Regioselective Opening of Epoxy Alcohols: Mild Chemo- and Stereoselective Preparation of Iodohydrins and 1,2-Diols[1]

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Received December 27, 1990

Several 2,3-epoxy alcohols have been opened, at −60 °C, with MgI_2, leading to the corresponding 3-iodo 1,2-diols with a high level of regio- and chemoselectivity. The iodohydrins can be reduced "in situ", by means of nBu_3SnH, to the corresponding 1,2-diols. The chemo-, regio-, and stereocontrol of the reaction makes the method of wide use. Furthermore, epoxy alcohol derivatives (acetyl, benzyl, or TBMS) still maintain a strong preference for C-3 attack of the nucleophile. The experimental data strongly suggest that a metal (Mg) centered chelate is formed throughout the reaction, which gives rise to the regioselective delivery of the iodide ion.

The regioselectivity of oxirane opening by means of metal iodides (mainly MgI_2) and the "in situ" subsequent radical reaction which leads to the corresponding reductive or cyclization product have been investigated recently in our laboratory.[2]

As a natural extension of these studies we decided to examine the behavior of 2,3-epoxy alcohols which are very attractive starting materials as they are readily available in optically pure form by the Sharpless asymmetric epoxidation.[3] Figure 1 shows what might be the possible role of MgI_2 in directing the nucleophilic attack, as reported recently for the reactions of 2,3-epoxy esters with metal iodides.[2b,4]

A recent communication by Martin et al.[5] on the regioselective opening of epoxy alcohols to the corresponding halohydrins (I_2 or Br_2 in the presence of $Ti(OiPr)_4$) has prompted us to report some results from our investigation of epoxide opening reactions.

As shown in Table I, a large number of epoxy alcohols were submitted to the standard conditions (MgI_2 in toluene and then eventually nBu_3SnH, see Experimental Section).

The results show that ring opening by MgI_2 greatly favors the 3-iodo 1,2-diols[6] (and the subsequent formation of the corresponding 1,2-diols) in most cases.[7]

The experimental data suggest the following generalizations:

1. This procedure gives rise to the corresponding 3-iodo 1,2-diols with regio and chemical yields and chemoselectivity[8] that are comparable or superior to those obtained by available methods.[5,9]

2. As described in the general procedure (see Experimental Section), the reaction sequence leading to the formation of 1,2-diols can be performed in one pot, without the isolation of the corresponding iodohydrins. The well known chemoselectivity (see compounds **3–5**, **7**, **8**, and **11**) displayed under radical conditions, makes our method more flexible than the known procedure for the reductive opening of 2,3-epoxy alcohols with hydride reagents (i.e., DIBAL or $LiBH_4$).[10]

3. The extremely interesting case of the protected (acetyl, benzyl, or TBMS group) epoxy alcohols **3–5** and **8**, represent significant improvements over other methodologies and makes these compounds particularly attractive for further synthetic elaboration; in other known procedures the free hydroxyl group is clearly essential to increase the rate and the regioselectivity of the ring opening, which does not happen in the experiments described here.

4. A previously postulated chelate complex[9a] between the metal (Mg) and the two oxygens of the epoxy alcohol seems to occur, without the need of other known coordinating species such as $Ti(OiPr)_4$.[5,9a,d] This chelate still functions in the cases of protected epoxy alcohols, in contrast with other reports. The regioselectivity observed for silyl derivative **5** is still to be understood, in view of the well-known inability of the *O*-silyl derivatives to chelate;[11] more studies are needed to explain this behavior, which greatly extends the usefulness of the procedure.

5. The cases of epoxy alcohols **11** and **12**, in which the opening of the oxirane ring is also favored by steric hindrance, further demonstrates the usefulness of this procedure.

In conclusion, an attractive alternative route to the regio- and chemoselective opening of epoxy alcohols is now available. This methodology leads to a series of useful chiral 3-iodo 1,2-diols or directly to 1,2-diols to be utilized in the synthesis of more complex molecules. We intend to apply the described methodology to other functionalized epoxides (i.e., secondary epoxy alcohols or derivatives).

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(1) Presented at "Chemioforum Ricerca 90" Battipaglia, Salerno, May 25–30, 1990.

(2) (a) Bonini, C.; Di Fabio, R. *Tetrahedron Lett.* **1988**, *29*, 819. (b) Bonini, C.; Di Fabio, R.; Sotgiu, G.; Cavagnero, S. *Tetrahedron* **1989**, *45*, 2895, (c) Bonini, C.; Di Fabio, R.; Mecozzi, S.; Righi, G. *Tetrahedron Lett.* **1990**, *31*, 5369.

(3) Katsuki, T.; Sharpless, K. B. *J. Am. Chem. Soc.* **1980**, *102*, 5974.

(4) Otsubo, K.; Inanaga, J.; Yamaguchi, M. *Tetrahedron Lett.* **1987**, *28*, 4435.

(5) Alvarez, E.; Nunez, M. T.; Martin, V. S. *J. Org. Chem.* **1990**, *55*, 3429.

(6) The regioisomer ratios were determined by ^1H NMR and ^{13}C NMR spectroscopy, as well by HPLC and GC/MS analyses (see Experimental Section for detailed data). The stereochemistry of the iodohydrins can be easily established by reconverting them to the starting epoxides. **General Procedure.** The iodohydrin (0.5 mmol) was dissolved in MeOH (1 mL) at −20 °C, and 0.2 M KOH in MeOH (2.5 mL, 0.5 mmol) was added. After TLC monitoring (3–6 h), the reaction was quenched with 1 N HCl solution, extracted with ether (twice), dried (Na_2SO_4), and concentrated in vacuo to yield the starting epoxy alcohol in quantitative yield.

(7) The presence of a homoallylic oxygen may be responsible for the observed low regioselectivity for compound **10**; geraniol epoxide **9** gave rise to several byproducts, although the only product which could be isolated was the corresponding 1,2-diol **29**.

(8) No trace of compounds arising from the attack of MgI_2 on other functional groups (acetyl, benzyl, benzoyl, silyl, or olefin) was detected.

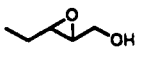
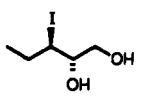
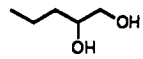
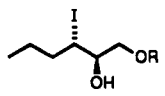
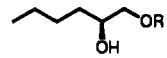
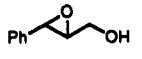
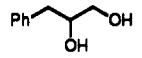
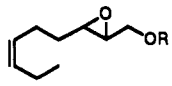
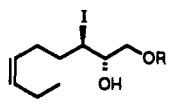
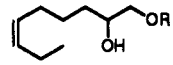
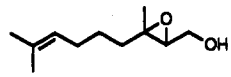
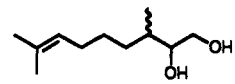
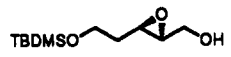
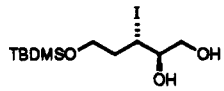
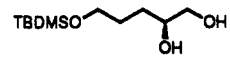
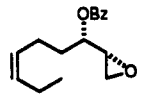
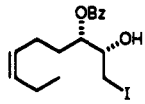
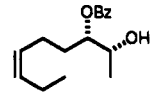
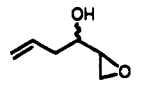
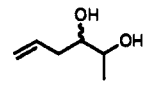
(9) (a) Caron, M.; Sharpless, K. B. *J. Org. Chem.* **1985**, *50*, 1557. (b) Lu, L. D.; Jonhson, R. A.; Finn, M. G.; Sharpless, K. B. *Ibid.* **1984**, *49*, 728. (c) Onaka, M.; Sugita, K.; Takeuchi, H.; Izumi, Y. *J. Chem. Soc., Chem. Commun.* **1988**, 1173. (d) Gao, L.; Murai., A. *Chem. Lett.* **1989**, 35.

(10) Finan, J. M.; Kishi, Y. *Tetrahedron Lett.* **1982**, *23*, 2719. Dai, L.; Lou, B.; Zhang, Y.; Gou, G. *Ibid.* **1986**, *27*, 4343.

(11) Kahn, S. D.; Keck, G. E.; Hehre, W. J. *Tetrahedron Lett.* **1987**, *28*, 279.

0022-3263/91/1956-6206$02.50/0

Table I. Structures and Stereochemistry of the Major Iodohydrins and 1,2-Diols from MgI_2-Promoted Opening of Epoxy Alcohols and Their Derivatives

epoxide[a]		major iodohydrin		major 1,2-diol	
structure	R no.	structure	no. (yield[b] (%))	structure	no. (ratio)[c] (yield[b] (%))
	1		13 (85)		21 (97:3) (75)
	H 2				22 (96:4) (77)
	Ac 3		14 (90)		23 (95:5) (75)
	Bn 4		15 (90)		24 (>99:1) (52)
	TBDMS 5		16 (93)		25 (>99:1) (78)
	6				26 (>99:1) (80)
	H 7		17 (85)		27 (96:4) (74)
	Bn 8		18 (85)		28 (>99:1) (72)
	9				29 (>99:1) (50)
	10		19 (65)		30 (70:30) (55)
	11		20 (90)		31 (98:2) (85)
	12				32 (>99:1) (85)

[a] Compounds 2, 10, and 11 used in enantiomeric form. [b] Combined yields on isolated products. [c] Ratio C_3:C_2 attack: the ratios are the same for the corresponding iodohydrins.

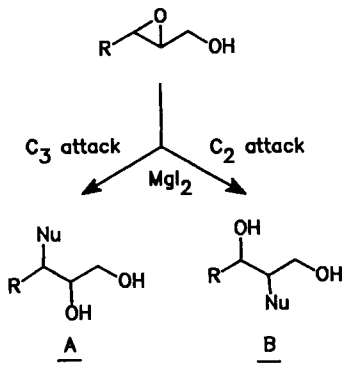


Figure 1.

These compounds as well as the regioselective opening of epoxy alcohols leading to the corresponding 2-iodo 1,3-diols or 1,3-diols are being investigated.

Experimental Section

General. Flash chromatography was carried out on silica gel (70–230 mesh). TLC analyses were performed on Merck Kieselgel 60 F-254 plates. All the solvents were redistilled and dried before use. Elemental analysis could not be performed satisfactorily for iodohydrins 13–20 because of their instability. ^1H and ^{13}C NMR spectra were determined at 200 and 50.3 MHz, respectively, in $CDCl_3$. HPLC analyses were carried out with a C_{18} column HP ODS Hypersil with CH_3CN/H_2O as eluent. GC/MS analyses were conducted with a SPB1 capillary column and a quadrupole mass spectrometer.

The regioisomer ratios of the iodohydrins were determined from ^1H and ^{13}C NMR spectra as well as HPLC and GC/MS analyses.

Preparation of the Starting Epoxy Alcohols 1–12. Compounds 1, 3–9, and 12 were prepared using the standard epoxidation procedure[12] from the corresponding available *E* allylic alcohols. Compound 10, a known compound as its enantiomer, was prepared according to refs 13 and 14. Compound 11 was prepared according to ref 2c and references cited therein.

Compounds 2, 6, and 9 are known compounds, and their spectroscopic and physical data were compared with the literature data.[15]

Representative Procedure for Preparation of 2,3-Epoxy Alcohols:[12] (2*S,3*S**,6*Z*)-2,3-Epoxy-6-nonen-1-ol (7).** A solution of (2*E*,6*Z*)-2,6-nonadien-1-ol[16] (1 g, 7.14 mmol) in dry CH_2Cl_2 (150 mL) was stirred and cooled at −20 °C under N_2, and $Ti(OiPr)_4$ (7.2 mmol) was added. After the solution was stirred for 20 min, a 3 M solution of *tert*-butyl hydroperoxide in toluene (7.2 mmol, 2.5 mL) was slowly added. The reaction was stopped after 3 h, (TLC monitoring) and quenched with a saturated solution of Na_2SO_3 (20 mL). The organic layer, diluted with ether (150 mL), was then washed with brine and dried over Na_2SO_4. After concentration in vacuo the crude residue was purified by silica gel chromatography (petroleum ether/ether (1/1) as eluent), affording pure compound 7 (900 mg, 82%) as a colorless oil: ^1H NMR 5.2–5.4 (m, 2 H), 3.9 (m, 1 H), 3.5 (m, 1 H), 2.9 (m, 2 H), 2.35 (bs, OH, 1 H), 2.10 (q, J = 7.2 Hz, 2 H), 2.0 (quintet, J = 7.2 Hz, 2 H), 1.6 (q, J = 7.2 Hz, 2 H), 0.91 ppm (t, J = 9 Hz, 3 H); ^{13}C NMR 132.86, 127.54, 62.64, 59.58, 55.50, 31.45, 23.32, 20.24, 14.00 ppm. Anal. Calcd for $C_9H_{16}O_2$: C, 69.18; H, 10.32. Found: C, 69.29; H, 10.27.

(2*S,3*S**)-2,3-Epoxypentan-1-ol (1):** colorless oil; yield 550 mg (78%); ^1H NMR 3.75 (dd, J = 3.6 and 12.7 Hz, 1 H), 3.55 (dd, J = 7.3 and 12.9 Hz, 1 H), 3.1 (m, 2 H), 2.9 (m, 1 H), 1.5 (m, 2 H), 0.95 ppm (t, J = 7.3 Hz, 3 H). Anal. Calcd for $C_5H_{10}O_2$: C,

(12) Sharpless, K. B.; Michaelson, R. C. *J. Am. Chem. Soc.* **1973**, *95*, 6136.
(13) Bonadies, F.; Di Fabio, R.; Gubbiotti, A.; Mecozzi, S.; Bonini, C. *Tetrahedron Lett.* **1987**, *28*, 703.
(14) Harold, P.; Mohr, P.; Tamm, C. *Helv. Chim. Acta* **1983**, *66*, 744.
(15) Gao, Y.; Hanson, R. M.; Klunder, J. M.; Ka, S. Y.; Masamune, H.; Sharpless, K. B. *J. Am. Chem. Soc.* **1987**, *109*, 5765.
(16) Vig, O. P.; Sharma, H. L.; Ganba, R. *Ind. J. Chem.* **1985**, *24B*, 313.

58.78; H, 9.87. Found: C, 58.65; H, 9.98.

(2S*,3S*)-1-Acetoxy-2,3-epoxyhexane (3) was prepared from racemic compound **2** by a standard acetylation procedure[17] in quantitative yields (250 mg, 98%): yellow oil; ^{1}H NMR 4.2–4.35 (m, 1 H), 3.8–3.9 (m, 1 H), 2.9 (m, 1 H), 2.75 (m, 1 H), 2.0 (m, 3 H), 1.4 (m, 4 H), 0.9 ppm (m, 3 H); ^{13}C NMR 170.95, 64.58, 56.25, 55.10, 33.25, 20.41, 18.87, 13.49 ppm. Anal. Calcd for $C_8H_{14}O_3$: C, 60.72; H, 8.92. Found: C, 60.59; H, 8.97.

(2S*,3S*)-1-(Benzyloxy)-2,3-epoxyhexane (4) was prepared from compound **2** with the same described procedure for compound **8** (benzylation of **7**, see below): yellow oil; yield 258 mg (58%); ^{1}H NMR 7.3 (m, 5 H), 4.5, 4.6 (2 d, J = 12.5 Hz, 2 H), 3.71 (dd, J = 3.6, 12 Hz, 1 H), 3.45 (dd, J = 5.4, 12 Hz, 1 H), 2.9 (m, 1 H), 2.8 (m, 1 H), 1.4 (m, 4 H); 0.9 ppm (bt, J = 7.3 Hz, 3 H); ^{13}C NMR 138.12, 128.48, 127.79, 73.16, 70.41, 56.80, 55.82, 35.50, 19.02, 13.64 ppm. Anal. Calcd for $C_{13}H_{18}O_2$ C, 75.68; H, 8.80. Found: C, 75.57; H, 8.86.

(2S*,3S*)-1-[(*tert*-Butyldimethylsilyl)oxy]-2,3-epoxyhexane (5) was prepared from **2** by a standard silylation procedure:[17] colorless oil; yield 351 mg (82%); ^{1}H NMR 3.75 (dd, J = 3.5 and 11.8 Hz, 1 H), 3.63 (dd, J = 4.7, 11.8 Hz, 1 H), 2.8 (m, 2 H), 1.5 (m, 4 H), 0.90 (m, 3 H), 0.86 (bs, 9 H), 0.1–0.0 ppm (2s, 6 H); ^{13}C NMR 63.64, 58.55, 56.13, 33.58, 25.69, 19.10, 18.15, 13.68, –5.60, –5.55 ppm. Anal. Calcd for $C_{13}H_{26}O_2$: C, 72.83; H, 12.23. Found: C, 72.96; H, 12.17.

(2S*,3S*,6Z)-1-(Benzyloxy)-2,3-epoxy-6-nonene (8). A solution of compound **7** (46 mg, 0.3 mmol) in THF (10 mL) was stirred at –20 °C under N_2. Then KH (35 mg, 0.3 mmol of a 35% suspension) was added, followed by dropwise addition of benzyl bromide (51 mg, 0.3 mmol). After TLC monitoring (10 min) the reaction mixture was quenched with saturated NH_4Cl, ether (15 mL) was added, and the organic layer washed with brine. After drying over Na_2SO_4, the organic phase was concentrated in vacuo; the crude mixture was then purified by silica gel chromatography (petroleum ether/ether (8/2) as eluent), affording pure compound **8** (37 mg, 52%) as a colorless oil: ^{1}H-NMR 7.3 (m, 5 H), 5.3–5.5 (m, 2 H), 4.55–4.6 (2 d, J = 12.5 Hz, 2 H), 3.7 (dd, J = 3.6 and 11 Hz, 1 H), 3.45 (dd, 5.4 and 11 Hz, 1 H), 2.95 (m, 1 H), 2.8 (m, 1 H), 2–2.2 (m, 4 H), 1.6 (m, 2 H), 0.95 ppm (t, J = 7.3 Hz, 3 H). Anal. Calcd for $C_{16}H_{22}O_2$: C, 77.99; H, 9.00. Found: C, 77.88; H, 9.08.

(2R,3S,6Z)-1,2-Epoxy-3-(benzoyloxy)-6-nonene (11): colorless oil; yield 48 mg (35%); ^{1}H NMR 8.0–8.1 (d, J = 6 Hz, 2 H), 7.4–7.6 (m, 3 H), 5.2–5.45 (m, 2 H), 4.9–5.0 (m, 1 H), 3.0–3.1 (m, 1 H), 2.7–2.85 (m, 2 H), 2.1–2.85 (m, 2 H) 0.8–2.1 (m, 4 H) 0.9 ppm (t, J = 8 Hz, 3 H); ^{13}C NMR 133.28, 130.17, 129.80, 128.56, 127.50, 73.19, 52.33, 45.37, 31.36, 22.53, 20.31, 14.03 ppm; $[\alpha]_D$ = 19.40° ($CHCl_3$, c = 1.8%). Anal. Calcd for $C_{16}H_{20}O_3$: C, 73.80; H, 7.74. Found: C, 73.28; H, 7.61.

1,2-Epoxy-5-hexen-3-ol (12): colorless oil; yield 127 mg (68%), mixture of diastereoisomers (erythro/threo (9/1)); ^{1}H NMR 5.8 (m, 1 H), 5.15 (m, 2 H), 3.8 (m, 1 H), 3.0 (m, 1 H), 2.7 (m, 2 H), 2.3 ppm (m, 2 H); ^{13}C NMR 133.68, 118.29, 68.07, 53.99, 43.75, 37.91 ppm. Anal. Calcd for $C_6H_{10}O_2$: C, 63.12; H, 8.84. Found: C, 63.01; H, 8.91.

Preparation of Iodohydrins 13–20. Representative Procedure for Preparation of 3-Iodo 2,3-Diols: (2S*,3R*,6Z)-3-Iodo-6-nonene-1,2-diol (17). A solution of epoxy alcohol **7** (312 mg, 2.1 mmol) in dry toluene (20 mL) was stirred and cooled at –60 °C under N_2, and MgI_2 (2.1 mmol) in ether (2 mL) was added. The reaction mixture was vigorously stirred with a magnetic apparatus, since MgI_2 is scarcely soluble in the toluene solution. The reaction can be followed by TLC, monitoring the formation of the iodohydrins (UV lamp and H_2SO_4 spray). After 1–2 h the reaction was completed and the temperature was raised to rt. After the reaction was quenched with saturated Na_2SO_3 (5 mL), the organic layer was diluted with ether and washed with brine. After being dried (Na_2SO_4), the solvents were evaporated in vacuo affording the crude mixture of iodohydrins, which was checked by ^{1}H and ^{13}C NMR spectroscopy *before purification*. The reaction mixture was then purified by silica gel chromatography (petroleum/ether (6/4) as eluent) affording pure compound **17** as a yellow oil; yield 481 mg (85%); ^{1}H NMR 5.2–5.5 (m, 2 H), 4.1–4.2 (m, 1 H), 3.6–3.9 (m, 2 H), 3.5–3.6 (m, 1 H), 3.0 (bs, OH, 1 H), 2.6 (bs, OH, 1 H), 2.0–2.3 (m, 4 H), 1.7–1.9 (m, 2 H), 0.9 (t, J = 8 Hz, 3 H); ^{13}C NMR 133.72, 126.75, 75.01, 65.72, 39.61, 35.16, 26.93, 20.52, 14.15 ppm.

For epoxy alcohols **3**, **4**, and **8**, the reaction was performed at –20 °C, because of the longer reaction times required (6 h), with no detectable changes in the regioselectivity of the reaction.

(2S*,3R*)-3-Iodopentane-1,2-diol (13): yellow oil; yield 220 mg (85%); ^{1}H NMR 4.1–4.25 (m, 1 H), 3.7 (d, J = 5.4 Hz, 2 H), 3.2–3.35 (m, 1 H), 2.8 (bs, OH, 1 H), 1.8–1.95 (m, 2 H), 1.05 ppm (t, J = 7.2 Hz, 3 H); ^{13}C NMR 74.69, 66.60, 44.99, 30.41, 14.30 ppm.

(2S*,3R*)-1-Acetoxy-3-iodohexan-2-ol (14): yellow oil; yield 120 mg (90%); ^{1}H NMR 4.1–4.4 (m, 3 H); 3.65 (m, 1 H); 2.5 (d, J = 6.6 Hz, OH, 1 H), 2.1 (s, 3 H), 1.6–1.9 (m, 2 H), 1.2–1.45 (m, 2 H), 0.9 ppm (t, J = 6.7 Hz, 3 H); ^{13}C NMR 171.51, 73.21, 67.84, 39.98, 22.76, 20.70, 12.95 ppm.

(2S*,3R*)-1-(Benzyloxy)-3-iodohexan-2-ol (15): yellow oil; yield 160 mg (90%); ^{1}H NMR 7.3–7.4 (bs, 5 H), 4.55 (s, 2 H), 4.1–4.2 (m, 1 H), 3.6–3.8 (m, 3 H), 2.7 (d, J = 4 Hz, OH, 1 H), 1.2–1.8 (m, 4 H), 0.9 ppm (t, J = 6 Hz, 3 H); ^{13}C NMR 137.76, 121.61, 128.04, 127.92, 73.60, 73.47, 73.20, 39.90, 36.99, 22.64, 12.98 ppm.

(2S*,3R*)-1-[(*tert*-Butyldimethylsilyl)oxy]-3-iodohexan-2-ol (16): yellow oil; yield 218 mg (93%); ^{1}H NMR 4.1 (m, 1 H), 3.9 (dd, J = 4.1 and 9 Hz, 1 H), 3.7–3.8 (dd, J = 5.1 and 9 Hz, 1 H), 3.6 (m, 1 H), 2.7 (m, OH, 1 H), 1.7–1.9 (m, 2 H), 1.3–1.7 (m, 2 H) 0.9 (t, J = 7.1 Hz, 3 H), 0.8 (s, 12 H), 0.1 ppm (s, 6 H); ^{13}C NMR 74.54, 66.08, 39.60, 37.04, 25.69, 22.57, 18.06, 13.03, 5.61 ppm.

(2S*,3R*,6Z)-1-(Benzyloxy)-3-iodo-6-nonen-2-ol (18): yellow oil; yield 45 mg (85%); ^{1}H NMR 7.3 (bs, 5 H), 5.2–5.5 (m, 2 H), 4.55 (s, 2 H), 4.1–4.2 (m, 1 H), 3.6–3.8 (m, 3 H), 2.6 (bs, OH, 1 H), 2.0–2.3 (m, 4 H), 1.8–1.9 (m, 2 H), 0.9 ppm (t, J = 8 Hz, 3 H); ^{13}C NMR 133.57, 128.66, 128.09, 127.95, 126.98, 73.56, 73.50, 73.18, 39.38, 35.04, 26.92, 20.61, 14.20 ppm.

(2S,3R)-5-[(*tert*-Butyldimethylsilyl)oxy]-3-iodopentane-1,2-diol (19): yellow oil; mixture of regioisomers, yield 29 mg (65%), ^{1}H NMR 4.35–4.5 (m, 0.7 H), 4.25–4.35 (m, 0.3 H), 3.5–3.95 (m, 4 H), 3.1–3.2 (m, 1 H), 2.3 (s, OH, 1 H), 2.0–2.1 (m, 2 H), 0.85 (s, 9 H), 0.1 ppm (s, 6 H); ^{13}C NMR 74.09, 71.27, 66.88, 66.55, 62.19, 61.24, 44.75, 39.82, 39.22, 38.91, 25.73, 25.68, 25.66, –5.65 ppm.

(2S,3S,6Z)-1-Iodo-3-(benzoyloxy)-6-nonen-2-ol (20): yellow oil; 27 mg (90%); ^{1}H NMR 8.05 (m, 2 H), 7.2–7.7 (m, 3 H), 5.2–5.5 (m, 2 H), 5.1–5.2 (m, 1 H), 3.8–4.0 (m, 1 H), 3.15–3.45 (m, 2 H), 2.5 (d, J = 4.4 Hz, OH, 1 H), 1.7–2.3 (m, 6 H), 0.9 ppm (t, J = 6.6 Hz, 3 H); ^{13}C NMR 166.25, 133.28, 133.09, 130.03, 129.86, 128.64, 127.29, 75.89, 72.90, 30.30, 22.72, 20.30, 13.98, 9.78 ppm.

Preparation of 1,2-Diols 21–32. Representative Procedure for Preparation of 1,2-Diols: (Z)-6-Nonene-1,2-diol (27). The previous procedure for the preparation of the iodohydrin from epoxy alcohol **7** (312 mg, 2.08 mmol) was followed. After the regioselective opening by MgI_2 was completed (TLC monitoring), the reaction mixture was allowed to warm to rt. Then AIBN (catalytic, 10 mg) and nBu_3SnH (611 mg, 2.1 mmol) were added and the temperature was raised to 70 °C. After 1 h (TLC monitoring, with a UV lamp), the reaction was stopped and most of the solvent was removed in vacuo. The concentrate was diluted with CH_3CN (50 mL) and washed with hexane (5 mL, three times) to remove most of the tin residues. The solvent was evaporated in vacuo. The crude mixture, checked before purification by NMR spectroscopy, HPLC, and GC, was then chromatographed on silica gel (petroleum ether, and then petroleum ether/Et_2O (1/1) as eluent) affording pure compound **27** as a colorless oil (230 mg, 74% overall yield from **7**): ^{1}H NMR 5.2–5.4 (m, 2 H), 3.5–3.7 (m, 2 H), 3.4 (m, 1 H), 2.8 (bs, OH, 2 H), 2.0 (m, 2 H), 1.4 (m, 2 H), 0.9 ppm (t, J = 8.2 Hz, 3 H); ^{13}C NMR 132.30, 128.68, 72.21, 66.74, 32.53, 26.80, 25.47, 20.34, 14.11 ppm. Anal. Calcd for $C_9H_{18}O_2$: C, 67.47; H, 11.78. Found: C, 67.53; H, 11.72.

Compounds **21** and **22** are commercially available products. Compound **26** is a known compound.[18]

1-Acetoxyhexan-2-ol (23): oil; yield 88 mg (75%); ^{1}H NMR 4.15 (dd, J = 3.3, 10 Hz, 1 H), 3.85 (dd, J = 6.7 and 10 Hz, 1 H),

(17) Greene, T. W. *Protective Groups in Organic Synthesis*; John Wiley & Sons: New York, 1981.

(18) Barluenga, J.; Flores, J.; Yus, M. *J. Chem. Soc., Perkin Trans 1* **1983**, *12*, 3019.

3.7–3.8 (m, 1 H), 2.2 (d, J = 5 Hz, OH, 1 H), 2.1 (s, 3 H), 1.2–1.5 (m, 4 H), 0.9 ppm (bt, J = 6 Hz, 3 H); ^{13}C NMR 171.50, 69.82, 68.69, 32.82, 27.31, 22.40, 20.68, 13.73 ppm. Anal. Calcd for $C_8H_{16}O_3$: C, 59.95; H, 10.17. Found: C, 59.87; H, 9.8.

1-(Benzyloxy)hexan-2-ol (24): oil, yield 65 mg (52%); ^{1}H NMR 7.3 (bs, 5 H), 4.5 (s, 2 H), 3.8 (m, 1 H), 3.5 (dd, J = 3.5, 8 Hz, 1 H), 3.3 (dd, J = 8, 8.8 Hz, 1 H), 2.3 (d, J = 4 Hz, OH, 1 H), 1.2–1.6 (m, 4 H), 0.9 ppm (bt, J = 6 Hz, 3 H); ^{13}C NMR 138.19, 128.69, 128.60, 128.03, 127.86, 74.65, 73.31, 70.42, 32.68, 27.51, 22.54, 13.78 ppm. Anal. Calcd for $C_{13}H_{20}O_2$: C, 74.94; H, 9.68. Found: C, 74.82; H, 9.66.

1-[(*tert*-Butyldimethylsilyl)oxy]hexan-2-ol (25): oil; yield 103 mg (78%); ^{1}H NMR 3.6 (m, 2 H), 3.3–3.4 (dd, J = 9, 10 Hz, 1 H), 2.45 (d, J = 3.3 Hz, OH, 1 H), 1.2–1.4 (m, 4 H), 0.9 (s, 12 H), 0.1 ppm (s, 6 H); ^{13}C NMR 71.78, 67.23, 32.32, 27.58, 25.70, 22.59, 18.08, 13.80, -5.62 ppm. Anal. Calcd for $C_{13}H_{28}O_2$: C, 72.15; H, 13.05. Found: C, 72.01; H, 13.0.

(6*Z*)-1-(Benzyloxy)-6-nonen-2-ol (28): oil; yield 30 mg (85%); ^{1}H NMR 7.3 (bs, 5 H), 5.2–5.4 (m, 2 H), 4.5 (s, 2 H), 3.8 (m, 1 H), 3.4–3.5 (m, 1 H), 3.2–3.3 (m, 1 H), 2.3 (d, J = 3.5 Hz, OH, 1 H), 2.0 (m, 2 H), 1.4 (m, 2 H), 0.9 ppm (t, J = 7.1 Hz, 3 H); ^{13}C NMR 132.17, 128.81, 128.59, 127.91, 127.86, 74.58, 73.31, 70.31, 32.49, 26.22, 25.43, 20.33, 14.15 ppm. Anal. Calcd for $C_{16}H_{24}O_2$: C, 77.36; H, 9.74. Found: C, 77.31; H, 9.76.

3,8-Dimethyl-7-nonene-1,2-diol (29): oil; mixture of diastereoisomers (erythro/threo (2/1)), yield 156 mg (50%); ^{1}H NMR 5.0–5.1 (m, 1 H), 3.4–3.8 (m, 3 H), 1.7–2.1 (m, 2 H), 1.65 (s, 3 H), 1.55 (s, 3 H), 1.6–1.1 (m, 5 H), 1.35 (s, OH, 1 H), 1.1 (s, OH, 1 H), 0.87 ppm (dd, J = 6.4 Hz, 3 H). Anal. Calcd for $C_{11}H_{22}O_2$: C, 70.90; H, 11.90. Found: C, 70.68; H, 11.97.

(2*S*)-5-[(*tert*-Butyldimethylsilyl)oxy]pentane-1,2-diol (30): oil; mixture of regioisomers, yield 18 mg (55%); ^{1}H NMR 3.2–4.0 (m, 5 H), 2.9 (bs, OH, 1 H), 1.4–2.1 (m, 4 H), 0.9 (s, 9 H), 0.1 ppm (s, 6 H). Anal. Calcd for $C_{12}H_{26}O_3$: C, 65.99; H, 12.00. Found: C, 65.81; H, 12.21.

(2*R*,3*S*,6*Z*)-3-(Benzoyloxy)-6-nonen-2-ol (31): oil; yield, 19 mg (85%); ^{1}H NMR 8.1 (m, 2 H), 7.2–7.6 (m, 3 H), 5.2–5.6 (m, 2 H), 5.0–5.2 (m, 1 H), 4.7 (d, J = 6.2 Hz, OH, 1 H), 3.9–4.1 (m, 1 H), 1.7–2.2 (m, 6 H), 1.2 (d, J = 6.6 Hz, 3 H), 0.9 ppm (t, J = 7.5 Hz, 3 H). Anal. Calcd for $C_{16}H_{22}O_3$: C, 73.24; H, 8.45. Found: C, 73.49; H, 8.98.

5-Hexene-2,3-diol (32): oil; mixture of diastereoisomers, yield 106 mg (85%); ^{1}H NMR 5.8–6.0 (m, 1 H), 5.1–5.35 (m, 2 H), 3.8–4.2 (m, 2 H), 1.7–2.1 (m, 2 H), 2.0 (bs, OH, 2 H), 1.2 (d, J = 6.5 Hz, 3 H). Anal. Calcd for $C_6H_{12}O_2$: C, 62.02; H, 10.42. Found: C, 61.89; H, 10.63.

Acknowledgment. This work was partially supported by a MURST grant and by C.N.R. Progetto Finalizzato "Chimica Fine e Secondaria".

Supplementary Material Available: ^{1}H and ^{13}C NMR spectra for all listed compounds (32 pages). Ordering information is given on any current masthead page.

Ab Initio Theoretical Studies on the Homotrimethylenemethane (HTMM) Diradical and Two Monomethyl-Substituted Derivatives

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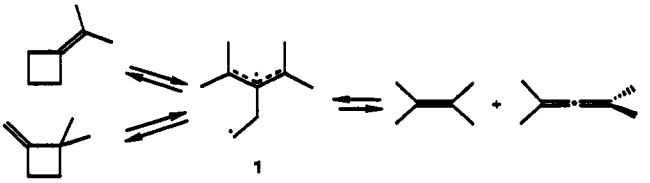
Received May 7, 1991

Ab initio calcuations have been carried out on the singlet and triplet states of the lowest energy conformation of the homotrimethylenemethane diradical **28** (HTMM) at the CASSCF, 4-31G level with full geometry optimization. At this level the lowest energy triplet state is only 0.77 kcal/mol^{-1} lower in energy than the singlet state, and the geometries are essentially identical, indicating that there is no interaction between the two radical centers in the intermediate. Geometry optimization calculations at the UHF 6-31G* level on the HTMM energy surface have located two other minimum-energy conformations **31** and **29** lying 0.56 and 1.61 kcal mol^{-1} higher in energy. Optimization calculations at the 6-31G* level indicate that the energy barriers for rotation about the C_1–C_2 and C_1–C_9 bonds in **28** are approximately 1.68 and 1.62 kcal mol^{-1}, respectively. The effect of the values of these energy barriers on the stereochemistry of the (2 + 2) cycloaddition reactions of optically active 1,3-dimethylallene are discussed. Calculations have been also carried out on the methyl-substituted HTMM's **24** and **25** at the 4-31G level as models for the substituted diradical intermediates formed in the (2 + 2) cycloaddition reactions of substituted allenes with variously substituted radicophiles, and rotational energy barriers for racemization processes in the diradical intermediates have been estimated. The results of these calculations are compared with the proposed structures of substituted HTMM's formed in the (2 + 2) cycloaddition reactions of substituted allenes and in the methylenecyclobutane rearrangement.

Introduction

Substituted homotrimethylenemethane diradicals (HTMM's, **1**) have been implicated as intermediates in the thermal rearrangement of methylenecyclobutanes[1] and as intermediates in the (2 + 2) cycloaddition reactions of substituted allenes. Several different conformations have been proposed for the substituted HTMM's formed in the rearrangement and (2 + 2) cycloaddition reactions.



1

Doering and Gilbert reported on the kinetics of the thermal equilibrium of **2** and **3** and suggested that in view of the fact that the observed activation energy exceeded the expected bond dissociation energy of the distal C_2–C_3 or C_3–C_4 bond the rearrangement proceeded via a diradical

(1) For a review see: Gajewski, J. J. *Hydrocarbon Thermal Isomerizations*, Academic Press, New York, 1981; pp 90–94.

0022-3263/91/1956-6209$02.50/0