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Silicon-guided rearrangement of 10-methyl-4,5-epoxydecalins. Methyl versus methylene migration

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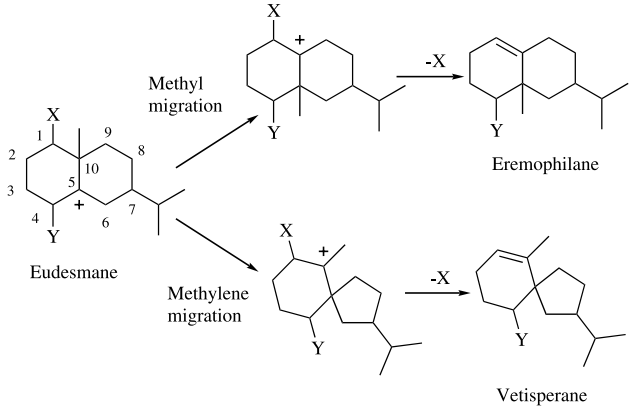
Abstract—The Lewis acid-promoted rearrangement of two 10-methyl-4,5-epoxydecalins bearing a trimethylsilyl (TMS) group on C-1 or C-9 has been studied. Migration of the C-9 methylene group to C-5 is the major reaction pathway when the TMS and the oxirane groups are on the same ring while methyl migration results exclusively when they are on different rings.

It is generally accepted that many biogenetic pathways leading to natural products involve Wagner–Meerwein rearrangements of carbenium ions. For instance, this is the case in the biogenetic transformation of eudesmanes into eremophilanes or spirovetivane sesquiterpenes, which involves the rearrangement of a C-5 carbenium ion related to a 10-methyldecalin system with 1,2-methyl or methylene migrations, respectively (Scheme 1, X = H, Y = CH_3).[1]

Following our interest in the synthesis of bioactive sesquiterpenes[2] we became interested in the use of such rearrangements in the laboratory as a synthetic route towards naturally occurring compounds. In particular, we were interested in the rearrangement of 4,5-epoxydecalins as a way to obtain 5-methyldecalin or spiro[4,5]decane-based compounds functionalized at C-4. However, a literature search showed only a small number of examples using this methodology for the synthesis of natural products.[3] This lack of use may be due to the possibility of different competitive pathways which complicate the overall picture of these rearrangements, such as the existence of different migrating groups, the 1,2-elimination of a vicinal proton[4] and, in the case of epoxides, the Grob-type fragmentation of the 1,3-hydroxycarbenium ions resulting, after the initial rearrangement, in carbonyl compounds.[5]



Scheme 1.

In order to simplify this picture we thought of introducing a trialkylsilyl group on a carbon vicinal to C-10, i.e. C-1 or C-9. The ability of the silicon atom to stabilize β carbocations (β-effect)[6] should promote rearrangement to a C-10 carbocation via methyl or methylene migration over the 1,2-elimination and other possible migrations. On the other hand, the faster elimination of the trialkylsilyl group (superproton behavior) in the rearranged intermediate would prevent the Grob-type fragmentation, giving a double bond between C-10 and the carbon atom initially bearing the silyl group (Scheme 1, X = $SiMe_3$, Y = O-LA).[6] To the best of our knowledge, this strategy based on the special features of silicon has only been applied in the case of a 5-hydroxyeudesmane rearrangement,[7] and no examples of the silicon-promoted rearrangement of 4,5-epoxydecalins have been described.

Keywords: epoxides; rearrangements; methyl shift; terpenes and terpenoids; eremophilanes; eudesmanes; spiro compounds.
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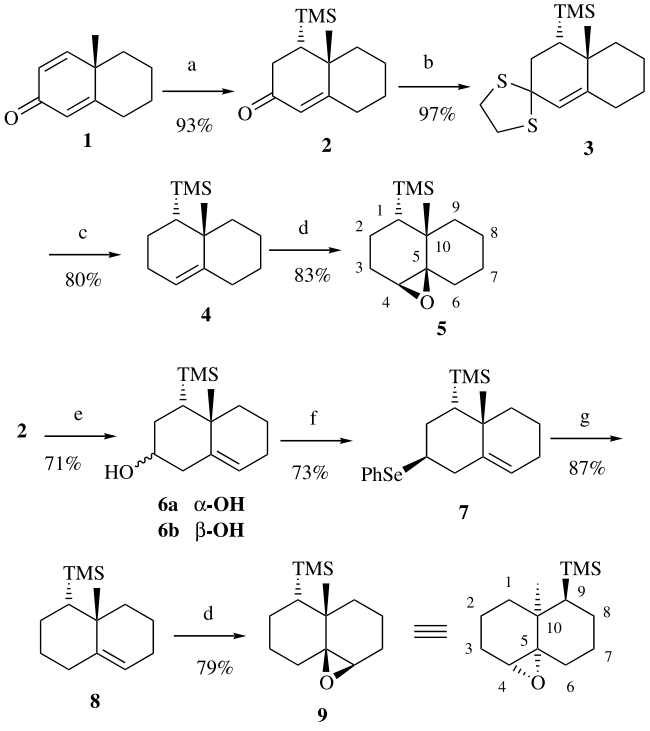
We have prepared two 10-methyl-4,5-epoxydecalins **5** and **9** differing in the relative location of the trimethylsilyl group and the oxirane ring. We have studied their rearrangement in acidic media in order to determine the applicability of this strategy with epoxydecalins and how the location of the TMS group in relation to the epoxide moiety can affect the selectivity of methyl versus methylene migration.

Compounds **5** and **9** were prepared from the enone **2**, which is easily prepared by treatment of dienone **1**[8] with trimethylsilyllithium in the presence of CuCN[9] (Scheme 2). Enone **2** was deoxygenated at C-3 in two steps by treatment with ethanedithiol in the presence of $BF_3{\cdot}Et_2O$ to give thioketal **3** followed by desulfuration with Ca in liquid ammonia.[7] Finally, epoxidation of the resulting olefin **4** with magnesium monoperoxyphthalate (MMPP) in methanol afforded epoxide **5** as the only diastereoisomer.

The synthesis of epoxide **9** from **2** required deconjugation of the enone moiety with migration of the double bond. This was achieved by treatment of compound **2** with potassium *tert*-butoxide in dioxane followed by reduction[10] of the ketone with $NaBH_4/CaCl_2$ to give two alcohols **6a** and **6b** that were isolated in 46% and 25% yields respectively. The major alcohol **6a** was transformed into phenylselenide **7** (73%) by reaction of its corresponding mesylate with PhSeNa generated from diphenyldiselenide and $NaBH_4$ in DMF.[11]



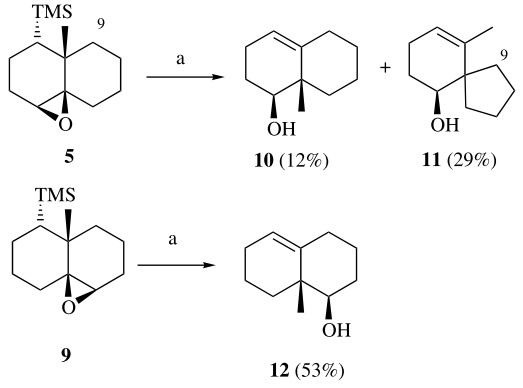
Scheme 2. *Reagents and conditions*: (a) TMSLi–CuCN, –23°C; (b) ethanedithiol–$BF_3{\cdot}Et_2O$, AcOH, rt; (c) Ca, NH_3; (d) MMPP, MeOH; (e) 1. KO*t*-Bu, dioxane; 2. $NaBH_4$, $CaCl_2$, EtOH; (f) 1. MsCl, py; 2. PhSeNa; (g) Raney Ni, MeOH.

Hydrogenolysis of the C–Se bond using Raney Ni gave alkene **8** in 87% yield.[12] Finally epoxidation of **8** with MMPP gave epoxide **9** as the only product.

With these two alkenes available we studied their rearrangement (Scheme 3). Treatment of compound **5** with $BF_3{\cdot}Et_2O$ in CH_3CN from –20 to 0°C furnished a ca. 3:1 mixture of two products that could be separated by column chromatography. The major product **11**[13] showed a molecular ion peak at 166.1363 in its HRMS corresponding to the formula $C_{11}H_{18}O$, indicating the presence of two rings and a double bond in the molecule. Two signals at δ 121.0 (d) and 138.5 (s) in the ^{13}C NMR were further proof of the structure of **11**. The spirocyclic structure of this compound, which would result from the migration of C-9 to C-10 and elimination of the TMS group was inferred from the quaternary carbon at δ 50.6 (s) corresponding to C-5 and from the ^1H NMR spectrum signal at δ 1.64 assigned to the olefinic methyl group. The minor product **10**[14] did not show the molecular peak in its HRMS but its isomeric relationship with **11** was inferred from the M^+–OH peak that appeared at 149.1321 ($C_{11}H_{17}$ requires 149.1330). The decalin structure of **10** resulting from the migration of the angular methyl and elimination of the TMS group was supported by spectral data. Significant differences with regards to compound **11** were found in the ^1H and ^{13}C NMR spectra. Thus, a signal corresponding to the bridgehead quaternary carbon of the decalin system appeared at δ 40.2 and, furthermore, the methyl group gave a singlet at δ 1.03 (s) in the ^1H NMR spectrum, indicating its position on the bridgehead carbon.

On the other hand, treatment of compound **9** with $BF_3{\cdot}Et_2O$ under similar conditions gave exclusively the decalin product **12**[15] resulting from migration of the angular methyl group and elimination of the TMS group. The spectral data for this compound were identical to those described in the literature.[16]

In summary, a TMS group on C-1 or C-9 promotes the acidic rearrangement of 10-methyl-4,5-epoxydecalins with exclusive migration of the methyl or methylene groups linked directly to C-10. The preference for the migration of these groups depends on the relative dis-



Scheme 3. *Reagents and conditions*: (a) $BF_3{\cdot}Et_2O$, CH_3CN, –20 to 0°C.

position of the epoxide and TMS groups. Thus, methyl migration is found when both groups are on the same ring, while methylene migration is preferred if they are placed on different rings. The TMS group also inhibits the Grob-type fragmentation of the rearranged products and determines the location of the new double bond in the final products.

Acknowledgements

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13. Compound **11**: $[\alpha]_D^{25}=+24.1$ (*c* 0.73, $CHCl_3$); MS (EI) *m*/*z* 166 (M^+, 10), 149 (9), 148 (70), 136 (26), 122 (100), 107 (62), 93 (43); HRMS: 166.1363 (M^+), $C_{11}H_{18}O$ requires 166.1358; IR (NaCl) ν_{max} 3411, 1456, 1049 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.31 (1H, br s), 3.57 (1H, dd, $J=2.1$; 6.6 Hz), 2.17–1.87 (2H, m), 1.85–1.40 (10H, m), 1.64 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.5 (s), 121.0 (d), 74.0 (d), 50.6 (s), 37.1 (t), 32.6 (t), 27.5 (t), 27.0 (t), 26.9 (t), 21.7 (t), 19.6 (q).
14. Compound **10**: $[\alpha]_D^{25}=-125.8$ (*c* 0.30, $CHCl_3$); MS (EI) *m*/*z* 149 (M^+-17, 10), 148 (82), 122 (100), 107 (50), 93 (53), 79 (42), 71 (42), 57 (75) 55 (56); HRMS: 149.1321 (M^+-OH), $C_{11}H_{17}$ requires 149.1330; IR (NaCl) ν_{max} 3393, 1437, 1025 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.21 (1H, br t, $J=2.3$ Hz), 3.50 (1H, dd, $J=7.5$; 8.1 Hz), 2.20–1.80 (4H, m), 1.75–1.30 (6H, m), 1.40–1.05 (2H, m), 1.03 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.9 (s), 118.6 (d), 78.4 (d), 40.2 (s), 38.6 (t), 31.9 (t), 27.7 (t), 27.0 (t), 24.5 (t), 22.0 (t), 17.1 (q).
15. Compound **12**: $[\alpha]_D^{25}=-85.3$ (*c* 0.70, $CHCl_3$); MS (EI) *m*/*z* 166 (M^+, 10), 149 (11), 148 (89), 133 (60), 109 (51), 105 (66), 91 (70); HRMS: 166.1359 (M^+), $C_{11}H_{18}O$ requires 166.1358;^1H NMR (300 MHz, $CDCl_3$) δ 5.40 (1H, br s), 3.30 (1H, dd, $J=4.3$; 11.5 Hz), 2.15–2.05 (1H, m), 1.95–1.85 (3H, m), 1.79–1.68 (3H, m), 1.65–1.30 (5H, m), 1.00 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.0 (s), 121.9 (d), 79.1 (d), 40.2 (s), 35.9 (t), 31.6 (t), 30.7 (t), 25.7 (t), 25.0 (t), 18.6 (t), 17.2 (q).
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