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Notes

A Reverse Vinylogous Aldol Condensation[1]

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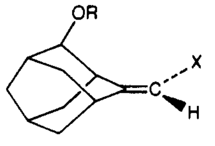
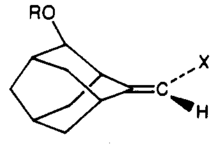
Heterolytic fragmentation in the case of adamantyl moieties are well documented.[2,3] An example,[2c] inter alia, is the ring opening of 3-chloro-1-adamantyl oxide. Homolytic cleavage reaction have also been demonstrated for the 1- and 2-adamantyloxyl radicals.[4] We report our results, which have a bearing on the oxide rearrangement.

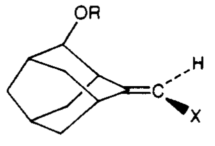
Desilylation of siloxy aldehyde **1** (R = *tert*-butyldimethylsilyl; X = CHO) with tetra-*n*-butylammonium fluoride gave besides the expected axial alcohol **1** (R = H; X = CHO) and three other epimeric alcohols **2**–**4** (R = H; X = CHO). The alcohols were separated by radial chromatography to give a 26% yield of a 1:1 mixture of **2** and **4** (R = H; X = CHO) in the less polar fraction and a 55% yield of a 3:2 mixture of **1** and **3** (R = H; X = CHO) in the more polar fraction. Similarly, desilylation of the *E* isomer (**3**, R = *tert*-butyldimethylsilyl; X = CHO) also produced a mixture of all four epimeric alcohols; a 56% yield of a 1:1 mixture of **2** and **4** (R = H, X = CHO) and a 35% yield of a 3:2 mixture of **1** and **3** (R = H; X = CHO).[5]



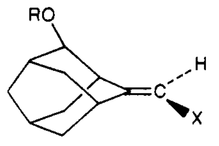
Z-(1*R*)-4(a)-**1**



Z-(1*R*)-4(e)-**2**



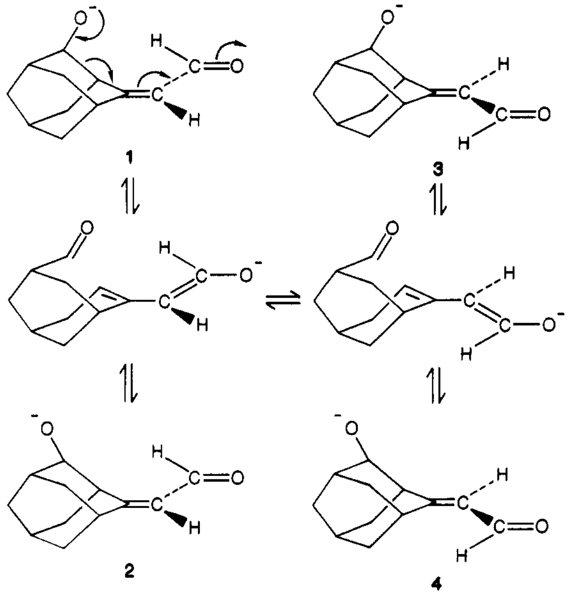
E-(1*R*)-4(a)-**3**



E-(1*R*)-4(e)-**4**

Suspecting that the 4-oxy anion was involved, we treated a sample of the *E* hydroxy aldehyde (**3**, R = H; X = CHO) with sodium hydride in THF, and again the four epimeric alcohols **2**, **4**, **1**, and **3** (R = H; X = CHO) were formed, in a ratio of 17:18:40:25, respectively, a result similar to that observed for the tetra-*n*-butylammonium fluoride cleavage of the silyl ethers. Treatment of the related methyl ketone (**3**, R = H; X = $COCH_3$) with sodium hydride also yielded **2**, **1**, **4**, and **3** (R = H; X = $COCH_3$), although with a somewhat different ratio of 27:32:8:33.

Scheme I



Treatment of the corresponding *Z* hydroxy ester (**1**, R = H; X = $COOCH_3$) or *E* hydroxy diene (**3**, R = H; X = $CH{=}CH_2$) with sodium hydride did not lead to the formation of epimeric alcohols but only to the recovery of starting material.

Scheme I describes a mechanism that accounts for the observations made. The oxide, whether formed by treatment of the precursor alcohol with sodium hydride or of the silyl ether with fluoride ions, can undergo an elimination to yield an aldehyde and a delocalized anion. This can be viewed as a reverse vinylogous aldol condensation reaction. The anion can isomerize, as shown, and subsequent aldol condensation leads to ring closure and the formation of a thermodynamic mixture of the four epimeric alcohols. Our results further indicate that this reverse aldol condensation occurs more readily when the anion formed is strongly delocalized by a carbonyl moiety (X = CHO or $COCH_3$) and not when X = $COOCH_3$ or $CH{=}CH_2$.

Experimental Section

High-pressure liquid chromatography (HPLC) was performed on a Beckman Model 334 gradient liquid chromatograph (serial nubmer 1421) employing a column of (4.6 mm × 25 cm) Ultrasphere Si with a 10:90 (2-propanol–heptane) solvent mixture with a flow rate of 1 mL/min and a Beckman 163 variable wavelength detector.

The preparations of the starting materials have been reported elsewhere.[5] All the products were fully characterized by the comparison of their spectral data and retention times with the authentic samples obtained in separate experiments.[5a]

Desilylation Reactions with Tetra-*n*-butylammonium Fluoride.[5b] (a) (*E*)-(1*R*)-4(a)-[(Dimethyl-*tert*-butylsilyl)oxy]-2-adamantylideneacetaldehyde (0.30 g, $[\alpha]^{25}_{\mathrm{Hg}}$ +23.26 ± 0.23°, 84% ee) in THF was treated with 3 equiv of tetra-*n*-butylammonium

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[1] This work was supported by a grant from the National Science Foundation for which we are grateful.

[2] (a) Grob, C. A. *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 535. (b) Becker, K. B.; Grob, C. A. *The Chemistry of Functional Groups*; Patai, S., Ed.; Wiley: New York, 1976; Suppl. Vol. 1, Chapter 8, p 653. (c) Fischer, W.; Grob, C. A. *Tetrahedron Lett.* **1975**, 3547.

[3] Adcock, W.; Kok, G. B. *J. Org. Chem.* **1987**, *52*, 356. Fischer, W.; Grob, C. A.; Katayama, H. *Helv. Chim. Acta* **1976**, *59*, 1953. Gagneaux, A. R.; Meier, R. *Tetrahedron Lett.* **1969**, 1365. Henkel, J. G.; Spector, J. H. *J. Org. Chem.* **1983**, *48*, 3657.

[4] Black, R. M.; Gill, G. B. *J. Chem. Soc., Chem. Commun.* **1970**, 972.

[5] (a) All four alcohols **1**–**4** (R = H, X = CHO) have been isolated in pure state and characterized, see accompanying paper. (b) The procedure used for desilylation by tetra-*n*-butylammonium fluoride is described in the accompanying paper. Walborsky, H. M.; Reddy, S. M.; Brewster, J. H. *J. Org. Chem.*, this issue.

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fluoride and stirred for 12 h at 25 °C under a N_2 atmosphere. After usual workup, the hydroxy aldehydes 1-4 (R = H; X = CHO) (0.16 g) were separated into two fractions. Less polar fraction I (0.096 g, 56%) was the 1:1 mixture (^{1}H NMR) of *E*-(1*R*)-4(e)-**4** and *Z*-(1*R*)-4(e)-**2**. Polar fraction II gave 0.06 g (35%) of a 4:6 mixture (^{1}H NMR) of *E*-(1*R*)-4(a)-**3** and *Z*-(1*R*)-4(a)-**1**, respectively.

(**b**) A solution of (*Z*)-(1*R*)-4(a)-[(dimethyl-*tert*-butylsilyl)oxy]-2-adamantylideneacetaldehyde (0.50 g, $[\alpha]^{25}_{Hg}$ −58.98 ± 0.18°, 84% ee) in THF was treated with tetra-*n*-butylammonium fluoride as above. The reaction mixture after workup and separation yielded two fractions. The less polar fraction I (0.08 g, 26%) was found to be a 1:1 mixture (^{1}H NMR) of *E*-(1*R*)-4(e)-**4** and *Z*-(1*R*)-4(e)-**2**, and the more polar fraction II (0.17 g, 55%), a 4:6 mixture (^{1}H NMR) of *E*-(1*R*)-4(a)-**3** and *Z*-(1*R*)-4(a)-**1** (R = H; X = CHO), respectively.

Reaction with NaH. (**a**) A mixture of methyl (*Z*)-(1*R*)-4-(a)-hydroxy-2-adamantylideneacetate (33 mg, $[\alpha]^{25}_{Hg}$ −46.89 ± 0.07°, 92% ee) and NaH (50 mg) in 2 mL of dry THF was stirred for 1 h. The reaction mixture was decomposed on ice and extracted with ether (2 × 15 mL). The combined ether solution was washed with water, dried (Na_2SO_4), and concentrated. The crude product upon ^{1}H NMR and HPLC analyses showed mainly the starting material **1** (R = H; X = $COOCH_3$).

(**b**) (*E*)-(1*R*)-4(a)-Hydroxy-2-adamantylideneacetaldehyde (36 mg, $[\alpha]^{25}_{Hg}$ +10.57 ± 0.41°, 92% ee) in dry THF was treated with NaH as above. The reaction mixture after workup and analytical HPLC analysis gave a ratio of 17:18:40:25 for the hydroxyaldehydes **2**, **4**, **1**, and **3** (R = H; X = CHO), respectively.

(**c**) A solution of 12 mg *E*-(1*R*)-4(a)-hydroxy-2-adamantylideneacetone ($[\alpha]^{24}_{Hg}$ +38.52 ± 0.82°, 92% ee) in dry THF was treated with NaH as earlier. After workup, a ratio of 27:32:7.7:33 was estimated, respectively, for the hydroxy methyl ketones **2**, **1**, **4**, and **3** (R = H; X = $COCH_3$) by HPLC analysis of the crude mixture.

(**d**) Via the earlier procedure, NaH was added to a stirred solution of (*E*)-(1*R*)-4(e)-hydroxy-2-adamantylidenepropene (16 mg, $[\alpha]^{27}_{Hg}$ +47.12 ± 0.27°, 92% ee) in dry THF. After 1 h the reaction mixture was worked up to give pure starting material **4** (R = H; X = $CH{=}CH_2$) (^{1}H NMR, HPLC).

Alternative Practical Syntheses of Spiro(poly)cyclic Imino Thio- and Selenoethers

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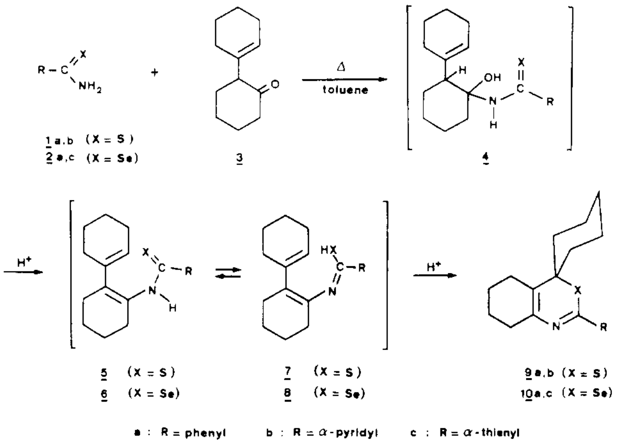
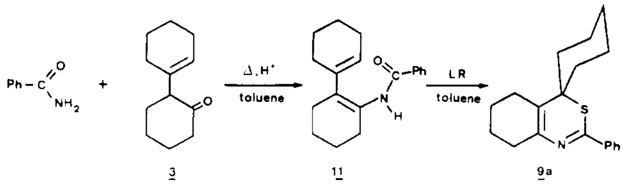
We recently reported[1] that aromatic and aliphatic dienamides, a class of little studied compounds, can serve as photochemical precursors of diversified imino ethers possessing a spiro heterocyclic framework. The present paper deals with the synthetic potential of these polyenic compounds and their use in the elaboration of a variety of spirothiazines and selenazines.

Thus the cyclohexanespiro-2-(5-aza-4-phenyl-3-thiabicyclo[4.4.0]deca-1(6),4-dienes) **9a,b** are easily accessible by direct condensation of the appropriate thiocarboxamide **1a,b** with 2-(cyclohex-1-enyl)cyclohexanone (**3**), a product of the aldol dimerization of cyclohexanone (Scheme I). Reactions are carried out in a Dean-Stark apparatus by refluxing an equimolar mixture of the aromatic thioamides and the β,γ-unsaturated ketone in toluene in the presence of a catalytic amount of β-naphthalenesulfonic acid. The results are listed in Table I. These reactions can be extended to the synthesis of the spiro seleno derivatives **10a,c** which are obtained from the bicyclic ketone **3** and the aromatic selenocarboxamides **2a,c**.[2] The spiro structure of **9a** and **10a** was confirmed mainly by 100-MHz ^{13}C NMR spectroscopy (Table II). The quaternary character of the carbon nucleus (D) α to the sulfur and selenium atoms was unambiguously established by comparison of DEPT spectra with different pulse angles θ.

Scheme I



Scheme II



Scheme III

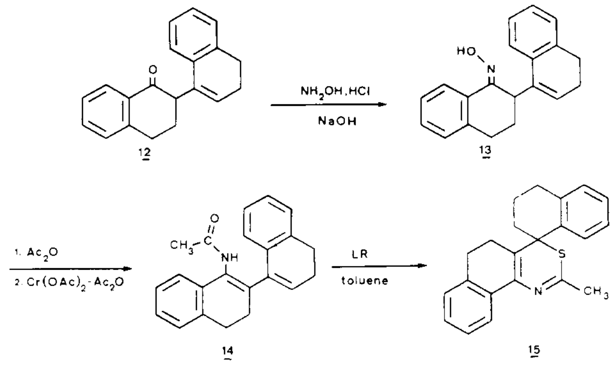


Table I. Yields of Products from Reactions of 1a,b, 2a,c and Benzamide with 3 and from Treatment of 11, 14, and 16 with the Lawesson Reagent

starting material		reaction product
method A[a]	method B[b]	(yield, %)
1a		**9a** (63)
1b		**9b** (55)
2a		**10a** (55)
2c		**10c** (49)
benzamide		**11** (65)
	11	**9a** (89)
	14	**15** (93)
	trans-16	*trans*-**17** (90)

[a] Direct condensation under acidic conditions with 2-(cyclohex-1-enyl)cyclohexanone (**3**). [b] Treatment with the Lawesson reagent.

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[1] Bochu, C.; Couture, A.; Granclaudon, P.; Lablache-Combier, A. *J. Chem. Soc., Chem. Commun.* 1986, 839.

[2] Obtained from the nitriles.[3]

[3] Cohen, V. I. *Synthesis* 1978, 668.

0022-3263/88/1953-4852$01.50/0