an endo proton in the ^1H NMR spectrum appearing as a singlet at δ ~4.7. The final ^1H NMR spectra were as follows. Maleic anhydride-1 adduct: δ 4.65 (1 H, s), 4.0 (1 H, d J = 7 Hz), 3.8 (1 H, d J = 7 Hz), 3.7 (3 H, s), 3.6 (3 H, s). Maleic anhydride-3 adduct: δ 4.7 (1 H, s), 4.2 (4 H, s), 3.9 (1 H, d J = 7 Hz), 3.7 (1 H, d J = 7 Hz). (See ref 5 for comparison.)

Oxidation of the Hydroquinone 13 to the Quinone 15 with DDQ. To a solution of 0.22 g (0.53 mmol) of the hydroquinone 13[2] in 40 mL of methanol in a flask fitted with a magnetic stirrer was added 0.23 g (1.0 mmol) of dichlorodicyanoquinone (DDQ) in small portions. After the addition of DDQ was complete, the solution was stirred for an additional 15 min at room temperature, and a yellow solid began to precipitate. When precipitation of the solid was complete, the mixture was filtered to yield the solid quinone: 0.15 g (70% yield); mp 260-263 °C; IR ($CHCl_3$) 1780, 1660, 1580, 1050-920 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.5-7.5 (4 H, m), 4.6 (1 H, s), 3.76 (3 H, s), 3.70 (3 H, s).

Triethylamine on Hydroquinone 13. The hydroquinone 13[2] was dissolved in benzene, and to this was added excess triethylamine. From the crude product was obtained a yellowish solid: IR (Nujol) 3400, 1800, 1620, 1100-1000 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.4-7.7 (5 H, m), 7.2 (1 H, s), 5.63 (1 H, s), 3.63 (3 H, s), 3.46 (3 H, s).

Triethylamine on Quinone 15. A few drops of triethylamine were added to a solution of quinone 15 in benzene, and the mixture was stirred for a few hours at room temperature. From the reaction was obtained a dark residue which yielded a yellow solid: IR (Nujol) 1800, 1690, 1590, 1100-1000 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.5-7.5 (4 H, m), 5.3 (1 H, s), 3.76 (3 H, s), 3.7 (3 H, s).

Registry No. 1, 3357-59-3; 1 *p*-benzoquinone adduct, 73286-38-1; 1 maleic anhydride adduct, 49672-95-9; 2, 2207-27-4; 3, 49672-92-6; 3 *p*-benzoquinone adduct, 73286-39-2; 3 maleic anhydride adduct, 73286-40-5; 4, 73286-15-4; 4 *p*-benzoquinone adduct, 73286-16-5; 5, 73346-47-1; 6, 73286-17-6; 7, 73286-18-7; 8, 73286-19-8; 9, 73295-92-8; 10, 73286-20-1; 11 (X = OMe, R = $CH_2CH_2O_2CCF_3$), 73286-21-2; 11 (X = OH, R = $CH_2CH_2O_2CCF_3$), 73286-22-3; 13, 73307-70-7; 14, 73307-71-8; 15, 73286-23-4; 16, 73307-72-9; hexachlorocyclopentadiene, 77-47-4; 1,2,3,4-tetrachloro-5,5-(ethylenedioxy)cyclopentadiene, 2082-08-8; 1,4-naphthoquinone, 130-15-4; *p*-benzoquinone, 106-51-4; maleic anhydride, 108-31-6; 2-(chloroethyl) 4-chloro-5,8-dihydro-5,8-dioxo-3-methoxy-1-naphthalenecarboxylate, 73286-24-5.

One-Step Annelation. A Convenient Method for the Preparation of Diols, Spirolactones, and Spiroethers from Lactones

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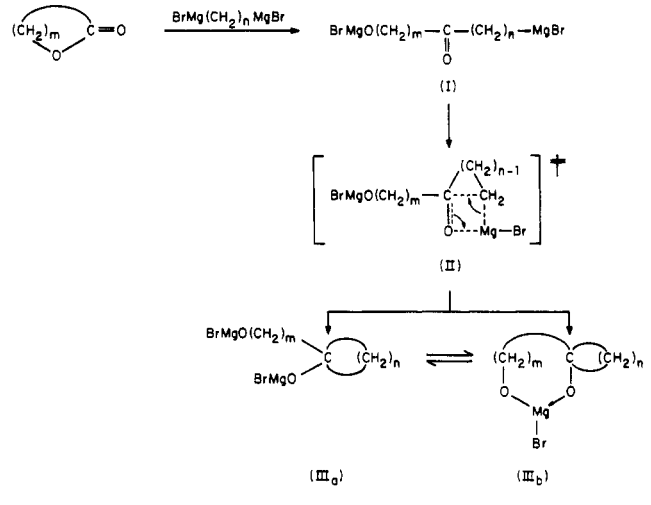
1-(ω-Hydroxyalkyl)cyclopentanols and -cyclohexanols were prepared in one step in high yields from butane-1,4-diyl- and pentane-1,5-diyldimagnesium dibromides and lactones in tetrahydrofuran. This method was found to be general and applicable to lactones of any size (β, γ, δ, and ε) and structure whether aliphatic, aromatic, bicyclic, or spirocyclic. Evidently important steric hindrance close to the carbonyl group prevents annelation and attack on the second nucleophilic center of the Grignard reagent. Furthermore, in the case of oxetan-2-one one obtains, in addition to the corresponding diol, products resulting from scission of the C-O bond. The diols by appropriate transformation afford new routes to spirolactones and spiroethers.

All methods for preparing 1-(ω-hydroxyalkyl)cycloalkanols require several steps which usually result in low overall yields. The only general method applicable to the entire series of such diols would be the reduction of 1-oxaspiroalkan-2-ones. However, the synthesis of such compounds presents serious difficulties.

Other methods require the introduction of the ω-hydroxyalkyl chain to the corresponding cycloalkanone. The products obtained depend upon the order in which the hydroxyl group is introduced into the ω-carbon atom in the chain. Thus for the synthesis of 1-(2-hydroxyethyl)-cycloalkanols the Reformatsky reaction has been used, followed by reduction of the hydroxy esters formed.[1] While the preparation of 1-(3-hydroxypropyl)cycloalkanols was accomplished by three different methods involving reaction of functional organometallic compounds on the cycloalkanones,[2-5] for the synthesis of 1-(4-hydroxybutyl)cycloalkanols, one of these three routes chosen was

Scheme I



the reaction of 3-butenylmagnesium bromide on the cycloalkanones followed by reduction of the double bond by oxidative hydroboration.[6] However, 1-(5-hydroxypentyl)cycloalkanols, as well as other diols, which we have now prepared have not been reported.

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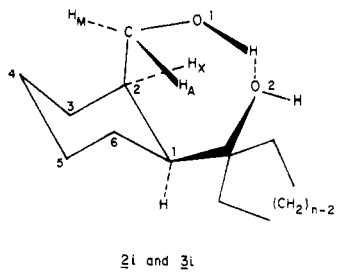
In the present work, we describe a novel and general one-step preparation of 1-(ω-hydroxyalkyl)cycloalkanols in high yields. Our synthesis which involves the reaction of bis(bromomagnesio)alkanes with lactones differs from those previously described in that the hydrocarbon ring and both hydroxyl groups are introduced simultaneously. As we have previously pointed out these bis(bromomagnesio)alkanes are readily prepared in tetrahydrofuran.[7-10] Their reaction with lactones leads to the formation of a new ring by attack on two nucleophilic centers. Annelation to give a five- or a six-membered ring occurs irrespective of the structure of the lactone concerned, be it monocyclic (β, γ, δ, ε), bicyclic, aromatic, or spiro. However, if there is pronounced steric hindrance close to the carbonyl group, the course of the reaction is altered. Diols with a primary hydroxyl can be subsequently converted in good yield to spirolactones and spiroethers which constitutes an indirect two-step route to spiro compounds.

A plausible course of the reaction is shown in Scheme I. Initially, attack of the organodimagnesium gives the complexed intermediate I which, according to the yields of diols obtained, reacts rapidly by intramolecular attack to form intermediate I by annelation to the dialcoholate II. This alcoholate occurs either as the open structure IIIa or the chelated structure IIIb. Possibly the two forms are in equilibrium depending upon the structure of the hydroxylates, and the lactone ring to form a hydrogen bond would explain the chelated form IIIb. On the other hand, diols which do not form a hydrogen bond would give the intermediate complex IIIa. Table I shows the lactones employed and the diols obtained with the yields and IR spectra in CCl_4 at a concentration of 0.5×10^{-3} M.

The yields of diols **2a** and **3a** from this annelation on oxetan-2-one **1a** are low particularly with pentane-1,5-diylmagnesium dibromide as shown by the values obtained by gas chromatographic analysis of the reaction mixture. Treatment of this mixture with 10% sodium hydroxide and continuous extraction to dissolve neutral substances followed by acidification of the aqueous solution indicated that acidic byproducts had also been formed. Spectra show bands characteristic of carboxyl groups [IR 1715–1710 (C=O), 3000–2600 (OH) cm^{-1}; NMR δ 13], as well as the presence of methyl groups (δ 0.82). This suggests that normal addition of the organomagnesium compound to the lactone carbonyl is accompanied by opening of the oxetan-2-one by the Grignard reagent on the CH_2O side by an S_N2 reaction.[14]

However, the action of α,ω-di-Grignard reagents on dihydrofuran-2(3*H*)-one (**1b**) and two derivatives resulted in excellent yields of the corresponding diols **2b**, **3b**, **2c**, **3c**, and **2d**, **3d**. Approximate calculation of the ratio of the bands of apparent integrated absorption intensity of the hydroxyl bound to the free hydroxyl (AB/AF) clearly show a higher value for the pair of diols **2d** and **3d** than for either pair of diols **2b**, **3b** or **2c**, **3c**. This result obtained for the diols **2d** and **3d** shows that the population of chelated forms has definitely increased. The lactone



2i and 3i

Figure 1.

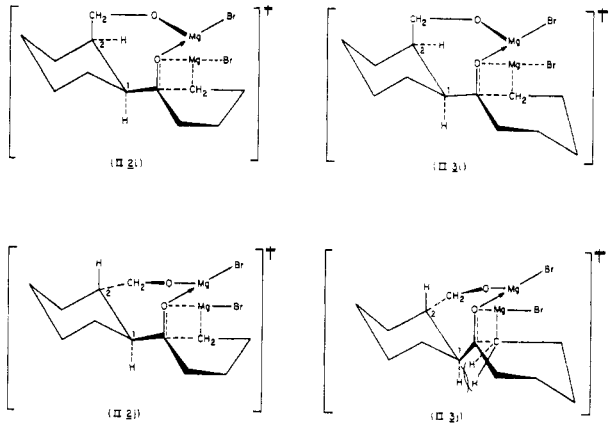


Figure 2.

1d is a mixture of diastereoisomers. As usual, the population of coiled forms is favored by alkyl substituents (cf. *gem*-dialkyl effect).

Furthermore, as we might have expected for the pair of diols **2e** and **3e** prepared by the action of the two organodimagnesium compounds of tetrahydro-2*H*-pyran-2-one (**1e**), as well as for the pair of diols **2f** and **3f** obtained from tetrahydroxepin-2(3*H*)-one (**1f**), we do not observe in the IR spectrum in dilute solutions the formation of intramolecular hydrogen bonding, due presumably to the length of the hydrocarbon chain. In addition the diols **2f** and **3f** prepared from lactone **1f** are partly dehydrated as shown in the regions δ 5.00–6.32 (ethylenic protons) and δ 2.1–2.24 (allylic protons) in the NMR.

A study of the IR spectra of the pair of diols **2g** and **3g** obtained from the aromatic lactone **1g** shows formation of a π bond between the aromatic ring and the hydroxyl group in diol **3g**. This same π bond probably exists in the spectrum of the diol **2g**, but is superimposed on the intramolecular OH bond. It is clear, however, that the pseudospirano chelated conformation is more hindered in the cyclohexyl diol **3g** than in the cyclopentyl diol **2g**.

We next attempted to extend the present method to the bicyclic lactones **1h-j** as well as the spirolactones **4b** and **5b**. The low yields of diols **2h** and **3h** obtained can be partly attributed to an impurity (25% α-campholide) in the lactone **1h**. The yields reported are based on impure starting material.

It is interesting to note that the value of the ratio AB/AF is greatly increased for the pair of diols **2i** and **3i** (Table I), suggesting that the pseudospiranic chelated cyclic conformations are more favored (by stabilization of the hydrogen bond) as an examination of molecular models shows. Likewise in the NMR spectrum, the H_A and H_M hydrogens (Figure 1) manifest a notable difference in chemical shift. It appears that H_A is affected by the paramagnetic zone of the oxygen of the tertiary hydroxyl and consequently forms an AMX system with the nonequivalent geminal methylenic proton of the hydroxymethyl group and the vicinal equatorial hydrogen H_X at

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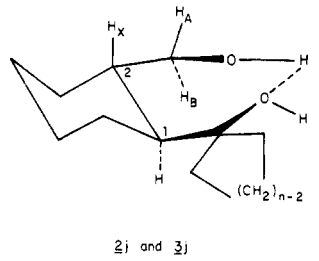


2j and 3j

Figure 3.

carbon 2. Thus, the presence in the NMR spectrum of an AMX system, rather than the ABX system one might expect if the diol had an open conformation, reinforces the observation that in diols **2i** and **3i** the pseudospiranic chelated conformations are favored (Figure 1).

Furthermore, experiments made with monocyclic lactones in order to compare the efficacy of the two bis(bromomagnesio)alkanes showed an appreciable difference in yields by VPC analysis, particularly in the case of oxetan-2-one (**1a**) where electronic rather than steric factors may play a role. On the other hand, the case of trans lactone **1j** is characterized by steric hindrance which prevents the formation of the cyclohexane ring and accounts for the considerable difference in yields of **2j** vs. **3j** (Figure 2).

With regard to the conformation of these diols (**2j** and **3j**) a study of their NMR spectra again leads to the favored conformation shown in Figure 3. In fact, the signal of proton H_X coincides with that of the ring protons since it lies in the cage of the diamagnetically protected ring protons. The methylene protons find themselves in a similar magnetic environment and appear between δ 3.3 and 3.8 as the AB multiplet of an ABX system.

The bicyclic diol **2k** can be prepared in excellent yields from either 1-oxaspiro[4.4]nonan-2-one (**4b**) and pentane-1,5-diyldimagnesium dibromide or 1-oxaspiro[4.5]decan-2-one (**5b**) and (butane-1,4-diyl)dimagnesium dibromide.

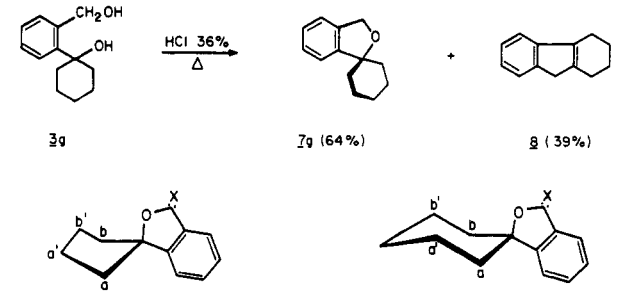
The reaction of the above bis(bromomagnesio)alkanes with 1,8,8-trimethyl-3-oxabicyclo[3.2.1]-octan-2-one (α-campholide) was attempted to determine the limits of our method of annelation. Because of appreciable steric hindrance in the vicinity of the carbonyl group only slight reactivity was expected, and considerable amounts of the lactone were recovered even after long reaction times accompanied by hydroxy unsaturated compound and the expected diol. Purification of the reaction mixture proved to be difficult.

In order to extend the scope of the reaction, we tried to react hexane-1,6-diyldimagnesium bromide with dihydrofuran-2(3*H*)-one to obtain a seven-membered-ring diol. However, a viscous liquid was obtained from which none of the expected diol could be isolated.

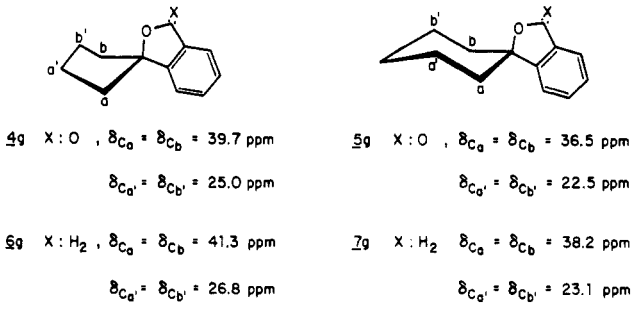
The (ω-hydroxyalkyl)cyclohexanols and (ω-hydroxyalkyl)cyclopentanols with primary hydroxyl groups were easily converted into spirolactones by Jones reagent.[15,16] In this oxidation the γ-spirolactones are immediately formed while in the case of the δ-spirolactones the corresponding hydroxy acid is also obtained, but fractional distillation of the mixture yields only the δ-spirolactone.

The same diols on intramolecular etherification give the corresponding spiroethers. The method of Reynolds and Kenyon,[17] which consists in reacting equimolar quantities

Scheme II



3g 7g (64%) 8 (39%)



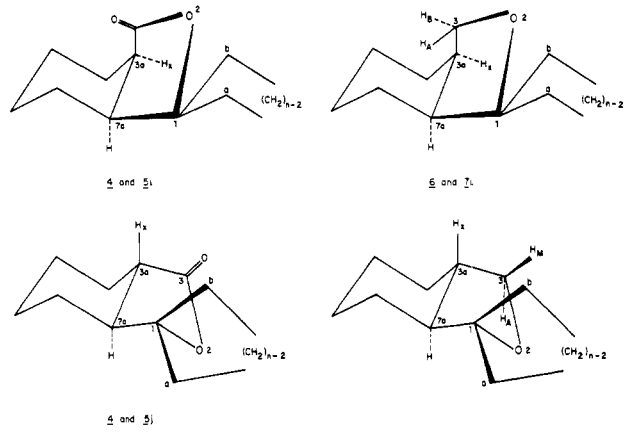
4g X : O , $\delta_{C_a} = \delta_{C_b} = 39.7$ ppm; $\delta_{C_{a'}} = \delta_{C_{b'}} = 25.0$ ppm

5g X : O , $\delta_{C_a} = \delta_{C_b} = 36.5$ ppm; $\delta_{C_{a'}} = \delta_{C_{b'}} = 22.5$ ppm

6g X : H_2 , $\delta_{C_a} = \delta_{C_b} = 41.3$ ppm; $\delta_{C_{a'}} = \delta_{C_{b'}} = 26.8$ ppm

7g X : H_2 $\delta_{C_a} = \delta_{C_b} = 38.2$ ppm; $\delta_{C_{a'}} = \delta_{C_{b'}} = 23.1$ ppm

Figure 4.



4 and 5; 6 and 7; 4 and 5

Figure 5.

of tosyl chloride and diol in pyridine, was employed to obtain the tetrahydrofurans while the tetrahydropyrans were prepared by the method of Picard.[12] The spirolactones and spiroethers are listed in Table II.

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Table I. Diols from the Action of Dimagnesium Compounds on Lactones

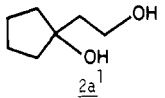
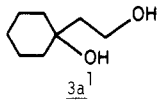
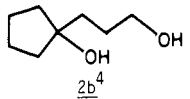
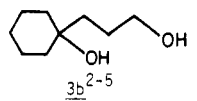
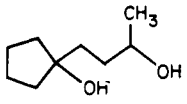
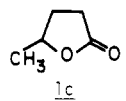
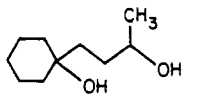
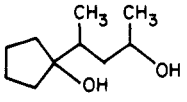
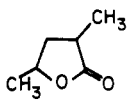
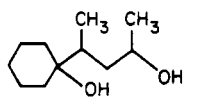
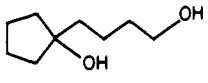
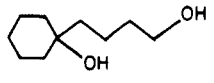
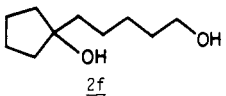
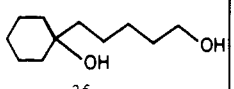
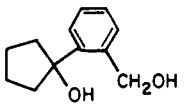
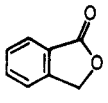
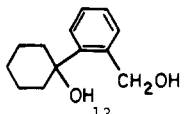
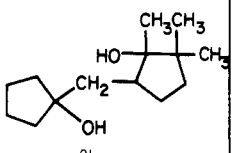
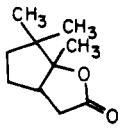
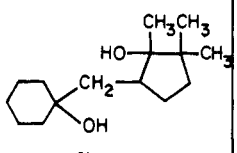
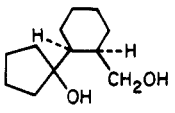
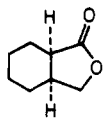
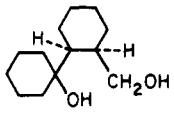
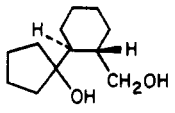
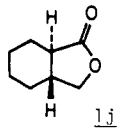
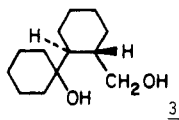
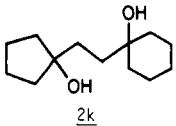
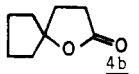
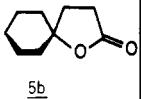
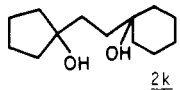
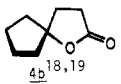
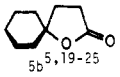
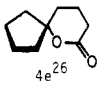
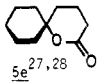
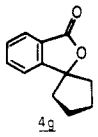
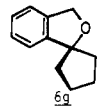
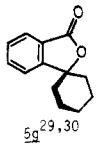
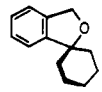
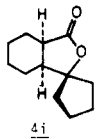
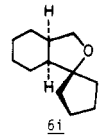
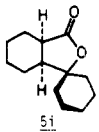
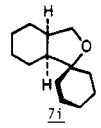
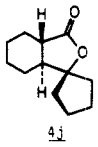
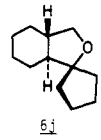
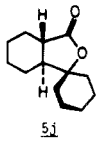
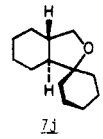
IR Hydroxyl Stretching (ν_{OH}) frequencies	Yield (%)	Product with $BrMg(CH_2)_4MgBr$	Lactone	Product with $BrMg(CH_2)_5MgBr$	Yield (%)	IR Hydroxyl Stretching (ν_{OH}) frequencies
ν_F 3640 cm^{-1} ν_B 3550 cm^{-1}	56(67)	 2a[1]	 1a	 3a[1]	37(46)	ν_F 3640 cm^{-1} ν_B 3550 cm^{-1}
ν_F 3640 cm^{-1} ν_B 3480 cm^{-1}	88(100)	 2b[4]	 1b	 3b[2-5]	80(90)	ν_F 3640 cm^{-1} ν_B 3480 cm^{-1}
ν_F 3640 cm^{-1} ν_B 3460 cm^{-1}	69(81)	 2c	 1c	 3c	60(70)	ν_F 3640 cm^{-1} ν_B 3460 cm^{-1}
ν_F 3630 cm^{-1} ν_B 3450 cm^{-1}	72	 2d	 1d	 3d	58	ν_F 3635 cm^{-1} ν_B 3450 cm^{-1}
ν_F 3640 cm^{-1} ———	70(88)	 2e[11]	 1e	 3e[12]	65(70)	ν_F 3645 cm^{-1} ———
ν_F 3655 cm^{-1} ———	81	 2f	 1f	 3f	73	ν_F 3655 cm^{-1} ———
ν_F 3620 cm^{-1} ν_B 3480 cm^{-1}	65(87)	 2g	 1g	 3g[13]	67	ν_F 3635 cm^{-1} ν_B 3505 cm^{-1} ν_π 3580 cm^{-1}
ν_F 3650 cm^{-1} ν_B 3500 cm^{-1}	42	 2h	 1h	 3h	33	ν_F 3650 cm^{-1} ν_B 3500 cm^{-1}
ν_F 3625 cm^{-1} ν_B 3465 cm^{-1}	92	 2i	 1i	 3i	78	ν_F 3630 cm^{-1} ν_B 3470 cm^{-1}
ν_F 3630 cm^{-1} ν_B 3470 cm^{-1}	86(100)	 2j	 1j	 3j	32(39)	ν_F 3635 cm^{-1} ν_B 3470 cm^{-1} ν_B 3540 cm^{-1}
ν_F 3620 cm^{-1} ν_B 3460 cm^{-1}	86	 2k	 4b  5b	 2k		

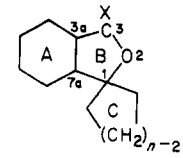
Table II. Spirolactones and Spiroethers from Diols 2 and 3

Diol	Spirolactone	Yield (%)	Spiroether	Yield (%)
2b	 4b[18,19]	82	 6b[4,31]	82
3b	 5b[5,19-25]	81	 7b[2,5,32]	85
2e	 4e[26]	61	 6e[31,33]	60
3e	 5e[27,28]	65	 7e[12,33,34]	68
2g	 4g	86	 6g	80
3g	 5g[29,30]	94	 7g	82
2i	 4i	80	 6i	88
3i	 5i	72	 7i	77
2j	 4j	83	 6j	83
3j	 5j	81	 7j	76

We have also prepared the spirophthaline **7g** by the action of hydrochloric acid on the corresponding diol **3g** by Parham's method.[13] The NMR spectrum of the reaction mixture revealed in addition to signals corresponding to the spiroether **7g** others which we attribute to 1,2,3,4-tetrahydrofluorene (**8**) by comparison with the signals in authentic 1,2,3,4-tetrahydrofluorene prepared by the action of hydrobromic acid on the diol **3g**. The use of hydrochloric acid therefore does not give the pure ether. GLC showed the presence of 39% 1,2,3,4-tetrahydrofluorene (Scheme II).

(34) Y. Leroux, N. V. P. DaRocha, and J. C. Combret, *C. R. Hebd. Seances Acad. Sci., Ser. C*, **267**, 1512 (1968).

Table III. ^{13}C NMR Chemical Shifts for Derivatives of Spiro[cycloalkane-1,1′(3′*H*)-isobenzofuran][a]



compd	X	*n*	C_1	C_3	C_{3a}	C_{7a}
4g	O	4	95.5	169.9	152.9	126.4
5g	O	5	86.9	170.0	155.1	125.1
6g	H_2	4	94.8	61.6	147.7	121.9
7g	H_2	5	86.5	62.1	148.6	122.6
4i	O	4	95.7	177.8	43.7	41.4
5i	O	5	85.6	177.7	41.8	39.6
6i	H_2	4	95.0	68.1	37.8	45.1
7i	H_2	5	85.4	68.8	36.8	43.6
4j	O	4	96.8	176.9	49.6	45.3
5j	O	5	86.9	177.0	53.0	43.6
6j	H_2	4	92.6	71.0	44.9	51.9
7j	H_2	5	82.0	71.0	43.7	55.8

[a] Chemical shifts are in δ (parts per million from Me_4Si), 0.75 mol/L in $CDCl_3$.

The conformation of the spirolactones and ethers **4g–7g**, **4i–7i**, and **4j–7j** may be studied from their ^1H NMR spectra and their ^{13}C NMR parameters. The latter are shown in Table III. Although rings B and C are always perpendicular to each other, and this is reflected in the spectra (Figure 4), the axial conformation of carbon 3 in the compounds with the cis configuration (**4i–7i**) puts ring C in a plane almost parallel to ring A, whereas, on the contrary, the equatorial conformation on carbon 3 with trans (**4j–7j**) configuration puts ring C almost perpendicular to the plane of ring A (Figure 5). These hypotheses for the proposed conformation are supported by the fact that carbons **3a** and **7a** of the cis compounds are more deshielded due to the perpendicular conformation of rings A and B (Table III).

A comparison of the ^1H NMR spectra of the cis ethers (**6i** and **7i**) and the trans ethers (**6j** and **7j**) shows that in the cis isomers proton H_X is, on account of its equatorial position and gauche relationship with the ethereal oxygen, deshielded and appears as a broad multiplet (δ 2.5–2.6) due to coupling to no less than 7 other hydrogens. The methylene protons H_A and H_B on carbon 3, being in a similar environment, form an ABX system with proton H_X. On the other hand, in the trans ethers (**6j** and **7j**) axial proton H_X is shielded and appears in the region of the other cycloalkyl protons and is superimposed upon them. The methylene protons H_A and H_M because of their different chemical shifts form an AMX system.

Finally, the definite differences observed for the chemical shifts in the ^{13}C NMR spectrum of spiro carbon C_1 between five- and six-membered rings must be emphasized. Thus, in general, the spirocyclohexyl compounds offer a diamagnetic protection on carbon 1 which is more pronounced than in the corresponding cyclopentyl compounds.

Experimental Section

Melting points were determined in capillary tubes with a Thomas-Hoover melting point apparatus and are uncorrected. Column chromatography was carried out on silica gel 60F-254 (70–230 mesh ASTM) for dry column chromatography. Gas chromatographic analyses were performed on a Hewlett-Packard

1620A research chromatograph equipped with a flame ionization detector under a nitrogen flow (22 mL/min) in a column (10% SE-30 on Chromosorb G). IR spectra were recorded on a Beckman IR-12 spectrophotometer. ^1H NMR spectra were determined on a Bruker HX-90 spectrometer and are reported in δ units downfield from Me_4Si. ^{13}C NMR spectra were determined on a Bruker WP-80 (20.1 MHz) apparatus in $CDCl_3$ solution by using Me_4Si as an internal standard. Mass spectra were obtained in a Varian M-66 spectrometer, and UV absorption spectra were measured on a DK-1A Beckman instrument in 95% EtOH solution. Microanalyses were performed by Chemalytics Inc.

Starting Materials. Oxetan-2-one (**1a**), dihydrofuran-2(3*H*)-one (**1b**), tetrahydro-2*H*-pyran-2-one (**1e**), 5-methyldihydrofuran-2(3*H*)-one (**1c**), tetrahydrooxepin-2(3*H*)-one (**1f**), and 1*H*-isobenzofuran-3-one (**1g**) were commercially available. 3,5-Dimethyldihydrofuran-2(3*H*)-one (**1d**) was prepared by decarboxylation of 2-allyl-2-methylmalonic acid followed by lactonization of the intermediate 2-methylpent-4-enoic acid by using the Bradsher reagent[35] in an overall yield of 48%; bp 68–70 °C (8 mmHg). The NMR spectrum of this product indicated that it was a mixture of *cis*- and *trans*-2,5-dimethyldihydrofuran-2(3*H*)-ones.[36] 3a,7a-*cis*-3a,4,5,6,7,7a-Hexahydro-1*H*-isobenzofuran-3-one (**1i**) was prepared by reduction of *cis*-cyclohexane-1,2-dicarboxylic anhydride with $LiAlH_4$ according to the method of Bloomfield:[37] bp 68–70 °C (0.2 mm); 72% yield; IR (film) ν_{max} 1770 (C=O) cm^{-1}; NMR (90 MHz, $CDCl_3$) δ 0.92–2.28 (8 H, very complex m, cyclohexane H), 2.28–2.83 (2 H, m, 3a,7a-H), 3.94 (1 H, 2d, AMX, $J_{AM} \simeq 8.5$ Hz, $J_{AX} \simeq 1$ Hz, 1-H_A), 4.24 (1 H, q, AMX, $J_{AM} \simeq 8.5$ Hz, $J_{MX} \simeq 4.5$ Hz, 1-H_M). 3a,7a-*trans*-3a,4,5,6,7,7a-Hexahydro-1*H*-isobenzofuran-3-one[38] (**1j**) was synthesized by the same method as above: bp 72–74 °C (0.4 mmHg); 63% yield; IR (film) ν_{max} 1780 (C=O) cm^{-1}; NMR (90 MHz, $CDCl_3$) δ 1.0–2.44 (10 H, 2 m, cyclohexane H), 3.76–3.96 (1 H, m, 1-H), 4.29–4.44 (1 H, m, 1-H). 1,8,8-Trimethyl-2-oxabicyclo[3.3.0]octan-3-one (**1h**) was prepared by the method of Sauers[39,40] by the Baeyer–Villiger oxidation of camphor in the presence of sodium acetate, and the desired lactone was obtained by the acid isomerization of the intermediate 1,8,8-trimethyl-2-oxabicyclo[3.2.1]octan-3-one in an overall yield of 68%; bp 70–72 °C (0.1 mmHg). NMR analysis of this product based on the integration of the methyl signals (δ 0.9, 1.08, and 1.29) in comparison with an authentic sample of α-campholide (CH_3 signals δ 0.96, 1.09, and 1.16) shows that it contains 25–28% α-campholide. This lactone was used without further purification.

Preparation of Diols 2 and 3. General Method. The corresponding lactone 1 (0.06 mol) in anhydrous THF (~50 mL) was added dropwise with vigorous stirring under nitrogen to 0.065 mol of the organodimagnesium compound in the same solvent (150 mL). The reaction mixture was stirred overnight under an atmosphere of nitrogen. After hydrolysis with saturated aqueous ammonium chloride, the organic layer was separated, the aqueous layer was extracted with ether, and the combined organic layers were dried (Na_2SO_4). After removal of the solvents, the residue was purified, either by distillation, crystallization, or column chromatography.

1-(2-Hydroxyethyl)cyclopentanol[1] **(2a)**: bp 100 °C (1.7 mmHg); yield 56%; IR (film) ν_{max} 3350 (OH stretch), 1380 (OH bend), 1085 (C–O stretch) cm^{-1}; NMR (90 MHz, $CDCl_3$) δ 1.22–1.89 (8 H, m, cyclopentane H), 1.72 (2 H, t, $J \simeq 6$ Hz, A_2X_2, 1′-H), 3.68 (2 H, t, $J \simeq 6$ Hz, A_2X_2, 2′-H), 3.95 (2 H, br s, OH).

1-(2-Hydroxyethyl)cyclohexanol[1] **(3a)**: bp 84–86 °C (0.8 mmHg); mp 32 °C; 37% yield; IR (film) ν_{max} 3370 (OH stretch), 1380 (OH bend), 1090 (C–O stretch) cm^{-1}; NMR (90 MHz, $CDCl_3$) δ 1.21–1.78 (10 H, m, cyclohexane H), 1.63 (2 H, t, $J \simeq 6$ Hz, A_2X_2, 1-H), 3.68 (2 H, t, $J \simeq 6$ Hz, A_2X_2, 2′-H), 3.70 (2 H, s, OH).

1-(3-Hydroxypropyl)cyclopentanol[4] **(2b)**: bp 110–113 °C (0.1 mmHg); mp 33–34 °C; 88% yield; IR (film) ν_{max} 3320 (OH stretch), 1065 (C–O stretch) cm^{-1}; NMR (90 MHz, $CDCl_3$) δ 1.39–1.89 (12 H, m, cyclopentane and aliphatic H), 3.66 (2 H, t, $J \simeq 6$ Hz, 3′-H), 4.34 (2 H, s, OH).

1-(3-Hydroxypropyl)cyclohexanol[2-5] **(3b)**: bp 108–110 °C (0.03 mmHg); 80% yield; IR (film) ν_{max} 3340 (OH stretch), 1060 (C–O stretch) cm^{-1}; NMR (90 MHz, $CDCl_3$) δ 1.22–1.88 (14 H, m, cyclohexane and aliphatic H), 3.62 (2 H, t, $J \simeq 6$ Hz, 3′-H), 2.94 (2 H, br s, OH).

1-(3-Hydroxybutyl)cyclopentanol (2c): mp 88–89 °C (Et_2O-pentane); bp 104–106 °C (0.05 mmHg); 69% yield; IR (KBr) ν_{max} 3305 (OH stretch), 1370, 1340 (OH bend), 1130 (C–O stretch) cm^{-1}; NMR (90 MHz, $CDCl_3$) δ 1.22 (3 H, d, $J \simeq 6$ Hz, CH_3), 3.84 (1 H, m, 3′-H), 1.44–1.91 (12 H, m, cyclopentane and aliphatic H), 2.27 (2 H, br s, OH); mass spectrum, *m/e* 112 ($M^+ - C_2H_5OH$, 72%), 86 ($M^+ - C_4H_8O$, 76%), 56 ($C_3H_4O^+$, 100%). Anal. Calcd for $C_9H_{18}O_2$: C, 68.31; H, 11.46. Found: C, 68.58; H, 11.46.

1-(3-Hydroxybutyl)cyclohexanol (3c): bp 100–103 °C (0.02 mmHg); 60% yield; IR (film) ν_{max} 3350 (OH stretch), 1375 (OH bend), 1170 (C–O stretch) cm^{-1}; NMR (90 MHz, $CDCl_3$) δ 1.2 (3 H, d, $J \simeq 6$ Hz, CH_3), 3.82 (1 H, m, 3′-H), 1.4–1.77 (14 H, m, cyclohexane and aliphatic H), 3.03 (2 H, br s, OH). Anal. Calcd for $C_{10}H_{20}O_2$: C, 69.72; H, 11.70. Found: C, 69.88; H, 11.75.

1-(3-Hydroxy-1-methylbutyl)cyclopentanol (2d) (mixture of diastereoisomers): bp 97–99 °C (0.01 mmHg); 72% yield; IR (film) ν_{max} 3350 (OH stretch), 1375 (OH bend), 1125 (C–O stretch) cm^{-1}; NMR (90 MHz, $CDCl_3$) δ 0.96 and 1.05 (3 H, d, $J \simeq 6$ Hz, 1′-CH_3), 1.21 and 1.24 (3 H, d, $J \simeq 6$ Hz, CH_3), 1.4–2.1 (11 H, m, cyclopentane and aliphatic H), 3.22 (2 H, very br s, OH), 3.93 (1 H, m, 3′-H). Anal. Calcd for $C_{10}H_{20}O_2$: C, 69.72; H, 11.70. Found: C, 69.84; H, 11.56.

1-(3-Hydroxy-1-methylbutyl)cyclohexanol (3d) (mixture of diastereoisomers): bp 100–101 °C (0.03 mmHg); 58% yield; IR (film) ν_{max} 3350 (OH stretch), 1375 (OH bend), 1125, 1060 (C–O stretch) cm^{-1}; NMR (90 MHz, $CDCl_3$) δ 0.93 and 0.97 (3 H, d, $J \simeq 6$ Hz, 1′-CH_3), 1.19 and 1.22 (3 H, d, $J \simeq 6$ Hz, CH_3), 1.05–2.22 (13 H, m, cyclohexane and aliphatic H), 3.55–4.17 (1 H, m, 3′-H), 2.77–4.00 (2 H, very br s, OH). Anal. Calcd for $C_{11}H_{22}O_2$: C, 70.92; H, 11.91. Found: C, 70.68; H, 11.88.

1-(4-Hydroxybutyl)cyclopentanol[11] **(2e)**: bp 88–90 °C (0.01 mmHg); mp 45–45.5 °C; 70% yield; IR (film) ν_{max} 3330 (OH stretch), 1335 (OH bend), 1060 (C–O stretch) cm^{-1}; NMR (90 MHz, $CDCl_3$) δ 1.33–2.00 (14 H, m, cyclopentane and aliphatic H), 3.62 (2 H, t, $J \simeq 6$ Hz, 4′-H), 2.85 (2 H, br s, OH).

1-(4-Hydroxybutyl)cyclohexanol[12] **(3e)**: bp 100–104 °C (0.005 mmHg); mp 41–42 °C; 65% yield; IR (film) ν_{max} 3340 (OH stretch), 1355 (OH bend), 1070 (C–O stretch) cm^{-1}; NMR (90 MHz, $CDCl_3$) δ 1.11–1.78 (16 H, m, cyclohexane and aliphatic H), 3.62 (2 H, t, $J \simeq 6$ Hz, 4′-H), 2.44–3.08 (2 H, very br s, OH).

1-(5-Hydroxypentyl)cyclopentanol (2f): bp 102–104 °C (0.02 mm); 81% yield; IR (film) ν_{max} 3340 (OH stretch), 1075, 1060 (C–O stretch) cm^{-1}; NMR (90 MHz, $CDCl_3$) δ 1.12–1.88 (16 H, m, cyclopentane and aliphatic H), 3.62 (2 H, t, $J \simeq 6$ Hz, 5′-H), 2.25 (2 H, s, OH). Anal. Calcd for $C_{10}H_{20}O_2$: C, 69.72; H, 11.70. Found: C, 72.43; H, 11.43 (partial dehydration).

1-(5-Hydroxypentyl)cyclohexanol (3f): bp 120–122 °C (0.2 mm); 73% yield; IR (film) ν_{max} 3350 (OH stretch), 1360 (OH bend), 1060 (C–O stretch) cm^{-1}; NMR (90 MHz, $CDCl_3$) δ 1.17–1.83 (18 H, m, cyclohexane and aliphatic H), 2.49 (2 H, br s, OH), 3.62 (2 H, t, $J \simeq 6$ Hz, 5′-H). Anal. Calcd for $C_{11}H_{22}O_2$: C, 70.92; H, 11.91. Found: C, 70.99; H, 11.67.

1-(*o*-Hydroxymethylphenyl)cyclopentanol (2g). This diol was purified by column chromatography using Et_2O–pentane (2:1) as the eluant; mp 50–51 °C (Et_2O–pentane); 65% yield; IR (KBr) ν_{max} 3250 (OH stretch), 1580 (C=C), 1370 (OH bend), 1125 (C–O stretch), 770 (C–H bend of Ph) cm^{-1}; NMR (90 MHz, $CDCl_3$) δ 1.55–1.95 (4 H, m, cyclopentane H), 1.95–2.33 (4 H, m, cyclopentane H), 4.01 (1 H, s, OH), 4.33–4.6 (1 H, br s, OH), 4.69 (2 H, s, *o*-CH_2Ph), 7.15–7.44 (4 H, m, C_6H_4); mass spectrum, *m/e* 192 (M^+, 17%), 174 ($M^+ - H_2O$, 23%), 145 ($M^+ - HO - C_2H_5$, 100%); UV (ethanol) λ_{max} 261 nm (ϵ_{max} 208). Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.96; H, 8.39. Found: C, 75.19; H, 8.42.

1-(*o*-Hydroxymethylphenyl)cyclohexanol[13] **(3g).** This diol was purified under the same conditions described for the diol **2g**; mp 68–69 °C (Et_2O–pentane); 67% yield; IR (KBr) ν_{max} 3350 (OH stretch), 1130, 1055 (C–O stretch), 755 (C–H bend of Ph) cm^{-1}; NMR (90 MHz, $CDCl_3$) δ 1.33–2.11 (10 H, very complex m, cy-

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clohexane H), 3.76 (2 H, s, OH), 4.76 (2 H, s, o-CH_2Ph), 7.11–7.44 (4 H, m, C_6H_4); UV (ethanol) λ_{max} 260 nm (ϵ_{max} 193.8).

1-[(2,3,3-Trimethyl-2-hydroxycyclopentyl)methyl]cyclopentanol (2h). After removal of the solvents the residual viscous oil was dried under vacuum for several hours and was crystallized by treating with pentane: mp 94 °C (Et_2O–pentane); 42% yield; IR (KBr) ν_{max} 3430 (OH stretch), 1380 (OH bend), 1150, 1050 (C–O stretch) cm^{-1}; NMR (90 MHz, $CDCl_3$) δ 0.89 (3 H, s, 3′-CH_3), 0.98 (3 H, s, 3′-CH_3), 1.09 (3 H, s, 2′-CH_3), 1.27–2.22 (17 H, very complex m, cyclopentane, aliphatic, and hydroxylic H). Anal. Calcd for $C_{14}H_{26}O_2$: C, 74.28; H, 11.58. Found: C, 74.31; H, 11.48.

1-[(2,3,3-Trimethyl-2-hydroxycyclopentyl)methyl]cyclohexanol (3h). This diol was separated by column chromatography eluting with Et_2O–hexane (1:1): mp 97 °C (Et_2O–pentane); 33% yield; IR (KBr) ν_{max} 3480 (OH stretch), 1385, 1370 (OH bend), 1100, 1070 (C–O stretch) cm^{-1}; NMR (90 MHz, $CDCl_3$) δ 0.86 (3 H, s, 3′-CH_3), 0.94 (3 H, s, 3′-CH_3), 1.03 (3 H, s, 2′-CH_3), 1.28 (2 H, s, OH), 1.11–2.10 (17 H, very complex m, cycloalkane and aliphatic H). Anal. Calcd for $C_{15}H_{28}O_2$: C, 74.95; H, 11.74. Found: C, 74.98; H, 11.73.

1-[1,2-*cis*-2-(Hydroxymethyl)cyclohexyl]cyclopentanol (2i): mp 89–90 °C (Et_2O–pentane); 78% yield; IR (KBr) ν_{max} 3230 (OH stretch), 1335, 1350 (OH bend), 1110, 1050 (C–O stretch) cm^{-1}; NMR (90 MHz, $CDCl_3$) δ 1.0–2.06 (17 H, m, cycloalkane H), 2.06–2.39 (1 H, m, 2′-H), 3.37–3.54 (1 H, q, AMX, $J_{AM} \simeq 11$ Hz, $J_{MX} \simeq 2.5$ Hz, 2′-methylenic H), 3.96–4.19 (1 H, t, AMX, $J_{AM} \simeq J_{AX} \simeq 11$ Hz, 2′-methylenic H), 4.12 (2 H, s, OH); mass spectrum, m/e 180 ($M^+ - H_2O$, 9.5%), 167 ($M^+ - CH_2OH$, 100%). Anal. Calcd for $C_{12}H_{22}O_2$: C, 72.68; H, 11.19. Found: C, 72.78; H, 11.03.

1-[1,2-*cis*-2-(Hydroxymethyl)cyclohexyl]cyclohexanol (3i): mp 108.5–109 °C (Et_2O–pentane); 91% yield; IR (KBr) ν_{max} 3200 (OH stretch), 1375 (OH bend), 1155 (C–O stretch) cm^{-1}; NMR (90 MHz, $CDCl_3$) δ 1.0–2.06 (19 H, complex m, cyclohexane H), 2.12–2.44 (1 H, m, 2′-H), 3.38–3.54 (1 H, q, AMX, $J_{AM} \simeq 11$ Hz, $J_{MX} \simeq 2.5$ Hz, 2′-methylenic H), 3.99–4.18 (1 H, t, AMX, $J_{AM} \simeq J_{AX} \simeq 11$ Hz, 2′-methylenic H), 3.88–4.44 (2 H, very br s, OH). Anal. Calcd for $C_{13}H_{24}O_2$: C, 73.54; H, 11.39. Found: C, 73.28; H, 11.41.

1-[1,2-*trans*-2-(Hydroxymethyl)cyclohexyl]cyclopentanol (2j). This diol was crystallized by pentane treatment followed by refrigeration: mp 65–66 °C (Et_2O–pentane); 86% yield; IR (KBr) ν_{max} 3340 (OH stretch), 1350 (OH bend), 1175, 1080 (C–O stretch) cm^{-1}; NMR (90 MHz, $CDCl_3$) δ 0.89–2.00 (18 H, complex m, cycloalkane H), 3.36–3.78 (2 H, m, 2′-methylenic H), 3.53 (2 H, s, OH). Anal. Calcd for $C_{12}H_{22}O_2$: C, 72.68; H, 11.19. Found: C, 72.57; H, 11.23.

1-[1,2-*trans*-2-(Hydroxymethyl)cyclohexyl]cyclohexanol (3j). This product was separated by column chromatography by eluting with Et_2O–hexane (1:1): mp 92.5–93 °C (Et_2O–pentane); 32% yield; IR (KBr) ν_{max} 3190 (OH stretch), 1340 (OH bend), 1060 (C–O stretch) cm^{-1}; NMR (90 MHz, $CDCl_3$) δ 0.8–1.95 (20 H, very complex m, cyclohexane H), 3.31–3.8 (2 H, m, 2′-methylene H), 3.78–4.33 (2 H, very br s, OH). Anal. Calcd for $C_{13}H_{24}O_2$: C, 73.54; H, 11.39. Found: C, 73.38; H, 11.45.

1-[2-(1-Hydroxycyclopentyl)ethyl]cyclohexanol (2k): mp 96–97 °C (Et_2O–pentane); 86% yield (from **5b**), 84% (from **4b**); IR (KBr) ν_{max} 3320 (OH stretch), 1335 (OH bend), 1155 (C–O stretch) cm^{-1}; NMR (90 MHz, $CDCl_3$) δ 1.22–1.89 (22 H, m, cycloalkane and aliphatic H), 2.4 (2 H, s, OH). Anal. Calcd for $C_{13}H_{24}O_2$: C, 73.54; H, 11.39. Found: C, 73.28; H, 11.21.

Spirolactone (4, 5) Preparation. General Method. Jones reagent (20 mL) was added dropwise with stirring at 0 °C to a solution of 20 mmol of the corresponding diol in acetone (40 mL). After the addition was complete, stirring was continued at 0 °C for 1 h, and then excess reagent was destroyed by adding a few drops of 2-propanol. The green layer of chromous salts was filtered off and the acetone was removed in vacuo. The residue was treated with water and extracted several times with chloroform. The organic layer was washed with water, dried ($MgSO_4$), and evaporated. The residual product was either crystallized or distilled under vacuum.

1-Oxaspiro[4.4]nonan-2-one[18,19] (4b): bp 59–61 °C (0.7 mmHg); 82% yield; IR (film) ν_{max} 1770 (C=O) cm^{-1}; NMR (90 MHz, $CDCl_3$) δ 1.55–2.0 (8 H, m, cyclopentane H), 2.1–2.33 (2 H, m, 4-H), 2.5–2.73 (2 H, m, 3-H).

1-Oxaspiro[4.5]decan-2-one[5,19–25] (5b): bp 63 °C (0.8 mmHg); 81% yield; IR (film) ν_{max} 1775 (C=O) cm^{-1}; NMR (90 MHz, $CDCl_3$) δ 1.21–1.91 (10 H, m, cyclohexane H), 1.91–2.14 (2 H, m, 4-H), 2.5–2.75 (2 H, m, 3-H).

5-Oxaspiro[4.5]decan-6-one[26] (4e): bp 58–60 °C (0.08 mmHg); 61% yield; IR (film) ν_{max} 1730 (C=O) cm^{-1}; NMR (90 MHz, $CDCl_3$) δ 1.5–2.11 (12 H, m, cyclopentane and 8,9-H), 2.44–2.67 (2 H, m, 7-H).

1-Oxaspiro[5.5]undecan-2-one[27,28] (5e): mp 45–46 °C (pentane); bp 90–92 °C (0.3 mm); 65% yield; IR (film) ν_{max} 1730 (C=O) cm^{-1}; NMR (90 MHz, $CDCl_3$) δ 1.22–2.06 (14 H, m, cyclohexane and 4,5-H), 2.38–2.61 (2 H, m, 3-H).

Spiro[cyclopentane-1,1′(3′*H*)-isobenzofuran]-3′-one (4g): mp 75 °C (Et_2O–pentane); bp 108–110 °C (0.08 mmHg); 86% yield; IR (KBr) ν_{max} 1752 (C=O), 1622, 1608 (C=C), 750 (C–H bend of Ph) cm^{-1}; NMR (90 MHz, $CDCl_3$) δ 1.88–2.22 (8 H, m, cyclopentane H), 7.32–7.9 (4 H, m, C_6H_4); mass spectrum, m/e 188 (M^+, 81.6%), 160 ($M^+ - CO$, 100%); UV (ethanol) λ_{max} 277 nm (ϵ_{max} 1823). Anal. Calcd for $C_{12}H_{12}O_2$: C, 76.57; H, 6.43. Found: C, 76.34; H, 6.46.

Spiro[cyclohexane-1,1′(3′*H*)-isobenzofuran]-3′-one[29,30] (5g): mp 78–79 °C (Et_2O–pentane); 94% yield; IR (KBr) ν_{max} 1770 (C=O), 1622, 1610 (C=C) cm^{-1}; NMR (90 MHz, $CDCl_3$) δ 1.52–2.00 (10 H, m, cyclohexane H), 7.28–7.86 (4 H, m, C_6H_4); UV (ethanol) λ_{max} 274, 282 nm (ϵ_{max} 1982, 1958).

3′a,7′a-*cis*-3′a,4′,5′,6′,7′,7′a-Hexahydrospiro[cyclopentane-1,1′(3′*H*)-isobenzofuran]-3′-one (4i): mp 80.5–81 °C (Et_2O–pentane); 80% yield; IR (KBr) ν_{max} 1775 (C=O) cm^{-1}; NMR (90 MHz, $CDCl_3$) δ 1.0–2.44 (17 H, very complex m, cycloalkane H), 2.79–3.1 (1 H, m, 3′a-H); mass spectrum, m/e 194 (M^+, 56%), 166 ($M^+ - CO$, 100%), 150 ($M^+ - CO_2$, 54%). Anal. Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 74.01; H, 9.12.

3′a,7′a-*cis*-3′a,4′,5′,6′,7′,7′a-Hexahydrospiro[cyclohexane-1,1′(3′*H*)-isobenzofuran]-3′-one (5i): bp 112–115 °C (0.05 mmHg); mp 55–56 °C; 72% yield; IR (film) ν_{max} 1775 (C=O) cm^{-1}; NMR (90 MHz, $CDCl_3$) δ 1.0–2.39 (19 H, very complex m, cycloalkane H), 2.86–3.08 (1 H, m, 3′a-H). Anal. Calcd for $C_{13}H_{20}O_2$: C, 74.96; H, 9.68. Found: C, 74.75; H, 9.65.

3′a,7′a-*trans*-3′a,4′,5′,6′,7′,7′a-Hexahydrospiro[cyclopentane-1,1′(3′*H*)-isobenzofuran]-3′-one (4j): mp 61.5–62 °C; 83% yield; IR (KBr) ν_{max} 1755 (C=O) cm^{-1}; NMR (90 MHz, $CDCl_3$) δ 1.03–2.33 (very complex m). Anal. Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 74.25; H, 9.46.

3′a,7′a-*trans*-3′a,4′,5′,6′,7′,7′a-Hexahydrospiro[cyclohexane-1,1′(3′*H*)-isobenzofuran]-3′-one (5j): mp 99–99.5 °C; 81% yield; IR (KBr) ν_{max} 1760 (C=O) cm^{-1}; NMR (90 MHz, $CDCl_3$) δ 1.0–2.39 (very complex m). Anal. Calcd for $C_{13}H_{20}O_2$: C, 74.96; H, 9.68. Found: C, 75.08; H, 9.81.

Preparation of Spiroethers (6, 7). General Method. To a stirred solution of 20 mmol of the corresponding diol in pyridine (50 mL) was added 20 mmol of TsCl in small portions with cooling. After being stirred for 1 h, the resulting solution was refluxed for 4 h. The mixture was poured into water and extracted several times with chloroform. The combined extracts were washed with water and 5% HCl and dried ($MgSO_4$). After removal of the solvent the residual oil was purified by distillation.

1-Oxaspiro[4.4]nonane[4,31] (6b): bp 42 °C (10 mmHg); 82% yield; NMR (90 MHz, $CDCl_3$) δ 1.0–2.2 (12 H, m, cyclopentane and 3,4-H), 3.5–3.72 (2 H, ~t, 2-H).

1-Oxaspiro[4.5]decane[2,5,32] (7b): bp 52 °C (8 mmHg); 85% yield; NMR (90 MHz, $CDCl_3$) δ 1.1–2.2 (14 H, m, cyclohexane and 3,4-H), 3.6–3.9 (2 H, ~t, 2-H).

5-Oxaspiro[4.5]decane[31,33] (6e). After addition of the TsCl the resulting solution was stirred at 0 °C for 2 h and then poured into ice–water. The mixture was extracted with ether, and the ether layer was washed with water and dried. After removal of the solvent in vacuo, the residual tosylate was dissolved in HMPT (20 mL) and then heated at 80 °C for 6 h. The mixture was treated with water and extracted with chloroform in the usual manner. The spiroether was separated by fractional distillation: bp 68–70 °C (10 mmHg); 60% yield; NMR (90 MHz, $CDCl_3$) δ 1.11–2.1 (14 H, m, cyclopentane and 7,8,9-H), 3.42–3.66 (2 H, ~t, 6-H).

1-Oxaspiro[5.5]undecane[12,33,34] (7e) was prepared by the method described for **6e**: bp 72–74 °C (8 mmHg); 68% yield; NMR (90 MHz, $CDCl_3$) δ 1.0–2.12 (16 H, m, cyclohexane and 3,4,5-H), 3.30–3.66 (2 H, ~t, 2-H).

Spiro[cyclopentane-1,1′(3′*H*)-isobenzofuran] (6g): bp 58–60 °C (0.05 mmHg); 80% yield; IR (film) ν_{max} 1620 (C=C), 755 (C–H bend of Ph) cm^{-1}; NMR (90 MHz, $CDCl_3$) δ 1.61–2.22 (8 H, m, cyclopentane H), 5.02 (2 H, s, 3′-H), 7.06–7.39 (4 H, m, C_6H_4); UV (ethanol) λ_{max} 265, 272 nm (ϵ_{max} 1155, 1222). Anal. Calcd for $C_{12}H_{14}O$: C, 82.72; H, 8.10. Found: C, 82.53; H, 7.99.

Spiro[cyclohexane-1,1′(3′*H*)-isobenzofuran] (7g): bp 64–66 °C (0.06 mm); 82% yield; IR (film) ν_{max} 1617 (C=C), 755 (C–H bend of Ph) cm^{-1}; NMR (90 MHz, $CDCl_3$) δ 1.5–1.94 (10 H, m, cyclohexane H), 5.05 (2 H, s, 3′-H), 7.02–7.33 (4 H, m, C_6H_4); UV (ethanol) λ_{max} 265, 272 nm (ϵ_{max} 1000, 1056). Anal. Calcd for $C_{13}H_{16}O$: C, 82.93; H, 8.57. Found: C, 83.12; H, 8.46.

3′a,7′a-*cis*-3′a,4′,5′,6′,7′,7′a-Hexahydrospiro[cyclopentane-1,1′(3′*H*)-isobenzofuran] (6i): bp 60–62 °C (0.05 mmHg); 88% yield; NMR (90 MHz, $CDCl_3$) δ 1.0–2.1 (17 H, m, cycloalkane H), 2.33–2.78 (1 H, br m, 3′a-H), 3.46–3.87 (2 H, complex m, 3′-H). Anal. Calcd for $C_{12}H_{20}O$: C, 79.94; H, 11.18. Found: C, 80.18; H, 11.03.

3′a,7′a-*cis*-3′a,4′,5′,6′,7′,7′a-Hexahydrospiro[cyclohexane-1,1′(3′*H*)-isobenzofuran] (7i): bp 78–80 °C (0.1 mmHg); 71% yield; NMR (90 MHz, $CDCl_3$) δ 1.0–2.0 (19 H, very complex m, cyclohexane H), 2.44–2.89 (1 H, br m, 3′a-H), 3.58–3.91 (2 H, complex m, 3′-H). Anal. Calcd for $C_{13}H_{22}O$: C, 80.35; H, 11.41. Found: C, 80.44; H, 11.23.

3′a,7′a-*trans*-3′a,4′,5′,6′,7′,7′a-Hexahydrospiro[cyclopentane-1,1′(3′*H*)-isobenzofuran] (6j): bp 70–72 °C (0.3 mmHg); 83% yield; NMR (90 MHz, $CDCl_3$) δ 0.89–2.22 (18 H, very complex m, cycloalkane H), 3.16–3.42 (1 H, q, AMX, $J_{AX} \simeq 9.5$ Hz, $J_{AM} \simeq 7$ Hz, 3′-H_A), 3.78–4.00 (1 H, t, AMX, $J_{AM} \simeq J_{MX} \simeq 7$ Hz, 3′-H_M). Anal. Calcd for $C_{12}H_{20}O$: C, 79.94; H, 11.18. Found: C, 80.12; H, 11.25.

3′a,7′a-*trans*-3′a,4′,5′,6′,7′,7′a-Hexahydrospiro[cyclohexane-1,1′(3′*H*)-isobenzofuran] (7j): bp 76–78 °C (0.2 mmHg); 76% yield; NMR (90 MHz, $CDCl_3$) δ 0.89–2.28 (20 H, very complex m, cyclohexane H), 3.18–3.38 (1 H, q, AMX, $J_{AX} \simeq 9.5$ Hz, $J_{AM} \simeq 7$ Hz, 3′-H_A), 3.79–4.00 (1 H, t, AMX, $J_{AM} \simeq J_{MX} \simeq 7$ Hz, 3′-H_{11}). Anal. Calcd for $C_{13}H_{22}O$: C, 80.35; H, 11.41. Found: C, 80.61; H, 11.41.

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Registry No. 1a, 57-57-8; **1b**, 96-48-0; **1c**, 108-29-2; *cis*-**1d**, 24405-07-0; *trans*-**1d**, 24405-08-1; **1e**, 542-28-9; **1f**, 502-44-3; **1g**, 87-41-2; **1h**, 5732-81-0; **1i**, 6939-71-5; **1j**, 7702-72-9; **2a**, 73089-93-7; **2b**, 73057-71-3; **2c**, 73061-24-2; **2d**, isomer 1, 73089-94-8; **2d**, isomer 2, 73104-79-7; **2e**, 52318-90-8; **2f**, 73089-95-9; **2g**, 73061-25-3; **2h**, 73089-96-0; **2i**, 73089-97-1; **2j**, 73089-98-2; **2k**, 73089-99-3; **3a**, 40894-17-5; **3b**, 6963-45-7; **3c**, 73061-26-4; **3d**, isomer 1, 73090-00-3; **3d**, isomer 2, 73090-01-4; **3e**, 57740-07-5; **3f**, 73090-02-5; **3g**, 58931-26-3; **3h**, 73090-03-6; **3i**, 73090-04-7; **3j**, 73090-05-8; **4b**, 33448-80-5; **4e**, 20127-07-5; **4g**, 73090-06-9; **4i**, 73090-07-0; **4j**, 73090-08-1; **5b**, 699-61-6; **5e**, 4481-78-1; **5g**, 5651-49-0; **5i**, 73090-09-2; **5j**, 73090-10-5; **6b**, 176-10-3; **6e**, 177-21-9; **6g**, 73090-11-6; **6i**, 73104-80-0; **6j**, 73090-12-7; **7b**, 176-91-0; **7e**, 180-79-0; **7g**, 171-80-2; **7i**, 73090-13-8; **7j**, 73090-14-9; **8**, 17057-95-3; 1,5-dibromopentane, 111-24-0; 1,4-dibromobutane, 110-52-1; 2-allyl-2-methylmalonic acid, 5281-63-0; 2-methylpent-4-enoic acid, 1575-74-2; *cis*-cyclohexane-1,2-dicarboxylic anhydride, 13149-00-3; *trans*-cyclohexane-1,2-dicarboxylic anhydride, 14166-21-3.

Regiocontrolled Synthesis of Hydroxyphthalides. Synthesis of (±)-Isoochracinic Acid and a Zealeranone Intermediate

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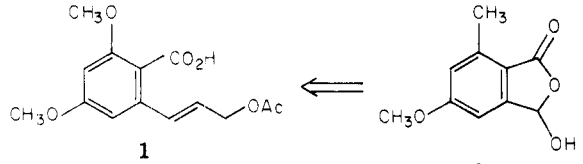
Metalation of 3-methoxy- and 3,5-dimethoxybenzyl alcohol followed by quenching with CO_2 provided the phthalides. Bromination and solvolysis generated 7-methoxy- and 5,7-dimethoxyphthalaldehydic acid in a fully regiocontrolled reaction. The former served as an intermediate in the synthesis of isoochracinic acid, a toxic metabolite from a parasite responsible for black spot disease of Japanese pears, in 44% overall yield from 3-methoxybenzyl alcohol. The latter served as an intermediate for the aromatic portion of zealeranone in a projected synthesis of this macrolide. A chemoselective reduction of an ester using an ate complex of DIBAL and *n*-butyllithium and the effect of tetra-*n*-hexylammonium bromide on the Wadsworth–Horner reaction are also reported.

In pursuing the synthesis of zealeranone[1] via organopalladium chemistry, we required **1** for the aromatic portion of the molecule. A suitable precursor was envisioned to be the lactol **2**. However, the obtainment of **2** from the corresponding phthalic anhydride proceeded in only 16% yield on a preparative scale.[2] The general importance of such intermediates in natural products encouraged us to seek a high-yield alternative route. In this paper, we wish to report such a sequence, (1) its application to the synthesis of **1**, (2) its application to a total synthesis of a toxin, isoochracinic acid (**3**), which arises from a parasite responsible for black spot disease of Japanese pears,[3] (3) a novel use of lithium trialkylaluminum hydride



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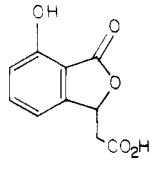
2



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