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AN UNUSUAL EFFECT OF SELENIUM SUBSTITUENTS ON THE REGIOCHEMISTRY OF A BAEYER-VILLIGER REARRANGEMENT

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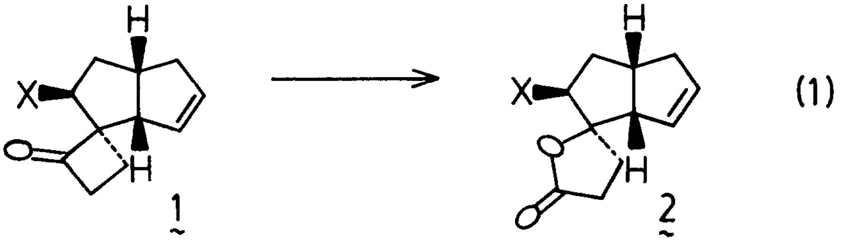
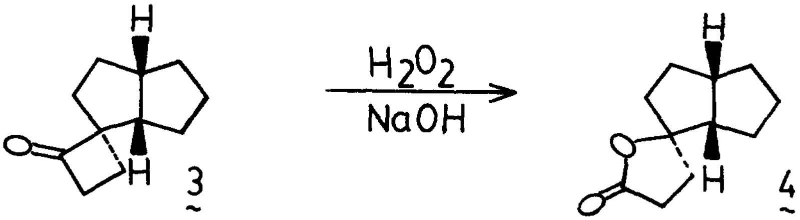
ABSTRACT: The regioselectivity of a Baeyer-Villiger oxidation of a cyclobutanone is dependent upon the oxidation state of a proximal selenium substituent.

The Baeyer-Villiger oxidation represents a major synthetic entry to lactones whose importance derives from their presence as structural units in many natural products as well as their utility for further structural elaboration. The dependence of the regioselectivity upon substitution of the migrating carbon and conformational factors is well recognized.[1] Recently, a subtle electronic effect of a proximal silicon substituent was reported.[2] In pursuing a spirolactonization study[3] directed toward allamandin,[4] we explored the rearrangement summarized in equation 1. In this letter, we wish to report an unusual effect of the X group on this transformation.

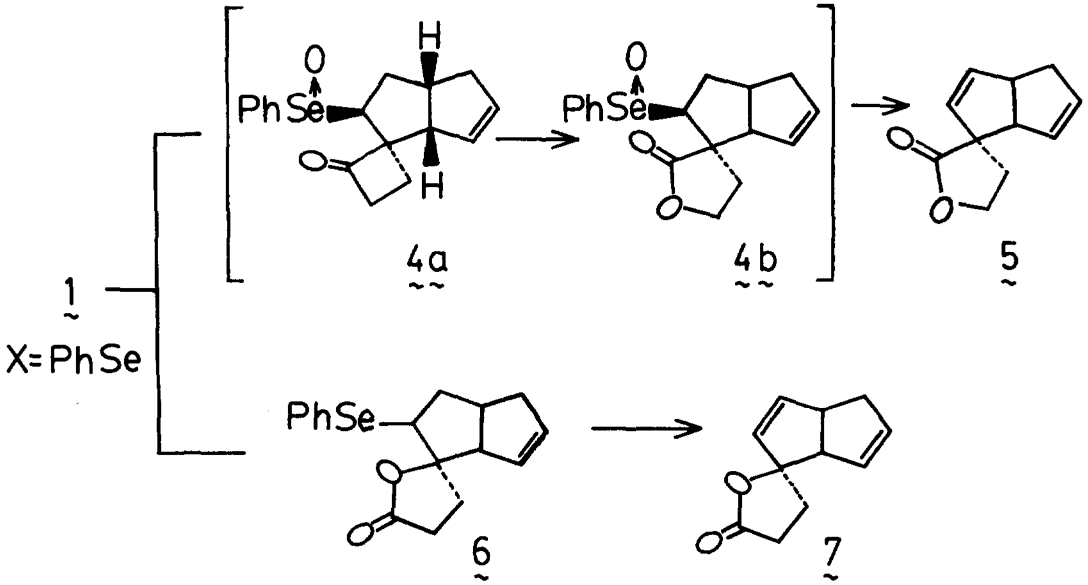


Previous studies[3] have shown that hydrogen peroxide induced Baeyer-Villiger oxidations of compounds like **1**, eg. **3**, lead to exclusive migration of the quaternary carbon as depicted. When X=OH in **1**,[4] this expected trend was observed and only **2** X=OH was obtained [IR (CCl_4) 3400, 1770 cm^{-1}; NMR ($CDCl_3$) δ5.9-5.7 (m, 1H), 5.7-5.5 (m, 1H), 3.8 (dd, J=11, 8 Hz, 1H), 3.3-3.1

(m, 1H), 3.0-1.6 (m, 10H); calc'd for $C_{11}H_{14}O_3$: 194.0943; found 194.0937].



Most unexpectedly, the product from 1 (X=PhSe)[4,5] depended critically upon the oxidation conditions. Treatment with hydrogen peroxide in refluxing

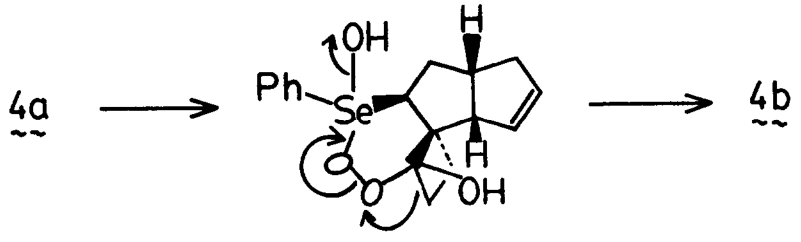


ethanol led to a single product [IR ($CHCl_3$) 1760 cm^{-1}; NMR ($CDCl_3$) δ 5.94 (1H, dd, J=5.5, 2.5 Hz), 5.84 (1H, ddd, J=5.5, 2.4, 1.4), 5.62 (1H, ddd, J=5.5, 2.0, 1.1), 5.55 (1H, dd, J=5.5, 1.5), 4.4 (2H, m), 3.75 (1H, m), 3.62 (1H, m), 2.62 (1H, ddq, J=17.5, 9.5, 2 Hz), 2.42 (1H, dt, J=14.5, 10 Hz), 2.28 (1H, dt, J=14.5, 1 Hz), 2.15 (1H, ddd, J=13.0, 6.5, 5.5 Hz). ^{13}C NMR δ 180.6, 139.1, 131.7, 128.9, 128.3, 66.1, 58.3, 55.3, 40.1, 38.0, 32.3]. This data clearly supports 5 as the correct structure. That the 2H, m at δ4.4 and the δ66.1 absorption in the ^{13}C NMR spectrum were indeed associated with the $-CH_2O\overset{O}{\overset{\|}{C}}-$ unit and not an artifact of the anisotropy of the double bonds, 5 was hydrogenated to its fully saturated derivative in which these absorptions occurred at δ4.25

and δ65.8. Thus, the methylene group of the cyclobutanone preferentially migrated.

The source of the abnormal regioselectivity does not lie with the benzeneselenyl group per se. In fact, treatment of **1** (PhSe) with hydrogen peroxide under basic conditions (K_2CO_3, CH_3OH, 0°) followed by acidification with $NaHSO_4$ to effect relactonization (partial hydrolysis of the initial lactone occurs) produced **6**. Treatment of **6** with hydrogen peroxide in refluxing ethanol gave the desired **7** [NMR ($CDCl_3$) δ5.95 (1H, dd, J=5, 2.5 Hz), 5.67 (1H, m), 5.65 (2H, m), 3.58 (1H, m), 3.34 (1H, m), 2.56 (3H, m), 2.37 (1H, m), 2.21 (1H, m), 2.11 (1H, m). ^{13}C NMR δ142.1, 131.3, 129.3, 128.0, 58.7, 47.0, 36.9, 30.3, 29.8 (the quaternary carbon and carbonyl carbon not visible)].

We interpret the striking difference in regioselectivity of the rearrangement to the difference in chemoselectivity in the initial oxidation. In the absence of base, selenide oxidation appears to be faster than the Baeyer-Villiger oxidation. If **4a** is the initial product, hydrogen peroxide can be envisioned to add to the selenoxide as well as the cyclobutanone carbonyl group to give an adduct such as **8**. Only the methylene group now can adopt the appropriate geometric relationship to the cleaving O-O bond and thus migrates exclusively. The facile exchange rate of the oxygen of selenoxides which has been interpreted as an indication of the facility of hydration[6] and the general stability of hypervalent selenium compounds[7] lends credence to this postulate.[8,9] Its potential as a general directive effect may increase the ability to control regioselectivity in such migrations to an unprecedented degree.



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