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A UNIQUE AND HIGHLY REMARKABLE BORON TRIFLUORIDE CATALYZED REARRANGEMENT OF 2, 2-DI-t-BUTYLOXIRANE INTO 2, 2, 3, 3, 4, 4-HEXAMETHYLTETRAHYDROFURAN

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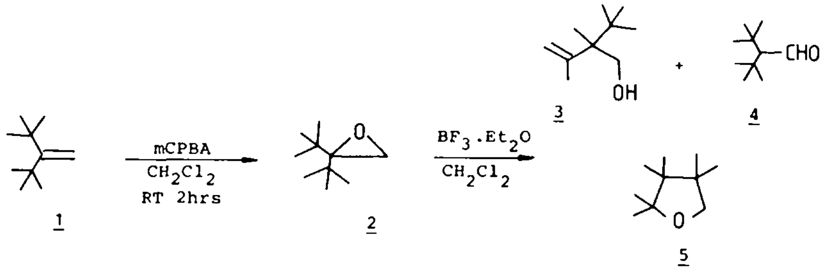
Abstract—The boron trifluoride catalyzed rearrangement of 2,2-di-t-butyloxirane, involving competitive reactions of transient carbenium ions, could be selectively directed towards either 2, 2, 3, 3, 4, 4-hexamethyltetrahydrofuran or 2-t-butyl-2,3-dimethyl-3-buten-1-ol. Hydride shift to afford 2,2-di-t-butylacetaldehyde was only observed to a minor extent.

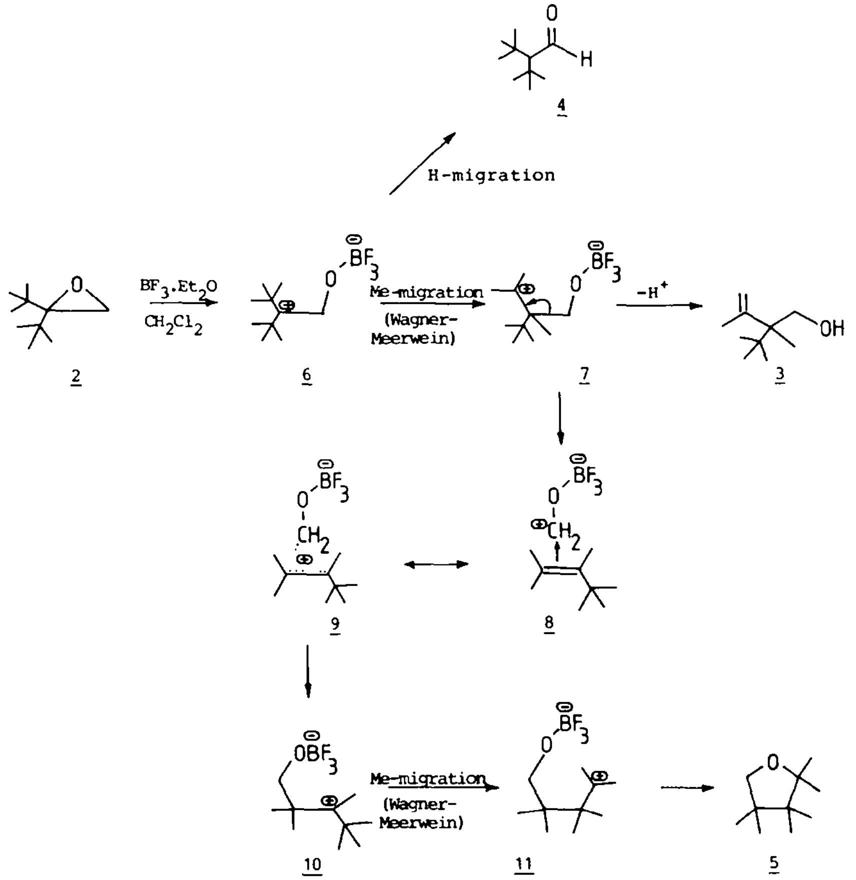
Based on stereochemical data, the boron trifluoride catalyzed rearrangement of epoxides has been most satisfactorily interpreted in terms of the intermediacy of a discrete carbenium ion.[2] Intramolecular hydride migration in terminal epoxides to such a carbenium centre often produced aldehydes.[2,3] Our attempted boron trifluoride catalyzed isomerization of 2, 2-di-t-butyloxirane **2**, obtained from mCPBA oxidation (CH_2Cl_2, room temperature 2 h) of 1, 1-di-t-butylethylene **1**,[4] failed to giye useful amounts of di-t-butylacetaldehyde **4**. The reaction proved to be highly dependent upon the reaction temperature. Slow addition of one molar equivalent of boron trifluoride etherate to a solution (10% w/v) of 2, 2-di-t-butyloxirane in dichloromethane at 0° resulted in the instantaneous formation of only 4% di-t-butylacetaldehyde **4**, next to 85% 2-t-butyl-2, 3-dimethyl-3-buten-1-ol **3** and 5% 2, 2, 3, 3, 4, 4-hexamethyltetrahydrofuran **5** (Scheme 1). The yield of the latter highly unusual ring-enlarged compound **5** could be drastically enhanced by carrying out the reaction at reflux temperature (one minute). Adding BF_3-etherate (one mol equiv) to a refluxing solution of 2, 2-di-t-butyloxirane **2** afforded 82–84% 2, 2, 3, 3, 4, 4-hexamethyltetrahydrofuran **5** and 8–12% di-t-butylacetaldehyde **4**, but no trace of the rearranged alcohol **3** was found (Scheme 1).

The formation of all three compounds **3**, **4** and **5** can be explained in terms of several competitive reactions of the intermediate carbenium ion **6** (Scheme 2).

The desired hydride migration to afford di-t-butylacetaldehyde **4** appeared to be a minor route irrespective of the temperature of the reaction. However, carbenium ion **6** also underwent methyl migration (Wagner–Meerwein rearrangement) to produce carbenium ion **7** which, by loss of a proton, afforded homoallylic alcohol **3**.[7] This process seems to be favored at lower temperature. Under more drastic conditions (reflux), carbenium ion **7** rearranged into oxolane **5** in an unusual way. The oxymethylene moiety migrates to the carbon bearing the positive charge, giving rise to carbenium ion **10**, which is again apt to undergo a Wagner–Meerwein type migration of a methyl group to generate **11**. The latter gives ring closure to the hexamethyltetrahydrofuran **5**. Whether the rearrangement of carbenium ion **7** into **10** occurs by migration of a formaldehyde unit, complexed with boron trifluoride as visualized by the π-complexes **8** and **9**, might be supported by the boron trifluoride catalyzed electrophilic addition of formaldehyde on 2, 3, 4, 4-tetramethyl-2-pentene (see complex **8**) (the Prins reaction[8]). We were not successful in the preparation of the latter olefin because the dehydration of alcohol **13**, easily obtained from di-isopropylketone **12** in a two-step sequence (Scheme 3), produced the isomeric terminal olefin **14**, exclusively, due to steric hindrance. Nevertheless, we tried to condense olefin **14** with paraformaldehyde in refluxing dichloromethane (2 min)) in the hope of affecting a similar addition and subsequent rearrangement into a five-membered ring species. The reaction mixture contained 3-isopropyl-2, 2, 3-trimethyltetrahydrofuran **15** as the major product (55%), besides some other unidentified higher boiling compounds. The reaction path leading from olefin **14** to oxolane **15** (Scheme 3) proceeds analogous to the proposed conversion of carbenium ion **7** into **5** and is a substantial support for the mechanistic explanation of the multi-step rearrangement of 2, 2-di-t-butyloxirane **2** into 2, 2, 3, 3, 4, 4-hexamethyltetrahydro-



Scheme 1.

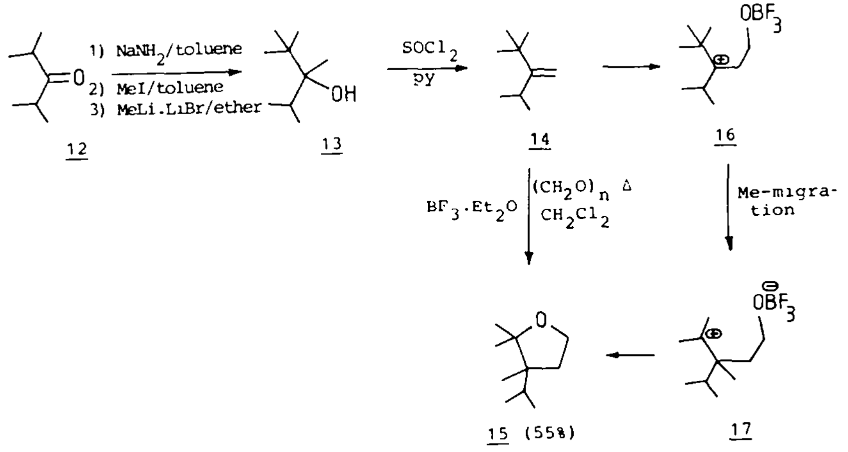


Scheme 2.

furan **5**. A support of this proposal involves the condensation of 2, 3, 3-trimethyl-1-butene with formaldehyde in aqueous sulfuric acid which affords 2, 2, 3, 3-tetramethyltetrahydrofuran, next to the normal expected 4-t-butyl-4-methyl-1, 3-dioxane.[9] Another related reaction is the reaction of 1-butene with formaldehyde in aqueous medium to yield 2-methyltetrahydrofuran.[10] Finally, further attempts to rearrange epoxide **2** into di-t-butylacetaldehyde **4** under various conditions (e.g. HCl/MeOH, TFA/CCl_4) failed because the normal Wagner–Meerwein rearrangement product **3** prevailed with respect to the desired aldehyde. In addition, surprisingly no reaction occurred between epoxide **2** and lithium bromide (CH_2Cl_2 or C_6H_6/HMPT) or lithium iodide (CH_2Cl_2) despite the known capacity of these reagents to induce epoxide rearrangements.[11,12]

EXPERIMENTAL

Infrared spectra were recorded with a Perkin–Elmer model 1310 spectrophotometer. ^{1}H-NMR spectra were mea-



Scheme 3.

sured with a Varian T-60 NMR spectrometer (60 MHz), while ^{13}C-NMR spectra were obtained with a Varian FT-80 NMR spectrometer (20 MHz). Mass spectra were recorded with a Varian Mat 112 mass spectrometer (direct inlet system; 70 eV). Gas chromatographic analyses were performed with a Varian 1700 gas chromatograph (10% SE 30 column; 5 metres).

Synthesis of 2, 2-*di-t-butyloxirane* **2**

A soln of 7.0 g (0.05 mol) of 1, 1-di-t-butylethylene **1** (prepared from di-t-butylketone according to a literature procedure[5]) in 200 ml of CH_2Cl_2, cooled in an ice bath, was treated portionwise with 0.055 mol of m-chloroperbenzoic acid (peracid content 80–85%). The mixture was additionally stirred at room temp for 2 h after which it was poured into 300 ml of 0.5 N aq KOH. The CH_2Cl_2 layer was isolated and the aqueous layer extracted with 50 ml CH_2Cl_2. The combined organic extracts were washed with brine, dried ($MgSO_4$) and evaporated *in vacuo* to give 7.5 g of a colorless oil. This oil contained about 94% epoxide **2** (NMR, GLC). Distillation *in vacuo* afforded pure 2, 2-di-t-butyloxirane **2** as a colorless oil, b.p. 61–68°/11 mm Hg (6.3 g, 80%). A small amount (0.5 g) of a mixture of epoxide **2** and unidentified material was isolated as a fraction boiling at 80–120°/11 mm Hg. In addition, the distillation resulted in some decomposition leaving a residual tar in the distillation flask. ^{1}H NMR: δ (CCl_4) 1.04 (18H, s, tBu_2), 2.54 (2H, s, CH_2). ^{13}C δ ($CDCl_3$) 29.11 (q, $(\underline{C}H_3)_3$), 36.25 (s, $\underline{C}Me_3$), 48.46 (t, $\underline{C}H_2$–O), 66.00 (s, $\underline{C}$–O).

Reaction of 2, 2-*di-t-butyloxirane* **2** *with boron trifluoride etherate at* 0°

To a soln of 2.82 g (0.018 mol) of 2, 2-di-t-butyloxirane **2** in 24 ml of CH_2Cl_2, cooled in an ice bath, was added dropwise a solution of 2.79 g (0.0198 mol) of boron trifluoride etherate in 6 ml of dichloromethane. After stirring for 15 min, the reaction mixture was poured into 5% aq Na_2CO_3 and the organic phase was isolated (if a persisting emulsion was formed, the mixture was filtered resulting in well separable phases). Drying ($MgSO_4$) and evaporation *in vacuo* afforded 2.8 g (quantitative yield) of a colorless oil. Gas chromatographic analyses revealed the presence of the following compounds: 2-t-butyl-2, 3-dimethyl-3-buten-1-ol **3** (85%), 2, 2-di-t-butylacetaldehyde (4%) and 2, 2, 3, 3, 4, 4-hexamethyltetrahydrofuran **5** (5%). This procentic composition corresponded to the values calculated from the ^{1}H NMR spectrum of the reaction mixture.

2-*t-Butyl*-2, 3-*dimethyl*-3-*buten*-1-*ol* **3**. ^{1}H NMR ($CDCl_3$) δ 0.89 (9H, s, t-Bu), 1.16 (3H, s, CH_3), 1.83 (3H, br, CH_3–C =), 1.5 (1H, s, br, OH), 3.44 and 4.00 (each 1H, d × d, AB, J = 11 Hz), 4.81 and 5.20 (each 1H, each m, C=CH_2). IR (NaCl): ν_{OH} 3100–3600 cm^{-1} (br), $\nu_{C=C}$ 1630 cm^{-1}. MS *m/e* (relative abundance): no M^+, 100 (7), 84 (16), 82 (43), 69 (16), 67 (20), 57 (100), 55 (23), 43 (36), 41 (72), 40 (23). ^{13}C NMR ($CDCl_3$): 18.20 (q, Me), 23.90 (q, Me), 26.71 q, $C\underline{Me}_3$, 35.56 (s, $\underline{C}Me_3$), 49.35 (s, $\underline{C}CH_2O$), 66.66 (t, $\underline{C}H_2$–O), 114.60 (t, $\underline{C}H_2$ = C), 147.57 (s, C=).

2, 2-*Di-t-butylacetaldehyde* **4** was completely identical with an authentic sample prepared according to the literature.[5]

2, 2, 3, 3, 4, 4-*Hexamethyltetrahydrofuran* **5**. ^{1}H NMR ($CDCl_3$): δ 0.85 (6H, s, Me_2), 0.98 (6H, s, Me_2), 1.16 (6H, s, Me_2), 3.51 (2H, s, CH_2O). ^{13}C NMR ($CDCl_3$): 22.21 (q), 24.33 (q), 26.97 (q), 44.30 (s, $\underline{C}Me_2$), 45.77 (s, $\underline{C}Me_2$), 77.27 (t, $\underline{C}H_2O$), 85.40 (s, $\underline{C}$–O). MS *m/e* (relative abundance): no M^+, 141 (4), 111 (2), 98 (25), 83 (100), 72 (3), 70 (5), 69 (17), 59 (4), 58 (3), 57 (32), 56 (9), 55 (33), 43 (70), 42 (7), 41 (42), 39 (11).

Reaction of 2, 2-*di-t-butyloxirane* **2** *with boron trifluoride etherate in dichloromethane at reflux temperature*

To a refluxing soln of 1.41 g (0.009 mol) of 2, 2-di-t-butyloxirane **2** in 24 ml of dichloromethane was rapidly added a solution of 1.40 g (0.0099 mol) of boron trifluoride etherate in 1.5 ml of dichloromethane. (CAUTION!! vigorous reaction). The soln was then refluxed for 1 min, poured into 5% aq Na_2CO_3 and the organic phase was isolated, dried ($MgSO_4$) and evaporated *in vacuo* to give 1.4 g (quantitative yield) of a colorless oil. GLC and ^{1}H-NMR revealed the presence of 82–84%, 2, 2, 3, 3, 4, 4-hexamethyltetrahydrofuran **5** and 8–12% 2, 2-di-t-butylacetaldehyde **4**.

Preparation of 3, 3-*dimethyl*-2-*isopropyl*-1-*butene* **14**

2, 2, 4-Trimethyl-3-pentanone was synthesized by a slightly modified procedure of Whitmore *et al.*[13] involving methylation of the sodio-enolate of 2, 4-dimethyl-3-pentanone **12**. Methyl iodide was used instead of dimethyl sulphate in the methylation step. The pure ketone boiled at 136–137°/760 mm Hg (lit[13] b.p. 132–134.5°/730 mm Hg) (yield 43%). The addition of methyllithium to 2, 2, 4-trimethyl-3-pentanone to afford 2, 2, 3, 4-tetramethyl-3-pentanol **13** (98% yield) and the dehydration of the latter with thionylchloride in pyridine to give 3, 3-dimethyl-2-isopropyl-1-butene **14** (94% yield) was essentially executed in the way described for the synthesis of 1, 1-di-t-butylethylene **1** from di-t-butylketone.[5] ^{1}H-NMR (CCl_4) of 2, 2, 3, 4-tetramethyl-3-pentanol **13**: δ 0.98 (9H, s, t-Bu), 0.95 (6H, d, J = 7 Hz, Me_2), 2.06 (1H, septet, J = 7 Hz, $C\underline{H}$), $O\underline{H}$ covered by the foregoing signals. ^{1}H NMR (CCl_4) of 3, 3-dimethyl-2-isopropyl-1-butene **14**: δ 1.05 (9H, s, t-Bu), 1.03 (6H, d, J = 7 Hz, Me_2), 3.29 (1H, septet, J = 7 Hz, $C\underline{H}$), 4.72 and 4.80 (each 1H, AB system).

Reaction of 3, 3-*dimethyl*-2-*isopropyl*-1-*butene* **14** *with paraformaldehyde*

A refluxing soln of 0.71 g (0.005 mol) boron trifluoride etherate and 0.45 g of paraformaldehyde (0.015 molar equiv of formaldehyde) in 10 ml of dichloromethane was treated in one portion with 0.63 g (0.005 mol) of 3, 3-dimethyl-2-isopropyl-1-butene **14**. The solution was refluxed for 2 min after which it was poured into aq Na_2CO_3. The organic phase was isolated, dried ($MgSO_4$) and evaporated *in vacuo* to afford 0.8 g of an oil. The main component (55%) was isolated by preparative GLC and was shown by spectrometric means to be 3-isopropyl-2, 2, 3-trimethyltetrahydrofuran **15** (m.p. 40°): ^{1}H NMR ($CDCl_3$) δ 0.94 and 0.89 (each 3H, 2d, J = 6 Hz, Me_2), 0.88, 1.15 and 1.23 (each 3H, s, 3 Me), 1.4–2.1 (3H, m, CH_2 and $C\underline{H}Me_2$), 3.90 and 3.75 (2H, d × d, br, J = 6.5 Hz, J = 8.5 Hz, $C\underline{H}_2O$). MS, no M^+, 98 (11), 83 (20), 70 (30), 59 (11), 55 (23), 44 (11), 43 (21), 40 (100). ^{13}C NMR ($CDCl_3$) 84.03 (s, $\underline{C}$–O), 62.89 (t, $\underline{C}H_2O$), 48.43 (s, $\underline{C}Me_2$), 40.70 (t, CH_2), 33.17 (d, $\underline{C}H$), 24.73, 23.61, 20.01, 17.64 and 14.70 (5 Me's). Several other compounds were present in the reaction mixture but were not identified because they could not be isolated in the pure state. One compound was tentatively identified as 4-t-butyl-4-isopropyl-1, 3-dioxane.

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[4] Peracid oxidation of 1, 1-di-t-butylethylene has been described already. Using peracetic acid in CH_2Cl_2 in the presence of NaOAc, the complex reaction mixture contained 30–50% epoxide **2**.[5] Another synthesis of epoxide **2** involves addition of phenylthiomethyllithium to di-t-butylketone, S-alkylation of the resulting β-hydroxysulfide and base-induced ring closure.[6]

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[7] The conversion of epoxide **2** into alcohol **3** was already tentatively reported,[5] according to which "... the BF_3-etherate catalyzed rearrangement of the epoxide yielded a complex mixture of at least seven compounds, one of which was an unsaturated alcohol to which we tentatively assign the structure 2-t-butyl-2, 3-dimethyl-3-buten-1-ol."[5]

[8] For reviews on the Prins reaction, see E. Arundale and L. A. Mikeska, *Chem. Rev.* **51**, 505 (1952); *Methoden der Organischen Chemie*, Band V/lb, p. 1040. Houben-Weyl, (1972); V. I. Isagulyants, T. G. Khaimova, V. R. Melikyan and S. V. Pokrovskaya, *Russ. Chem. Rev.* **37**, 17 (1968).

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