Synthesis of Adamantane Derivatives. Part 53.[1] Simple Synthesis of 7-Thiaprotoadamantane (7-Thiatricyclo[4.3.1.0^{3,8}]decane) and Related Derivatives *via* a Regiospecific and Stereoselective Intramolecular Friedel–Crafts Reaction

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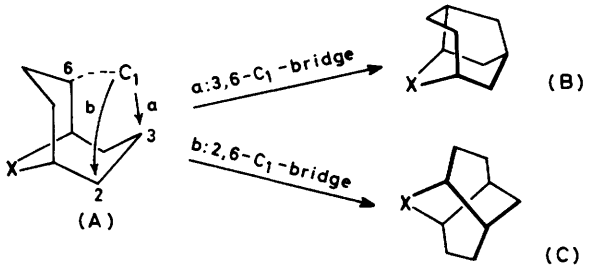
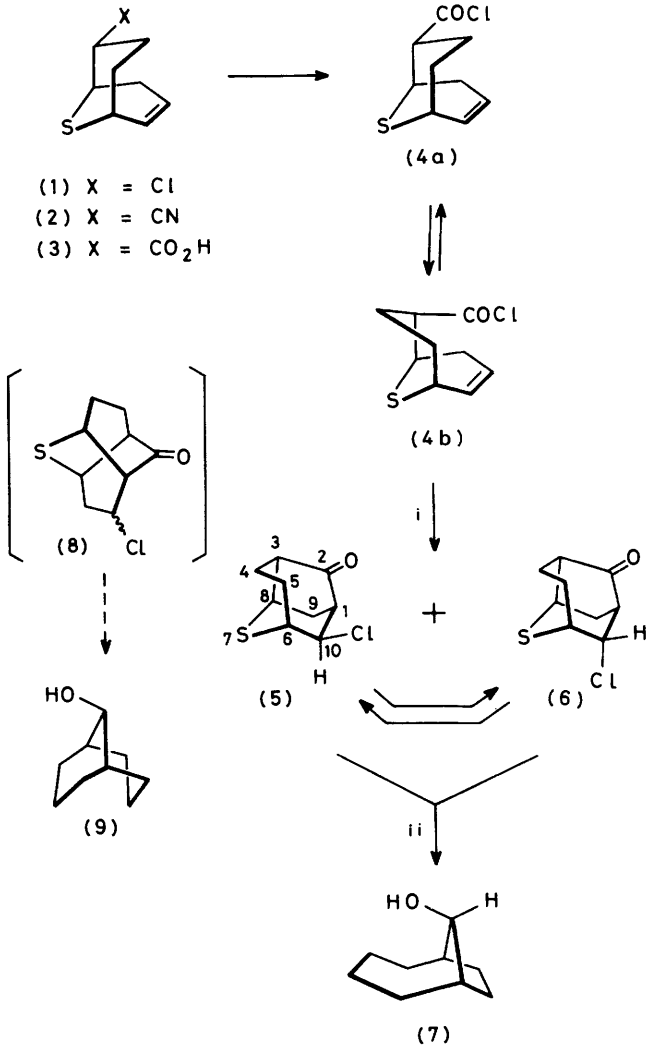
When heated under reflux in carbon tetrachloride in the presence of aluminium chloride, 9-thiabicyclo[3.3.1]-non-2-ene-6-carbonyl chloride (4) gave 10*eq*-chloro- (5) and 10*ax*-chloro-7-thiaprotoadamantan-2-one (6), in a ratio which depended on the conditions. The 10*eq*-chloro-group of (5) was more reactive than the 10-*ax*-chloro-group of (6) in lithium aluminium hydride reduction, alkaline hydrolysis, and azido-substitution reactions. 7-Thiaprotoadamantane (7-thiatricyclo[4.3.1.0^{3,8}]decane) and some related derivatives were prepared.

SINGLE bridging (a or b in A) with a one-carbon unit between the 3- or 2- and 6-positions of the 9-X-bicyclo-[3.3.1]nonane ring system (A) [2,3] provides the 7-X-protoadamantane (7-X-tricyclo[4,3,1,0^{3,8}]decane) (B) or the 2-X-twistane (2-X-tricyclo[4.4.0.0^{3,8}]decane) (C) skeletons. However, the synthesis by this bridging route of these ring systems seems to have received much less attention than syntheses of dihetero-analogues *via* heteroatom bridging [4,5] and syntheses of the adamantane ring *via* 3,7-bridging of the bicyclo[3.3.1]nonane ring system.[6] This might be due to difficulties in a- or b-type bridging of (A) compared with heteroatom bridgings. Recently, however, the synthesis of the carbocyclic protoadamantane skeleton *via* an intramolecular aldol condensation (a route) has been reported by Bishop, Parker, and Stevenson,[7] and the synthesis of the carbocyclic twistanone skeleton *via* route b has been recorded by Hamon and Young.[8] We report here another example of an a bridging route using the 9-thiabicyclo-[3.3.1]nonene system, which involves a Friedel–Crafts reaction.



RESULTS AND DISCUSSION

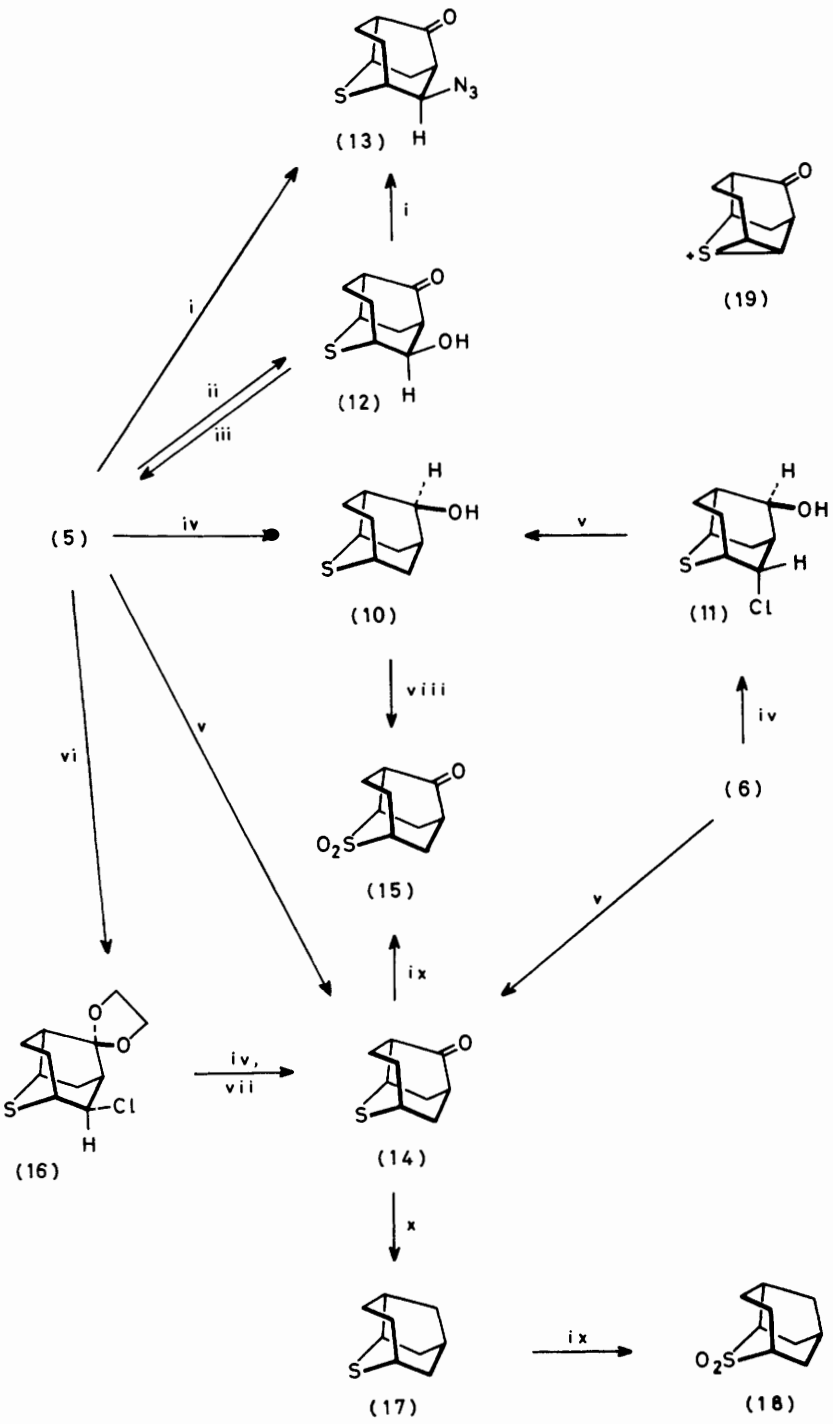
The chloro-9-thiabicyclononene (1), readily obtainable from the sulphur dichloride adduct of cyclo-octa-1,5-diene, was converted into the acid chloride (4) *via* (2) and (3) [9,10] in an overall 83% yield. Compound (4) cyclized when heated in carbon tetrachloride in the presence of aluminium chloride to afford the chloroketones (5) and (6) in a ratio which depended on reaction conditions (Scheme 1 and Table). The data in the Table show clearly that (6) is produced initially by kinetic control but equilibrates slowly with (5) by thermodynamic control. Compounds (5) and (6) isolated by chromatography (silica gel) were also interconvertible to



SCHEME 1 *Reagents*: i, $AlCl_3$, CCl_4; ii, H_2, Raney nickel

give the equilibrium mixture [(5) : (6) = 4 : 1] when heated for 10 days with aluminium chloride (1.24 mol equiv.) in carbon tetrachloride.

Compounds (5) and (6) were characterized as the 10-*eq*-chloro- and 10*ax*-chloro-7-thiaprotoadamantan-2-one, respectively, on the basis of analytical and spectral data. Both compounds showed strong i.r. absorptions assignable to the cyclopentanone moiety, at 1 760 and 1 755 cm^{-1}, respectively. Their ^1H n.m.r. spectra ($CDCl_3$) showed characteristic signals at δ 4.57 (dd, *J* 4.5 and 2.5 Hz, 1 H) and at δ 4.15 (dd, *J* 4.2 and 2.7 Hz, 1 H) assignable to 10*ax*-H of (5) and 10*eq*-H of (6), respectively. The skeletal assignments for (5) and (6) were based on the following chemical conversions. Reductions of (5) and



SCHEME 2 *Reagents*: i, NaN_3, 57% H_2SO_4; ii, 5% aq. $NaHCO_3$; iii, $SOCl_2$; iv, $LiAlH_4$; v, Bu^n_3SnH; vi, H^+, $HOCH_2CH_2OH$; vii, H^+, H_2O; viii, CrO_3, aq. AcOH; ix, *m*-$ClC_6H_4CO_3H$; x, Wolff–Kishner reduction

(6) with Raney nickel (W-5 type) afforded *syn*-9-hydroxybicyclo[4.2.1]nonane (7) [11,12] in 93 and 94% yields, respectively. The identification of (7) was based on its m.p. and ^{1}H n.m.r. data, which are similar to those reported,[11] together with its oxidation to the corresponding

Intramolecular cyclization of (4) [a]

Mol equiv. of $AlCl_3$	Reflux time/h	Ratio of (5) : (6) [b]	Yield (%) [c]	Recovered (4) (%) [c,d]
1.5	200	81 : 19	83.0	Trace
1.0	53	80 : 20	75.8	10.0
0.60	78	47 : 53	66.3	29.2
0.34	144	37 : 63	50.2	37.9
0.10	72	trace : 99	59.2	40.2
0	144		0	97.0

[a] The reactions were carried out for 0.035M solutions of (4) in CCl_4 under N_2. [b] G.l.c. analysis. [c] Isolated yield. [d] As acid (3).

ketone [12] and ^{13}C n.m.r. data.[13] In these catalytic reductions, no trace of 9-hydroxybicyclo[3.3.1]nonane [14] (9), the product expected from the chlorotwistanone structure (8), was detected on g.l.c. analysis with an authentic sample for comparison. These facts supported the above skeletal assignments for (5) and (6). The assignment of the stereochemistry of the 10-chloro-substituents of (5) and (6), based on the chemical shift difference of the 10-H signals (ascribable mainly to the C=O shielding effect on $H_{10\,eq}$),[15] was also corroborated by the unique chemical reactivity of the 10*eq*-chloro-group of (5) as shown in Scheme 2.

On lithium aluminium hydride reduction in ether at room temperature, compound (5) was converted into the *endo*-alcohol (10) in high yield, whereas (6) was transformed quantitatively into the chloro-alcohol (11) under similar conditions, indicating the higher reactivity of the 10*eq*-chloro-substituent of (5). The *endo*-stereochemistry of the 2-hydroxy-group shown in structures (10) and (11) was demonstrated by the ^{1}H n.m.r. signal coupling patterns at δ 4.33 (dd, $J_{2,3}$ 9.1 and $J_{2,1}$ 4.6 Hz) and at δ 4.37 (dd, $J_{2,3}$ 9.4 and $J_{2,1}$ 4.6 Hz) due to 2-H [16] in (10) and (11), respectively, as well as the reduction of (11) to (10) with tri-n-butyltin hydride. Furthermore, the 10*eq*-chloro-group of (5) could be readily replaced by OH on hydrolysis in aqueous sodium hydrogen carbonate–chloroform, and by N_3 on treatment with sodium azide in 57% sulphuric acid–dichloromethane, affording (12) and (13), respectively, in good yields, whereas the 10*ax*-chloro-group of (6) was stable under these conditions. The hydroxy-ketone (12) was reconverted quantitatively into the chloro-ketone (5) with thionyl chloride, supporting the skeletal integrity during the hydrolysis. The azido-ketone (13) was also obtained from (12) in 94% yield by the method previously reported.[17] The observed higher reactivity of (5) than (6) is consonant with the given 10*eq*-chloro-stereochemistry because backside participation of the 7-S atom facilitates substitution *via* an episulphonium ion (19),[18] whereas such participation is impossible for (6) having a 10*ax*-chloro-group.

The parent 7-thiaprotoadamantane (17) and 7-thiaprotoadamantan-2-one (14) were readily obtainable from (5) and (6). Reductions of (5) and (6) with tri-n-butyltin hydride afforded (14) in 25—91% yields after work-up. Oxidation of (14) with *m*-chloroperbenzoic acid gave the corresponding sulphone (15) (53%) which was also obtained from the alcohol (10) by chromic acid oxidation (50%). Compound (14) was also prepared *via* the ethylene acetal (16) from (5) in 36% yield. Wolff–Kishner reduction of (14) afforded 7-thiaprotoadamantane (17) as a readily sublimable colourless solid (87%), m.p. 266—269 °C, which exhibited 9 lines (4d + 5t) for 9 carbon atoms in its ^{13}C n.m.r. spectrum.[13] Oxidation of (17) with *m*-chloroperbenzoic acid gave the corresponding sulphone (18) (Scheme 2).

In summary, the intramolecular cyclization of the acid chloride (4) under Friedel–Crafts conditions, in spite of the requirement for it to adopt a chair–boat conformation, *i.e.* (4b) affords exclusively the less strained chloroprotoadamantanones (5) and (6) *via* a-type (3,6-C_1) bridging. The calculated strain-energy difference between the carbocyclic twistane and protoadamantane is *ca.* 33 kJ/mol [19] and, hence, chloroprotoadamantanone may be less strained than chlorotwistanone. The initial cyclization product (6), a *trans*-addition product of $-CO^+$ and Cl^-, equilibrates slowly *via* (19) to the more stable isomer (5) which has fewer 1,3-repulsions. It should be noted that neighbouring group participation of the S atom may not be involved in a bridged acylium ion intermediate [20] at the initial cyclization stage because intervention of the episulphonium ion (19) should lead to the *cis*-addition product (5) initially. This reaction sequence is rather similar to the π-route cyclization of bicyclo[3.3.1]non-2-ene-7-acylium ion (3,7-C_1 bridging) to 2,4-disubstituted adamantanes; [21] however, the clean cyclization of the present example compared with the monocycloalkenyl-carbonyl chloride [20] demonstrates the practical utility of the intramolecular Friedel–Crafts reaction as a method for 3,6-C_1 bridging of the bicyclo[3.3.1]nonane ring to provide a regiospecifically and stereoselectively functionalized protoadamantane skeleton.

EXPERIMENTAL

M.p.s were taken in a sealed tube on a Yanagimoto micro-melting point apparatus. All pure products were colourless. I.r. spectra were obtained on a Jasco IRA-1 spectrometer. ^{1}H N.m.r. and ^{13}C n.m.r. spectra were recorded on a JEOL JMN-C-60HL instrument at 60 MHz and a JEOL JNM-FX-60 FT spectrometer at 15.04 MHz, respectively. Chemical shifts are reported in p.p.m. (δ) relative to Me_4Si as an internal standard in $CDCl_3$ or CD_3SOCD_3. Mass spectra were obtained with a JEOL JMS-D10 mass spectrometer at 75 eV. Microanalyses were performed with a Perkin-Elmer 240B elemental analyser. G.l.c. analyses were carried out using a JEOL JGC-20K gas chromatograph on 1 or 2 m Silicone SE-30 columns.

9-*Thiabicyclo*[3.3.1]*non*-2-*ene*-6-*carbonitrile* (2).—A mixture of 6-chloro-9-thiabicyclo[3.3.1]non-2-ene (1) [9] (2.17 g, 12.4 mmol), sodium cyanide (650 mg, 13.0 mmol), and 18-crown-6 (1,4,7,10,13,16-hexacyclo-octadecane) (264 mg, 1.00 mmol) in $CHCl_3$ (15 ml) was heated to reflux under

argon for 4 h. The cooled mixture was diluted with water (10 ml) and extracted with chloroform (3 × 20 ml). The combined extracts were washed with water and dried (Na_2SO_4). Removal of the solvent gave the crude nitrile which was recrystallized from methanol to give (2) as colourless crystals (2.00 g, 100%), m.p. 55—58 °C (lit.,[9] m.p. 59—59.5 °C).

9-Thiabicyclo[3.3.1]*non-6-ene-6-carboxylic Acid* (3).—A mixture of the nitrile (2) (16.5 g, 0.10 mol), sodium hydroxide (9.0 g) in water (20 ml), and ethanol (60 ml) was heated under reflux for 15 h. The cooled mixture was concentrated under reduced pressure and diluted with water to dissolve the resulting precipitate. The homogeneous solution was acidified with concentrated hydrochloric acid to afford a colourless precipitate of the crude acid. Two reprecipitations from 10% aqueous sodium hydroxide with concentrated hydrochloric acid gave the acid (3) (15.3 g, 83.0%), m.p. 161—164 °C (lit.,[9] m.p. 157—158 °C).

9-Thiabicyclo[3.3.1]*non-2-ene-6-carbonyl Chloride* (4).—A solution of the acid (3) (1.86 g, 10.1 mmol) in thionyl chloride (5 ml) was heated at reflux for 15 h. Removal of the excess of thionyl chloride under reduced pressure gave the acid chloride (4) as an oil (2.05 g, 100%), $\nu_{max.}$ (film) 1 805 cm^{-1} (C=O).

Intramolecular Friedel–Crafts Cyclization of the Acid Chloride (4). 10-eq-*Chloro-* (5) *and* 10-ax-*Chloro-7-thiaprotoadamantan-2-one* (6).—To a stirred and refluxing solution of (4) (2.05 g, 10.1 mmol) in carbon tetrachloride (250 ml) was added powdered aluminium chloride (2.01 g, 15.1 mmol) under nitrogen and the stirring and heating were continued for 200 h. The cooled mixture was treated with 5% aqueous sodium hydrogen carbonate and dried (Na_2SO_4). Removal of the solvent gave crude product as a brown tar which was purified on a silica gel column (Kieselgel 60; 115 g) with chloroform as eluant to afford a mixture (81 : 19) of (5) and (6) as a solid after treatment with n-hexane (1.70 g, 83.0%). Further purification of the mixture on a silica gel column (Mallinckrodt 100 mesh) with n-hexane–dichloromethane as eluant gave pure (5) (120 mg) and (6) (190 mg). The 10eq-*chloro-compound* (5) had m.p. 208—211 °C (from n-hexane) (Found: C, 53.25; H, 5.55. $C_9H_{11}ClOS$ requires C, 53.3; H, 5.45%), $\nu_{max.}$ (CCl_4) 2 960, 2 870, 1 760, 1 750 (shoulder), 1 450, 1 260, 1 175, 1 155, and 1 125 cm^{-1}; δ_H ($CDCl_3$) 4.57 (dd, *J* 4.5 and 2.2 Hz, 10*ax*-H), 3.6—3.2 (m, 6- and 8-H), 3.0—2.6 (m, 1- and 3-H), and 2.5—1.5 (m, 3 × CH_2); δ_C ($CDCl_3$) 214.0 (s, 1 C, C-2), 60.9 (d, 1 C, C-10), 53.9 (d, 1 C), 45.5 (d, 1 C), 41.1 (t + d, 1 C + 1 C), 37.6 (d, 1 C), 21.2 (t, 1 C), and 19.6 (t, 1 C); *m/z* 204 (M^+ + 2, 40.9%), 203 (M^+ + 1, 5.5), 202 (M^+, 100), 167 (54.1), 139 (86.0), 110 (63.9), 105 (80.3), 99 (62.3), and 97 (60.7). The 10ax-*chloro-compound* (6), had m.p. 203—206 °C (from n-hexane) (Found: C, 53.3; H, 5.5%), $\nu_{max.}$ (CCl_4) 2 950, 2 870, 1 755, 1 450, 1 260, and 1 180 cm^{-1}; δ_H ($CDCl_3$) 4.15 (dd, *J* 4.2 and 2.7 Hz, 10eq-H), 3.6—3.1 (m, 6- and 8-H), 3.0—2.5 (m, 1- and 3-H), and 2.5—1.2 (m, 3 × CH_2); δ_C ($CDCl_3$) 215.9 (s, 1 C, 2-C), 60.2 (d, 1 C, 10-C), 53.5 (d, 1 C), 44.7 (d, 1 C), 44.5 (d, 1 C), 38.3 (d, 1 C), 32.7 (t, 1 C), 27.7 (t, 1 C), and 22.6 (t, 1 C); *m/z* 204 (M^+ + 2, 35.0%), 203 (M^+ + 1, 10.9), 202 (M^+, 91.2), 167 (46.5), 139 (100), 110 (59.6), 105 (69.3), 99 (57.0), and 97 (50.5). For the yields and product ratios under other reaction conditions, see the Table.

Isomerization of (5) *and* (6).—A mixture of the chloro-compound (5) or (6) (35 mg, 0.17 mmol) and aluminium chloride (28 mg, 0.21 mmol) in carbon tetrachloride (5 ml) was heated at reflux for 10 days. The cooled mixture was treated with 5% aqueous sodium hydrogen carbonate and dried (Na_2SO_4). Removal of the solvent and sublimation (140—160 °C at 0.2 mmHg) gave a 78 : 22 mixture of (5) and (6) (8.0 mg, 23.0%), as shown by ^1H n.m.r. analysis.

Raney Nickel Reduction of (5) *and* (6) *to* syn-9-*Hydroxybicyclo*[4.2.1]*nonane* (7).—A mixture of (5) (132 mg, 0.651 mmol) and Raney nickel (W-5 type) (3.4 ml) in ethanol (10 ml) was stirred under hydrogen for 3 days at room temperature. The mixture was filtered through Celite and the filtrate was diluted with water (15 ml) and extracted with dichloromethane (7 × 5 ml). The combined extracts were washed with water and dried (Na_2SO_4). Removal of the solvent gave the crude product which was sublimed (90 °C at 20 mmHg) to afford (7) as a solid (84 mg, 93.0%). Similarly, reduction of (6) (212 mg, 1.05 mmol) under the same conditions afforded the *alcohol* (7) (138 mg, 94.0%). Compound (7) was fully characterized; only its m.p. and ^1H n.m.r. data in carbon disulphide have been reported previously.[11] Compound (7) had m.p. 173—176 °C (lit.,[11] m.p. 176—177 °C) (Found: C, 77.3; H, 11.2. $C_9H_{10}O$ requires C, 77.1; H, 11.5%); $\nu_{max.}$ (CCl_4) 3 640, 3 500, 2 940, 2 870, 1 470, 1 450, 1 095, and 935 cm^{-1}; δ_H ($CDCl_3$) 4.27 (t, *J* 6.7 Hz, 1 H), 2.32br. (s, 2 H), and 2.0—1.2 (m, 13 H, 12 H on shaking with D_2O); δ_C ($CDCl_3$) 78.5 (d, 1 C), 40.1 (d, 2 C), 30.6 (t, 2 C), 28.2 (t, 2 C), and 25.5 (t, 2 C); *m/z* 140 (M^+, 40.3%), 122 (23.1), 94 (29.0), 93 (37.3), 81 (47.1), 80 (100), 79 (43.9), 67 (44.7), 55 (30.6), 43 (21.2), and 39 (19.2).

A mixture of (7) (40 mg, 0.29 mmol) and Jones reagent [22] (0.2 ml) in acetone (5 ml) was stirred at 20—25 °C for 15 h. The acetone solution was decanted from the precipitate, concentrated, and diluted with chloroform (20 ml). The mixture was washed with 5% aqueous sodium hydrogen carbonate and dried (Na_2SO_4). Removal of the solvent gave the crude oxidation product which was sublimed (90—95 °C at 20 mmHg) to afford bicyclo[4.2.1]nonan-9-one (40 mg, 100%), m.p. 107—110 °C (lit.,[12] m.p. 109—111 °C); i.r. and ^1H n.m.r. data were in agreement with those reported; [12] δ_C ($CDCl_3$) 222.4 (s, 1 C), 45.7 (d, 2 C), 30.5 (t, 2 C), 26.6 (t, 2 C), and 24.9 (t, 2 C); *m/z* 138 (M^+, 58.1%), 110 (25.4), 95 (21.3), 93 (21.3), 92 (28.6), 82 (82.4), 81 (49.6), 68 (25.3), 67 (100), 55 (25.2), 54 (58.9), and 39 (26.4).

2-endo-*Hydroxy-7-thiaprotoadamantane* (10).—A mixture of (5) (150 mg, 0.74 mmol) and lithium aluminium hydride (380 mg, 1.00 mmol) in anhydrous ether (30 ml) stirred at room temperature for 20 h and at reflux for 20 min. The cooled mixture was diluted with wet ether and the precipitate was filtered off and washed with ether. The combined filtrate and washings were dried (Na_2SO_4). Removal of the solvent gave the crude product which was sublimed (100 °C at 0.4 mmHg) to afford the *alcohol* (10) (110 mg, 88.0%), m.p. 290—293 °C (Found: C, 63.7; H, 8.1. $C_9H_{14}OS$ requires C, 63.5; H, 8.3%); $\nu_{max.}$ (KBr) 3 350, 2 940, 2 840, 1 450, 1 435, 1 330, 1 310, and 1 090 cm^{-1}; δ_H ($CDCl_3$) 4.33 (dd, *J* 9.2 and 4.5 Hz, 1 H), 3.3—2.9 (m, 2 H), and 2.8—1.6 (m, 11 H, 10 H on shaking with D_2O); δ_C ($CDCl_3$) 77.4 (d, 1 C), 40.7 (d, 1 C), 39.8 (d, 1 C), 38.1 (t, 1 C), 37.8 (d, 1 C), 36.3 (d, 1 C), 35.2 (t, 1 C), 30.5 (t, 1 C), and 20.4 (t, 1 C); *m/z* 170 (M^+, 100%), 142 (56.5), 119 (31.3), 115 (24.1), 113 (37.1), 111 (23.2), 105 (31.3), 100 (23.2), 99 (38.6), 98 (25.5), 97 (51.6), 95 (26.1), 93 (26.1), 92 (32.2), 91 (39.4), 87 (23.2), 85 (23.5), 83 (22.6), 81 (23.8), 79 (47.8), 77 (53.0), 73 (27.0), 67 (45.8), and 65 (31.3).

10ax-*Chloro*-2-endo-*hydroxy-7-thiaprotoadamantane* (11).—A mixture of (6) (116 mg, 0.57 mmol) and lithium alumin-

ium hydride (110 mg, 1.90 mmol) in anhydrous ether (20 ml) was stirred at room temperature for 12 h and at reflux for 10 min. Work-up as in the preceding experiment and chromatography (silica gel; CH_2Cl_2) afforded the *chloro-alcohol* (11) as crystals (116 mg, 100%), m.p. 254—257 °C (Found: C, 52.9; H, 6.3. $C_9H_{13}ClOS$ requires C, 52.8; H, 6.4%); $\nu_{max.}$ (Kbr) 3 440, 2 959, 2 860, 1 450, 1 305, 1 245, and 1 085 cm^{-1}; δ_H ($CDCl_3$) 4.37 (dd, *J* 9.4 and 4.6 Hz, 1 H), 4.45 (dd, *J* 3.8 and 1.8 Hz, 1 H), 3.3—3.0 (m, 2 H), 2.43 (s, 1 H, disappeared on shaking with D_2O), and 2.9—1.5 (m, 9 H); δ_C ($CDCl_3$) 75.7 (d, 1 C), 62.8 (d, 1 C), 48.0 (d, 1 C), 45.5 (d, 1 C), 40.8 (d, 1 C), 36.6 (d, 1 C), 32.7 (t, 1 C), 28.7 (t, 1 C), and 21.1 (t, 1 C); *m/z* 206 ($M^+ + 2$, 45.6%); 205 ($M^+ + 1$, 29.8), 204 (M^+, 100), 185 (27.4), 169 (59.1), 151 (78.6), 150 (30.2), 112 (38.1), 110 (99.8), 105 (32.1), 97 (82.3), 91 (38.1), and 79 (57.7).

Tri-n-butyltin Hydride Reduction of (11) *to* (10).—A mixture of (1) (83 mg, 0.41 mmol), tri-n-butyltin hydride (160 mg, 0.55 mmol) and azobisisobutyronitrile (AIBN) (1 mg) in anhydrous cyclohexane (20 ml) was heated at reflux for 8 h. The cooled mixture was concentrated under reduced pressure, diluted with acetonitrile (20 ml), and washed with n-hexane (2 × 10 ml).[23] Removal of acetonitrile gave the crude product which was purified on a silica gel column with chloroform as eluant to afford (10) [25 mg, 71% based on (11) consumed] and unchanged (11) (40 mg, 48% recovery).

10eq-*Hydroxy*-7-*thiaprotoadamantan*-2-*one* (12).—A mixture of (5) and (6) (48.3 : 51.7; 1.55 g, 7.66 mmol) in chloroform (30 ml) and 5% aqueous sodium hydrogen carbonate (20 ml) was stirred vigorously at 20—25 °C for 10 days. The chloroform layer was separated off and the water layer was extracted with chloroform (5 × 10 ml). The combined chloroform layer and extracts were dried (Na_2SO_4) and concentrated to afford the *hydroxy-ketone* (12) as plates (418 mg). Purification of the mother liquor on a silica gel column with chloroform–methanol as eluant gave unchanged (6) (800 mg, 100% recovery) and (12) (264 mg, total yield = 100%), m.p. 240—243 °C (Found: C, 58.9; H, 6.45. $C_9H_{12}O_2S$ requires C, 58.7; H, 6.6%); $\nu_{max.}$ (KBr) 3 400, 2 950, 2 880, 1 720, 1 455, 1 260, and 1 060 cm^{-1}; δ_H (CD_3SOCD_3) 5.32 (d, *J* 2.9 Hz, 1 H, OH), 3.86 (dd, *J* 3.9 and 2.0 Hz, 1 H), 3.5—2.9 (m, 2 H), and 2.7—1.3 (m, 8 H); δ_C (CD_3SOCD_3) 215.4 (s, 1 C), 69.5 (d, 1 C), 69.4 (d, 1 C), 53.3 (d, 1 C), 44.7 (d, 1 C), 38.6 (t, 1 C), 36.9 (d, 1 C), 19.4 (t, 1 C), and 19.0 (t, 1 C); *m/z* 184 (M^+, 93.0%), 156 (40.8), 128 (43.7), 99 (100), and 95 (40.8).

Reaction of (12) *with Thionyl Chloride*.—A mixture of (12) (212 mg, 1.15 mmol) and thionyl chloride (2 ml) was stirred at 20—25 °C for 22 h. Removal of the excess of thionyl chloride under reduced pressure gave crude product which was sublimed (105 °C at 0.5 mmHg) to afford the chloroketone (5) (233 mg, 100%).

10eq-*Azido*-7-*thiaprotoadamantane*-2-*one* (13).—To a stirred and ice-cooled mixture of (12) (200 mg, 1.09 mmol), 57% (w/v) sulphuric acid (10 ml), and dichloromethane (10 ml) was added, in small portions, solid sodium azide (300 mg, 4.61 mmol).[17] The mixture was stirred for 2 h at room temperature, poured on to ice–water, and extracted with dichloromethane (4 × 10 ml). The combined extracts were washed with 5% aqueous sodium hydrogen carbonate (10 ml) and dried (Na_2SO_4). Removal of the solvent gave an oil which solidified overnight to give the *azide* (13) (214 mg, 94.0%), m.p. 64—66 °C (Found: C, 51.8; H, 5.3; H, 20.4. $C_9H_{11}N_3OS$ requires C, 51.7; H, 5.3; N, 20.1%); $\nu_{max.}$ (KBr) 2 940, 2 880, 2 100, 1 740, 1 440, and 1 260 cm^{-1}; δ_H ($CDCl_3$) 4.09 (dd, *J* 4.7 and 2.6 Hz, 1 H), 3.6—3.1 (m, 2 H), 2.9—2.5 (m, 2 H), 2.5—2.3 (m, 2 H), and 2.1—1.7 (m, 4 H). The reaction of a mixture (51 : 49) of the chlorides (5) and (6) under similar conditions for 1 day at 20—25 °C also gave (13) but only from (5) (70% conversion from g.l.c. analysis); (6) remained unchanged.

7-*Thiaprotoadamantan*-2-*one* (14).—(A) *From* (5) *and* (6). A mixture of (5) and (6) (73 : 27; 2.65 g, 13.1 mmol), tri-n-butyltin hydride (5.30 g, 18.2 mmol), and AIBN (5 mg) in cyclohexane (50 ml) was heated to reflux under argon for 35 h. The cooled mixture was concentrated under reduced pressure and purified on a silica gel column with n-hexane–dichloromethane as eluant to afford the *ketone* (14) as crystals (2.00 g, 91.0%), m.p. 283—286 °C (Found: C, 64.2; H, 7.2. $C_9H_{12}OS$ requires C, 64.25; H, 7.2%); $\nu_{max.}$ (KBr) 2 940, 2 880, 1 735, 1 440, 1 195, and 1 130 cm^{-1}; δ_H ($CDCl_3$) 3.6—3.0 (m, 2 H) and 3.0—1.3 (m, 10 H); δ_C ($CDCl_3$) 219.1 (s, 1 C), 46.0 (d, 1 C), 45.6 (d, 1 C), 38.1 (t + d, 2 C), 36.5 (t, 1 C), 35.1 (d, 1 C), 28.6 (t, 1 C), and 20.1 (t, 1 C); *m/z* 168 (M^+, 100%), 140 (37.1), 99 (52.1), 97 (36.6), 79 (24.8), and 65 (23.9). Similarly, reduction of (5) (210 mg, 1.04 mmol) with tri-n-butyltin hydride (360 mg, 1.24 mmol) in refluxing cyclohexane (10 ml) for 27 h gave (14) (44 mg, 25.0%) after the usual work-up, and reduction of (6) (210 mg, 1.04 mmol) with tri-n-butyltin hydride (360 mg, 1.24 mmol) in refluxing cyclohexane (15 ml) for 40 h gave (14) (68 mg, 39.0%).

(B) *From* (16). A mixture of the acetal (16) (30 mg, 0.12 mmol) (see next experiment) and lithium aluminium hydride (190 mg, 5.0 mmol) in anhydrous ether (20 ml) was stirred for 20 h at room temperature. The mixture was diluted with wet ether and filtered, 5% sulphuric acid (20 ml) was added to the filtrate, and the mixture was stirred for 12 h at room temperature. The organic layer was washed with 5% aqueous sodium hydrogen carbonate and water and dried (Na_2SO_4). Removal of the solvent gave a solid which was sublimed to afford (14) (15 mg, 73%).

10eq-*Chloro*-7-*thiaprotoadamantan* -2-*one Ethylene Acetal* (16).—A mixture of (5) (150 mg, 0.74 mmol), toluene-*p*-sulphonic acid (20 mg) and ethylene glycol (4 ml) in anhydrous benzene (50 ml) was heated under reflux for 25 h. The cooled nixture was diluted with water (10 ml) and the organic layer was washed with water and dried (Na_2SO_4). Removal of the solvent gave an oil which was purified on a silica gel column (CH_2Cl_2) to give the *acetal* (16) as a paste (70 mg, 50%) (Found: C, 53.75; H, 6.35. $C_{11}H_{15}ClO_2S$ requires C, 53.5; H, 6.1%), $\nu_{max.}$ (film) 2 960, 2 890, 1 450, 1 325, 1 110, 1 040, and 950 cm^{-1}; δ_H ($CDCl_3$) 4.39—4.20 (m, 1 H), 4.1—3.8 (m, 4 H), 3.4—3.0 (m, 2 H), and 2.7—1.5 (m, 8 H).

7-*Thiaprotoadamantan*-2-*one* 7,7-*Dioxide* (15).—(A) *From* (14). A mixture of (14) (34 mg, 0.20 mmol) and *m*-chloroperbenzoic acid (*m*-CPBA) (69 mg of 95% purity reagent, 0.40 mmol) in dichloromethane (5 ml) was stirred for 1 day at room temperature. After confirming the disappearance of the peracid (negative starch–iodine paper test), the mixture was washed with 5% aqueous sodium hydrogen carbonate (5 × 10 ml) and dried (Na_2SO_4). Removal of the solvent gave a solid which was recrystallized from n-hexane–dichloromethane to afford the *dioxide* (15) (21 mg, 53%), m.p. >300 °C (Found: C, 54.0; H, 6.0. $C_9H_{12}O_3S$ requires C, 54.0; H, 6.0%); $\nu_{max.}$ (KBr) 2 940, 2 880, 1 750, 1 450, 1 295, 1 120, and 1 040 cm^{-1}; δ_H ($CDCl_3$) 3.8—3.2 (m, 2 H), 3.2—2.8 (m, 2 H), and 2.8—1.5 (m, 8 H); δ_C ($CDCl_3$) 214.4 (s, 1 C), 58.2 (d, 1 C), 53.9 (d, 1 C), 47.0 (d, 1 C), 43.1

(d, 1 C), 33.0 (t, 1 C), 30.6 (t, 1 C), 26.4 (t, 1 C), and 16.8 (t, 1 C); *m/z* 200 (M^+, 9.3%), 178 (37.2), 139 (19.7), 135 (22.0), 107 (54.4), 91 (25.6), 80 (25.8), 79 (100), and 67 (24.4).

7-Thiaprotoadamantane (*7-Thiatricyclo*[4.3.1.$0^{3,8}$]*decane*) (17).—A mixture of (14) (320 mg, 1.90 mmol), hydrazine dihydrochloride (80 mg, 0.76 mmol) and hydrazine hydrate (0.75 ml, 16 mmol) in diethylene glycol (10 ml) was heated under reflux for 3 h. To the cooled mixture was added sodium hydroxide (0.50 g, 13 mmol), excess of hydrazine hydrate was then distilled off, and the remaining mixture was heated under reflux for a further 4 h. The sublimed solid in the condenser was dissolved in ether. The combined ether washings were evaporated to give a solid which was sublimed twice (80—90 °C at 20 mmHg) to afford *7-thiaprotoadamantane* (17) (254 mg, 87.0%), m.p. 266—269 °C (Found: C, 69.95; H, 9.3. $C_9H_{14}S$ requires C, 70.1; H, 9.15%); $\nu_{max.}$ (K Br) 2 940, 2 860, 1 475, 1 450, 1 440, 1 310, 1 280, 1 090, 1 045, 960, 790, and 720 cm^{-1}; δ_H ($CDCl_3$) 3.3—2.8 (m, 2 H) and 2.8—1.5 (m, 12 H); δ_C ($CDCl_3$) 43.5 (t, 1 C), 41.8 (d, 1 C), 41.1 (t, 1 C), 36.2 (t, 1 C), 36.0 (d, 1 C), 35.8 (d, 1 C), 34.9 (d, 1 C), 27.7 (t, 1 C), and 24.8 (t, 1 C); *m/z* 154 (M^+, 100%), 126 (27.2), and 79 (45.8).

7-Thiaprotoadamantan 7,7-Dioxide (18).—A mixture of (17) (30 mg, 0.19 mmol) and *m*-CPBA (165 mg of 85% purity reagent, 0.81 mmol) in dichloromethane (5 ml) was stirred for 5 h at room temperature. The mixture was washed with 10% aqueous sodium hydrogen sulphite until a starch–iodine paper test became negative, and 5% aqueous sodium hydrogen carbonate and water successively, and dried (Na_2SO_4). Removal of the solvent gave a solid which was sublimed (130 °C at 0.5 mmHg) to afford the *sulphone* (18) (31 mg, 86%), m.p. >300 °C (Found: C, 58.3; H, 7.3. $C_9H_{14}O_2S$ requires C, 58.0; H, 7.6%); $\nu_{max.}$ (CCl_4) 2 950, 2 880, 1 310, 1 295, 1 220, 1 120, and 905 cm^{-1}; δ_H ($CDCl_3$) 3.5—3.0 (m, 2 H) and 3.0—1.2 (m, 12 H); δ_C ($CDCl_3$) 61.6 (d, 1 C), 54.4 (d, 1 C), 39.6 (t, 1 C), 37.4 (d, 1 C), 36.0 (t, 1 C), 35.6 (t, 1 C), 33.3 (d, 1 C), 26.4 (t, 1 C), and 21.6 (t, 1 C); *m/z* 186 (M^+, 4.6%), 121 (72.6), 93 (49.3), 81 (36.1), 80 (100), 79 (83.5), 67 (44.2), and 66 (29.2).

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