Pergamon

Tetrahedron 56 (2000) 4555–4563

TETRAHEDRON

Synthesis of Tertiary Cyclobutanols through Stereoselective Ring Expansion of Oxaspiropentanes Induced by Grignard Reagents

Angela M. Bernard, Costantino Floris, Angelo Frongia and Pier P. Piras*

Dipartimento di Scienze Chimiche, Università di Cagliari, Complesso Universitario di Monserrato, S.S. 554, Bivio per Sestu, I-09042 Monserrato (Cagliari), Italy

Received 25 January 2000; revised 7 April 2000; accepted 27 April 2000

Abstract—The stereoselectivity of the ring expansion of oxaspiropentanes to cyclobutanols induced by Grignard reagents has been studied. It has been found that the reaction occurs through the intermediacy of a cyclobutanone, formed stereospecifically, whereas the attack of the Grignard reagent on the carbonyl group of the cyclobutanone is stereospecific only in the case of the oxaspiropentanes derived from aldehydes.

Introduction

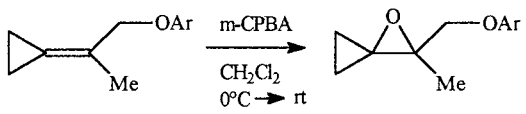
Oxaspiropentanes are very important intermediates in organic synthesis[1,2] and are usually prepared by peracid oxidation of methylenecyclopropanes,[3–9] through nucleophilic addition of 1-lithio-1-bromocyclopropanes to ketones at low temperatures[10–12] or through reaction of sulphur ylides with carbonyl compounds.[13–17] They have also been proposed as intermediates in the addition of diazomethane to ketones[9] and in the reaction of dimethylsulphonium methylide with α-haloketones.[13] Their versatility as synthetic tools is clearly demonstrated by their capability to react with nucleophiles[18] and bases[15–17,19,20] to give cyclopropanols, and to undergo ring expansion to cyclobutanones by reaction with acidic reagents like protonic acids, lithium or europium salts,[1,2,5,6,15–18,20,21] or by thermal treatment.[22,23]

Results and Discussion

We report here on the reaction of oxaspiropentanes with Grignard reagents as a useful method to prepare very efficiently tertiary cyclobutanols.[24] Oxaspiropentanes **2a**,**b** were prepared by oxidation with *m*-CPBA of the previously reported[25] 2-cyclopropylidene-aryloxy propanes **1a**,**b** (Scheme 1).

Occasionally variable amounts of cyclobutanones **9a**,**b** were obtained if an excess of *m*-CPBA was used, but in this case the chromatographic purification of the oxaspiropentane posed no problem. The cyclobutanones **9a**,**b** were also prepared by treating the corresponding oxaspiropentanes with LiI or TsOH in refluxing dichloromethane for 24 h. When we reacted **2a**,**b** with a set of Grignard reagents (Scheme 2) at −70°C, good yields of cyclobutanols **3a**, **3b**–**7b** were obtained as mixtures of diastereoisomers separable by column chromatography.

In the case of 2-methyl-1-(4-methylphenyl)-2-(phenoxymethyl) cyclobutanol **4b** only the **(*E*)-4b** product was isolated from the reaction mixture, while the diastereoisomer **(*Z*)-4b** was always obtained as an enriched mixture, from which discernible ^{1}H and ^{13}C NMR data were reported. The separation of **(*E*)-7b** from its diastereoisomer **(*Z*)-7b** was more easily carried out from the mixture obtained from the reaction of cyclobutanone **9b** with benzylmagnesium chloride using the same experimental conditions. As can be seen from Scheme 2 and from the data reported in Table 1, aromatic, aliphatic and vinylic Grignard reagents gave cyclobutanols, whereas the reaction with benzylmagnesium chloride led to a 60:40 mixture of cyclobutanols (diastereoisomeric ratio 6:4) and the cyclopropanol **8**, probably coming from a nucleophilic attack on the epoxide ring of the oxaspiropentane.



1a,b **2a,b**

a : Ar = *p*-MeO-C_6H_4 , 75%

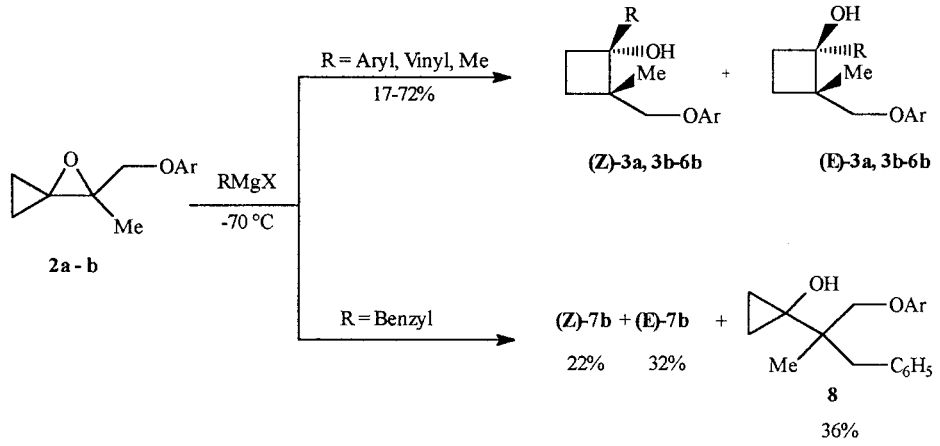
b : Ar = C_6H_5 , 90%

Scheme 1.

Keywords: cyclopropanes; oxaspiropentanes; cyclobutanones; cyclobutanols; stereoselectivity; ring expansion; Grignard reagents.

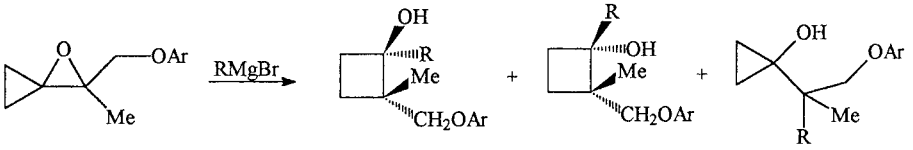
* Corresponding author. Fax: +390-70-675-4388;
e-mail: pppiras@vaxca1.unica.it

0040–4020/00/$ - see front matter
PII: S0040-4020(00)00369-0

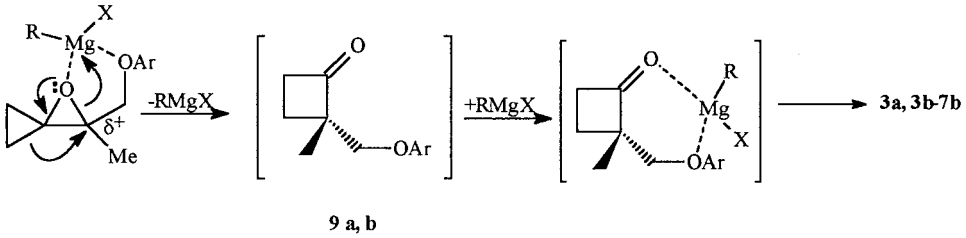


Scheme 2.

Table 1. Reaction of oxaspiropentanes **2a**,**b** with Grignard reagents



Entry	R	X	Reaction condition	Ar	Derivatives **3a**, **3b**–**7b**	Cyclobut./cycloprop.	(*E*)/(*Z*) ratio	Yields
1	C_6H_5	Br	Et_2O/THF	*p*-MeO-C_6H_4	**3a**	100:0	80:20	90
2	C_6H_5	Br	Et_2O/THF	C_6H_5	**3b**	100:0	75:25	75
3	*p*-Me-C_6H_4	Br	Et_2O/THF	C_6H_5	**4b**	100:0	80:20	84
4	$CH{=}CH_2$	Br	THF	C_6H_5	**5b**	100:0	68:32	90
5	CH_3	I	Et_2O/THF	C_6H_5	**6b**	100:0	45:55	80
6	$C_6H_5CH_2$	Cl	Et_2O/THF	C_6H_5	**7b**	60:40	60:40	90

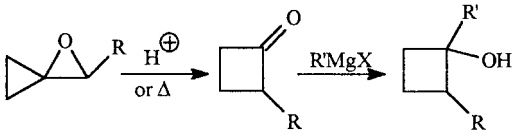


Scheme 3.

As a possible rationale of this reaction we believe that, due to its electrophilic character,[26] the metal atom of the Grignard reagent, coordinates with both the oxygen atom of the epoxide and of the aryloxy group creating an electronic deficiency on the non-cyclopropylic carbon of the epoxide ring. At this point the oxaspiropentane undergoes a ring expansion to the corresponding cyclobutanones **9a**,**b**, which then react with the Grignard reagents to give the final cyclobutanols (Scheme 3).

Strong support for this hypothesis is given by the fact that the cyclobutanols **3b**–**7b** are also obtained, in the same diastereoisomeric ratio, by reaction of the corresponding Grignard reagents with cyclobutanone **9b**. This reaction represents an unprecedented example of the use of Grignard reagents to trigger the ring expansion of oxaspiropentanes to cyclobutanones.

If the final target is a tertiary cyclobutanol, this approach saves one reaction step in comparison with the usual



Scheme 4.

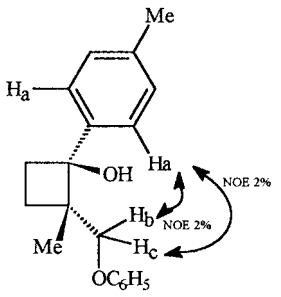


Figure 1.

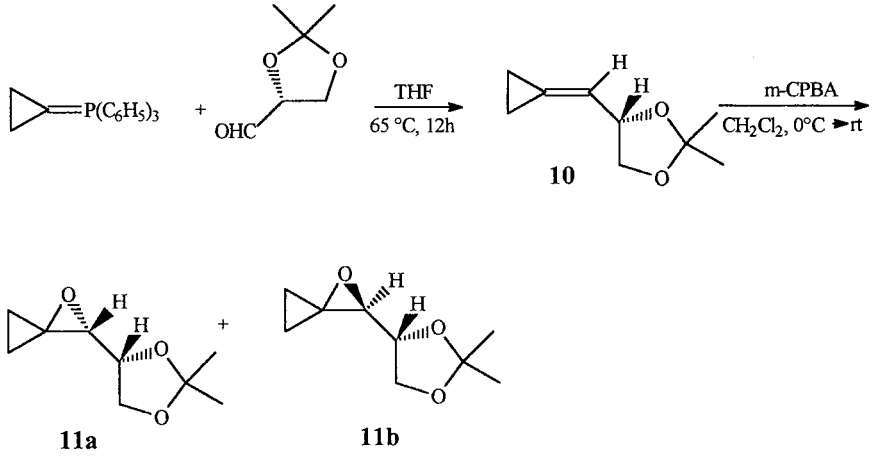
methods, that allow the synthesis of the final product by first preparing the cyclobutanone using either protonic acids or lithium salts (Scheme 4).

In these cases the stereochemistry of the epoxide carbon involved in the migration is normally inverted, and Trost and coworkers have clearly demonstrated[1,15–18] that the stereospecificity of the rearrangement strongly depends on the type of acid used. In this way, changing from protonic acids to the Lewis acidic cations of lithium or europium, the transformation of the oxaspiropentane generates the relative diastereoisomeric cyclobutanones with increasing levels of stereospecificity. Using the oxaspiropentanes **2a**,**b** we can say nothing about the stereoselectivity of the ring expansion, although it appears that the attack of the intermediate cyclobutanone is occurring with moderate diastereoselectivity, probably as a consequence of a chelation of the magnesium with the oxygen atom of the ether group. This chelation leads to preferential attack of the cyclobutanone from the same side of the ether group to give cyclobutanols with the *E* geometry, except in the case of methyl magnesium iodide, that gives the corresponding cyclobutanol **6b** with practically no stereoselectivity. The stereochemical assignments of the geometric isomers of the cyclobutanols were made on the basis of the differences in the chemical shifts of the methyl and the methylene hydrogens, determined by the well known shielding effects exerted by the phenyl group on *cis*-located groups in a four membered ring system, and on the opposite effect exerted by an hydroxy group.[27] These assignments have been confirmed by the presence of a definite NOE enhancement between H_c and H_b (3.39 and 3.48 ppm, AB q) and the aromatic proton H_a (7.28–7.30 ppm) of **(*E*)-4b**. (Fig. 1).

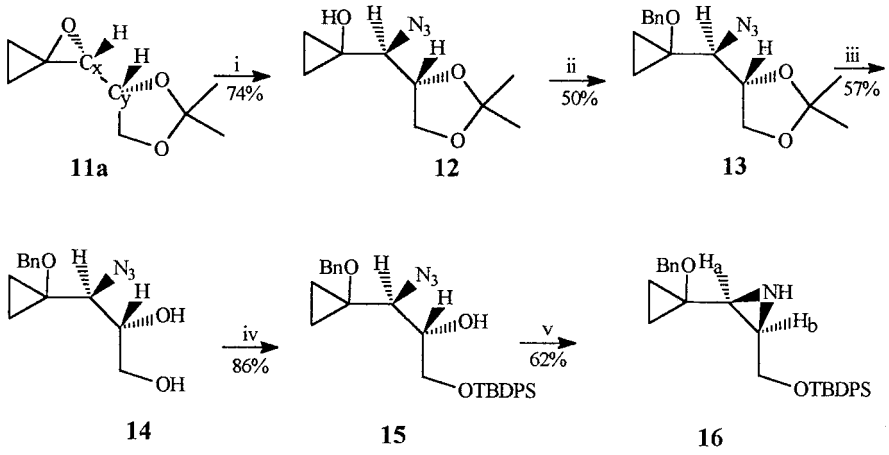
To obtain information regarding the stereoselectivity of this ring expansion using Grignard reagents we decided to use a chiral oxaspiropentane. For this purpose we prepared the oxaspiropentane **11** by peracid oxidation of (*S*)-4-cyclopropylidenemethyl-2,2-dimethyl-1,3-oxadiolane **10** (easily obtained by the Wittig reaction of cyclopropylidenetriphenylphosphorane with (*R*)-2,3-*O*-isopropylideneglyceraldehyde[28] under McMurry's conditions).[29] The oxaspiropentane **11** was obtained as a 70:30 mixture of the expected epoxides, (2*R*)- and (2*S*)-2-[(4*R*)-2,2-dimethyl-1,3-dioxolan-4-yl]-oxaspiropentanes **11a** and **11b** (Scheme 5).

Despite the not particularly high chiral induction, the two diastereoisomers were easily separated by column chromatography (light petroleum/diethyl ether 10:1) and this constitutes an advantage for their synthetic exploitation. The structures have been assigned on the basis of their ^{1}H NMR and the stereochemistry is based on the coupling constant of the doublets of the epoxidic C*H* in the two diastereoisomers.[30–32] As a matter of fact the *syn* stereochemistry has been assigned to the major component of the mixture (J=5.1 Hz) while the *anti* has been assigned to the minor one (J=6.3 Hz). The stereochemical assignment was further corroborated by the transformation of the oxaspiropentane **11a** into the aziridine **16** where the C_x–C_y bond is inserted in a conformationally blocked structure, through the sequence indicated in Scheme 6.

The oxaspiropentane **11a** has been regioselectively and stereospecifically[33–36] opened by reaction with sodium azide to give the azido alcohol **12**, with inversion of configuration, that has been protected with benzyl bromide to give the benzyl ether **13**. Subsequently, **13** has been opened with trifluoroacetic acid and the primary alcoholic group of **14** has been protected as a TBDPS ether to give **15**. Final transformation of **15** into the aziridine **16** has been carried out with PPh_3/THF[37] at reflux for 7 h. The resulting aziridine **16** shows a coupling constant of 6.5 Hz for the protons of the aziridinic ring, a value that is characteristic of a *syn* configuration,[37–39] that is further confirmed by the appearance of a definite NOE enhancement between the two



Scheme 5.



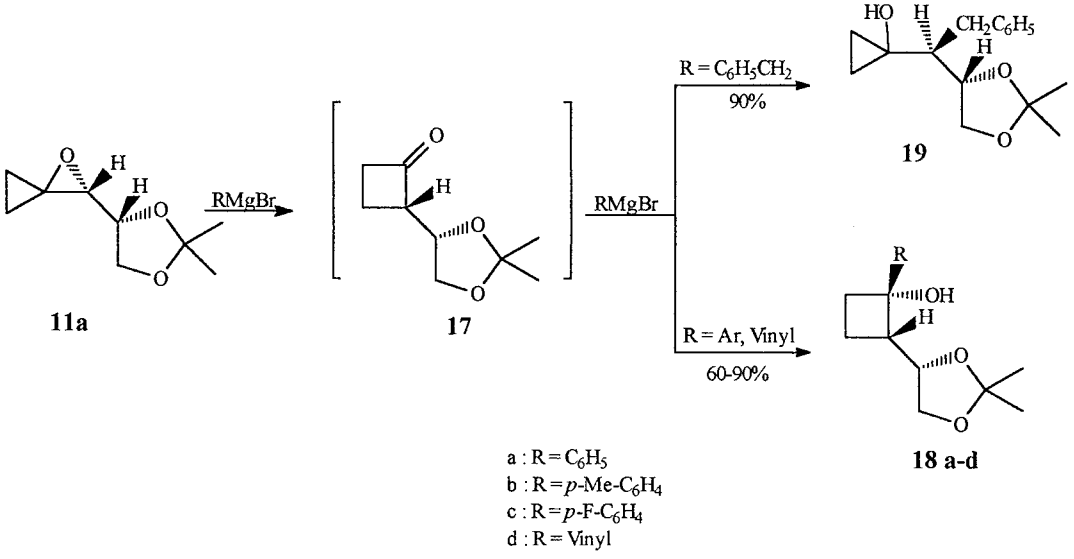
Scheme 6. i: NaN_3/MeOH-H_2O(8:1), NH_4Cl, 80°C, 12 h. ii: NaH, BnBr, n-Bu_4NI, imidazole(cat)THF, 0°C=>50°C. iii: TFA.Dioxane:H_2O-10:1, rt, 48 h. iv: TBDPSCl, DMAP, imidazole, CH_2Cl_2, rt, 20 h. v: PPh_3, THF, 65°C, 7 h.

above mentioned hydrogens. As the transformation of the oxaspiropentane **11b** into the aziridine entails two steps that occur with inversion of configuration,[40] it follows that both the aziridine **16** and the oxaspiropentane **11a** should have the same *syn* configuration.

Once we confirmed the oxaspiropentane configuration, we treated it with a set of Grignard reagents to transform it into the corresponding cyclobutanols **18a–d** and into cyclopropanol **19** in the case of benzyl magnesium chloride (Scheme 7).

During this reaction the chiral epoxidic centre of the oxaspiropentane **11a** is transformed into the chiral C_2 centre of the intermediate cyclobutanone **17**, and a new stereocentre is created by reaction of the Grignard reagent on the carbonyl group to generate the tertiary cyclobutanol. As the stereocentre of the glyceraldehyde derivative is stereochemically stable towards the Grignard reagents,[41,42] we should expect a maximum of four diastereoisomers. In this case we were only able to find evidence for the presence of one diastereoisomer of the expected cyclobutanols **18**. However it was not possible to obtain pure **18** due to the fragility of the oxadiolane ring. As a matter of fact, when examined by glc-mass spectrometry, the products were always accompanied by small amounts of cyclobutanols deprotected at the oxadiolane ring that could not be separated from the protected ones. This result tentatively demonstrates that the transformation induced by Grignard reagents of oxaspiropentanes into cyclobutanones is stereospecific. The attack of the Grignard reagent on the carbonyl of the intermediate cylobutanones occurs with low selectivity in the case of derivatives **9a**,**b** giving mixtures of *Z* and *E* derivatives, but with remarkably high stereoselectivity in the case of the intermediate **17** leading to the corresponding *Z* cyclobutanols **18a–d** where the stereochemistry of the three stereocentres is completely controlled. This assignment is further confirmed by NOE enhancement as shown in Fig. 2.

The *trans* selective addition normally observed for the nucleophilic addition to a carbonyl group of a substituted cyclobutanone[43,44] is explained by the fact that it occurs at the requisite angle of attack[45] (θ=110°) from the *exo* face of



Scheme 7.

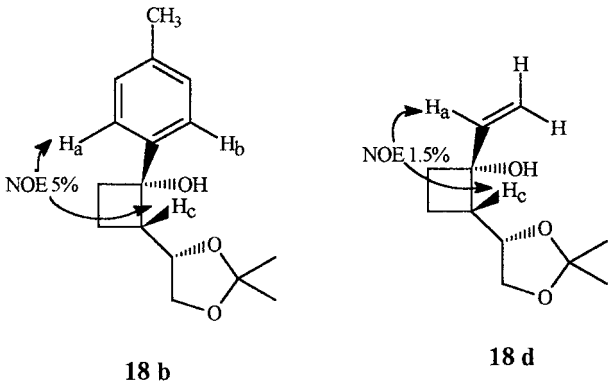


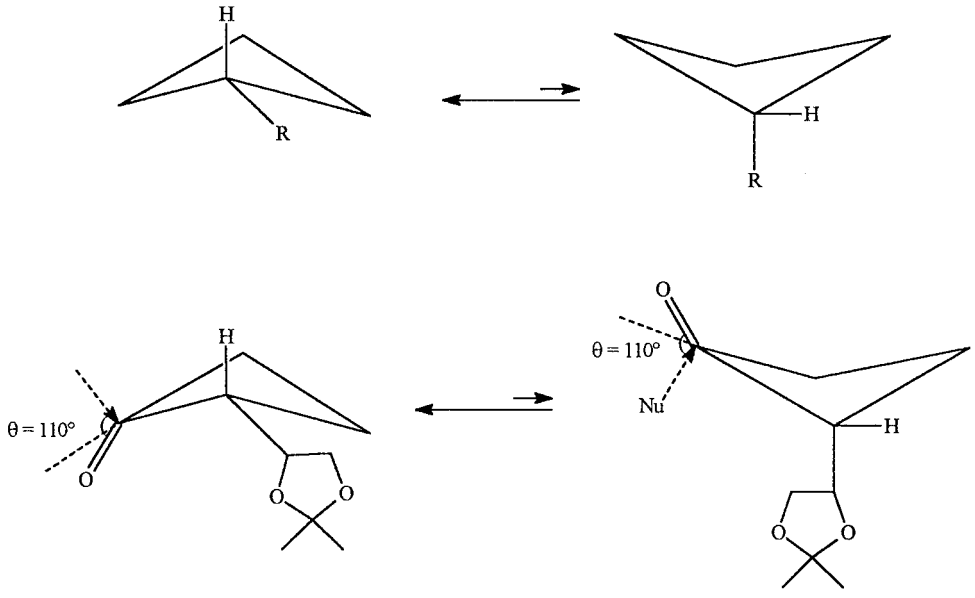
Figure 2.

its most stable conformation, that is the one carrying the substituent in the pseudo equatorial position (Scheme 8).

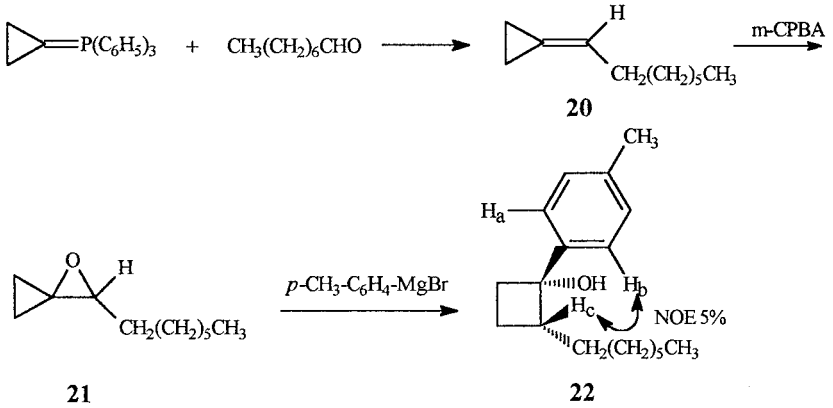
This observation is in agreement with the result we obtained in the case of the intermediate **17**, where it will be the large oxadiolane ring which remains in the equatorial position, avoiding non-bonded repulsions present in the axial conformation, while the lack of stereoselectivity with derivatives **9a**,**b** is explainable on the basis that both the methyl and the aryloxymethylene groups can occupy the equatorial position in conformations of comparable energy.

Finally, as both the oxaspiropentanes **2a**,**b** and **11a**,**b** carry an ether function we decided to check if the presence of the oxygen atom of the ether function was important in the ring expansion induced by Grignard reagents. For this purpose we prepared the oxaspiropentane **21** by *m*-CPBA oxidation of the known cyclopropylidene derivative **20**[46] and reacted it with *p*-tolylmagnesium bromide (Scheme 9).

In this case the corresponding tertiary cyclobutanol **22** was also obtained in good yields, with the *cis* geometry being determined by the presence of a NOE enhancement between the hydrogen H_c (2.51–2.62 ppm) and the aromatic protons H_a and H_b (7.30–7.32 ppm). This result is a clear indication that even an oxaspiropentane lacking a second oxygen atom can undergo ring expansion to a cyclobutanone, giving a tertiary cyclobutanol as the final product.



Scheme 8.



Scheme 9.

Conclusions

A new use of Grignard reagents has been found, as catalysts for the ring expansion of oxaspiropentanes to cyclobutanols, through the intermediacy of cyclobutanones. The reaction represents a shortcut for the synthesis of cyclobutanols by using cyclopropyl derivatives. Furthermore, the complete stereocontrol in the ring expansion and, with aldehyde derivatives, in the attack on the carbonyl group, allows the easy synthesis of cyclobutanols whilst controlling the stereochemistry of several stereogenic centres. Application of this reaction to the synthesis of natural products is currently under investigation and the results will be presented in due course.

Experimental

Reagent-grade commercially available reagents and solvents were used. Analytical TLC plates and silica gel were purchased from Merck. IR spectra were recorded on a Perkin–Elmer 1310 grating spectrophotometer using NaCl plates. ^{1}H and ^{13}C NMR spectra were recorded on a Varian VXR-300 spectrometer with tetramethylsilane as internal reference; δ values are given in ppm and J values in Hz. Mass spectra were obtained at 70 eV with a Hewlett-Packard 5989A mass spectrometer. Optical activity was determined on a Perkin–Elmer 241 polarimeter with a path length of 1 dm. Concentrations are given in g/100 ml. Microanalyses were carried out on a Carlo Erba 1106 Elemental Analyzer. Analytical data of products **2a**, **2b**, **3a**, **7b**, **8**, **9b** have previously reported.[24]

General method for the synthesis of 2a, 2b

To a stirred solution of **1a** or **1b** (0.017 mol) in dichloromethane (80 ml) at 0°C, *m*-CPBA (0.017 mol) was added portion wise. After stirring for 20 h at room temperature, the solution was filtered and treated several times with a saturated solution of sodium bicarbonate. The organic phase was dried (Na_2SO_4) and after filtration evaporated under vacuum. The remaining oil was chromatographed on a silica gel column (light petroleum/diethyl ether 5:1) to give the purified product in 75–90% yields.

Analytical data of cyclobutanols 3b–6b

Following the reported general method[24] cyclobutanols **3a**, **3b**–**7b** and cyclopropanol **8** were prepared.

(*E*)-2-Methyl-2-(phenoxymethyl)-1-phenylcyclobutanol (3b). Yield: 56%. Pale yellow oil. ^{1}H NMR ($CDCl_3$) δ: 1.47 (s, 3H), 1.84–1.91 (m, 2H), 2.16–2.25 (m, 1H), 2.81 (br s, 1H), 2.78–2.87 (m, 1H), 3.26, 3.36 (AB q, 2H, J=9.3 Hz), 6.59–7.44 (m, 10H). ^{13}C NMR ($CDCl_3$) δ: 18.52, 25.01, 30.68, 47.50, 73.06, 79.01, 114.34, 120.32, 125.76, 127.35, 128.05, 129.06, 142.49, 158.99. MS *m/z*: 250 ($M^+-18(<1)$), 175 (71), 148 (18), 133 (62), 105 (100), 94 (48), 77 (41). Anal. Calcd for $C_{18}H_{20}O_2$: C, 80.56; H, 7.51. Found: C, 80.30; H, 7.60.

(*Z*)-2-Methyl-2-(phenoxymethyl)-1-phenylcyclobutanol (3b). Yield: 19%. Pale yellow oil. ^{1}H NMR ($CDCl_3$) δ: 082 (s, 3H), 1.57–1.66 (m, 1H), 2.14–2.35 (m, 2H), 2.79–2.88 (m, 1H), 2.92 (br s, 1H), 4.02, 4.30 (AB q, 2H, J=9.3 Hz), 6.92–7.54 (m, 10H). ^{13}C NMR ($CDCl_3$) δ:21.69, 25.13, 30.89, 46.99, 72.71, 80.63, 114.68, 121.09, 126.21, 127.12, 128.09, 129.52, 143.53, 158.81. MS *m/z*: 250 ($M^+-18(<1)$), 175 (66), 148 (17), 133 (50), 105 (100), 94 (52), 77 (40). Anal. Calcd for $C_{18}H_{20}O_2$: C, 80.56; H, 7.51. Found: C, 80.36; H, 7.40.

(*E*)-2-Methyl-1-(4-methylphenyl)-2-(phenoxymethyl) cyclobutanol (4b). Yield: 67%. Pale yellow oil. ^{1}H NMR ($CDCl_3$) δ: 1.47 (s, 3H), 1.84–1.90 (m, 2H), 2.13–2.23 (m, 1H), 2.26 (br s, 1H), 2.31 (s, 3H), 2.75–2.84 (m, 1H), 3.39, 3.48 (AB q, 2H, J=9.0 Hz), 6.73–7.42 (m, 9H). ^{13}C NMR ($CDCl_3$) δ: 18.52, 20.95, 25.07, 30.68, 47.47, 73.17, 78.95, 114.39, 120.30, 125.67, 128.79, 129.06, 136.95, 139.56, 159.10. MS *m/z*: 265 ($M^+-17(<1)$), 189 (80), 161 (10), 134 (51), 119 (100), 91 (40). Anal. Calcd for $C_{19}H_{22}O_2$: C, 80.22; H, 7.85. Found: C, 80.30; H, 7.65.

(*Z*)-2-Methyl-1-(4-methylphenyl)-2-(phenoxymethyl) cyclobutanol (4b). Yield: 17%. Pale yellow oil. (Discernible data from mixture of *E*/*Z* **4b**): ^{1}H NMR ($CDCl_3$) δ: 0.84 (s, 3H), 0.81–0.98 (m, 1H), 1.54–1.62 (m, 1H), 2.24–2.32 (m, 2H), 2.26 (s, 3H), 2.35 (br s, 1H), 4.00, 4.25 (AB q, 2H, J=9.3 Hz), 6.68–7.43 (m, 9H). ^{13}C NMR ($CDCl_3$) δ: 21.05, 21.73, 25.18, 30.80, 46.90, 72.68, 80.54, 114.68, 121.01, 126.16, 128.79, 129.51, 136.69, 140.67, 158.89. MS *m/z*: 267 ($M^+-15(<1)$), 189 (71), 161 (11), 134 (47), 119 (100), 91 (34).

(*E*)-2-Methyl-2-(phenoxymethyl)-1-vinylcyclobutanol (5b). Yield: 61%. Pale yellow oil. ^{1}H NMR ($CDCl_3$) δ: 1.35 (s, 3H), 1.61–1.67 (m, 2H), 2.08–2.16 (m, 1H), 2.21–2.28 (m, 2H; one is D_2O exchangeable), 3.68, 3.77 (AB q, 2H, J=9.0 Hz), 5.11 (dd, 1H, ^3J=10.8 Hz, ^2J=1.3 Hz), 5.28 (dd, 1H, ^3J=17.4 Hz, ^2J=1.3 Hz), 6.12 (dd, 1H, Calcd J=17.4 Hz, ^3J=10.8 Hz), 6.84–7.27 (m, 5H). ^{13}C NMR ($CDCl_3$) δ: 18.42, 23.95, 30.62, 46.80, 73.01, 76.92, 112.83, 114.48, 120.51, 129.25, 139.82, 159.08. MS *m/z*: 218 ($M^+(<1)$), 148 (8), 133 (86), 94 (95), 77 (10), 55 (100). Anal. Calcd for $C_{14}H_{18}O_2$: C, 77.03; H, 8.31. Found: C, 77.22; H, 7.95.

(*Z*)-2-Methyl-2-(phenoxymethyl)-1-vinylcyclobutanol (5b). Yield: 29%. Pale yellow oil. ^{1}H NMR ($CDCl_3$) δ: 1.10 (s, 3H), 1.46–1.56 (m, 1H), 1.92–2.01 (m, 1H), 2.13–2.33 (m, 2H), 2.65 (br s, 1H), 3.98, 4.15 (AB q, 2H, J=9.0 Hz), 5.18 (dd, 1H, ^3J=10.6 Hz, ^2J=1.5 Hz), 5.31 (dd, 1H, ^3J=17.4 Hz, ^2J=1.5 Hz), 6.09 (dd, 1H, ^3J=17.4 Hz, ^3J=10.6 Hz), 6.93–7.32 (m, 5H). ^{13}C NMR ($CDCl_3$) δ: 20.52, 24.17, 31.31, 46.49, 73.09, 78.01, 112.45, 114.60, 121.01, 129.39, 140.45, 158.69. MS *m/z*: 218 ($M^+(<1)$), 148 (8), 133 (31), 94 (100), 77 (6), 55 (94). Anal. Calcd for $C_{14}H_{18}O_2$: C, 77.03; H, 8.31. Found: C, 77.30; H, 8.10.

(*E*)-1,2-Dimethyl-2-(phenoxymethyl) cyclobutanol (6b). Yield: 36%. Pale yellow oil. ^{1}H NMR ($CDCl_3$) δ: 1.33 (s, 3H), 1.38 (s, 3H), 1.50–1.57 (m, 2H), 1.88–1.96 (m, 2H; one is D_2O exchangeable), 2.04–2.18 (m, 1H), 3.74, 3.88 (AB q, 2H, J=9.3 Hz), 6.88–7.30 (m, 5H). ^{13}C NMR ($CDCl_3$) δ: 18.60, 23.61, 29.69, 33.42, 46.00, 72.99, 74.38, 114.48, 120.60, 129.37,159.18. MS *m/z*: 206

(M^+(<1)), 148 (5), 133 (26), 94 (100), 77 (5), 55 (40). Anal. Calcd for $C_{13}H_{18}O_2$: C, 75.69; H, 8.80. Found: C, 75.22; H, 8.95.

(*Z*)-1,2-Dimethyl-2-(phenoxymethyl) cyclobutanol (6b). Yield: 44%. Pale yellow oil. ^{1}H NMR ($CDCl_3$) δ: 1.12 (s, 3H), 1.33 (s, 3H), 1.37–1.49 (m, 1H), 1.81–2.01 (m, 2H), 2.13–2.21 (m, 1H), 2.75 (br s, 1H), 3.99, 4.07 (AB q, 2H, J=9.0 Hz), 6.92–7.31 (m, 5H). ^{13}C NMR ($CDCl_3$) δ: 19.40, 23.96, 24.38, 34.62, 46.07, 73.45, 75.52, 114.66, 121.08, 129.47, 158.89. MS *m/z*: 206 (M^+(<1)), 148 (4), 133 (20), 94 (100), 77 (4), 55 (33). Anal. Calcd for $C_{13}H_{18}O_2$: C, 75.69; H, 8.80. Found: C, 75.52; H, 8.65.

2-[(4-Methoxyphenoxy)methyl]-2-methylcyclobutanone (9a). A solution of **2a** (1 g, 4.5 mmol) in dichloromethane (10 ml) was treated with LiI (0.30 g, 0.22 mmol, 5 mol%) and refluxed for 24 h. The mixture was washed repeatedly with brine and then dried over Na_2SO_4. Evaporation of dichloromethane left an oil that was purified by chromatography on silica gel column (light petroleum/diethyl ether 3:1) to give 0.87 g of the expected cyclobutanone as a white solid, m.p. 44°C. Yield: 87%. ^{1}H NMR ($CDCl_3$) δ: 1.26 (s, 3H), 1.78–1.88 (m, 1H), 2.35–2.43 (m, 1H), 3.00–3.18 (m,2H), 3.75 (s, 3H), 3.77–3.98 (AB q, 2H, J=9.0 Hz), 6.81 (s, 4H). ^{13}C NMR ($CDCl_3$): 17.49, 21.47, 43.05, 54.98, 63.68, 70.83, 114.09, 115.15, 152.45, 153.65, 212.35. IR (nujol, cm^{-1}): 1785. MS *m/z*: 220 (M^+ (12)), 124 (100), 109 (23), 95 (5), 69 (19). Anal. Calcd for $C_{13}H_{16}O_3$: C, 70.89; H, 7.32. Found: C, 71.06; H, 7.40.

(*S*)-4-Cyclopropylidene-2,2-dimethyl-1,3-oxadiolane (10). To a stirred suspension of pentane washed sodium hydride (60% in oil, 8 g, 0.2 mol) in dry tetrahydrofuran (80 ml), (3-bromopropyl) triphenylphosphonium bromide (46.4 g, 0.1 mol) was added under an argon atmosphere. After adding few drops of absolute ethanol the solution was kept at 70°C (external oil bath). After 6 h at this temperature (*R*)-2,3-*O*-isopropylideneglyceraldehyde (6.4 g, 0.05 mol) dissolved in THF (10 ml) together with TDA-1 (1.6 g, 5 mmol), was added dropwise. The solution was kept at the same temperature for 14 h and then poured onto brine after cooling. The aqueous phase was repeatedly extracted with diethyl ether and then the organic phase was dried over Na_2SO_4. After evaporation of the solvent the viscous residue was washed several times with light petroleum while stirring manually with a glass rod. Evaporation of the light petroleum gave an oil that after purification by column chromatography on a silica gel column (light petroleum/diethyl ether 10:1) left 5.4 g of the pure product as a colourless oil. Yield: 70%. $[\alpha]_D^{20}$=+13.7 (*c* 4, CH_2Cl_2), ^{1}H NMR ($CDCl_3$), δ: 1.07–1.16 (m, 4H), 1.38 (s, 3H), 1.43 (s, 3H), 3.67 (m, 1H), 4.09 (m, 1H), 4.70 (m, 1H), 5.82 (m, 1H); ^{13}C NMR ($CDCl_3$), δ: 1.91, 2.19, 25.91, 26.76, 69.13, 76.72, 108.97, 116.02, 127.92. MS *m/z*: 139 (M^+−15 (10)), 109 (22), 96 (16), 72 (27), 43 (100). Anal. Calcd for $C_9H_{14}O_2$: C, 70.10; H, 9.15. Found: C, 69.90; H, 9.00.

Following the method used for the synthesis of **2a**, **2b** the oxaspiropentanes **11a**, **11b** have been prepared.

(2*R*)-2-[(4*R*)-2,2-Dimethyl-1,3-dioxolan-4-yl]-oxaspiropentane (11a). Colourless liquid. Yield: 49%. $[\alpha]_D^{25}$=+25.82 (*c* 10, $CHCl_3$),^{1}H NMR ($CDCl_3$), δ: 0.92–1.18 (m, 4H), 1.38 (s, 3H), 1.46 (s, 3H), 3.57 (d, 1H, J=5.1 Hz), 4.00–4.13 (m, 3H);^{13}C NMR ($CDCl_3$), δ: 1.69, 2.90, 25.32, 26.53, 57.88, 58.62, 66.43, 75.88, 109.70. MS *m/z*: 155 (M^+−15 (16)), 101 (6), 72 (26), 55 (35), 43 (100). Anal. Calcd for $C_9H_{14}O_3$: C, 63.51; H, 8.29. Found: C, 63.80; H, 8.10.

(2*S*)-2-[(4*R*)-2,2-Dimethyl-1,3-dioxolan-4-yl]-oxaspiropentane (11b). White waxy solid. Yield: 21%. $[\alpha]_D^{25}$=−3.58 (*c* 3, $CHCl_3$), ^{1}H NMR ($CDCl_3$), δ: 0.91–1.15 (m, 4H), 1.38 (s, 3H), 1.46 (s, 3H), 3.56 (d, 1H, J=6.3 Hz), 3.76–4.07 (m, 2H), 4.12–4.19 (m, 1H); ^{13}C NMR ($CDCl_3$), δ: 1.82, 1.93, 25.33, 26.62, 55.91, 59.22, 65.41, 76.90, 110.00. MS *m/z*: 155 (M^+−15 (10)), 101 (4), 83 (7), 72 (13), 55 (25), 43 (100). Anal. Calcd for $C_9H_{14}O_3$: C, 63.51; H, 8.29. Found: C, 63.65; H, 8.40.

1-{(*S*)-Azido [(4*S*)-2,2-dimethyl-1,3-dioxolan-4-yl] methyl} cyclopropanol (12). The oxaspiropentane **11a** (2 g, 13 mmol) was dissolved in 50 ml of methanol/water (8:1) together with sodium azide (4.2 g, 65 mmol) and ammonium chloride (1.4 g, 26 mmol). The solution was stirred at 80°C (external oil bath temperature) for 6 h. The reaction mixture was then poured onto brine and extracted with dichloromethane. After drying and evaporation of the solvent the residue was chromatographed on a silica gel column with a 5:1 light petroleum/diethyl ether mixture, to obtain 2 g of pure product as an oil. Yield: 74%. $[\alpha]_D^{25}$=−22.0 (*c* 4, $CHCl_3$); ^{1}H NMR ($CDCl_3$), δ: 0.61–0.92 (m, 4H), 1.40 (s, 3H), 1.48 (s, 3H), 2.88 (d, 1H, J=6.9 Hz), 3.37 (br s, 1H), 3.89–4.14 (m, 2H), 4.41–4.48 (m, 1H). ^{13}C NMR ($CDCl_3$), δ: 12.14, 12.51, 25.34, 26.34, 56.69, 66.17, 68.16, 77.35, 109.93. IR (neat, cm^{-1}): 3440, 2100. MS *m/z*: 198 (M^+−15 (4)), 155 (2), 113 (5), 101 (45), 43 (100). Anal. Calcd for $C_9H_{15}N_3O_3$: C, 50.68; H, 7.09; N, 19.71. Found: C, 50.95; H, 7.10; N, 19.45.

(4*S*)-4-{(*S*)-Azido [1-(benzyloxy) cyclopropyl] methyl}-2,2-dimethyl-1,3-dioxolane (13). A suspension of sodium hydride (2.2 g of a 65% dispersion in mineral oil, 59 mmol) in anhydrous tetrahydrofuran (35 ml) was treated at 50°C with a solution of benzyl bromide (4.8 g, 28 mmol) also in anhydrous tetrahydrofuran (5 ml). A solution of **12** (5 g, 23.4 mmol) in anhydrous tetrahydrofuran (10 ml) was then added dropwise over 1 h, and the reaction mixture was kept at this temperature for 18 h. After cooling, the reaction mixture was treated carefully with water to destroy the excess of sodium hydride. Dilution with diethyl ether and evaporation of the washed (water) organic solution afforded the crude benzyl ether which was chromatographed on a silica gel column with a 1:1 mixture of light petroleum/diethyl ether to give 3.5 g of pure oily product. Yield: 50%. $[\alpha]_D^{27}$=−19.7 (*c* 9, $CHCl_3$); ^{1}H NMR ($CDCl_3$), δ: 0.73–0.98 (m, 4H), 1.36 (s, 3H), 1.43 (s, 3H), 3.21 (d, 1H, J=8.4 Hz), 3.89–4.15 (m, 2H), 4.35–4.42 (m, 1H), 4.49, 4.74 (AB q, 2H, J_{AB}=11.7 Hz), 7.23 (m, 5H). ^{13}C NMR ($CDCl_3$), δ: 9.81, 13.25, 25.54, 26.79, 62.06, 66.55, 69.00, 71.15, 77.72, 109.45, 127.30, 127.63, 128.38, 138.03. IR (neat, cm^{-1}): 2100. MS *m/z*: 288 (M^+−15 (<1)), 174 (4), 147 (3), 101 (15), 91 (100). Anal. Calcd for $C_{16}H_{21}N_3O_3$: C, 63.33; H, 6.98; N, 13.86. Found: C, 63.50; H, 6.90; N, 13.45.

(2*S*,3*S*)-3-Azido-3-[1-(benzyloxy) cyclopropyl]-1,2-propanediol (14). To a solution of the protected azido alcohol **13** (2.5 g, 8.2 mmol) in dioxane/water (1:1, 40 ml), trifluoroacetic acid (1.7 ml) was slowly added under magnetic stirring. After 48 h the reaction mixture was diluted with dichloromethane and the organic phase was washed with sodium bicarbonate and brine. After drying (Na_2SO_4) and evaporation of the solvent, the crude reaction mixture was chromatographed (ethyl acetate/light petroleum 1:1) on a silica gel column previously deactivated with methanol/water (95:5) and then with methanol. 1.24 g of pure product were obtained as a clear oil. Yield: 57%. $[\alpha]_D^{27}=-32.0$ (*c* 2, $CHCl_3$); ^{1}H NMR ($CDCl_3$), δ: 0.80–1.17 (m, 4H), 2.92 (br s, 2H), 3.23 (d, 1H, *J*=6.9 Hz), 3.74–3.86 (m, 2H), 4.00–4.06 (m, 1H), 4.55, 4.87 (AB q, 2H, J_{AB}=11.4 Hz), 7.28 (m, 5H). ^{13}C NMR ($CDCl_3$), δ: 10.14, 12.66, 62.13, 62.90, 69.18, 71.58, 72.82, 127.41, 127.81, 128.48, 137.58. IR (neat, cm^{-1}): 3440, 2100. MS *m/z*: 220 (M^+-43 (<1)), 146 (2), 118 (100), 104 (2), 91 (95). Anal. Calcd for $C_{13}H_{17}N_3O_3$: C, 59.30; H, 6.51; N, 15.96. Found: C, 59.66; H, 6.60; N, 15.81.

(1*S*,2*S*)-1-Azido-1-[1-(benzyloxy) cyclopropyl]-3-{[*tert*-butyl (diphenyl) silyl]oxy}–2-propanol (15). A solution of the diol **14** (1.6 g, 6 mmol) in dry dichloromethane (30 ml) was treated with Et_3N (0.72 g, 7 mmol), *t*-butyl diphenylsilyl chloride (1.8 g, 6.5 mmol) and DMAP (0.029 g, 0.24 mmol) and stirred at room temperature for 24 h. The reaction mixture was diluted with water and extracted with dichloromethane. The combined organic extracts were dried (Na_2SO_4), concentrated in vacuo and chromatographed on a silica gel column (ethyl acetate/light petroleum 4:1) to yield 2.6 g of a pure oil. Yield: 86%. $[\alpha]_D^{27}=-3.9$ (*c* 13, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ: 0.80–1.11 (m, 4H), 1.06 (s, 9H), 2.79 (d, *J*=4.2 Hz, 1H), 3.36 (br s, 1H), 3.72–3.91 (m, 2H), 4.10–4.16 (m, 1H), 4.52, 4.82 (AB q, *J*=11.4 Hz 2H), 7.19–7.73 (m, 15H). ^{13}C NMR ($CDCl_3$): δ=10.47; 12.63; 19.24; 26.89; 62.71; 64.28; 68.09; 71.29; 73.11; 127.37; 127.80; 128.40; 129.89; 132.84; 133.00; 135.53; 137.97. IR (neat, cm^{-1}): 3440, 2100. MS *m/z*: 416 (M^+-85 (<1)), 241 (14), 199 (20), 163 (24), 91 (100). Anal. Calcd for $C_{29}H_{35}N_3$ O_3Si: C, 69.43; H, 7.03; N, 8.38. Found: C, 69.60; H, 7.10; N, 8.73.

(2*R*,3*S*)-2-[1-(Benzyloxy) cyclopropyl]-3-({[*tert*-butyl (diphenyl) silyl]oxy} methyl) aziridine (16). To a stirred solution of triphenylphosphine (1.3 g, 5.1 mmol) in dry tetrahydrofuran (20 ml) the product **15** (2.6 g, 5.1 mmol) was added. After refluxing for 7 h the mixture was diluted with water (30 ml) and extracted with dichloromethane. The combined organic extracts were dried (Na_2SO_4), concentrated in vacuo and chromatographed on a silica gel column (ethyl acetate/light petroleum 1:4) to yield 1.6 g (62%) of a pure oil. $[\alpha]_D^{27}=-4.5$ (*c* 30, $CHCl_3$), ^{1}H NMR ($CDCl_3$), δ: 0.58–0.99 (m, 4H), 1.05 (s, 9H), 2.37 (dt, 1H, *J*=6.0, 4.5 Hz), 2.48 (br s, 1H), 2.58 (d, 1H, *J*=6.0 Hz), 3.79–3.84 (m, 1H), 3.97–4.01 (m, 1H), 4.43, 4.64 (AB q, 2H, *J*=11.4), 7.30–7.62 (m, 15H); ^{13}C NMR ($CDCl_3$), δ: 10.24, 11.26, 19.17, 26.84, 34.59, 37.95, 60.37, 63.25, 69.94, 127.47, 127.54, 128.17, 129.53, 133.63, 135.55, 135.60, 138.59. MS *m/z*: 458 (M^+-15 (<1)), 288 (7), 240 (60), 188 (20), 162 (21), 91 (100). Anal. Calcd for $C_{29}H_{35}NO_2Si$: C, 76.10; H, 7.71; N, 3.06. Found: C, 76.51; H, 7.63; N, 3.10.

Synthesis of cyclobutanols 18a–d and cyclopropanol 19

18a–d and **19** have been prepared and purified by following the same procedure described for **3a**, **3b–7b** and **8**. NMR data of **18 a-d**, **19** were obtained from compounds containing 5–10% of cyclobutanols deprotected at the oxadiolane ring.

(1*S*,2*S*)-2-[(4*S*)-2,2-Dimethyl-1,3-dioxolan-4yl]-1-phenylcyclobutanol (18a). Yield: 90%. Colourless oil. ^{1}H NMR ($CDCl_3$), δ: 1.25 (s, 3H), 1.31 (s, 3H), 1.68–1.88 (m, 2H), 2.20–2.42 (m, 2H), 2.75 and 2.78 (dt 1H *J*=8.7, 8.1 Hz), 3.50–3.60 (m, 1H), 3.60 (br s, 1H), 3.96–4.02 (m, 1H), 4.39–4.44 (m, 1H), 7.10–7.60 (m, 5H). ^{13}C NMR ($CDCl_3$), δ: 16.97, 25.31, 26.61, 33.26, 46.92, 67.10, 75.56, 77.71, 108.95, 125.01, 126.68, 127.90, 146.84. MS *m/z*: 233 (M^+-15 (2)), 190 (12), 162 (12), 145 (28), 120 (63), 43 (100).

(1*S*,2*S*)-2-[(4*S*)-2,2-Dimethyl-1,3-dioxolan-4yl]-1-(4-methylphenyl) cyclobutanol (18b). Yield: 90%. Colourless oil. ^{1}H NMR ($CDCl_3$) 1.33 (s, 3H), 1.38 (s, 3H), 1.70–1.93(m, 2H), 2.25–2.40 (m, 2H), 2.32 (s, 3H), 2.78 and 2.81 (dt, 1H *J*=8.0, 8.7 Hz), 3.35 (br s, 1H), 3.59–3.65(m, 1H), 4.00–4.09 (m, 1H), 4.42–4.56 (m, 1H), 7.10–7.39 (m, 4H); ^{13}C NMR ($CDCl_3$), δ: 16.97, 20.90, 25.42, 26.74, 33.40, 47.06, 67.42, 76.04, 77.82, 109.25, 125.01, 128.79, 136.50, 143.93. MS *m/z*: 247 (M^+-15 (<1)), 204 (7), 159 (23), 119 (100), 105 (8), 91 (33).

(1*S*,2*S*)-2-[(4*S*)-2,2-Dimethyl-1,3-dioxolan-4yl]-1-(4-fluorophenyl) cyclobutanol (18c). Yield: 65%, colourless oil; ^{1}H NMR ($CDCl_3$), δ: 1.35 (s, 3H), 1.37 (s, 3H), 1.84–1.91 (m, 2H), 2.33–2.44 (m, 2H), 2.70–2.82 (m, 1H), 3.01 (br s, 1H), 3.60–3.65 (m, 1H), 4.02–4.55 (m, 1H), 4.46–4.55 (m, 1H), 6.99–7.52 (m, 4H); ^{13}C NMR ($CDCl_3$), δ: 17.15, 25.51, 26.86, 33.64, 47.33, 67.59, 76.22, 77.55, 109.37,114.79, 115.08, 143.02, 163.45. MS *m/z*: 251 (M^+-15 (<1)), 209 (<1), 191 (3), 163 (26), 123 (100), 109 (7), 95 (20).

(1*R*,2*S*)-2-[(4*S*)-2,2-Dimethyl-1,3-dioxolan-4yl]-1-vinylcyclobutanol (18d). Yield: 60%, colourless oil. ^{1}H NMR ($CDCl_3$), δ: 1.35 (s, 3H), 1.40 (s, 3H), 1.70–1.84 (m, 2H), 2.06–2.28 (m, 2H), 2.37–2.48 (m, 1H), 3.17 (br s, 1H), 3.58–3.66 (m, 1H), 4.02–4.08 (m, 1H), 4.41–4.48 14 (m, 1H), 5.05 (dd, 1H *J*=10.8, 1.2 Hz), 5.27 (dd, 1H *J*=17.4, 1.2 Hz), 6.09 (dd, 1H *J*=10.8, 17.4 Hz). ^{13}C NMR ($CDCl_3$): δ=16.46, 25.53, 26.99, 32.27, 46.57, 67.59, 73.94, 75.97, 76.38, 109.19, 111.24, 143.67. MS *m/z*: 183 (M^+-15 (<1)), 109 (35), 99 (40), 70 (70), 55 (100).

1-{(1*S*)-1-[(4*S*)-2,2-Dimethyl-1,3-dioxolan-4-yl]-2-phenylethyl cyclopropanol (19). Yield: 90%. White crystals, mp 123–124°C. ^{1}H NMR ($CDCl_3$), δ 0.01–0.07 (m, 1H), 0.28–0.36 (m, 1H), 0.53–0.60 (m, 1H), 0.64–0.71 (m, 1H), 1.26–1.33 (m, 1H), 1.40 (s, 3H), 1.49 (s, 3H), 2.57 (brs, 1H), 2.89–3.09 (AB q, 1H, *J*=13.8 Hz), 2.91–3.06 (AB q, 1H, *J*=13.8 Hz), 3.84–3.91 (m, 1H), 4.06–4.11 (m, 1H), 4.42–4.48 (m, 1H), 7.10–7.27 (m, 5H). ^{13}C NMR ($CDCl_3$)=2.54; 13.48; 25.23; 26.47;32.82; 49.51; 56.91; 67.14; 78.08;

108.92; 125.93; 128.23; 129.28; 140.72. MS *m*/*z*: 247 (M^+-15 (2)), 204 (26), 187 (13), 161 (21), 131 (33), 91 (100).

2-Heptyl-1-oxaspiro[2.2] pentane (21). To a well stirred suspension of potassium fluoride (318 mg, 5.5 mmol) in dry dichloromethane (8 ml), was added *m*-CPBA (552 mg, 3.2 mmol) and the resulting suspension was stirred at room temperature for 1 h. Then a solution of **20** (500 mg, 3.2 mmol) dissolved in 8 ml of dry dichloromethane was added at room temperature and the reaction was stirred for 1 h. The mixture was filtered through a layer of silica gel and the solvent evaporated under vacuum. The residue was purified by column chromatography on silica gel using light petroleum/diethyl ether 5:1 as eluent. Yield: 90%, colourless oil. ^{1}H NMR ($CDCl_3$), δ=0.85 1.12 (m, 7H), 1.20–1.82 (m, 12H), 3.45 (t, 1H, J=6 Hz). ^{13}C NMR ($CDCl_3$): δ=13.96; 16.80; 22.54; 25.72; 26.95; 29.03; 29.32; 29.48; 31.70; 44.26; 60.53. MS *m*/*z*: 168 (M^+ (1)), 150 (3), 124 (2), 112 (10), 98 (100), 84 (33), 70 (30). Anal. Calcd for $C_{11}H_{20}O$: C, 78.51; H, 11.98. Found: C, 78.32; H, 12.07.

(*Z*)-2-Heptyl-1-(4-methylphenyl) cyclobutanol (22). The synthesis of **22** was carried out by following the same procedure described for cyclobutanols **18**. Colourless oil. Yield: 78%. ^{1}H NMR ($CDCl_3$), δ=0.87 (t, J=6.3 Hz, 3H), 1.25 (m, 10H), 1.42–1.63 (m, 2H), 1.71–1.86 (m, 1H), 1.88–2.00 (m, 1H), 2.04 (br s, 1H), 2.08–2.19 (m, 1H), 2.24–2.41 (m, 1H), 2.31 (s, 3H), 2.51–2.62 (m, 1H), 7.11–7.32 (m, 4H). ^{13}C NMR ($CDCl_3$): δ=14.04; 20.93; 21.84; 22.61; 26.99; 29.26; 29.31; 29.78; 31.82; 34.11; 45.75; 78.62; 124.68; 128.88; 136.39; 144.39. MS *m*/*z*: 260 (M^+ (4)), 232 (4), 157 (1), 134 (100), 119 (45), 91 (22). Anal. Calcd for $C_{18}H_{28}O$: C, 83.02; H, 10.84. Found: C, 83.32; H, 11.06.

Acknowledgements

Financial support from the Ministero dell'Università e della Ricerca Scientifica e Tecnologica, Rome, and by the University of Cagliari (National Project 'Stereoselezione in Sintesi Organica. Metodologie ed Applicazioni') and from C.N.R. (Italy) is gratefully acknowledged. One of us (A. Frongia) gratefully acknowledges financial support from the Regione Autonoma of Sardinia (Grant no. 178, art. 37 L.R. 2/94)

References

1. Trost, B. M. *Top. Curr. Chem.* **1986**, *133*, 3.
2. Salaun, J. *Top. Curr. Chem.* **1988**, *144*, 1.
3. Crandall, J. K.; Paulson, D. R. *J. Org. Chem.* **1968**, *33*, 991.
4. Crandall, J. K.; Paulson, D. R. *J. Org. Chem.* **1968**, *33*, 3291.
5. Salaun, J.; Conia, J. M. *J. Chem. Soc., Chem. Commun.* **1971**, 1579.
6. Salaun, J.; Champion, J.; Conia, J. M. *Org. Synth.* **1977**, *57*, 36.
7. Aue, D. H.; Meshishnek, M. J.; Shellhamer, D. F. *Tetrahedron Lett.* **1973**, 4799.
8. Erden, I.; de Meijere, A.; Rousseau, G.; Conia, J. M. *Tetrahedron Lett.* **1980**, *21*, 2501.
9. Wiseman, J. R.; Chan, H. F. *J. Am. Chem. Soc.* **1970**, *92*, 4749.
10. Makosza, M.; Wawrzyniewicz, M. *Tetrahedron Lett.* **1969**, 4569.
11. Dammann, R.; Braun, M.; Seebach, D. *Helv. Chim. Acta* **1976**, *59*, 2821.
12. Hiyama, T.; Takehara, S.; Kitatani, K.; Nozaki, H. *Tetrahedron Lett.* **1974**, 3295.
13. Wiechert, R. *Angew. Chem., Int. Ed. Engl.* **1970**, *9*, 27; *Angew. Chem.* **1970**, *82*, 219.
14. Johnson, C. R.; Katekar, G. F.; Huxol, R. F.; Janiga, E. R. *J. Am. Chem. Soc.* **1971**, *93*, 71.
15. Bogdanowicz, M. J.; Trost, B. M. *Tetrahedron Lett.* **1972**, 887.
16. Bogdanowicz, M. J.; Trost, B. M. *J. Am. Chem. Soc.* **1973**, *95*, 289.
17. Bogdanowicz, M. J.; Trost, B. M. *J. Am. Chem. Soc.* **1973**, *95*, 5311.
18. Trost, B. M.; Scudder, P. H. *J. Am. Chem. Soc.* **1977**, *99*, 7601.
19. Trost, B. M.; Kurozumi, S. *Tetrahedron Lett.* **1974**, 1929.
20. Salaun, J.; Conia, J. M. *J. Chem. Soc., Chem. Commun.* **1971**, 1579.
21. Chevtchouk, T.; Ollivier, J.; Salaun, J. *Tetrahedron: Asymmetry* **1997**, *8*, 1011.
22. Johnson, C. R. *Acc. Chem. Res.* **1973**, *6*, 341.
23. Trost, B. M. *Acc. Chem. Res.* **1974**, *7*, 85.
24. Preliminary communication: Bernard, A. M.; Floris, C.; Frongia, A.; Piras, P. P. *Synlett* **1998**, 668.
25. Bernard, A. M.; Piras, P. P. *Synlett* **1997**, 585.
26. Raston, C. L.; Salem, G. In *The Chemistry of the Metal–Carbon Bond*; Hartley, F. R., Ed.; Wiley: New York, 1987; pp 4–159.
27. Miller, D. D.; Hsu, Fu-L.; Salman, K. N.; Patil, P. N. *J. Med. Chem.* **1978**, *19*, 180.
28. Schmid, C. R.; Bryant, J. D.; Dowlatzedah, M.; Phillips, J. L.; Prather, D. E.; Schantz, R. D.; Sear, N. L.; Vianco, C. S. *J. Org. Chem.* **1991**, *56*, 4056.
29. Stafford, J. A.; McMurry, J. E. *Tetrahedron Lett.* **1988**, *29*, 2531.
30. Horton, D.; Hughes, J. B.; Thomson, J. K. *J. Org. Chem.* **1968**, *33*, 728.
31. Mihelich, E. D. *Tetrahedron Lett.* **1979**, 4729.
32. Yang, Z.; Zhou, W. *Tetrahedron* **1995**, *51*, 1429.
33. Rao, A. S.; Paknikar, S. K.; Kirtane, J. K. *Tetrahedron* **1983**, *39*, 2323.
34. Crotti, P.; Ferretti, M.; Macchia, F.; Stoppioni, A. *J. Org. Chem.* **1984**, *49*, 4706.
35. Chini, M.; Crotti, P.; Macchia, F. *Tetrahedron Lett.* **1990**, *31*, 5641.
36. Zamboni, R.; Rocach, J. *Tetrahedron Lett.* **1983**, *24*, 331.
37. Scriven, E. F. V.; Turnbull, K. *Chem. Rev.* **1988**, 297.
38. Shaw, K. J.; Luly, J. R.; Rapoport, H. *J. Org. Chem.* **1985**, *50*, 4515.
39. Batterham, T. J. *NMR Spectra of Simple Heterocycles*, Wiley: New York, 1973; pp 138–139.
40. Ittah, Y.; Sasson, Y.; Shahak, I.; Tsaroom, S.; Blum, J. *J. Org. Chem.* **1978**, *43*, 4271.
41. Mulzer, J.; Angerman, A. *Tetrahedron Lett.* **1983**, *24*, 2843.
42. Jurczak, J.; Pikul, S.; Bauer, T. *Tetrahedron* **1986**, *42*, 447 (and literature therein).
43. Baldwin, J. E.; Adlington, R. M.; Parisi, M. F.; Ting, H.-Hoi *Tetrahedron* **1986**, *42*, 2575.
44. Overman, L. E.; Okazaki, M. E.; Jacobsen, E. J. *J. Org. Chem.* **1985**, *50*, 2403.
45. Baldwin, J. E. *J. Chem. Soc., Chem. Commun.* **1976**, 738.
46. Nemoto, H.; Miyata, J.; Hakamata, H.; Nagamochi, M.; Fukumoto, K. *Tetrahedron* **1995**, *51*, 5511.