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SELECTIVE REARRANGEMENTS OF 4a,5-EPOXIDES OF 4,4-DIMETHYL-1,2,3,4,6,8a-HEXAHYDRONAPHTHALENES.[1]

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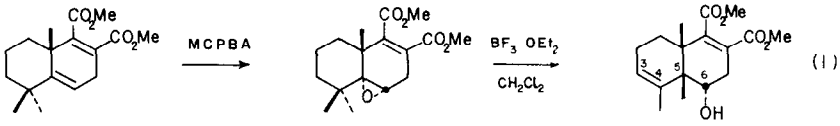
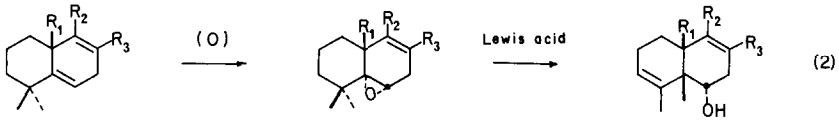
Summary: *Epoxidation selectivity of a number of 4,4-dimethyl-1,2,3,4,6,8a-hexahydronaphthalenes* **4** *were examined. Exposure of the isolated α-epoxides* **7** *provided excellent yields (79-92%) of rearranged fused indene-oxetanes* **8**. *Treatment of β-epoxides* **5** *with* $BF_3 \cdot OEt_2$ *also yields oxetanes* **8** *and related alcohols* **9** *and* **10**.

As part of another project, we examined the reaction sequence described in equation 1. The direction of epoxidation of **1**[5a] was confirmed by single crystal x-ray analysis of **2**[6]; which indicated that the 4β- and 10β-CH_3 groups of **2** were ideally disposed in the chair-like A-ring for migration upon rupture of the C-5-O bond.[7] In the event, treatment of **2** with $BF_3 \cdot OEt$ (CH_2Cl_2, 0°) provided **3** in 76% yield. The migration of the 4-CH_3 group was expected based upon precedent[7,1] but a priori the effect of the 8,9-double bond was unknown.



1 **2** (90%) **3** (76%)



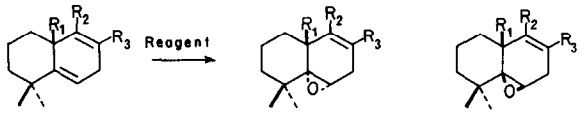
4 **5** **6**

These observations (eq. 1) and the close structural similarity of the C-3 to C-6 portion of **3** to the clerodane diterpenes,[8] ajugarin IV,[8a] and arenarol[8c] suggested that such compounds might be approached as outlined in equation 2 (R_1 = H). With proper choice of R_2 and R_3, **6** might be readily converted to cis-clerodanes; and with epimerization at C-10, trans-clerodanes would be obtained. The success of this strategy depends upon selective epoxidation of **4** (eq. 2, R_1 = H) and a directed rearrangement of **5** to **6**. We have examined the epoxidation selectivity and subsequent rearrangement of a variety of hexahydronaphthalenes **4**[1] as described below.

The first substrates treated with $BF_3 \cdot OEt_2$ (1.25 eq., CH_2Cl_2, 0°) were the β-epoxides **7c-f**. The reaction of **7f** with $BF_3 \cdot OEt_2$ (Table 2) provided a single compound, oxetane **8f**,[9] in 92% yield. The nature of **8f** was apparent from an inspection of spectral data;[9,10,11]

particularly, EI/MS (70eV): m/e 204 ($M-C_3H_6O$);[10,11] ^{1}H-NMR (250 MHz, $CDCl_3$)[9]: δ = 4.75 (br m, 4-H),[12a,b] 2.80 (br t, J = 8.3 Hz, 9-H), 2.76 (dd, J = 18.8, 2.3 Hz, 3-H), 2.26 (dd, J = 18.8, 4.2 Hz, 3-H); and ^{13}C-NMR (68.9 MHz, $CDCl_3$): δ = 83.7 (s, C-10) and 81.8 (d, C-4).[12b] Extensive decoupling studies (^{1}H-NMR) suggested the C-9, C-1 through C-4 arrangement shown. The nature of the ring system was demonstrated by exposure of **8f** to NaOMe, MeOH providing the related 1,3-diene-5-C$(CH_3)_2$OH ring-opened material (75%).[9] Reaction of the dienol with pyridinium chlorochromate afforded expected dihydroindene diester[9,13] which was identical in all respects when compared to literature data[14a] and an authentic sample.[14b] The cis relationship of the bridging oxetane to the ring-fusion hydrogen was indicated by nuclear Overhouser difference spectroscopy (NOEDS).[15] The isolation of oxetanes **8** from BF_3 OEt_2 treatment of epoxide **7** was unexpected;[7] however, an inspection of molecular models

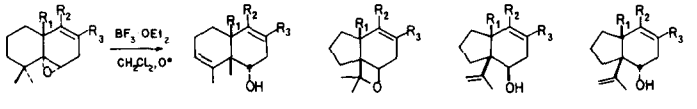
TABLE 1



4 5 7

Compound	R_1	R_2	R_3	Reagent	Yield(%)	Ratio(5:7)
4a	Me	CO_2Et	H	MCPBA	81	95:5
4b	Me	H	CO_2Et	MCPBA	90	95:5
4c	H	CO_2Et	H	MCPBA	82	10:90
4c	H	CO_2Et	H	NBS, aq. tBuOH	94	100:0
4d	H	CO_2Me	Me	MCPBA	78	11:89
4d	H	CO_2Me	Me	NBS, aq. tBuOH	54	100:0
4e	H	H	CO_2Et	MCPBA	77	33:67
4e	H	H	CO_2Et	NBS, aq. tBuOH	60	85:15
4f	H	CO_2Me	CO_2Me	MCPBA	95	45:55

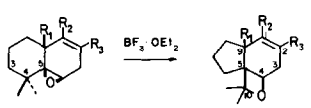
TABLE 3



5 3 8 9 10

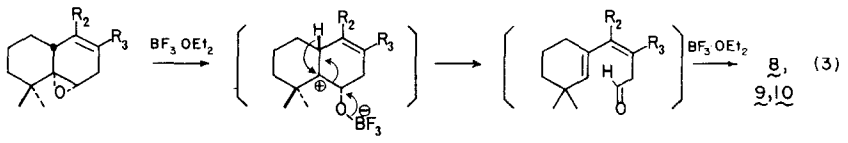
Compound	R_1	R_2	R_3	Yields			
5a	Me	CO_2Et	H	81%	—	—	—
5c	H	CO_2Et	H	—	60%	30%	—
5e	H	H	CO_2Et	—	52%	27%	10%
5f	H	CO_2Me	CO_2Me	—	53%	30%	8%

TABLE 2



7 8

Compound	R_1	R_2	R_3	Yield(%)
7c	H	CO_2Et	H	80
7d	H	CO_2Me	Me	79
7e	H	H	CO_2Et	87
7f	H	CO_2Me	CO_2Me	92



5c-f 11 8, 9,10 (3)

demonstrates the ideal positioning of the C-3-C-4 ring bond of **7** for migration with respect to the breaking C-5-O bond, giving **8** after ring closure. Similar epoxides **7c**, **7d** and **7e** provided oxetanes **8c** (80%), **8d** (79%), and **8e** (87%), respectively.

The α-epoxide **5a** (Table 3) provided the expected CH_3-migration product **3a** (1.25 eq., $BF_3 \cdot OEt_2$, CH_2Cl_2, 0°; 81%) as expected by analogy to equation 1. However, epoxides **5c**, **5e**, and **5f** failed to give even trace quantities of the desired products **3**, yielding instead oxetanes **8** (52-60%), and alcohols **9** (27-30%) and **10** (0-10%). The oxetanes **8c**, **8e**, and **8f** were compared to those isolated from rearrangement of epoxides **7** and were found to be identical. Alcohols **9** and **10** were separated, acetylated and compared with the 4-OAc, 5-isopropenyl compounds derived from oxetanes **8** (pTsOH, Ac_2O, PhH-reflux, 3 hrs.).[9] The acetates prepared from the major alcohols **9** were indistinguishable from those derived from oxetanes **8**. The structures of alcohols **10** were secured after conversion of the acetates of **9** and **10** to single dienes (KOtBu, THF).

The conversion of **5** to oxetanes **8** requires an inversion of configuration at C-5 and C-6 of the parent **5** with respect to the 9-H. Such a process might occur as outlined in equation 3. Rupture of the C-5-O bond, accompanied by 10-H migration of the C-5-C-6 ring bond, could give **11**. Further reaction of **11** with $BF_3 \cdot OEt_2$ could eventually lead to **8**.[5h,10]

The processes described above illustrate the importance of remote substituents (10-CH_3) and functional groups (8,9-double bond) in directing the epoxidation of dienes **4** and the rearrangement of epoxides **5** and **7**. Efforts to replace the C-10 H with a hydrogen equivalent to produce clerodane intermediates **6** are under study. These results will be reported in due course.

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REFERENCES

1. For syntheses of 4,4-Dimethyl-1,2,3,4,6,8a-hexahydronaphthalenes, see Tanis, S.P.; Abdallah, Y.M., manuscript in preparation.

2. Recipient of a Camille and Henry Dreyfus Grant for Young Faculty in Chemistry, 1980-1984.

3. Dedicated to Professor Koji Nakanishi on the occasion of his 60th birthday.

4. a) Burton, L.P.J.; White, J.D. J. Am. Chem. Soc. **1981**, 103, 3226;
   b) White, J.D.; Burton, L.P.J. J. Org. Chem. **1985**, 50, 357.

5. a) White has reported a similar preference for α-epoxidation and hydroboration; see ref. 4.

6. Tables of final atomic co-ordinates, bond lengths and angles, and anisotropic thermal parameters along with a computer generated plot with atom labels are available as supplementary data. See Announcement to Authors, Tetrahedron Lett. **1983**, 47, 5154.

7. a) Ramage, R.; Southwell, I.A. J. Chem. Soc. Perkin Trans. I **1984**, 1323.
   b) Bridge, A.W.; Morrison, G.A. J. Chem. Soc. Perkin Trans. I **1983**, 2933.
   c) Selover, S.J.; Crews, P. J. Org. Chem. **1980**, 45, 69.
   d) Maione, A.M.; Torrini, I.; Romeo, A. J. Chem. Soc. Perkin Trans. I **1979**, 775.
   e) Ireland, C.; Faulkner, D.J.; Solheim, B.A.; Clardy, J. J. Am. Chem. Soc. **1979**, 100, 1002.
   f) Ireland, R.E.; Beslin, P.; Giger, R.; Hengartner, U.; Kirst, H.A.; Maag, H. J. Org. Chem. **1977**, 42, 1267.

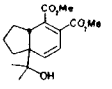
g) Guest, I.G.; Marples, B.A. J. Chem. Soc. Perkin Trans. I **1973**, 900.
h) Whitlock, H.W., Jr.; Olson, A.H. J. Am. Chem. Soc. **1970**, 93, 5383.
i) Blackett, B.N.; Coxon, J.M.; Hartshorn, M.P.; Richards, K.E. Tetrahedron **1969**, 25, 4999.
j) Hikino, H.; Kohama, T.; Takemoto, T. Tetrahedron **1969**, 25, 1037.
k) Blunt, J.W.; Hartshorn, M.P.; Kirk, D.N. Tetrahedron **1969**, 25, 149.
l) Blunt, J.W.; Hartshorn, M.P.; Kirk, D.N. J. Chem. Soc. (C) **1968**, 325.

8. a) Kubo, I.; Klocke, J.A.; Miura, I.; Fukuyama, Y. J. Chem. Soc. Chem. Commun. **1982**, 618.
b) McCrindle, R.; Nakamura, E.; Anderson, A.B. J. Chem. Soc. Perkin Trans. I **1976**, 1590.
c) Schmitz, F.J.; Lakshmi, V.; Powell, D.R.; van der Helm, D. J. Org. Chem. **1984**, 49, 241.

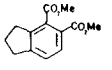
9. 5f: EI/MS (70eV): 294 (M^+H, 4.5), 279 (0.75), 263 (21.7), 247 (13.2), 234 (51.5), 219 (27.9), 202 (17.3), 191 (21.9), 165 (base). ^{1}H-NMR (250 MHz, $CDCl_3$): δ = 3.77 (s, 3), 3.70 (s, 3), 3.35 (t, J = 1.5 Hz, 1), 3.08 (dm, J = 19.2 Hz, 1), 3.05 (m, 1), 2.52 (dm, J = 19.2 Hz, 1), 1.2-1.8 (6), 1.11 (s, 3), 0.80 (s, 3).

7f: EI/MS (70eV): 294 (M^+, 2.1), 279 (0.9), 263 (28.5), 247 (16.4), 234 (15.7), 219 (36.4), 202 (23.0), 191 (30.0), 165 (base). ^{1}H-NMR (250 MHz, $CDCl_3$): δ = 3.74 (s, 3), 3.71 (s, 3), 3.33 (brd, J = 2.1 Hz, 1), 3.01 (brd, J = 13 Hz, 1), 2.93 (dt, J = 19, 2.1 Hz, 1), 2.67 (dt, J = 19, 2.1 Hz, 1), 2.12 (dt, J = 13.7, 2.5 Hz, 1), 1.61 (m, 3), 1.1-1.5 (2), 1.08 (s, 3), 0.80 (s, 3).

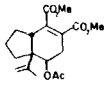
8f: IR (neat): 2945, 2860, 1720(br), 1645, 1430, 1375, 1360, 1260(br), 1190, 1105, 1070, 855, 830, 725 cm^{-1}. EI/MS (70eV): 295 (M^+1, 0.6), 263 (5.9), 236 (1.4), 204 (M-60, 55.4), 176 (base), 145 (32.4), 117 (42.9), 105 (50.8), 91 (31.7). ^{1}H-NMR (250 MHz, $CDCl_3$): δ = 4.76 (brt, J = 2 Hz, 1), 3.82 (s, 3), 3.76 (s, 3), 2.80 (brt, J = 8.3 Hz, 1), 2.76 (dd, J = 18.8, 2.3 Hz, 1), 2.26 (dd, J = 18.8, 4.2 Hz, 1), 2.12 (m, 1), 1.90 (t, J = 8.3 Hz, 2), 1.55 (m, 3), 1.44 (s, 3), 1.22 (s, 3). ^{13}C-NMR (68.9 MHz, $CDCl_3$): δ = 169.4(s), 167.6(s), 142.2(s), 129.0(s), 83.7(s), 81.8(d), 53.1(s), 52.2(q), 52.1(q), 41.7(d), 33.7(t), 32.7(t), 30.3(t), 26.5(q), 24.5(q), 23.9(t). IR (neat): 3520(br), 2950, 2870, 1715(br), 1640, 1595, 1580, 1430, 1260(br), 1080, 1030, 950 cm^{-1}.



EI/MS (70eV): 263 (0.7), 236 (3.6), 204 (11.3), 176 (base). ^{1}H-NMR (250 MHz, $CDCl_3$): δ = 6.19 (d, J = 10.07 Hz, 1), 5.71 (d, J = 10.07 Hz, 1), 3.80 (s, 3), 3.78 (s, 3), 3.00 (brt, J = 8.7 Hz, 1), 2.27 (m, 2), 1.51 (m, 5), 1.21 (s, 3), 1.15 (s, 3).



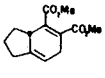
EI/MS (70eV): 234 (M^+, 3.1), 203 (43.8), 202 (base), 201 (20.9), 175 (2.8), 187 (11.1), 144 (9.8), 115 (25.1). ^{1}H-NMR (250 MHz, C_6D_6): δ = 7.64 (d, J = 8.3 Hz, 1), 6.69 (d, J = 8.3 Hz, 1), 3.68 (s, 3), 3.46 (s, 3), 2.82 (t, J = 7.3 Hz, 2), 2.43 (brt, J = 7.3 Hz, 2), 1.60 (m, 2).



^{1}H-NMR (250 MHz, $CDCl_3$): δ = 4.97 (dd, J = 10, 5 Hz, 1), 4.86 (brs, 1), 4.70 (brs, 1), 3.71 (s, 3), 3.63 (s, 3), 2.95 (brt, J = 8.3 Hz, 1), 2.65 (brdd, J = 17.5, 5 Hz, 1), 2.21 (ddd, J = 17.5, 10, 1.67 Hz, 1), 1.99 (s, 3), 1.77 (brs, 3), 1.5-2.1(6).

10. Demole, E.; Enggist, P.; Borer, C. Helv. Chim. Acta **1971**, 54, 1845.

11. A comparison of the EI/MS fragmentation of 8f after loss of C_3H_6O with the EI/MS (70eV) prepared from 1-vinyl cyclopentene and dimethyl acetylenedicarboxylate suggests a strong structural similarity. i: EI/MS (70eV): 236 (M^+, 0.2), 204 (45.1), 176 (base), 145 (43.8), 117 (70.4), 105 (72.9), 91 (35.9).



12. Similar ^{1}H-NMR and ^{13}C-NMR chemical shifts for oxetane resonances have been previously reported, see for example:
a) Okuma, K.; Tanaka, Y.; Kaji, S.; Ohta, H. J. Org. Chem. **1983**, 48, 5133.
b) Garcia-Alvarez, M.C.; Lukacs, G.; Neszmelyi, A.; Piozzi, F.; Rodriguez, B.; Savona, G. J. Org. Chem. **1983**, 48, 5123. See also:
c) Welch, S.C.; Prakasa Rao, A.S.C.; Lyon, J.T.; Assercq, J.-M. J. Am. Chem. Soc. **1983**, 105, 252; and references cited therein.

13. White (ref. 4b) has recently reported a related aromatization.

14. a) Prinzbach, H.; Schmidt, H.-G. Chem. Ber. **1974**, 107, 1988.
b) prepared by aromatization (DDQ) of the precursor diene (see ref. 11).

15. Hall, L.D.; Sanders, J.K.M. J. Am. Chem. Soc. **1980**, 102, 5703.

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