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THE METHYLLITHIUM-PROMOTED DEHALOGENATIVE RING FISSION OF B-IODOTETRA-HYDROFURANS GIVES NO EVIDENCE OF A FREE RADICAL COMPONENT

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We have recently reported the alkyllithium-promoted dehalogenative ring fission of diiodides derived from 1,4:3,6-dianhydrohexitols (1) to give 2-(1-iodo-2-hydroxyethyl)-2,5-dihydrofurans (2).¹ Here we wish to report evidence relevant to the mechanism of the above reaction (eq. 1).



Of major concern to us was the question of whether the reaction takes place, at least in part, by way of an outer sphere electron transfer process (SET).² Since such a mechanism would imply free radical intermediates, the substrate chosen for our study was 2-(1-iodo-5-hexenyl)tetrahydrofuran, 3, having a built-in free radical probe.³ Dissociative electron transfer⁴ to 3 is expected to give radical 4 which would undergo, *inter alia*, cyclization to a cyclopentylmethyl radical 5 to eventually give hydrocarbon 6. Thus formation of 6, under conditions where anionic cyclization does not compete,⁵ would provide evidence of radical intermediates, hence of an ET process.

Treatment of the *erythro* isomer **3e** with MeLi (1.05 eqs in THF at -78°) followed by aq NH₄Cl quenching gave the ring opened diene alcohols E- and Z-4,9-decadien-1-ol **8** and **9** in a 9:1 ratio.⁶ The same products were obtained from the *threo* isomer, **3t**, although in a reversed ratio, Z:E = 7:3. No reduction product, 2-(5-hexenyl)tetrahydrofuran, **10**, or cyclization products **6** could be detected. Coupling products were also absent.⁷



The above results provide no evidence in favor of an electron transfer mechanism. To gain further insight it was desirable to establish a comparison with what arises from the same substrates reacting with an authentic ET reagent. Thus the reactions of both **3e** and **3t** with sodium or lithium naphthalenide were investigated (eq. 2).

$$3e (or 3t) \xrightarrow{M^{+}C_{10}H_{8}^{-}}_{THF/-78^{\circ}} 8 + 9 + 10 \quad (eq. 2)$$

$$M = Li \quad 8/9 = 3 \qquad (8+9)/10 = 9$$

$$Na \qquad " \qquad 3 \qquad " \qquad 1.5$$

$$Na^{*} \qquad " \qquad 3 \qquad " \qquad 0.2$$

$$*_{t-BuNH_{2}}(3 eq)$$

The diene alcohols 8 and 9 were again produced; however, their ratio was identical for both *erythro* and *threo* starting materials, E/Z = 3, quite different with respect to the MeLi-eliminations. Moreover, and unlike the latter, an unrearranged reduction product, 10, was also formed in substantial amount (eq. 2).⁸ Interestingly, while the E/Z ratio appears not to depend on the metal counterion (Li⁺ or Na⁺) nor on the presence of a weak proton donor such as t-BuNH₂, the proportion between elimination (8 + 9) and reduction does. The observed dependence suggests 8, 9, and 10 arise from a common intermediate, an ion pair M⁺7, undergoing competitive Elcb ring opening to the alkoxides of 8 and 9, a process likely to be favored by the more electrophilic counterion (Li⁺), or proton capture from the solvent, or from the added H⁺-donor, to give 10. No cyclization products could be

detected. This implies that electron transfer from sodium naphthalenide to radical 4 (to give carbanion 7) is much more rapid than intramolecular cyclization of 4 to give 5. Since the latter is a well characterized clock reaction³ and our experiments are conducted at 0.01 *M* concentration, a lower limit of the second order specific rate for electron transfer from NaC₁₀H₈ to radical 4 at -78 °C can be set at ca $4 \times 10^6 M^{-1} s^{-1}$.¹¹

The comparison between the naphthalenide and the MeLi results provides strong support for the latter not proceeding by way of SET. The MeLi elimination is stereoselective (largely anti) while the bona fide ET reaction (naphthalenide) is not. Since both radical 4 and carbanion 7 are configurationally labile, neither species can be an intermediate in the MeLi reaction. That a carbanion, free or paired with a metal cation, is not an intermediate is also consistent with the absence of H^+ -capture product (10) in the MeLi-promoted elimination.

What mechanism does this reaction follow our experiments do not allow a clear cut conclusion. They are consistent with either a concerted X-philic displacement¹⁵ or with a two step process via a hypervalent iodine complex (eq. 3, path **b** or **a**, respectively). The



latter pathway is the more likely in view of recent studies where the existence and low temperature stability of such species have been convincingly demonstrated. 16

References and Notes.

- 1. V. Cerè, C. Paolucci, S. Pollicino, E. Sandri, and A. Fava, <u>Tetrahedron Lett.</u>, 1989, 6737.
- 2. E.C. Ashby, Acc.Chem.Res. 1988, 21, 414.
- 3. D. Griller and K.U. Ingold, Acc.Chem.Res. 1980, 13, 317. The cyclization of the 5-hexenyl radical is characterized by $k_c = 1 \times 10^5 \text{ s}^{-1}$ at 25° and $E_a = 6.1 \text{ kcal/mol}$.
- 4. C.P. Andrieux, I. Gallardo, J.M. Savéant, and K-B. Su, J.Am.Chem.Soc. 1986, 108, 638.
- W.F. Bailey, J.J. Patricia, V.C. DelGobbo, R.M. Jarret, and P.J. Okarma, <u>J.Org.Chem.</u> 1985, 50, 1999.
- 6. Glc analyses were carried out using suitable internal standards calibrated against authentic materials (however, see footnote 7). New materials had analytical data (C, H, I), 1 H-, and 13 C NMR spectra consistent with the assigned structures. For space limitation only the more relevant 13 C NMR resonances are reported below. Assignments

based on signals' multiplicities (by DEPT) and substituent effects. For numbering of **3t**, **3e**, and **10**, see structure **10**.

3t and **3e**: (the first and second δ value refer to the *threo* and *erythro* isomer, respectively) 138.1, 138.2 (C₁₀); 115.0, 114.9 (C₁₁); 82.4, 82.4 (C₂); 68.9, 69.0 (C₁); 42.2, 43.2 (C₆); 35.8, 36.0 (C₇); 32.9, 33.0 (C_g); 30.9, 32.4 (C₃); 29.0, 28.7 (C₈); 26.2, 26.0 (C₄).

- 6: Four inseparable isomers were obtained (80%) by Bu_3SnH reduction-cyclization of 3t and 3e (Et₂0; r.t.) along with reduction product 10 (20%) which could be separated by flash chromatography (petroleum ether: Et₂0 99:1): δ 83.90, 81.99, 81.50, 80.60 (CH0); 67.82, and 67.69 (three resonance) (CH₂0); 51.95, 51.73, 49.29, 48.81 (CHCH₃); 21.05, 20.43, 15.36, 14.97 (CH₃). The remaining 24 CH₂'s signals are comprised between 35.50 and 22.67 ppm.
- 8: 138.56 (C_g); 130.56, 129.75 (C₄, C₅ interchangeable); 114.35 (C₁₀); 62.19 (C₁); 32.97, 32.24 (C₂, C₈ interch.); 31.72 (C₇); 28.64, 28.57 (C₃, C₆ interch.).
- **9:** 138.67 (C_g); 130.26, 129.29 (C₄, C₅ interch.); 114.51 (C₁₀); 62.44 (C₁); 33.34, 32.63 (C₂,C₈ interch.); 28.95 (C₇); 26.66 (C₆); 23.64 (C₃).
- **10:** $13\overline{8}.99$ (C₁₀); 114.31 (C₁₁); **79.39** (C₂); 67.63 (C₅); 35.61 (C₆) 33.77 (C₉), 31.41 (C₃); 29.05 (C₈); 25.93, 25.75 (C₄, C₇ interch.).
- 7. For greater ease in the preparation of the authentic material required for analysis, the search for coupling products was carried out on the product mixture resulting from the BuLi-promoted elimination of 2-(l-iodomethyl)tetrahydrofuran. No trace (0.01%) of 2-pentyltetrahydrofuran could be detected (glc).
- 8. This contrasts with findings by Garst that no detectable methyltetrahydrofuran is formed in the reaction of tetrahydrofurfuryl halides with $NaC_{10}H_{B}$.
- 9. I.T. Barbas and J.F. Garst, unpublished observations quoted by J.F. Garst.¹⁰
- 10. J.F. Garst, <u>Acc.Chem.Res.</u> 1971, <u>4</u>, 400.
- 11. This figure arises from an extrapolated cyclization rate of radical 4, $k_c = 7.5 \times 10^2 \text{ s}^{-1}$ at -78°,³ and assuming our analytical method would be sensitive enough to detect at least 2% of cyclic product 6. For electron transfer from sodium naphthalenide to 5-hexenyl radical a specific rate $k = 1.10^9 M^{-1} \text{ s}^{-1}$ had been estimated by Garst^{10,12} at 25 °C in DME, a value abundantly compatible with our lower limit above, even though accounting for the 105 °K temperature difference. More recent data by the same author, however, seem to imply a k_r value much lower than previously estimated. By applying the criterion of the cis/trans 1,2-dimethylcyclopentane product ratio,¹³ and having suppressed anion cyclization, Garst, Hines, and Brunkke concluded that the purely radical cyclization of the 1-methyl-5-hexenyl radical competes comparably with electron transfer from NaC₈H₁₀ 0.1-04 M.¹⁴ From their data a k_r value can be deduced ranging from 2 to $8.10^6 M^{-1} \text{ s}^{-1}$, much larger than the previous estimate.¹⁰ Further experimental work is desirable for resolving this discrepancy.
- 12. J.F. Garst and F.E. Barton, II, Tetrahedron Lett. 1969, 587.
- 13. J.F. Garst and J.B. Hines, <u>J.Am.Chem.Soc.</u> 1984, <u>106</u>, 6443.
- 14. J.F. Garst, J.B. Hines, and J.D. Bruhnke, Tetrahedron Lett. 1986, 1963.
- 15. N.S. Zefirov and D.I. Makhon'kov, Chem.Rev. 1982, 82, 615.
- 16. a. H.J. Reich and N.H. Phillips, J.Am.Chem.Soc., 1985, 107, 4101; b. H.J. Reich, D.P. Green, and N.H. Phillips, ibid. 1989, 111, 3444.

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