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BORON TRIFLUORIDE-CATALYZED REARRANGEMENTS OF SOME TETRASUBSTITUTED NEOTRITERPENE EPOXIDES—II

HOPENE-II OXIDE AND ITS ANALOGUE IN THE A:B-NEOALLOBETULIN SERIES

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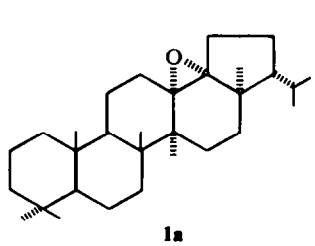
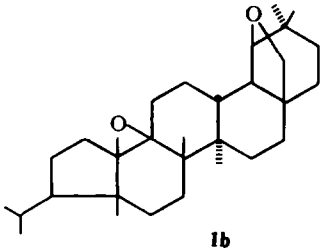
Abstract—While hopene-II oxide is converted by HCl into the 11,13(18)-diene, it rearranges quantitatively under the action of BF_3-ether complex to the 19(18 → 13)-abeo-18-oxo derivative. The structurally similar 9,10β:19β, 28-diepoxy-A:B-neo-18α-oleanane, prepared from allobetulin, behaves in an entirely analogous manner.

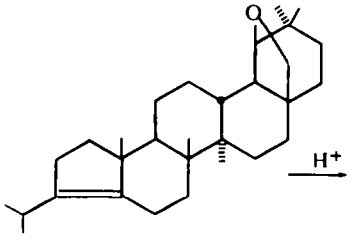
IN A previous paper we reported on the acid-catalyzed rearrangements of some A′- and A-neotriterpene epoxides.[1] We wish now to discuss the results obtained in a similar study on the epoxides **1a**[2] and **1b**, belonging respectively to B′:A′- and to the



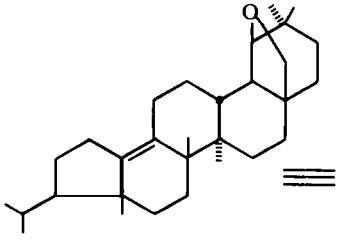
1a



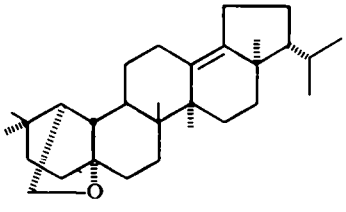
1b



2b



3b

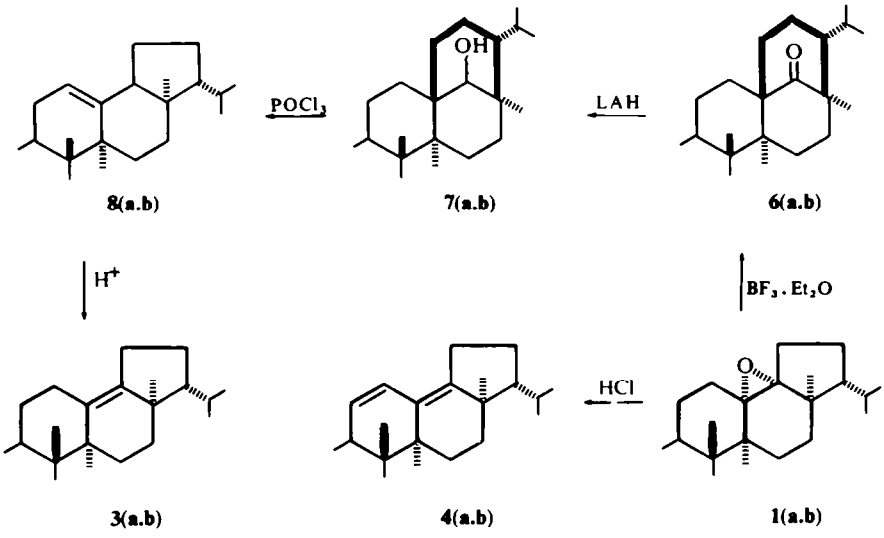


A:B-neo- series.[3] Both compounds contain a tetrasubstituted epoxide function on the six-membered ring of the hydrindane moiety, and have the same structures and configurations in the three rings adjacent to the oxirane ring.

RESULTS

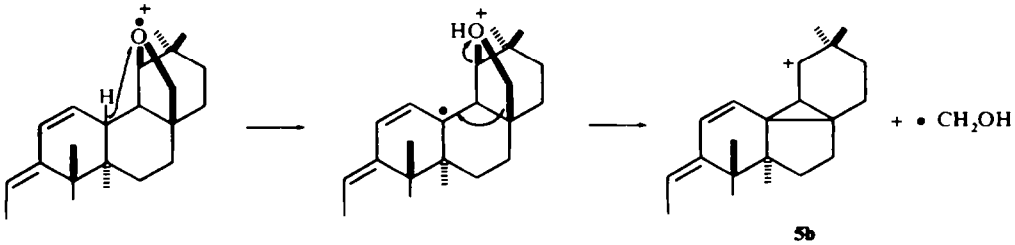
Treatment of α-apoallobetulin (**2b**)[4] with H_2SO_4 converted it into an isomer with a tetrasubstituted double bond, for which structure **3b** was deduced by analogy with the similar conversion of hopene-I into hopene-II (**3a**).[5] Compound **3b** was converted into the corresponding 9,10-epoxide **1b** by the action of *p*-nitroperoxybenzoic acid.

CHART 1



A proof that the location of the epoxide ring in **1b**, and consequently also that of the double bond in **3b**, are correct, was obtained by the easy transformation of the former compound, by treatment with HCl in EtOH, into a conjugated heteroannular diene for which structure **4b** was deduced from spectral evidence. The NMR spectrum of this compound shows signals, that can be assigned to the AB part of an ABX system from the two protons at the 11,12 double bond; the same pattern is found in the NMR spectrum of **4a**.[6] Thus, the behaviour of **1b** towards protic acids exactly parallels that of hopene-II oxide (**1a**).[6] The most abundant ion in the mass spectrum of **4b** is at *m/e* 391, and is originated from the molecular ion (relative intensity 41 %) by loss of 31 a.m.u. This can only be CH_3O. Inspection of Dreiding models shows that the allylic βH atom at C-13 is very near to the oxygen of the 19,25-epoxy group. A route leading to the M^+-31 ion (**5b**) could tentatively be formulated as shown in Chart 2.

CHART 2



All other peaks in the mass spectrum (down to *m/e* 70) are of very low intensity (< 7%). In the mass spectrum of **4a** the molecular ion is the most abundant, all other peaks down to *m/e* 95 being below 10%.

The reaction of epoxides **1a** and **1b** with BF_3-ether complex gave results completely different from those obtained with HCl. No olefinic products were isolated, only a high yield of a ketone from each of the epoxides, for which we propose structures **6a** and **6b**. There are no H atoms in position α with respect to the CO group, as deduced from NMR spectra and resistance to attack by bromine. The positive Cotton effects fit well with the octant diagrams. Reduction with LAH afforded the corresponding alcohols (**7a** and **7b**), the dehydration of which with $POCl_3$ proceeded with rearrangement to yield trisubstituted olefins. Structures **8a** and **8b** were deduced for these two compounds on the following grounds. The base peak in the mass spectrum of **8a** (Fig. 1) is at *m/e* 218; this fragment should contain rings A′ and B′ since it gives

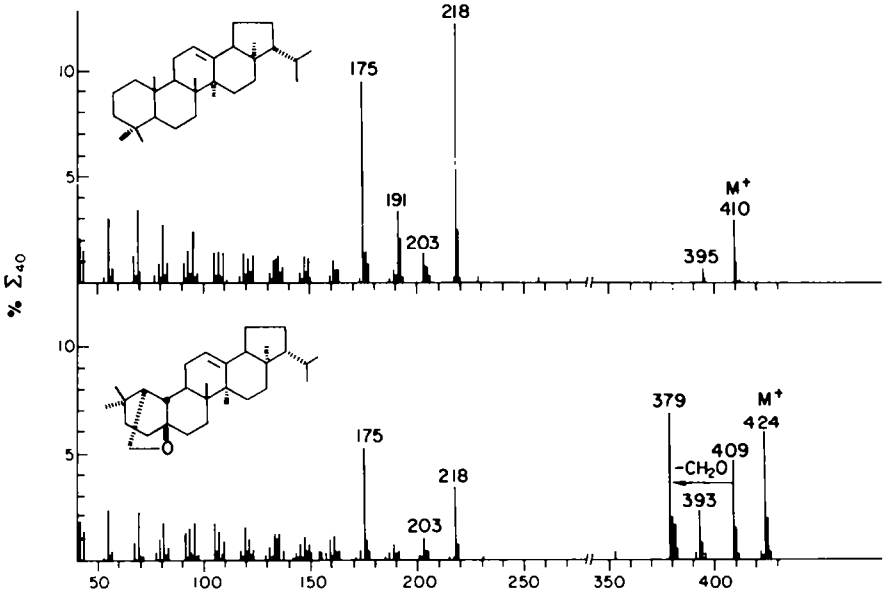
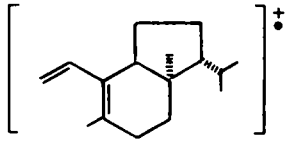


FIG. 1. Mass spectra of compounds **8a** and **8b**.

rise (metastable peaks) to ions at *m/e* 203 (—$CH_3^{\cdot}$) and at *m/e* 175 (—$C_3H_7^{\cdot}$). The structure of the *m/e* 218 ion is very probably **9**, its formation involving a retro Diels–Alder fragmentation of the molecular ion from **8a**.[5] The *m/e* 218, 203 and 175 ions are also present in the mass spectrum of **8b**. The abundances of these ions are lower in **8b**



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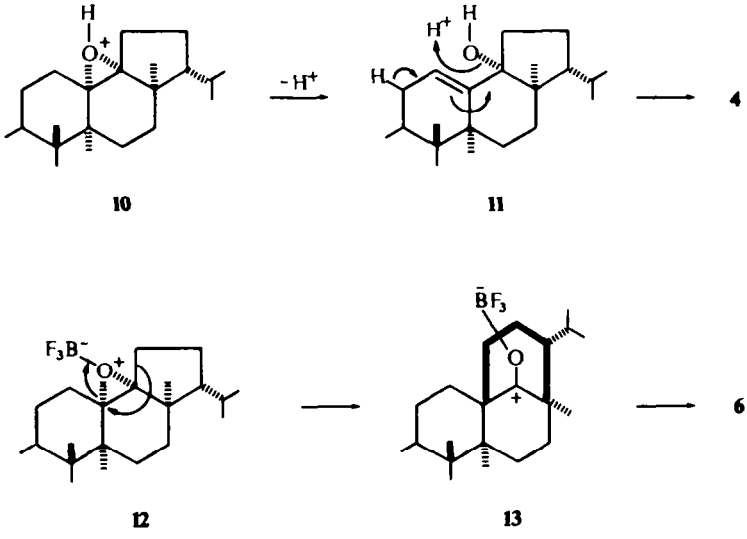
than in **8a**, because of competing fragmentation processes which can be initiated at the oxygen function. In this case the loss of Me followed by loss of CH_2O is of great importance. Mild acid treatment of **8a** and **8b** caused transformation into hopene-II (**3a**) and, respectively, **3b**. Moreover, structure **8a**, which was proposed in our preliminary paper,[2] was later independently confirmed.[7]

DISCUSSION

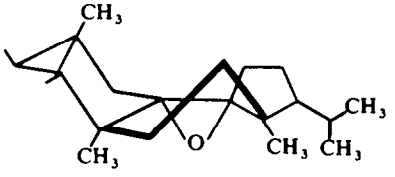
The present work provides a confirmation of the observation previously made with the 17,21-epoxides of the same series[1] that protic and aprotic acids give completely different products. The conversion of **1** into **4** by HCl in EtOH can be visualized as involving C–O bond cleavage in the protonated epoxide **10** (Chart 3) to give the allyl alcohol **11**, followed by the 1,4-elimination of water, to give directly **4**, as shown in Chart 3, or by formation of the 12,18-diene, followed by isomerization to the more stable diene **4**. In the less polar medium and in the absence of a good proton acceptor, the BF_3-epoxide complex (**12**), rather than lose a proton, will preferentially undergo a bond migration leading to the ketone **6**, via **13**.

CHART 3



Some comments are in order to justify the hypothesized configurations. The stereochemistry of **3b** follows from that of **2b**, except for the configuration of the isopropyl group at C-3. This has been tentatively assumed to be *cis* to the Me at C-5, on the basis of the reasonable hypothesis that in the conversion of **2b** into **3b** the protonation at C-3 takes place *anti* to the migrating Me group. A similar hypothesis was made for the entirely analogous conversion of hopene-I (**2a**) into hopene-II (**3a**);[5] however this hypothesis is still awaiting rigorous confirmation. As for the configuration of the epoxide ring, the conversion of **1** into **6** is strongly in favour of its being *cis* to the Me groups at C-14 and C-17 of **1a** (C-8 and C-10 of **1b**). From a casual examination of the structures **3** it could appear as somewhat surprising that their epoxidation takes

place from the apparently more hindered side (*cis* to two Me and one isopropyl group). Therefore the oxide derived from **3a** had previously been assigned the β configuration.[6] However, models show that in the most stable conformation of **3a** and **3b** (ring B or B′ in a distorted half-chair form), the Me group at C-8 of **3a** (C-14 of **3b**) leans towards the double bond providing a greater shielding than usual to epoxidation from the same side. On the other hand, while the α-epoxide can exist in a half-chair form (**14**) in which the two Me groups at C-14 and C-17 are sufficiently far from each other, in the β-epoxide the ring could only assume a boat conformation (**15**) in which there would be a prohibitively high "flagpole-bowsprit" interaction.



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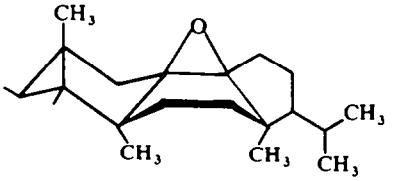

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Guilleux and Mme. Mousseron-Canet[8] in a detailed examination of the conformational situation in a somewhat similar case (a $\Delta_{9,10}$ Westphalen rearrangement product) reached opposite conclusions; however in the latter case only one Me group was present, and the double bond was exocyclic to two cyclohexane rings, and not to a cyclohexane and a cyclopentane ring as here.

An analogy with the conversion of **7** into **8** can be found in the transformation of bicyclo[4.3.1]decyl derivatives into hydroazulenes, which constituted one of the key steps in the synthesis of bulnesol;[9] although the reaction conditions (solvolysis of mesylate in AcOH) are quite different, the outcome is the same.

EXPERIMENTAL

(For general information, see Part I.)[1]

Hopane series

B′:A′-*Neogammacer*-13(18)-*ene* (*hopene*-II, **3a**) was prepared by BF_3-catalyzed rearrangement of fern-9(11)-ene.[10]

13,18 α-*Epoxy*-B′:A′-*neogammacerane* (**1a**). A soln of **3a** (0·400 g) and *m*-chloroperoxybenzoic acid (0·205 g) in $CHCl_3$ (20 ml) was stored at 5° for 18 hr, then worked up in the usual manner to give crude **1a** (0·390 g), which was crystallized from hexane to yield the pure product (0·250 g), m.p. 202–204°; $[\alpha]_D$ + 30·1°; IR band at 11·55 μ (epoxide). (Lit.[11] m.p. 199–201°; $[\alpha]_D$ + 45°). (Found: C, 84·49; H, 11·90; Calc. for $C_{30}H_{50}O$: C, 84·44; H, 11·81%).

19(18 → 13)-Abeo-B′:A′-*neogammaceran*-18-*one* (**6a**). A soln of **1a** (0·300 g) in $CHCl_3$ (30 ml), treated with $BF_3 \cdot Et_2O$ (3 ml), was left 30 min at room temp., washed with Na_2CO_3 aq, dried ($MgSO_4$) and evaporated. The product, dissolved in pet. ether, was chromatographed over alumina. After passing 500 ml of pet. ether through the column, C_6H_6 eluted **6a** (0·280 g), m.p. 278–282° dec (from $CHCl_3$—MeOH); $[\alpha]_D$ + 16·5; λ_{CO} 5·87 μ; CD, $\Delta\varepsilon_{314}$ + 1·19, $\Delta\varepsilon_{304}$ + 1·73, $\Delta\varepsilon_{296}$ + 1·50. (Found: C, 84·41; H, 11·86. $C_{30}H_{50}O$ requires C, 84·44; H, 11·81%.)

When **6a** in AcOH was treated with an excess of Br_2 in the presence of a catalytic amount of HBr the starting material was recovered completely unchanged. No reaction took place also with PhCHO in the presence of base, nor under the conditions of the Bayer–Villiger (*p*-nitroperoxybenzoic and trifluoroacetic acids), or Haller–Bauer reactions ($NaNH_2$ in xylene).

19(18 → 13)-Abeo-B′:A′-*neogammaceran*-18 ξ-*ol* (**7a**). A soln of **6a** (0·150 g) in Et_2O (60 ml) was refluxed for 2 hr with LAH (0·240 g). Addition of AcOEt, H_2O, filtration and evaporation gave **7a** (0·120 g after crystallization from $CHCl_3$—MeOH), m.p. 263–276° dec; $[\alpha]_D$ + 37·4°. (Found: C, 83·98; H, 12·34. $C_{30}H_{52}O$ requires: C, 84·04; H, 12·23%.)

B′:A′-*Neogammacer*-12-*ene* (**8a**). A soln of **7a** (65 mg) in pyridine (4 ml) was treated with $POCl_3$ (0·4 ml) and heated 2 hr on a steam bath. Usual work-up, followed by filtration of a soln of the product in pet. ether through Al_2O_3 and crystallization from $CHCl_3$—MeOH gave **8a** (40 mg), m.p. 124–128°; $[\alpha]_D$ + 20·0°, NMR, one olefinic H at δ 5·28 ppm (Lit.[7] m.p. 134–137°; $[\alpha]_D$ + 18·4). [Found: C, 87·39; H, 12·44; MW, 410 (mass spec). $C_{30}H_{50}$ requires: C, 87·73; H, 12·27%; MW, 410.]

Conversion of **8a** *into* **3a**. A soln of **8a** (50 mg) in $CHCl_3$ (30 ml), saturated with dry HCl, was stored at room temp. for 5 hr. Evaporation and crystallization from $CHCl_3$—MeOH gave **3a** (35 mg), m.p. 198–200°; $[\alpha]_D$ + 1·5°.

Apoallobetulin series

19β, 28-*Epoxy*-A:B-*neo*-18α-*olean*-9-*ene* (**3b**). A soln of α-apoallobetulin[3] (**2b**, 0·800 g) in C_6H_6 (75 ml), AcOH (315 ml) and H_2SO_4 (58 ml) was left 20 hr at room temp., then diluted with H_2O. The organic phase was washed with 2N NaOH and evaporated. The residue was dissolved in pet. ether and chromatographed over Al_2O_3. Elution with pet. ether containing 5% Et_2O gave **3b** (0·550 g), m.p. 158–161°; $[\alpha]_D$ + 58·3°. [Found: C, 84·56; H, 11·20; MW, 424 (mass spec). $C_{30}H_{48}O$ requires: C, 84·84; H, 11·39%; MW, 424].

9,10β:19β,28-*Diepoxy*-A:B-*neo*-18α-*oleanane* (**1b**). Treatment of **3b** (0·470 g) in $CHCl_3$ (24 ml) with *p*-nitroperoxybenzoic acid (0·250 g) for 24 hr at 0°, followed by usual work-up and crystallization from Me_2CO—MeOH gave **1b** (0·350 g), m.p. 195–198°; $[\alpha]_D$ + 72·3°. (Found: C, 81·94; H, 10·95. $C_{30}H_{48}O_2$ requires: C, 81·76; H, 10·98%).

19β,28-*Epoxy*-A:B-*neo*-18α-*oleana*-9,11-*diene* (**4b**). A soln of **1b** (0·100 g) in EtOH (100 ml) and conc HCl (10 ml) was refluxed for 90 min. Dilution with H_2O, usual work-up and crystallization from $CHCl_3$—MeOH gave **4b** (70 mg), m.p. 173–176°, $[\alpha]_D$ + 106°; λ_{max} 246, 254, 264 nm (ε 23,900, 28,000, 18,600)*; NMR: olefinic protons at δ 5·30 (broad doublet, 1 H) and 6·15 ppm (quartet, 1 H), J_{AB} 10·5 Hz, J_{AX} 3 Hz. [Found: C, 85·04; H, 10·80; MW, 422 (mass spec). $C_{30}H_{46}O$ requires: C, 85·24; H, 10·57%; MW, 422].

1(10→9)-Abeo-19β,28-*epoxy*-A:B-*neo*-18α-*oleanan*-10-*one* (**6b**). Treatment of **1b** (0·250 g) in $CHCl_3$ (13 ml) with $BF_3 . Et_2O$ (1·3 ml) for 30 min at room temp., followed by washing with 2N Na_2CO_3, usual work-up and crystallization from $CHCl_3$—MeOH gave **6b** (0·190 g), m.p. 227–231°; $[\alpha]_D$ + 29·3°; λ_{CO} 5·89 μ; CD, $\Delta\varepsilon_{314}$ + 1·12, $\Delta\varepsilon_{304}$ + 1·65, $\Delta\varepsilon_{295}$ + 1·43. (Found: C, 81·40; H, 10·89. $C_{30}H_{48}O_2$ requires: C, 81·76; H, 10·98%).

1(10→9)-Abeo-19β,28-*epoxy*-A:B-neo-18α-*oleanan*-10ξ-*ol* (**7b**). Reduction of **6b** (0·185 g) with LAH, under the conditions described above for the preparation of **7a**, gave **7b** (0·120 g, from $CHCl_3$—MeOH), m.p. 246–250°; $[\alpha]_D$ + 47·4°. (Found: C, 81·30; H, 11·29. $C_{30}H_{50}O_2$ requires: C, 81·39; H, 11·38%).

19β,28-*Epoxy*-A:B-*neo*-18α-*olean*-9(11)-*ene* (**8b**). The reaction of **7b** (0·100 g) with $POCl_3$ pyridine, under the conditions described above for the preparation of **8a**, gave **8b** (80 mg), m.p. 141–144° (from $CHCl_3$—MeOH); $[\alpha]_D$ + 90°; NMR, one olefinic H at δ 5·30 ppm. [Found: C, 84·76; H, 11·15; MW, 424 (mass spec). $C_{30}H_{48}O$ requires: C, 84·84; H, 11·39%; MW, 424].

Conversion of **8b** *into* **3b**. Isomerization of **8b** (40 mg) under the conditions described above for the conversion of **8a** into **3a**, gave **3b** (35 mg), m.p. 157–160°; $[\alpha]_D$ + 58°.

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*These data are in good agreement with those reported for **4a** (λ_{max} 247, 256, 267 nm; ε 23,500, 28,000, 17,700)[6] and with the expectations for a tetrasubstituted diene system exocyclic to a cyclopentane ring; see L. Dorfman, *Chem. Rev.* **53**, 59 (1953)

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