Pergamon

Tetrahedron Letters, Vol. 35, No. 48, pp. 8947-8950, 1994
Elsevier Science Ltd
Printed in Great Britain
0040-4039/94 $7.00+0.00

0040-4039(94)01961-4

CARBANION-INDUCED INTRAMOLECULAR BETA-CLEAVAGE REACTIONS OF 2-OXETANONES

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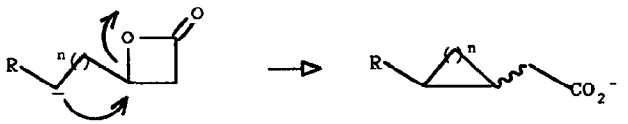
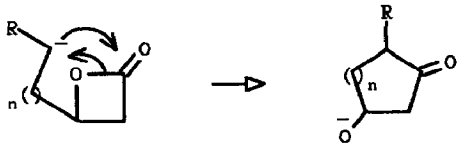
Abstract: Intramolecular β-cleavage reactions of β-lactones, or 2-oxetanones, by stabilized enolates have been demonstrated. Three-, four-, five-, and six-membered carbocyclic rings have been prepared.

Intramolecular ring opening reactions of epoxides by internally generated carbanions are well documented in the literature.[1] By contrast, related reactions of 2-oxetanones, or β-lactones, have not been investigated.[2] In undertaking this study, we set out to determine if the β-cleavage mode (eq.1) would be favored over acyl attack (eq.2) if the attacking carbanion is sufficiently *soft*,[3] providing a new route to functionalized cycloalkanes.



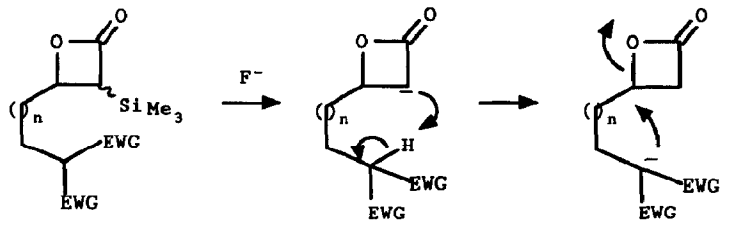
(1)



(2)

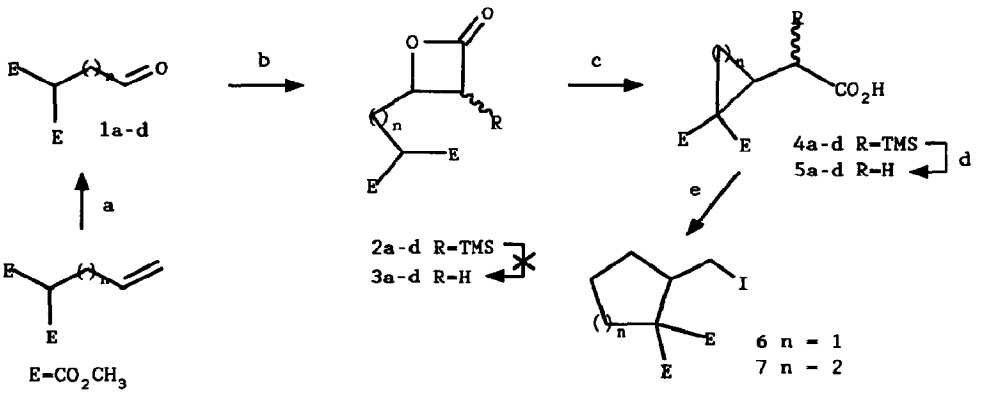
A doubly stabilized enolate was chosen as a suitable nucleophile for our studies. The regioselective generation of this carbanion in the presence of labile ring protons was not anticipated to present problems. Our first initiative was to use α-trimethylsilyl 2-oxetanones as substrates (Scheme I). In addition to their readily availability from aldehydes by 2π + 2π cycloaddition with trimethylsilylketene,[4] tetra-n-butylammonium enolates can be generated from these derivatives by treatment with TBAF.[5] Using this reaction, we initially hoped to generate the desired anions for ring opening by inducing an internal proton exchange. This exchange, we reasoned, might be particularly facile when n=1, i.e. leading to the possibility of four-membered ring formation, as the transition state for this conversion would be six-membered in nature.

Scheme I



A series of aldehydes, **1a-d** (Scheme II), was prepared by ozonolysis of their terminal alkene precursors and converted to the corresponding lactones **2a-d** as cis/trans mixtures.[6] Unfortunately, the reaction sequence outlined in Scheme I was not realized, as treatment of compounds **2a-d** with TBAF in THF, at a variety of temperatures, gave a complex mixture of products in each case. Furthermore, attempts to convert structures **2a-d** to the unsubstituted substrates **3a-d** using a variety of standard reagents (e.g. $KF.2H_2O$, CH_3CN) led to an identical outcome.

Scheme II



(a) O_3, CH_2Cl_2, -78°C; Me_2S; (b) Trimethylsilylketene, cat. $BF_3.OEt_2$
(c) NaH, THF, 0°C; (d) $KF.2H_2O$, CH_3CN; (e) $Pb(OAc)_4$, LiCl; NaI

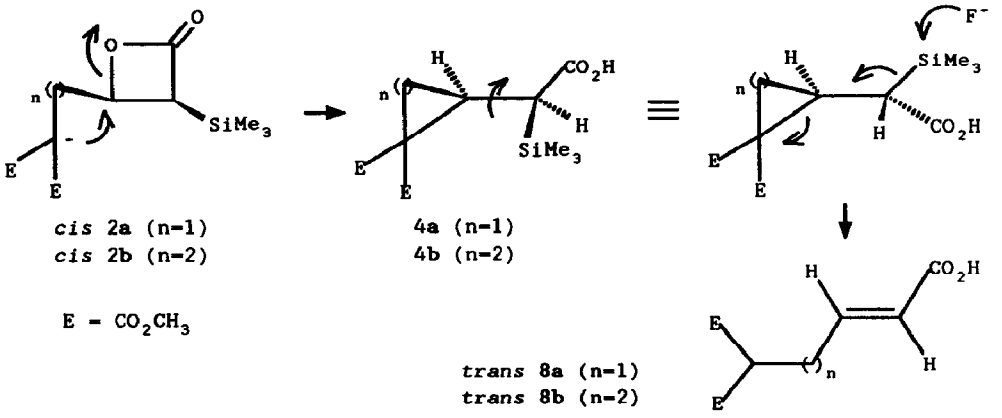
Cyclic products **4a-d**[7] were eventually formed in good yield (see Table I) by addition of a THF solution of each of the lactones **2a-d** to a rapidly stirred suspension of NaH in THF cooled to ice bath temperature. As shown (entries 3 and 4), the 5- and 6-membered rings remained completely intact when the acids **4c** and **4d** were treated with potassium fluoride to give **5c**[8] and **5d**,[9] respectively. The subsequent conversion of these materials to the known compounds **6**[10] and **7**,[10] respectively, provided additional evidence for our structural assignments.

TABLE I. Formation of Carbocycles 4 from 2-Oxetanones 2 and their Reactions with Potassium Fluoride.

Entry	1	n	2(c:t)[a]	1 -> 4(%)[b]	4 -> 5(%)[b]	4 -> 8(%)[b]	8(c:t)[c]
1	**a**	1	69:31	78	45	30	33:67
2	**b**	2	76:24	75	53	25	36:64
3	**c**	3	65:35	80	84	0	---
4	**d**	4	65:35	80	85	0	---

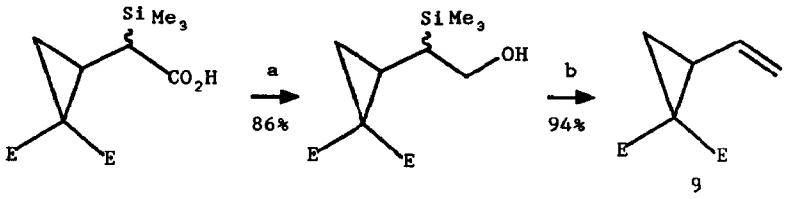
[a]Ratios were determined by integration of the trimethylsilyl signals in the ^{1}H NMR spectra of isomeric mixtures. [b]Yields quoted refer to isolated yields of purified products. All products were fully characterized by IR, ^{1}H NMR, ^{13}C NMR, and MS. [c]Ratios were determined by integration of vinylic hydrogens in the ^{1}H NMR spectra of isomeric mixtures.

With the smaller ring systems **4a** and **4b** (entries 1 and 2), formation of **5a** and **5b** on fluoride treatment was accompanied by alkene product formation, resulting from a reverse ring opening. The correlation between the ratios of cis/trans isomers of 2-oxetanones **2a** and **2b** with the double bond geometries of their product alkenes **8a** and **8b**, respectively, arises from the stereospecificity of both lactone ring opening[11] and alkene formation. As shown below, the predominant cis isomers of **2** give the predominant trans isomers of **8**.



Supporting evidence for the assignment of the isomeric structures **4a** was provided by their conversion to the known vinyl cyclopropane **9**.[12]

Intramolecular β-cleavage of 2-oxetanones is the exclusive mode of ring opening when the β-appendaged internal nucleophile is a doubly-stabilized enolate. Importantly, cycloalkane ring formation by this mechanism appears to be stereoelectronically favorable for all systems studied. Application of this methodology to the construction of larger ring systems will be the focus of future work.



(a) BH_3-THF; (b) $BF_3.OEt_2$, CH_2Cl_2

Acknowledgment: We thank the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this research. This work was also supported in part by the National Science Foundation EPSCoR program (Grant EHR 91-08767), The State of Mississippi, and Mississippi State University.

References and notes:

1. See: F. Benedetti, F. Berti, S. Fabrissin, and T. Gianferrara, J. Org. Chem. **1994**, 59, 1518 and references cited therein.
2. For the one documented example of this reaction, see: M. Kawashima and T. Fujisawa, Chem. Lett., **1983**, 1273.
3. For examples of intermolecular ring opening of 2-oxetanones by *hard* and *soft* nucleophiles, see: L. D. Arnold, T. H. Kalantar, and J. C. Vederas, J. Am. Chem. Soc., **1985**, 107, 7105; For examples of intramolecular β-cleavage of 2-oxetanones by oxygen nucleophiles, see: K. T. Mead and S. K. Pillai, Tetrahedron Lett. **1993**, 34, 6997; K. T. Mead and H.-L. Yang, J. Org. Chem. **1990**, 55, 2991.
4. W. T. Brady and K. Saidi, J. Org. Chem. **1979**, 44, 733.
5. K. T. Mead and M. Park, J. Org. Chem. **1992**, 57, 2511.
6. Structure **2a** is representative. ^{1}H NMR ($CDCl_3$) δ ppm: 0.18 (9H, s, Me_3Si of *trans*), 0.22 (9H, s, Me_3Si of *cis*), 2.30 (2H, m, CH_2), 2.98 (1H, d, J=4.3Hz, CHTMS of *trans*), 3.40 (1H, d, J=6.2Hz, CHTMS of *cis*), 3.56 (1H, t, CH(CO_2Me), 3.71 (6H, s, 2 x CO_2CH_3 of *trans*), 3.74 (6H, s, 2 x CO_2CH_3 of *cis*), 4.35 (1H, m, ring TMSCHCH of *trans*), 4.56 (1H, m, ring TMSCHCH of *cis*); IR (neat) cm^{-1}: 1808, 1738.
7. **4a** ^{1}H NMR ($CDCl_3$) δ ppm: 0.15 (9H, s), 0.90 (3H, m), 2.10 (1H, d, J=6.0Hz), 3.71 (3H, s), 3.74 (3H, s); IR (neat) cm^{-1}: 3200-3600 (OH), 1733 (ester C=O), 1711 (acid C=O); **4b** ^{1}H NMR ($CDCl_3$) δ ppm: 0.15 (9H, s), 1.20 (2H, m), 1.85 (3H, m), 2.21 (1H, d, J=6.1), 3.71 (3H, s), 3.74 (3H, s); **4c** ^{1}H NMR ($CDCl_3$) δ ppm: 0.15 (9H, s), 1.70-1.90 (4H, m), 2.01-2.10 (3H, m), 2.55 (1H, d, J=6.2Hz), 3.71 (3H, s), 3.74 (3H, s); **4d** ^{1}H NMR ($CDCl_3$) δ ppm: 0.15 (9H, s), 1.58-1.70 (2H, m), 1.80-1.97 (4H, m), 2.06-2.21 (3H, m), 2.60 (1H, d, J=6.1Hz), 3.71 (3H, s), 3.74 (3H, s)
8. **5c** ^{1}H NMR ($CDCl_3$) δ ppm: 1.60-1.90 (4H, m), 2.05-2.20 (3H, m), 2.51 (1H, dd, J=5.4, 13.8Hz), 2.62 (1H, dd, J=6.1, 13.8Hz), 3.71 (3H, s), 3.74 (3H, s); ^{13}C NMR ($CDCl_3$) δ ppm: 20.94, 21.88, 32.19, 32.40, 52.48, 52.76, 64.45, 78.20, 168.88, 169.47, 170.74
9. **5d** ^{1}H NMR ($CDCl_3$) δ ppm: 1.60 (2H, m), 1.73-1.92 (4H, m), 2.08-2.21 (3H, m), 2.55 (1H, dd, J=5.6, 14.0Hz), 2.61 (1H, dd, J=6.0, 14.0Hz), 3.71 (3H, s), 3.74 (3H, s); ^{13}C NMR ($CDCl_3$) δ ppm: 21.84, 22.60, 29.99, 31.05, 52.23, 52.44, 60.02, 64.43, 78.17, 168.85, 169.43, 170.71
10. D. P. Curran and C.-T. Chang, J. Org. Chem. **1989**, 54, 3140.
11. For proof of stereospecificity of this ring opening in related systems, see: K. T. Mead and H.-L. Yang, Tetrahedron Lett. **1989**, 30, 6829.
12. M. Jones, Jr., W. Ando, M. E. Hendrick, A. Kulczycki, Jr., P. M. Howley, K. F. Hummel, and D. S. Malament, J. Am. Chem. Soc. **1972**, 94, 7469.

(*Received in USA* 2 *February* 1994; *revised* 8 *September* 1994; *accepted* 3 *October* 1994)