Tetrahedron Vol 47, No.34, pp 7037-7044, 1991
Printed in Great Britain

0040-4020/91 $3 00+ 00
Pergamon Press plc

SAMARIUM DIIODIDE PROMOTED SPIROLACTONIZATION OF CYCLOALKANONES

RENÉ CSUK*[a], ZHONG HU[a], MOHAMED ABDOU[b], AND CHRISTOPH KRATKY[b]

[a])PHARMAZEUTISCH-CHEMISCHES INSTITUT, UNIVERSITÄT HEIDELBERG, IM NEUENHEIMER FELD 364, D-W6900 HEIDELBERG, F R G [b]) INSTITUT FÜR PHYSIKALISCHE CHEMIE, UNIVERSITÄT GRAZ, HEINRICHSTRASSE 28, A-8010 GRAZ, AUSTRIA

(*Received in Germany* 29 *April* 1991)

Summary- Reaction of cycloalkanones with methyl 3-bromopropionate and SmI_2 afforded formation of spiroanellated γ-lactones, pinacols and unprecedented 3-(1-hydroxycycloalkyl)-1-oxaspiro[n,m]alkan-2-ones

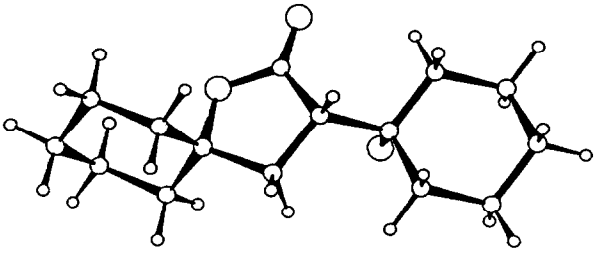
Introduction.- During a project dealing with glycosidase inhibition we became interested in the synthesis of spiro-anellated γ-lactones To obtain these compounds, many routes can be followed resting on quite different strategies such as acid catalyzed, [1-3] oxidative [4-8] or anion based [9-15] reactions as well as sequences involving the reactions of ylides [16-18] or of Grignard reagents [6,19] or by electrochemical transformations [20, 21], also oxazolines [22] α-chloraldonitrones [23] or 1-alkoxy-1-silyloxycyclopropanes [24] have been used as key intermediates
Although a zinc based approach [25] seems quite promising its scope, however, remains limited Alternatively, the use of cerium metal was reported to overcome the difficulties and low yields usually encountered in the formation of γ-lactones in metal (0) catalyzed reactions of ß-halogenated alkanoates with carbonyl compounds [26, 27]

Results and discussion.- Reaction of alkyl 3-bromopropionates with $Ce^{(0)}$ [26, 27] with carbonyl compounds in the presence of catalytic amounts of iodine, however, resulted only in low yields of desired γ-lactones but high yields of the corresponding pinacols, this fact is in excellent accord with previous results [28-30] Neither alterations of the conditions such as temperature, solvent, nor changing the amount of iodine from catalytic to stoichiometric nor using alkyl 3-iodopropionates instead of the corresponding bromo compounds improved the yields in a substantial way Using a cerium graphite surface compound which was easily obtained from anhydrous $CeCl_3$ by reduction with stoichiometric amounts of C_8K in tetrahydrofuran afforded excellent yields of the corresponding pinacols [31] but no improvements in the yields of the γ-lactones were observed Using a zinc-silver couple highly dispersed on the surface of graphite [32] gave similar high yields of pinacols but only insignificant amounts of lactones [31]
Among many other routes for the synthesis of such spirofused γ-lactones two $Sm^{(II)}$-iodide based ways have recently been reported starting either from α,β-unsaturated esters [33-35] or from alkyl 3-bromopropionate,[36] hence further enlarging the scope of applicability of $Sm^{(II)}$-mediated reactions

which have previously successfully been used in organic syntheses for intramolecular reductive coupling reactions generating functionalized carbocycles [37] or for intramolecular Barbier-[36-40] as well as Reformatsky-type [41-43] reactions Since the reported procedures for spirolactonization are quite controversial in as much as the addition of a proton source is concerned [33-35] a re-investigation of this reaction under conditions without addition of alcohols [33] seemed appropriate Reaction of cyclohexanone (**1**) with methyl acrylate according to literature [33, 34] in the presence or absence of an additional proton source gave the expected complex mixture [34] which on exhaustive chromatographic separations among other products afforded the desired lactone **2**, pinacol **3** and **4** as crystals of unknown constitution- albeit of low yield On the other hand, reaction of **1** with methyl 3-bromopropionate (**5**) [36] under addition of HMPA to the reaction mixture increased the yields of the spirolactone **2** but invariably of the conditions substantial amounts of **4** were formed

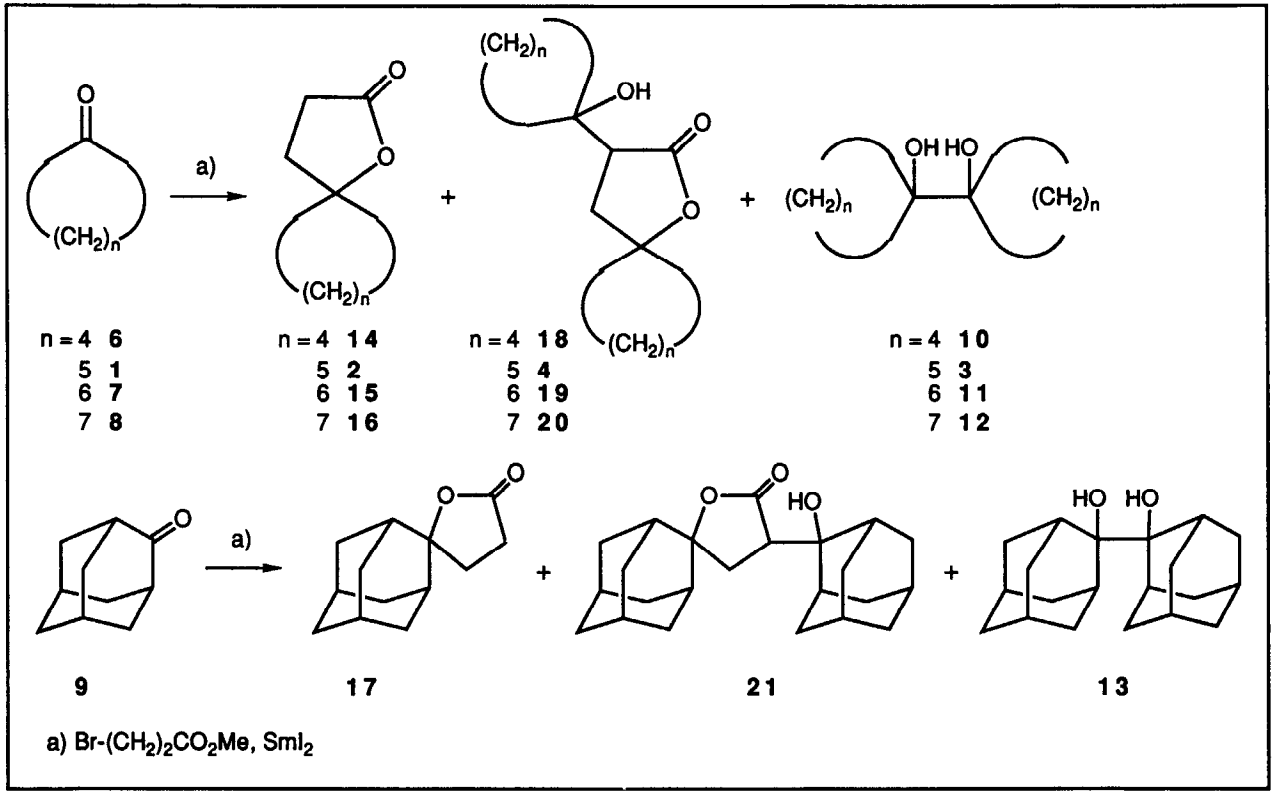
The 400 MHz ^{1}H-NMR spectrum of **4** showed an exchangeable one-proton doublet assigned to an hydroxy function at δ= 3 19 ppm and two distinct signals at δ 2 85 and 3.19 ppm each appearing as a doublet of doublets. A broad and unseparated multiplet between 1 1 and 1 9 ppm showed an integral corresponding to 21 H From the IR spectrum the presence of the hydroxy group was confirmed by a broad absorption at 3140 cm^{-1} A strong signal at 1735 cm^{-1} gave good evidence for the presence of a 5-membered lactone ring which was confirmed by taking a ^{13}C-NMR spectrum of **4** exhibiting among its 15 signals one singulet at δ= 177 62 ppm attributed to the carbonyl group of the lactone Two singulets at δ= 83 83 and 71 39 ppm, respectively, evidence the presence of two quaternary carbon atoms, one of them was attributed to the spiro-centre whereas the other one was assigned by its multiplicity and the value of its chemical shift to bear the hydroxy function and to serve as the connecting point to the spiro fused system. As far as this spiro system is concerned its connecting carbon atom to the second cyclohexane ring has to appear in the ^{13}C-NMR spectrum as a doublet, which was actually detected at δ= 49 87 ppm From these data the structure of **4** seemed already clear, further confirmation was found in its MS spectra Using chemical ionization with isobutane a peak with *m/z* = 253 was attributed to M+1, and another of *m/z*= 235 corresponded to M-H_2O+1 The break-down of the molecule (see Experimental) as found in its e i -MS-spectrum gave final proof for the structure of **4** which was assigned to be a 3-(1-hydroxycyclohexyl)-1-oxaspiro[4 5]decan-2-one

For both final proof of this proposed constitution as well as for the determination of the conformation of **4** which is not deducible from the crowded NMR-spectra a X-ray crystal structure analysis was carried out Its result is presented in the figure



Molecular conformation of **4** as observed in the crystal Only halve the asymmetric unit (which contains two crystallographically non-equivalent molecules of opposite chirality) is shown

SmI_2 mediated reaction of cycloalkanones with methyl 3-bromopropionate



The product was shown to be the *syn* isomer, this observation is in excellent agreement with the selectivity of $Sm^{(II)}$-mediated allylations [45] and iodomethylations [46] but contrasts earlier findings for SmI_2 mediated reactions of 4-*tert* butylcyclohexanone with ethyl acrylate. [34]

Similarly to the reaction of cyclohexanone, cyclopentanone (**6**), cycloheptanone (**7**), cyclooctanone (**8**) and 2-adamantanone (**9**) each afforded separable mixtures of the corresponding pinacols **10-13**, spirolactones **14-17** and tricyclic **18-21** respectively Benzophenone (**22**), however, afforded under these conditions only its pinacol **23** in almost quantitative yield (cf Table 1)

Table 1. Product distribution for the SmI_2 mediated reaction of cycloalkanones with methyl 3-bromopropionate

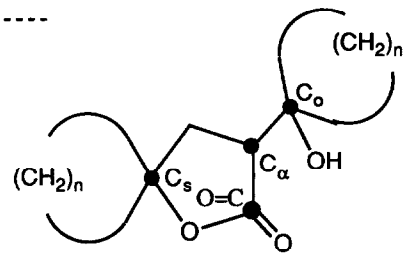
educt	lactone [%]		tricyclo [%]		pinacol [%]	
1	**2**	28 7	**4**	41 2	**3**	20.4
6	**14**	26 6	**18**	38 5	**10**	31 8
7	**15**	10 8	**19**	8 6	**11**	19 5
8	**16**	15 2	**20**	10 3	**12**	17 0
9	**17**	16 8	**21**	22 1	**13**	traces
22	--	--	--	--	**23**	97 5

Paralleling the proposed mechanism [34] for the SmI_2 mediated reductive coupling of α,ß-unsaturated esters with carbonyl compounds it seems reasonable to assume that the reaction of ß-bromo alkanoates in the system SmI_2-THF-HMPA [34, 36] also proceeds mainly by a radical rather than by an ionic mechanism involving a samarium ester enolate Thus, the reduction of the carbonyl compound to a ketyl is followed by a subsequent coupling to a radical resulting from a one electron transfer from Sm^{2+} to the halogenated compound, a second radical coupling completes the sequence Albeit at lower yield, **4** was obtained from the SmI_2 mediated reaction of **1** and **2**

^{13}C-NMR data show general findings throughout both series of the spirolactones **2**, **14-17** as well as of the novel compounds **4**, **18-21** In these spectra (cf Table 2) the value of the chemical shifts for the spiranic carbon varies according to the ring size For both series, in the five-membered ring the spiro-carbon is much more deshielded than in the six-membered ring ($\Delta\delta$= 9 0 and 8 6 ppm, respectively) The same dependency can be seen for the carbon bearing the hydroxyl group ($\Delta\delta$= 9 9 ppm), whereas the nuclear shielding of the carbonyl carbon is not affected by the size of the spiranic ring at all

Table 2 Selected ^{13}C-NMR data for spiro-anellated compounds (δ in ppm from TMS)

product	C_S	C=O	C_O	C_α
4	83 83	177 62	71 39	49 87
18	92 80	177 91	81 25	50 06
19	87 75	178 04	74 78	51 29
20	87 38	177 64	74 28	50 46
21	87 49	176 82	74 88	44 71
2	86 00	176 60		
14	94 60	176 60		
15	90 19	176 77		
16	88 95	176 17		
17	90 61	176 60		



Experimental

Melting points are uncorrected (Reichert micro-hot-stage apparatus), NMR spectra for solutions in $CDCl_3$ (internal Me_4Si) were recorded using a Bruker AM250 instrument (δ given in ppm, *J* in Hz), IR spectra on a Perkin-Elmer 298 (KBr or film) TLC was performed on silica gel (Merck 5554) All reactions were performed under argon

Crystal structure analysis of 4.- Diffraction data were collected at a temperature of 97 (1) K on a modified STOE diffractometer equipped with an ENRAF-NONIUS cold-stream low temperature device using graphite monochromated MoK_α radiation (λ = 0 71069 Å) Unit cell parameters were obtained by least square refinement against the setting angles of 32 reflections with $15° < 2\vartheta < 28°$ Crystals are tetragonal, space group $P4_12_12$ with 16 formula units $C_{15}H_{24}O_3$ (formula weight 252 35) in the unit cell a = 10 895 (7) Å, c = 46 308 (20) Å, V = 5497 (1) $Å^3$, d_{calc} = 1 22 g/cm^3 (calculated with the 97 K unit cell constants)
Intensity data (ω-scan, Δω = 0 8°) were collected for one octant of reciprocal space ($0 \le h \le 12$, $0 \le k \le 12$, $0 \le l \le 53$, $5\,5° \le 2\vartheta \le 48°$), yielding 7396 observed, 3916 unique (assuming Friedel's law) and 2544 significant ($F_{obs} > 3\,\sigma(F)$) structure factors Lp correction and an empirical absorption correction were applied to the data
The structure was solved with direct methods and refined with least-squares, including isotropic atomic displacement parameters (a d p 's) for all non-hydrogen atoms H atoms attached to C were included at calculated positions The two alcoholic protons were neither observed nor calculated R = 0 089 (unit weights) for 145 parameters and 3810 (non-centrosymmetric) observations A final difference electron density map showed features up to 0 8(1) e/$Å^3$ Atomic coordinates have been deposited at the Cambridge Crystallographic Data Centre [44] Computer programs are listed in reference 47
The asymmetric unit of the crystal structure contains two crystallographically non-equivalent molecules of opposite chirality but otherwise (within experimental error) identical conformation

General procedure.- To a slurry of Sm-powder (1 5 g, 10 mmol, Aldrich) in dry THF (30 ml) a solution of 1,2-diiodoethane (2 82 g, 10 mmol) in THF (10 ml) was slowly added at room temperature The resultant olive-green slurry was stirred at ambient temperature for 30 min, then refluxed for additional 20 min after which time the resulting dark blue slurry of SmI_2 formed was cooled to room temperature After addition of HMPA (5 ml) methyl 3-bromopropionate (0 75 g, 4 5 mmol) and the respective cycloalkanone (4 5 mmol) as a solution in THF (5 ml) was added

dropwise After stirring at ambient temperature until completion of the reaction (as evidenced by TLC, hexane/ ethyl acetate 5 1 (*v/v*)) N HCl (10 ml) was added, stirred for 15 min and the resulting mixture was extracted with ether (5 times 20 ml each) The extract was washed with a saturated $Na_2S_2O_3$-solution and brine (10 ml each), dried over Na_2SO_4 and evaporated The resulting syrupy residue was subjected to repeated column chromatography (hexane/ ethyl acetate 10 1 and 3 1 (*v/v*))

1- Oxaspiro[4.4]nonan-2-one (14), 3-(1-hydroxycyclopentyl)-1-oxaspiro[4.4] nonan-2-one (18) and **bicyclopentyl-1,1'-diol (10)** - From **6** (0 84 g) **14** (0 37 g, 27%), **18** (0 43 g, 38 5%) and **10** (0 27 g, 32%) were obtained after chromatographic separation

Data for **14** obtained as an oil [8, 20] IR (film) 2940 (*bs*), 2865 (*s*), 1770 (*s*), 1465 (*m*), 1250 (*m*), 1190 (*m*), 1160 (*m*), 1050 (*m*), 1040 (*m*), Lit [8, 20] 1770 cm^{-1} ^{1}H-NMR 2 50-2 75 (*m*, 2 H), 2 15-2 28 (*m*, 2 H), 1 55-2 05 (*m*, 8 H) MS (c I isobutane) 141 (M+1)

Data for **18** obtained as a solid mp 94-95° IR (KBr) 3500 (*bm*), 2960 (*s*), 2880 (*m*), 1770 (*s*), 1455 (*w*), 1435 (*w*), 1425 (*w*), 1350 (*m*), 1285 (*w*), 1240 (*m*), 1165 (*s*) ^{1}H-NMR 3 04 (*dd*, 1 H, *J* 9 4, 11 5 Hz,), 2 99 (*bs*, 1 H, exchangeable with D_2O, OH), 2 23 (*virt bs*, 1 H), 2 19 (*virt d*, 1 H, *J* 2 9 Hz, on irradiation at δ= 3 04 these both signals form a complex multiplet), 1 55-2 1 (*m*, 16 H) MS (e I) 224 (4), 206 (28), 195 (8), 182 (40), 177 (23), 160 (7), 149 (10), 140 (82), 122 (33), 111 (21) *Anal calcd for* $C_{13}H_{20}O_3$ (224 30) C, 69 61, H, 8 99 *Found* C, 69 73, H, 9 11%

Data for **10** mp 110-112° (Lit [48] 111 4-112 4°)

1- Oxaspiro[4.5]decan-2-one (2), 3-(1-hydroxycyclohexyl)-1-oxaspiro[4.5] decan-2-one (4), and **bicyclohexyl-1,1'-diol (3)** - Following the general procedure **1** (0 98 g) afforded after chromatographic separation **2** (0 44 g, 29%), **4** (0 52 g, 41%) and **3** (0 2 g, 20%)

Data for **2** obtained as an oil [8, 13] IR (film) 2940 (*bs*), 2880 (*m*), 1770 (*s*), 1465 (*m*), 1420 (*m*), 1250 (*m*), 1190 (*m*), 1160 (*m*), 1045 (*m*), 1030 (*m*) ^{1}H-NMR 2 51-2 69 (*m*, 2 H), 2 00-2 10 (*m*, 2 H), 1 25-1 98 (*m*, 10H) MS (e I) 154 (30), 125 (10), 112 (19), 111 (10), 99 (15), 98 (30), 97 (2)

Data for **4** obtained as a solid, mp 110-112°, IR (KBr). 3440 (*bs*), 2930 (*s*), 2860 (*s*), 1735 (*s*), 1450 (*m*), 1400 (*w*), 1375 (*w*), 1310 (*m*), 1280 (*m*), 1265 (*m*), 1235 (*m*), 1220 (*m*), 1135 (*m*), ^{1}H-NMR 3 19 (*d*, 1 H, *J* 1 5 Hz, exchangeable with D_2O, OH), 2 85 (*dd*, 1 H, *J* 9 6, 12 0 Hz), 2 16 (*dd*, 1 H, *J* 9 6, 12 8 Hz), 1 1-1 9 (*m*, 21 H) ^{13}C-NMR 177 62 (*s*, CO), 83 83 (*s*), 71 39 (*s*), 49 87 (*d*), 37 99 (*t*), 35 99 (*t*), 35 60 (*t*), 35 32 (*t*), 32 34 (*t*), 25 39 (*t*), 24 76 (*t*), 21 17 (*t*), 21 10 (*t*) MS (c I, isobutane) 253 (M+1), 235 (M-H_2O+1), (e I) 252 (19), 234 (41), 196 (19), 178 (11), 154 (100) *Anal calcd for* $C_{15}H_{24}O_3$ (252 36) C, 71 40, H, 9 59 *Found* C, 71 20, H, 9 61%

Data for **3** mp 126-128° (Lit [49] 128 5°)

From **1** (0 49 g) and methyl acrylate following the general procedure (HMPA substituted by the addition of 0 37 g of *tert* butanol) **2** (0 25 g, 16 5%) and **4** (0 17 g, 13 3%) were isolated **3** was detected but not isolated

1- Oxaspiro[4.6]undecan-2-one (15), 3-(1-hydroxycycloheptyl)-1-oxaspiro [4.6] undecan-2-one (19), and **bicycloheptyl-1,1'-diol (11)** - From **7** (1 12 g) **15** (0 18 g, 10 8 %), **19** (0 12 g, 9%), and **11** (0 22 g, 19 5%) were obtained

Data for **15** [6, 16, 17] obtained as an oil IR (film) 2930 (*s*), 2860 (*s*), 1770 (*s*), 1460 (*m*), 1245 (*m*), 1185 (*m*), 1160 (*m*), 1045 (*m*), 1040 (*m*) ^{1}H-NMR 2 52 (*t*, 2 H, *J* 7 8 Hz), 2 04 (*t*, 2 H, *J* 7 6 Hz), 1 3-1 95 (*m*, 12 H) MS (c I) 168 (12), 139 (6), 125 (13), 113 (15), 111 (100) *Anal calcd for* $C_{10}H_{16}O_2$ (168 24) C, 71 39, H, 9.59 *Found* C, 71 62, H, 9 47%

Data for **19** obtained as a solid, mp 62-65° IR (KBr) 3440 (*bs*), 2920 (*s*), 2860 (*s*), 1740 (*s*), 1455 (*m*), 1150 (*m*), 1070 (*m*), 1050 (*m*) ^{1}H-NMR 3 47 (*bs*, 1 H, exchangeable with D_2O, OH), 2 88 (*dd*, 1 H, *J* 9 1, 12 2 Hz), 2 21 (*dd*, 1 H, *J* 9 1, 12 6 Hz); 2.04 (*dd*, 1 H, *J* 8 1, 12 7 Hz), 1 3-2 0 (*m*, 24 H) ^{13}C-NMR 178 04 (*s*, COO), 87 75 (*s*), 74 78 (*s*), 51 29 (*d*), 41 91 (*t*), 40 17 (*t*), 38 42 (*t*), 37 08 (*t*), 36 56 (*t*), 29 09 (*t*), 28 91 (*t*), 28 86 (*t*), 28 82 (*t*), 22 23 (*t*), 22 12 (*t*), 21 81 (*t*) MS (e I) 280 (7), 263 (5), 235 (3), 223 (15), 210 (20), 205 (14), 192 (12), 168 (100), 153 (13), 150 (24) *Anal calcd for* $C_{17}H_{28}O_3$ (280 41) C, 72 82, H, 10 06 *Found* C, 73 03, H, 9 89%

Data for **11** mp 76-78°, (Lit [50] 78°).

1- Oxaspiro[4.7]dodecan-2-one (16), 3-(1-hydroxycyclooctyl)-1- oxaspiro[4.7] dodecan-2-one (20), and **bicyclooctyl-1,1'-diol (12)** - From **8** (1 26 g) **16** (0 28 g, 15%), **20** (0 16 g, 10%) and **12** (0 22 g, 17%) were obtained after chromatographic separation

Data for **16**·[11] IR (film)· 2940 (*s*), 2870 (*s*), 1760 (*s*), 1460 (*m*), 1250 (*m*), 1185 (*m*), 1165 (*m*), 1050 (*m*), 1045 (*m*) ^{1}H-NMR· 2.45-2 55 (*m*, 2 H), 2 10-2 20 (*m*, 2 H), 1 40-2 10 (*m*, 14 H). MS (c ı , ısobutane) 183 (M+1)

Data for **20**· obtained as a solid, mp 85-88° IR (KBr). 3440 (*bs*), 2925 (*s*), 2860 (*m*), 1725 (*s*), 1475 (*m*), 1455 (*m*), 1260 (*m*), 1205 (*m*), 1060 (*w*) ^{1}H-NMR 2.93 (s, 1 H, exchangeable with D_2O, OH); 2 85 (*dd*, 1 H, *J* 9 3, 12 1 Hz), 2.21 (*dd*, 1 H, *J* 9 3, 12 6); 1 25-2 15 (*m*, 29 H) ^{13}C-NMR 177 64 (*s*), 87 38 (*s*), 74.28 (*s*), 50 46 (*d*), 37 26 (*t*), 35 66 (*t*), 31 37 (*t*), 28 09 (*t*), 28 01 (*t*), 27 97 (*t*), 27 89 (*t*), 27 79 (*t*), 24 88 (*t*), 22.41 (*t*), 21 75 (*t*), 21 32 (*t*). MS (e.ı) 308 (3), 290 (18), 224 (10), 206 (9), 182 (58), 167 (17), 127 (98) *Anal calcd for* $C_{19}H_{32}O_3$ (308 47) C, 73 98, H, 10 46 *Found*· C, 73 81, H, 10 27%

Data for **12** mp 90-92° (Lit [51] 93-94°)

2-Hydroxyadamantanepropionic acid γ-lactone (17) and **adamantane-2-spiro-4'-tetrahydro-3'-(2-hydroxyadamantanyl)-2'-furanone (21).**- From **9** (1 5 g) **17** (0 35 g, 17%) and **21** (0 39 g, 22%) were ısolated after chromatography Traces of the corresponding adamantanone-pınacol **13** were detected by MS (c ı , ısobutane, 311, M+1) [52] In addition, unchanged startıng materıal **9** (0 73 g, 49%) was recovered

Data for **17**. obtaıned as a solid, mp 127-129° (Lıt [9] 124-128°), IR (KBr) 2910 (*s*), 2860 (*s*), 1770 (*s*), 1465 (*m*), 1450 (*m*), 1420 (*w*), 1390 (*w*), 1370 (*m*), 1365 (*m*), 1315 (*m*), 1290 (*m*), 1245 (*s*), 1225 (*m*), 1205 (*m*), 1070 (*w*), 1040 (*w*), 1020 (*w*), 1000 (*w*) ^{1}H-NMR 2 58 (*dt*, 2 H, *J* 0 6, 8 3 Hz), 2 05-2 24 (*m*, 4 H), 1 50-1 86 (*m*, 12 H) ^{13}C-NMR 176 60 (*s*), 90 61 (*s*), 37 38 (*t*), 37 18 (*d*), 34 46 (*t*), 33 18 (*t*), 31 21 (*t*), 28 83 (*t*), 26 67 (*d*), 26 56 (*d*) MS (c ı ısobutane) 207 (M+1), MS (e ı) 206 (71), 162 (99), 151 (100), 147 (10), 134 (13), 133 (21), 121 (11), 120 (7), 119 (16) *Anal calcd for* $C_{13}H_{18}O_2$ (206 29) C, 75 69, H, 8 79 *Found*· C, 75 81, H, 8 50%

Data for **21**· obtaıned as a solid, mp 210-212° IR (KBr) 3430 (*bs*), 2970 (*m*), 2940 (*s*), 2920 (*s*), 2860 (*s*), 1735 (*s*), 1450 (*m*), 1385 (*w*), 1365 (*m*), 1330 (*m*), 1290 (*m*), 1245 (*s*), 1125 (*w*), 1105 (*m*), 1055 (*m*), 1040 (*w*), 1020 (*w*), 1000 (*s*) ^{1}H-NMR 2 59 (*virt t*, *J* 8 7 Hz, 2 H), 2 03-2 29 (*m*, 7 H, after D_2O exchange 6 H), 1 49-1 96 (*m*, 23 H) ^{13}C-NMR 176 82 (*s*), 87 49 (*s*), 74 88 (*s*), 44 71 (*d*), 38 93 (*d*), 38 01 (*t*), 37 45 (*t*), 35 67 (*d*), 35 53 (*t*), 34 91 (*t*), 34 85 (*d*), 34.03 (*d*), 33 67 (*t*), 33 59 (*t*), 32 72 (*t*), 32 58 (*t*), 32 47 (*t*), 32 41 (*t*), 26 76 (*d*), 26 71 (*d*), 26 65 (*d*) MS (e ı) 356 (3), 338 (5), 310 (4), 294 (5), 206 (100), 191 (26), 188 (13), 151 (39), 148 (66) *Anal calcd. for* $C_{23}H_{32}O_3$ (356 51) C, 77 49; H, 9 05 *Found*· C, 77 30, H, 9 14%

Acknowledgements.- We are ındebted to Professor Dr R Neıdleın, Pharmazeutısch-Chemısches Institut, Univ Heidelberg, for hıs ınterest and gratefully acknowledge the donatıon of chemicals by Boehrınger Ingelheim as well as computatıonal support by IBM, Munchen

References and Notes

1 J T Edward, E Cooke, T C Paradellıs, *Can J Chem* **1981**, *59*, 597
2 W Sucrow, U Klein, *Chem Ber.* **1975**, *108*, 48
3 M F Ansell, J E Emmett, B. E Grımwood, *J. Chem Soc (C)* **1969**, 141
4 M Bertrand, A Meou, A Tubul, *Tetrahedron Lett* **1982**, *23*, 3691
5 D H Aue, M J Meshıshnek, D F Shellhamer, *Tetrahedron Lett* **1973**, 4799
6 M F Schlecht, H -J Kım, *Tetrahedron Lett* **1985**, *26*, 127
7 R G Salomon, S Roy, M F Salomon, *Tetrahedron Lett* **1988**, *29*, 769
8 P Canonne, G B Foscolos, D Bélanger, *J Org Chem* **1980**, *45*, 1828
9 E Ehlınger, P Magnus, *J Am Chem Soc* **1980**, *102*, 5004
10 D Ayalon-Chass, E Ehlınger, P Magnus, J *Chem Soc , Chem Comm* **1977**, 772
11 J Barluenga, J R Fernández, C Rubıera, M Yus, *J Chem Soc , Perkın Trans I* **1988**, 3113
12 R M Jacobson, G P Lahm, J W Clader, *J Org Chem* **1980**, *45*, 395
13 R M Jacobson, J W Clader, *Tetrahedron Lett* **1980**, *21*, 1205
14 J C Carretero, S De Lombaert, L Ghosez, *Tetrahedron Lett* **1987**, *28*, 2135
15 D Caıne, A S Frobese, *Tetrahedron Lett* **1978**, 883
16 M J Bogdanowıcz, T Ambelang, B M Trost, *Tetrahedron Lett* **1973**, 923
17 B M Trost, M J Bogdanowıcz, J *Am Chem. Soc* **1973**, *95*, 5321
18 G Sturtz, B Corbel, J -P Paugam, *Tetrahedron Lett* **1976**, 47
19 a) P Canonne, D Bélanger, *J Chem Soc , Chem Comm* **1980**, 125, b) P Canonne, D Belánger, G Lemay, G B Foscolos, *J Org Chem* **1981**, *46*, 3091

20 S Torii, T Okamoto, H Tanaka, *J. Org Chem.* **1974**, *39*, 2486
21 B J Mayall, D Pletcher, C Z. Smith, *J Chem. Soc, Perkin Trans I* **1976**, 2035
22 A I Meyers, E D Mihelich, R L Nolen, J *Org. Chem.* **1974**, *39*, 2783
23 T K. Das Gupta, D Felix, U M Kempe, A Eschenmoser, *Helv. Chim Acta* **1972**, *55*, 2198
24 E. Nakamura, H Oshino, I Kuwajima, *J. Am Chem Soc.* **1986**, *108*, 3745
25 Y Tamaru, T Nakamura, M. Sakaguchi, H Ochiai, Z Yoshida, *J. Chem Soc, Chem. Commun.* **1988**, 610
26 S-I Fukuzawa, T Fujinami, S. Sakai, *J Chem Soc, Chem Commun.* **1986**, 475
27 S-I Fukuzawa, N Sumimoto, T Fujinami, S Sakai, *J Org. Chem* **1990**, *55*, 1628
28 J L Namy, J Souppe, H B Kagan, *Tetrahedron Lett.* **1983**, 24, 765
29 T Imamoto, T Kusumoto, Y Hatanaka, M Yokohama, *Tetrahedron Lett* **1982**, *23*, 1353
30 a) for an intramolecular pinacolic coupling· G A. Molander, C Kenny, *J. Org. Chem.* **1988**, *53*, 2134, b) for an Yb mediated synthesis Z Hou, K Yakamine, Y Fujiwara, H Taniguchi, *Chem. Lett* **1987**, 2061
31 R Csuk, Z Hu, unpublished results
32 R Csuk, B I Glänzer, A Fürstner, *Adv Organomet Chem* **1988**, *28*, 85
33 S-I Fukuzawa, A Nakanishi, T Fujinami, S Sakai, *J Chem Soc, Chem Commun.* **1986**, 624
34 S-I Fukuzawa, A Nakanishi, T Fujinami, S Sakai, *J Chem Soc, Perkin Trans I* **1988**, 1669
35 K Otsubo, J. Inanaga, M Yamaguchi, *Tetrahedron Lett* **1986**, *27*, 5763
36 K Otsubo, K Kawamura, J Inanaga, M Yamaguchi, *Chem Lett* **1987**, 1487
37 G A Molander, C Kenny, *J Am. Chem Soc* **1989**, *111*, 8236
38 G A Molander, J B Etter, *J Org Chem.* **1986**, *51*, 1778
39 G A Molander, J B Etter, P W Zinke, *J Am. Chem Soc* **1987**, *109*, 453
40 G A Molander, J B Etter, *Synth Commun* **1987**, *17*, 901
41 G A Molander, J B Etter, *J Am Chem Soc* **1987**, *109*, 6556
42 T Tabuchi, K Kawamura, J Inanaga, M. Yamaguchi, *Tetrahedron Lett* **1986**, *27*, 3889
43 E Vedejs, S Ahmad, *Tetrahedron Lett* **1988**, *29*, 2291
44 The atomic coordinates are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB21EW Any request should be accompanied by the full literature citation for this communication
45 P Girard, J L Namy, H B Kagan, *J Am Chem Soc* **1980**, *102*, 2693
46 T Tabuchi, J Inanaga, M Yamaguchi, *Tetrahedron Lett* **1986**, *27*, 3891
47 (a) G M Sheldrick SHELXS-86, a Computer Program for Crystal Structure Solution, Univ of Göttingen, FRG, **1986**, (b) G M Sheldrick SHELX-76, a Computer Program for Crystal Structure Determination, Univ of Cambridge, England,1976, (c) DIFABS N Walker, D Stuart, *Acta Crystallogr A*, **1983**, *39*, 158, (d) A L Spek PLATON, in D Sayre (ed) Computational Crystallography, Clarendon Press, Oxford, 528 (1982), (e) S Motherwell Program PLUTO, University of Cambridge, England
48 P A Naro, J A Dixon, *J Am Chem Soc* **1959**, *81*, 1681
49 G Leuschner, K Pfordte, *Liebigs Ann Chem* **1958**, *619*, 1
50 *Beilstein*, Handbuch der Organ Chemie, *6 (EII)*, 76
51 L Ruzicka, H A Boekenoogen, *Helv Chim Acta* **1931**, *14*, 1319
52 H Wynberg, E Boelema, J H Wieringa, J Strating, *Tetrahedron Lett* **1970**, 3613