its utility for the synthesis of more complex natural products. We are also investigating the stereoelectronic requirements[25] of this remarkably facile Ramberg-Bäcklund ring contraction.

Acknowledgements

We are grateful to the S.E.R.C. for the award of a studentship to Guy Casy and to the Royal Society of Chemistry for the award of the Hickinbottom Fellowship to Richard Taylor. We are also grateful to Dr. C.J. Moody for providing n.m.r. spectra of authentic samples for comparison.

EXPERIMENTAL

General directions

Infrared spectra were recorded on a Perkin-Elmer 297 spectrometer as neat liquid films, unless stated otherwise. ^{1}H n.m.r. spectra were recorded on a Jeol PMX 60 spectrometer (60 MHz) unless stated otherwise. 400 MHz ^{1}H-n.m.r. spectra were recorded using a Jeol JNM GX-400 spectrometer. ^{13}C-n.m.r. spectra were recorded on a Jeol FX 100 spectrometer (25.05 MHz). N.m.r. spectra were recorded in $CDCl_3$ solution using tetramethylsilane (or $CHCl_3$ in the case of silicon-containing compounds) as internal standard. Mass spectra were recorded on either a Kratos MS 25 spectrometer (low resolution) or a V.G. Analytical ZAB-IF instrument (high resolution) using chromatographically homogeneous samples.

A normal work-up procedure consisted of three extractions with the

specified solvent, washing of the combined extracts where indicated, drying ($MgSO_4$), and removal of the solvent on a rotary evaporator under reduced pressure. Column chromatography was performed using either Merck 7734 or Merck 15111 silica gel at medium pressure (hand bellows).

Petrol is light petroleum (b.p. 40-60°C) and was distilled before use, ether is diethyl ether. Ether and THF were dried by distillation from Na-benzophenone, tetrachloromethane from P_2O_5, morpholine and tert-butanol from Na, Me_3SiCl from CaH_2 and DMF by storage over CaH_2. The following were obtained from commercial sources and used as received: $CuBr.SMe_2$, Me_3SiI and $^tBuMe_2SiCl$. Pyridinium p-toluenesulphonate[26] and $Pd(PPh_3)_4$[27] were prepared by literature procedures.

3-Allyl-2-butylthian-4-one 1,1-dioxide ethylene acetal (10)

A mixture of 3-allyl-2-butylthian-4-one (9)[4] (500 mg, 2.35 mmol), 1,2-ethane diol (440 mg, 7.05 mmol), p-toluenesulphonic acid (5 mg) and dry benzene (100 ml) was heated under azeotropic reflux (Dean-Stark apparatus) for 5 h, cooled, washed with saturated aqueous sodium hydrogen carbonate, dried, and concentrated under reduced pressure to leave a pale yellow oil (600 mg; recovery consistent with 100% acetalisation). Without further treatment a portion of this material (50 mg, ca. 0.195 mmol) was dissolved in methanol (2 ml). Water (2 ml) and sodium periodate (125 mg, 0.585 mmol) were added to this solution and the mixture was heated at 60°C with stirring for 5 h. After cooling to room temperature, the mixture was filtered, and the filtrate concentrated under reduced pressure to remove methanol. The residual aqueous suspension was subjected to a normal ether work-up. Column chromatography (dichloromethane) gave the title compound (10) as a soapy white solid (40 mg, 71%), m.p. 55-57°C; $\nu_{max.}$(nujol) 3080, 1315, 1125, and 1100 cm^{-1}; δ 6.13-4.85 (3H, m), 4.01 (4H, s), and 3.45-0.67 (17H, m); m/z 288 (M^+) and 99 ($C_5H_7O_2$). (Found: C, 57.9; H, 8.05. $C_{14}H_{24}O_4S$ requires C, 58.30; H, 8.34%).

Ramberg-Bäcklund reaction on sulphone 10 using Meyers' conditions[8]

Powdered potassium hydroxide (2.3 g, 41 mmol) was added in one portion to a stirred solution of 3-allyl-2-butylthian-4-one 1,1-dioxide ethylene acetal (10) (200 mg, 0.69 mmol) in dry tetrachloromethane (25 ml) and dry tert-butanol (10 ml). The mixture was heated at 50°C under nitrogen for 12 h, then cooled to room temperature, washed with 3 portions of water, dried, and concentrated under reduced pressure. Column chromatography (petrol-dichloromethane, 4:1) gave two compounds, which were separately distilled bulb-to-bulb under reduced pressure to give:

2-allyl-3-butyl-3-cyclopenten-1-one ethylene acetal (11) as a colourless oil (35 mg, 23%), b.p. 65-70°C/1.5 mm Hg; $\nu_{max.}$3080, 1640, and 1120 cm^{-1}; δ 6.22-5.51 (1H, m), 5.32 (1H, br t, J 2Hz), 5.26-4.78 (2H, m), 3.90 (4H, s), and 2.74-0.72 (14H, m); δ_c 145.7 (s), 137.3 (d), 119.8 (d), 117.9 (s), 115.3 (t), 64.8 and 63.7 (2 x t), 53.3 (d), 42.4, 32.5, 29.8, 29.2 and 22.5 (5 x t), and 14.0 (q); m/z 222 (7% M^+) and 181 (100%, $M^+-C_3H_5$) (Found: M^+, 222.1617. $C_{14}H_{22}O_2$ requires M^+, 222.1620), and

2-allyl-3-butyl-4-chloro-3-cyclopenten-1-one ethylene acetal (12) as a colourless oil (25 mg, 14%), b.p. 75-90°C/7 mm Hg; $\nu_{max.}$3080 and 1640 cm^{-1}; δ 6.10-5.54 (1H, m), 5.35-4.84 (2H, m), 3.90 (4H, s), and 2.97-0.69 (14H, m); δ_c 138.8 (s), 136.6 (d), 122.4 (s), 115.95 (t), 114.4 (s), 64.9 and 63.8 (2 x t), 53.1 (d), 48.0, 32.2, 29.0, 26.2 and 22.4 (5 x t), and 13.9 (q); m/z 258 [1%; M^+ (^{37}Cl)], 256 [4%, M^+ (^{35}Cl)]. (Found: M^+, 258.1199 and 256.1233. $C_{14}H_{21}ClO_2$ requires M^+, 258.1201 and 256.1230).

3-Allyloxycarbonylthiin-4-one (2b)

Allyl alcohol (6.0 ml, 88 mmol) and 1,1,3,3-tetrabutyl-3-chloro-1-hydroxydistannoxane[28] (94 mg, 0.18 mmol) were added to a solution of 3-methoxycarbonylthiin-4-one (2a)[5] (2.99 g, 17.6 mmol) in dry toluene (100 ml). the mixture was heated under azeotropic reflux (Soxhlet apparatus, 4A molecular sieves) with stirring under nitrogen, for 7 h, cooled to room temperature, and then concentrated under reduced pressure. The semi-solid residue was purified by column chromatography (dichloromethane-ethyl acetate, 3:1) followed by bulb-to-bulb distillation under reduced pressure, to give the title compound (2b) as a viscous colourless oil (2.215 g, 64%), b.p. 150-170°C/0.03 mm Hg; $\nu_{max.}$ 3040, 1735 and 1620 cm^{-1}; δ 8.53 (1H, d, J 4Hz), 7.76 (1H, dd, J 10 and 4Hz), 7.05 (1H, d, J 10Hz), 6.35-5.11 (3H, m), and 4.77 (2H, br d, J 5.5Hz); m/z 139 (34%; $\underline{M}^+$-CH_2=$CHCH_2O$) and 111 (12%; $\underline{M}^+$-CO_2CH_2CH=CH_2). (Found: C, 55.0; H, 4.15. $C_9H_8O_3S$ requires C, 55.09; H, 4.11%).

3-Allyl-2-butyl-6-iodothian-4-one 1,1-dioxide ethylene acetal (16)

Similar experimental procedures to those employed in the dicranenone synthesis described below were employed to convert 3-allyloxycarbonylthiin-4-one (2b) in 5 steps (see Scheme 3) into the title compound (16) obtained as a white solid, m.p. 148-150°C (di-isopropyl ether), $\nu_{max.}$ (CH_2Cl_2) 1325, 1310, and 1130 cm^{-1}; δ (400 MHz) 5.73-5.61 (1H, m), 5.24-5.05 (2H, m), 4.11-3.86 (4H, m), 3.22 (1H, ddd, J 9, 4.3, and 1.6Hz), 2.79 (1H, dt, J 11 and 4.3Hz), 2.67-2.48 (2H, m), 2.12-1.52 (7H, m), 1.38-1.195 (2H, m), and 0.90 (3H, t, J 7.1Hz); δ_c 134.6, 118.3 108.0, 65.8, 64.9, 60.6, 45.7, 45.4, 32.1, 29.5, 25.9, 25.6, 22.8, and 13.9; m/z 287 (16%; $\underline{M}^+$-I) and 195 (100%; $C_{12}H_{19}O_2$). (Found: C,. 40.55; H, 5.5. $C_{14}H_{23}IO_4S$ requires C, 40.59; H, 5.60%).

2-Allyl-3-butyl-3-cyclopenten-1-one ethylene acetal (11) by Ramberg-Bäcklund reaction of iodosulphone (16)

A solution of potassium tert-butoxide (freshly sublimed; 24 mg, 0.21 mmol) in dry THF (2 ml) was added dropwise to a stirred solution of 3-allyl-2-butyl-6-iodothian-4-one 1,1-dioxide ethylene acetal (16) (72.0 mg, 0.174 mmol) in dry THF (5 ml) at -78°C under nitrogen. The resulting orange solution was stirred for 30 min, and then water (20 ml) was added. The mixture was warmed to room temperature, diluted with brine, and subjected to a normal ether work-up incorporating a brine wash. Column chromatography (petrol-ether, 9:1) gave the title compound (11) (30.1 mg, 78%), identical to that prepared from sulphone 10 using Meyers' conditions.

2-Allyl-3-butyl-3-cyclopenten-1-one (17)

A solution of the acetal 11 (25.0 mg, 0.112 mmol) and pyridinium p-toluenesulphonate (8.5 mg, 0.034 mmol) in acetone (8 ml) and water (2 ml) was heated under gentle reflux with stirring, under nitrogen for 18 h, and then concentrated under reduced pressure on a rotary evaporator. The residue was dissolved in ether, washed with saturated aqueous sodium hydrogen carbonate and brine, dried, and then concentrated under reduced pressure (> 12 mm Hg). Examination of the crude product by ^1H n.m.r. and t.l.c. indicated the presence of a small quantity (< 5%) of the Δ^2-isomer 18. Column chromatography (petrol-ether, 19:1) gave the title compound (17) as a colourless oil (15.5 mg, 77%), $\nu_{max.}$ 3080, 1750 and 1645 cm^{-1}; δ 5.90-4.78 (4H, m), 3.02-1.94 (7H, m), and 1.71-0.70 (7H, m); m/z 178 (60%; $\underline{M}^+$), 137 (18%; $\underline{M}^+$-C_3H_5), and 111 (14%; $\underline{M}^+$-C_4H_9). (Found: $\underline{M}^+$, 178.1347. $C_{12}H_{18}O$ requires $\underline{M}^+$, 178.1358.

2-Allyl-3-butyl-2-cyclopenten-1-one (18)
Dilute hydrochloric acid (5%, 0.5 ml) was added to a solution of acetal 11 (6.0 mg, 0.027 mmol) in THF (1 ml). The mixture was stirred at room temperature for 20 h, and then diluted with ether, washed with water and brine, dried, and concentrated under reduced pressure. Column chromatography (petrol-ether, 4:1) gave the title compound (18) as a colourless oil (3.9 mg, 81%); $\nu_{max.}$ 1701 and 1640 cm^{-1}; δ 5.72-4.77 (3H, m), 2.96 (2H, br d, J ca. 3.5Hz), 2.44 (2H, br t, J ca. 7Hz), and 1.96-0.76 (11H, m); m/z 178 (42%; M^+). (Found: M^+, 178.1357. $C_{12}H_{18}O$ requires M^+, 178.1358).

2-(8-tert-Butyldimethylsilyloxyoctyl)-2,3-dihydro-3-(2-pentynyl)-thiin-4-one (21)
(a) A solution of 8-bromo-1-(tert-butyldimethylsilyloxy)octane (readily prepared from 8-bromooctan-1-ol[20] by silylation[21,22]) (7.92 g, 24.5 mmol) in dry THF (20 ml) was added dropwise over 45 min to a stirred suspension of magnesium turnings (0.625 g, 25.7 mmol) in dry THF (40 ml), heated under reflux under nitrogen. Refluxing was continued for 75 min, to obtain a solution of Grignard reagent 19, which was cooled to -78°C, and then a solution of copper(I) bromide-dimethyl sulphide complex (0.125 g, 0.61 mmol) in dry dimethyl sulphide (4 ml) was added. The mixture was stirred for 15 min and a solution of 3-allyloxycarbonylthiin-4-one (2b) (4.00 g, 20.4 mmol) in dry THF (40 ml) was added dropwise over 45 min. Stirring was continued for 1 h and then saturated aqueous ammonium chloride (80 ml) was added. The mixture was warmed to room temperature, filtered through Celite, and subjected to a normal ether work-up incorporating a brine wash. Column chromatography (petrol-ether, 49:1 → 9:1) gave the 3-allyloxycarbonyl-2-(8-tert-butyldimethylsilyloxyoctyl)-2,3-dihydrothiin-4-one as a yellow oil (5.10 g, 57%) as a mixture of keto and enol tautomers (ratio ca. 1:4): $\nu_{max.}$ 1750, 1645, and 1610 cm^{-1}; δ 12.21 (0.8H, s), 7.38 (0.2H, d, J 10Hz), 6.75 (0.8H, dd, J 10 and 2Hz), 6.34-5.64 (1H, m), 6.12 (1H, d, J 10Hz), 5.52-5.12 (2H, m), 4.68 (2H, br d, J 5.5Hz), 4.09-3.35 (3.2H, m), 1.97-1.03 (14H, m), 0.93 (9H, s), and 0.06 (6H, s); m/z 383 (25%; $M^+-C_4H_9$). (Found: $M^+-C_4H_9$, 383.1720. $C_{19}H_{31}O_4SSi$ requires 383.1712.)

In a similar experiment, 2 equivalents of the Grignard reagent were reacted with 3-allyloxycarbonylthiin-4-one (2b) to give the same product in 60% yield.

(b) Granular sodium hydride (0.77 g, 32 mmol) was added to a stirred solution of the above β-keto ester (4.78 g, 10.8 mmol) and 1-bromo-2-pentyne (27) (2.38 g, 16.2 mmol) in dry DMF (75 ml) and dry benzene (25 ml), at 0°C under nitrogen. After 30 min, the cooling bath was removed, and the mixture was stirred at room temperature for 4 h. After cooling to 0°C, water (100 ml) was added to quench the reaction; the mixture was diluted with brine (100 ml) and additional water (100 ml) and then subjected to a normal ether work-up incorporating a brine wash. Column chromatography (petrol-ether, 19:1 → 9:1) gave 3-allyloxycarbonyl 2-(8-tert-butyldimethylsilyloxyoctyl)-2,3-dihydro-3-(2-pentynyl)thiin-4-one as a diastereomeric mixture as a pale yellow oil (4.78 g, 82%); $\nu_{max.}$ 1740 and 1670 cm^{-1}; δ 7.41 (1H, d, J 10Hz), 6.27 (1H, d, J 10Hz), 6.13-5.58 (1H, m), 5.44-5.03 (2H, m), 4.58 (2H, br d, J 5.5Hz), 4.05-3.77 (1H, m), 3.58 (2H, t, J 6Hz), 3.21, 2.89 and 2.61 (2H, ca. 0.8:0.8:0.4, respectively, each t, J 2.5Hz), 2.39-1.02 (19H, m), 0.92 (9H, s) and 0.05 (6H, m); m/e 449 (31%; $M^+-C_4H_9/OCH_2CH{=}CH_2$). (Found: C, 66.35; H, 9.15. $C_{28}H_{46}O_4SSi$ requires C, 66.69; H, 9.39%).

(c) To a stirred solution of the above alkylated β-keto ester (4.42 g, 8.72 mmol) in dry THF (100 ml) at room temperature, under nitrogen, were added successively morpholine (7.6 ml, 8.7 mmol), dropwise, and tetrakis(triphenylphosphine)palladium(0) (0.51 g, 0.44 mmol) in one portion. The mixture was stirred for 1.5 h , then passed through a column of silica gel (Merck 7734; 50 g), eluting with ether (150 ml). The eluate was concentrated under reduced pressure; column chromatography (petrol-ether, 19:1 → 9:1) gave the title compound (21) as a pale yellow oil (3.43 g, 93%); $\nu_{max.}$ 1670 and 1100 cm^{-1}; δ 7.26 (1H, br dd, J 10 and 2Hz), 6.09 (1H, d, J 10Hz), 3.61 (2H, br t, J 6Hz), 3.26-0.99 (23H, m), 0.94 (9H, s), and 0.08 (6H, s); m/z 407 (3%; M^+-CH_3) and 365 (100%; $M^+-C_4H_9$). (Found: C, 68.2; H, 10.0. $C_{24}H_{42}O_2SSi$ requires C, 68.37; H, 9.89%).

2-(8-Hydroxyoctyl)-6-iodo-3-(2-pentynyl)thian-4-one 1,1-dioxide ethylene acetal (22)

(a) mCPBA (80% grade; 1.62 g, 7.5 mmol) was added to a stirred solution of the sulphide 21 (3.16 g, 7.48 mmol) in dry dichloromethane (100 ml) containing suspended anhydrous sodium carbonate (1.59 g, 15 mmol), at -5°C, under nitrogen. After stirring at 0°C for 1 h, a second portion of mCPBA (1.62 g, 7.5 mmol) was added, and the cooling bath was removed. The mixture was stirred at room temperature for 3 h, then diluted with ether, and washed with water, saturated aqueous sodium metabisulphite, saturated aqueous sodium hydrogen carbonate, and brine. The organic solution was dried and concentrated under reduced pressure; column chromatography (petrol-ether, 9:1 → 7:3) gave 2-(8-tert-butyldimethylsilyloxyoctyl)-2,3-dihydro-3-(2-pentynyl)thiin-4-one 1,1-dioxide as a mixture of 2,3-cis- and 2,3-trans-isomers (by n.m.r.) as an oil (2.835 g, 83%); $\nu_{max.}$ 1700, 1325 and 1135 cm^{-1}; δ 7.08 and 7.03 (1H combined, 2 x br d, J 11Hz), 6.32 and 6.26 (1H combined, 2 x br d, J 11Hz), 3.88-1.01 (25H, m), 0.89 (9H, s), and 0.04 (6H, s); m/z 439 (2%; M^+-CH_3) and 397 (52%; $M^+-C_4H_9$). (Found: M^+-CH_3, 439.2315; $M^+-C_4H_9$, 397.1874. $C_{23}H_{39}O_4SSi$ requires 439.2338; $C_{20}H_{33}O_4SSi$ requires 397.1869).

(b) Iodotrimethylsilane (0.43 ml, 3.02 mmol) was added dropwise to a stirred solution of the above enone (0.62 g, 1.36 mmol) in dry acetonitrile (10 ml) at room temperature under nitrogen. The mixture was stirred for 1 h, and then 1,2-ethanediol (0.38 ml, 6.81 mmol) was added dropwise. Stirring was continued for 18 h, then the mixture was diluted with ether and washed with aqueous sodium hydrogen carbonate (3%), aqueous sodium thiosulphate (5%) and brine. The organic solution was dried, and concentrated under reduced pressure; column chromatography (petrol-ethyl acetate., 7:3 → 1:1) gave the title compound (22) as a diastereomeric mixture (n.m.r.) as a viscous pale yellow oil (0.455 g, 65%); $\nu_{max.}$ 3400 br, 1315 and 1130 cm^{-1}; δ (400 MHz) 5.24-5.07 (1H, m), 4.18-3.82 (4H, m), 3.625 and 3.62 (2H, 2 x t, J 6Hz), 2.90-1.19 (23H, m), 0.93 and 0.92 (3H, 2 x t, J 7.3Hz); m/z 512 (2%; M^+), 385 (16%; M^+-I). (Found: M^+, 512.1090. $C_{20}H_{33}IO_5S$ requires M^+, 512.1092). ^{13}C-N.m.r. spectroscopy indicated the presence of 3 diastereoisomers.

In a similar experiment, iodotrimethylsilane was generated in situ (chlorotrimethylsilane-sodium iodide).[17] Title compound (22) was isolated in 32% yield.

3-(8-Hydroxyoctyl)-2-(2-pentynyl)-3-cyclopenten-1-one ethylene acetal (23)
A solution of potassium tert-butoxide (freshly sublimed; 162 mg, 1.44 mmol) in dry THF (3ml) was added dropwise to a stirred solution of the β-iodo acetal 22 (359 mg, 0.701 mmol) in dry THF (10 ml), at -78°C under nitrogen. The mixture was stirred for 1 h, poured onto brine (50 ml) and ice (50 ml), and warmed to room temperature. A normal ether work-up incorporating a brine wash, followed by column chromatography (petrol-ethyl acetate, 3:1) gave the title compound (23) as a colourless oil (145 mg, 65%); $\nu_{max.}$ 3400 br, 1125, and 865 cm^{-1}; δ (400 MHz) 5.38 (1H, br d, J 1.5Hz), 4.06-3.90 (4H, m), 3.63 (2H, t, J ca. 7Hz), 2.61-2.04 (9H, m), 1.60-1.16 (12H, m), and 1.10 (3H, t, J 7Hz) (OH not detected); m/z 320 (13%; M^+) and 253 (100%; M^+-C_5H_7). (Found: M^+, 320.2351. $C_{20}H_{32}O_2$ requires M^+, 320.2351).

3-(8-Hydroxyoctyl)-2-(2-pentynyl)-2-cyclopenten-1-one (24)
A solution of the acetal 23 (10.0 mg, 0.031 mmol) in THF (2 ml) and dilute hydrochloric acid (5%; 1 ml) was stirred at room temperature for 40 h, then diluted with ether and washed with water and brine. The organic solution was dried and concentrated under reduced pressure; column chromatography (petrol-ethyl acetate, 7:3) gave the title compound (24) as a colourless oil (8.2 mg, 95%); $\nu_{max.}$ 3420 br, 1700 and 1640 cm^{-1}; δ (400 MHz) 3.65 (2H, t, J 6.6Hz), 3.02 (2H, br s), 2.59-2.35 (6H, m), 2.12 (2H, tq, J 7.5 and 2.4Hz), 1.74-1.17 (12H, m), and 1.09 (3H, t, J 7.5Hz) (OH not detected); m/z 276 (46%; M^+) and 161 [100%; M^+-$(CH_2)_7OH$]. (Found: M^+, 276.2084. $C_{18}H_{28}H_2$ requires M^+, 276.2089).

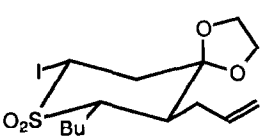
3-(8-Hydroxyoctyl)-2-[(Z)-2-pentenyl]-2-cyclopenten-1-one (25)
A solution of the hydroxy alkyne 24 (25 mg, 0.090 mmol) in ethanol (2 ml), containing palladium on charcoal (10%; 2 mg) was stirred vigorously under hydrogen at atmospheric pressure for 3 h (complete disappearance of 24 indicated by t.l.c. analysis). The mixture was filtered through Celite, washing the filter cake with dichloromethane. The combined filtrate and washings were concentrated under reduced pressure. Column chromatography (petrol-ethyl acetate, 7:3) gave the title compound (25) as a colourless oil (21.5 mg, 86%); $\nu_{max.}$ 3400 br, 1700 and 1630 cm^{-1}. ^{1}H-n.m.r. and mass spectral analysis indicated that the title compound (25) was contaminated by the corresponding (E)-isomer, and 3-(8-hydroxyoctyl)-2-pentyl-2-cyclopenten-1-one (approximate ratio respectively 4:1:1). The 400 MHz n.m.r. spectrum was consistent with that of an authentic sample[2] and the high resolution mass spectrum was in accord with the assigned structure. (Found: M^+, 278.2234. $C_{18}H_{30}O_2$ requires 278.2246.)

3-(8-tert-Butyldimethylsilyloxyoctyl)-2-(2-pentynyl)-2-cyclopenten-1-one (26)
tert-Butylchlorodimethylsilane (11 mg, 0.073 mmol), dry triethylamine (10 μl, 0.072 mmol), and 4-dimethylaminopyridine (1.3 mg, 0.011 mmol) were added to a stirred solution of alkyne 24 (10 mg, 0.036 mmol) in dry dichloromethane (1 ml) at room temperature under nitrogen. The mixture was stirred for 4 h, then diluted with ether, and washed with saturated aqueous ammonium chloride, water, and brine. The organic solution was dried, and concentrated under reduced pressure; column chromatography (petrol-ether, 4:1) gave the title compound (26) as a colourless oil (12.5 mg, 87%), which had spectroscopic properties in accord with those of an authentic sample:[2] $\nu_{max.}$ 2250, 1700, 1645, and 1100 cm^{-1}; δ (400 MHz) 3.60 (2H, t, J 6.7Hz), 3.05 (2H, br s), 2.59-2.34 (6H, m),

2.12 (2H, tq, J 7.6 and 2.4Hz), 1.65-1.24 (12H, m), 1.088 (3H, t, J 7.6Hz), 0.90 (9H, s), and 0.05 (6H, s); m/z 390 (12.3%; M^+), and 333 (66%; M^+-Bu^t). (Found: M^+, 390.2939. $C_{24}H_{42}O_2Si$ requires M^+, 390.2954).

References and notes

1. R.A. Ellison, Synthesis, 1973, 397; J.B. Hendrickson and P.S. Palumbo, J. Org. Chem., 1985, 50, 2110; J. Ollivier and J. Salaun, J. Chem. Soc., Chem. Commun., 1985, 1269.
2. C.J. Moody, S.M. Roberts, and J. Toczek, J. Chem. Soc., Chem. Commun., 1986, 1292.
3. Preliminary communication: G. Casy and R.J.K. Taylor, J. Chem. Soc., Chem. Commun., 1988, 454.
4. S. Lane, S.J. Quick, and R.J.K. Taylor, J. Chem. Soc., Perkin Trans 1, 1985, 893.
5. G. Casy, S. Lane, and R.J.K. Taylor, J. Chem. Soc., Perkin Trans. 1, 1986, 1397.
6. L.A. Paquette, Org. React., 1977, 25, 1, and references therein.
7. H. Matsuyama, Y. Miyazawa, Y. Takei, and M. Kobayashi, J. Org. Chem., 1987, 52, 1703; H. Matsuyama, Y. Miyazawa, and M. Kobayashi, Chem. Lett., 1986, 433; H. Matsuyama, Y. Miyazawa, Y. Tokei, and M. Kobayashi, Chem. Lett., 1984, 833.
8. C.Y. Meyers, A.M. Malte, W.S. Matthews, J. Am. Chem. Soc., 1969, 91, 7510.
9. J. Kattenberg, E.R. de Waard, and H.O. Huisman, Tetrahedron Lett., 1973, 1481.
10. D.S. Tarbell and P. Hoffman, J. Am. Chem. Soc., 1954, 76, 2451; I. Isaka, M. Murakami, T. Ozasa, and Y. Murakami, Jap. P., Japan Kokai, 76,113,873 (Chem. Abstr., 1977, 86, 189719f).
11. J. Otera, T. Yano, A. Kawabata, and H. Nozaki, Tetrahedron Lett., 1986, 27, 2383.
12. D.P. Roelofsen, Chem. Ind. (London), 1966, 1622; C.E. Rehberg, Org. Synth., Coll. Vol. III, 1955, 146; H. Yazawa, K. Tanaka, and K. Kariyone, Tetrahedron Lett., 1974, 3995; O. Meth-Cohn, J. Chem. Soc., Chem. Commun., 1986, 695.
13. H. Kunz and H. Waldmann, Angew. Chem., Int. Ed. Engl., 1984, 23, 71.
14. G. Casy, A.G. Sutherland, and R.J.K. Taylor, Manuscript in preparation.
15. R.D. Miller and D.R. McKean, Tetrahedron Lett., 1979, 2305.
16. G. Gil, Tetrahedron Lett., 1984, 25, 3805.
17. G.L. Larson and R. Klesse, J. Org. Chem., 1985, 50, 3627.
18. R. Sterzycki, Synthesis, 1979, 724.
19. K. Sakai, T. Fujimoto, M. Yamashita, and K. Kondo, Tetrahedron Lett., 1985, 26, 2089, and references therein.
20. B. Maurer and A. Grieder, Helv. Chim. Acta., 1977, 60, 1155.
21. E.J. Corey and A. Venkateswarlu, J. Am. Chem. Soc., 1972, 94, 6190.
22. M. Gill and R.W. Rickards, J. Chem. Soc., Perkin Trans 1, 1981, 599.
23. R. Couffignal, M. Gaudemar, and P. Perriot, Bull. Soc. Chim. France, 1967, 3909.
24. P.N. Rylander, Hydrogenation Methods, Academic Press, London, 1985.
25. Examination of the model Ramberg-Bäcklund precursor 16 by 400MHz ^{1}H-n.m.r. spectroscopy and ^{13}C-n.m.r. spectroscopy indicated that it was predominantly a single diastereomer, probably the all equatorial isomer 16a:



16a

The dicranenone Ramberg-Bäcklund precursor 22, on the other hand, appeared to be a mixture of 3-diastereomers by ^{13}C-n.m.r. spectroscopy. The ease with which both compounds undergo ring-contraction implies that the W-plan arrangement of participating atoms (X-CR_2-SO_2-CR_2-H), which is often a prerequisite for Ramberg-Bäcklund reactions of cyclic substrates,[6] is not essential in these systems. Further work is in progress to confirm this observation and to see whether other halide leaving groups also give facile ring contractions in these systems.
26. M. Mayashita, A. Yoshikoshi, and P.A. Grieco, J. Org. Chem., 1977, 42, 3772.
27. D.R. Coulson, Inorg. Synth., 1972, 13, 121.
28. P.L. Alleston, A.G. Davies, and M. Hancock, J. Chem. Soc., 1964, 5744.