J. Chem. Research (S), 1998, 258–259†

Direction of Ring Opening of Styrene Oxide and Butadiene Monoxide by Ester Carbanions†

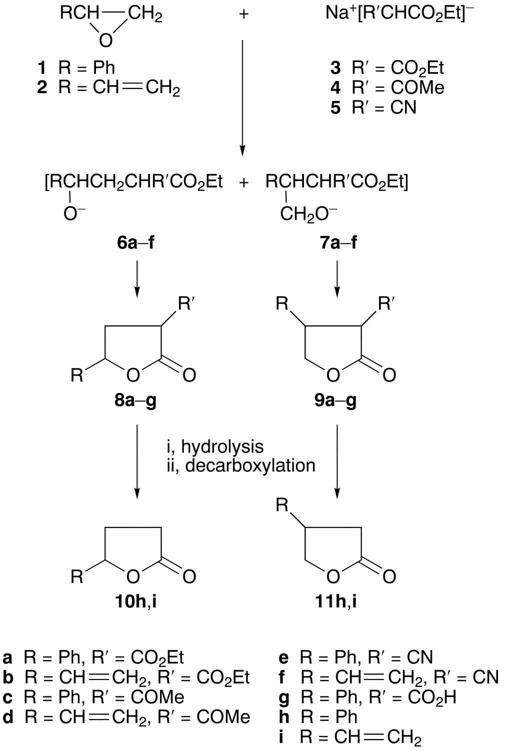
Stefan T. Orszulik*,‡ **and Maurice Porter**

Malaysian Rubber Producers' Research Association, Tun Abdul Razak Laboratory,
Brickendonbury, Hertford, Herts SG13 8NL, UK

Attack takes place at both primary and secondary epoxy carbons of styrene oxide and butadiene monoxide on reaction with ester carbanions, providing evidence for the conjugative effect in these systems.

Styrene oxide **1** and butadiene monoxide (3,4-epoxybut-1-ene) **2** have been used extensively in the investigation of the influence of conjugative effects on the direction of ring opening of epoxides by nucleophiles[1,2] but the results have been confused by structural misassignments and failure to identify some significant products. Early workers,[3,4] who did not have available the benefits of modern analytical methods, claimed that diethyl sodiomalonate **3** attacks **1** exclusively at the terminal carbon to give eventually the 4-phenyl lactone **10h** *via* the sequence shown (Scheme 1). This finding was widely quoted[1,5–7] but later shown to be incorrect, evidence being obtained that both **10h** and **11h** are formed in significant amounts,[8–11] though one worker[12] obtained only **11h** *via* the isolated acid **9g**.

Reaction of **3** with the vinyl epoxide **2** was claimed also to take place exclusively at the primary epoxide carbon atom to give **10i**[3,4] and this assertion has also received wide acceptance;[1,6,7] similarly the reaction of sodiocyanoacetate with styrene oxide **1**[13] and with butadiene monoxide **2**[13] was claimed to proceed by attack on the terminal carbon to give the products **10h** and **10i** respectively. In these cases the reactions do not appear to have been studied thoroughly since: there is one report[11] in which styrene oxide **1** has been shown to give both 3- and 4-phenyl lactones on reaction with cyanoacetate **5**, though there is some confusion regarding the melting points given in this report (see below).



a R = Ph, R′ = CO_2Et
b R = CH=CH_2, R′ = CO_2Et
c R = Ph, R′ = COMe
d R = CH=CH_2, R′ = COMe
e R = Ph, R′ = CN
f R = CH=CH_2, R′ = CN
g R = Ph, R′ = CO_2H
h R = Ph
i R = CH=CH_2

Scheme 1

Table 1 Ions **6a–f** and **7a–f** formed by attack of ester carbanions **3–5** on epoxides **1** and **2** deduced from the literature

	Ion(s) formed from	
Ester carbanion	Styrene oxide **1**	Butadiene monoxide **2**
Malonate **3**	**6a**[3,4] **7a**[12] **6a**+**7a**[8–11]	**6b**[3,4] **6b**+**7b**[a] (30:70)
Acetoacetate **4**	**6c**[16]	**6d**+**7d**[16]
Cyanoacetate **5**	**6e**[13b] **6e**+**7e**[a] (46:54)	**6f**[13] **6f**+**7f**[a] (32:68)

[a]This paper. [b]Almost certainly **7e**, see text.

The position of attack on epoxides such as **1** and **2** by nucleophiles like **3**, **4** and **5** has been thought to be determined by a balance between the conjugative effect exerted by the phenyl or vinyl group, which should facilitate attack at the neighbouring secondary carbon atom to give the ion **7**, and steric hindrance, which will predispose attack at the primary carbon to give ion **6**. As can be seen from Table 1, the experimental observations prior to this paper have produced a confusing picture. The degree of steric hindrance in the attacking carbanion falls in the order: $\mathbf{3} > \mathbf{4} \gg \mathbf{5}$, whilst that of the epoxide is $\mathbf{1} > \mathbf{2}$. At first sight, the results for **4** and **5** are anomalous since these should produce much larger proportions of the isomers **7**. However, reference to the original literature shows that the identification of **6c** and **6f** is doubtful. Identification of **6e** is almost certainly wrong, the product isolated having been assigned[13] the structure **8e** on the basis of its hydrolysis to **8g** and comparison with a supposedly authentic sample of **8g**,[4] the source of which is doubtful.[9] Comparison of melting points of the acids **8g**[10] and **9g**[9–12] given in the literature suggests that the product said to be **8e** is almost certainly **9e**, derived from the ion **7e**.

Since we required a pure sample of lactone **10i** for another purpose, we attempted its preparation using the reaction conditions of Russell and VanderWerf.[3] In fact, this procedure gave us a 30:70 mixture of **10i** and **11i** with an overall yield of 54%. The two isomers were cleanly separated by preparative HPLC and were identified by their ^1H NMR spectra.[14]

In our hands reaction of ethyl cyanoacetate **5** with styrene oxide **1** using established conditions[13] gave a mixture of **8e** and **9e**, separated by fractional crystallisation and identified by their ^1H NMR spectra.[15] Zuidema *et al.*[13] claim to have obtained the diastereoisomers of **8e**, the melting points of which correspond to those of **8e** and **9e** of the present work.[17] The melting point of the acid **8g** given by Zuidema

---

*To receive any correspondence (*e-mail:* stefan@orszulik.demon.co.uk).

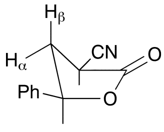
†This is a **Short Paper** as defined in the Instructions for Authors, Section 5.0 [see *J. Chem. Research (S)*, 1998, Issue 1]; there is therefore no corresponding material in *J. Chem. Research (M)*.

‡Present address: 6 The Kestrels, Grove, Wantage, Oxfordshire OX12 0QA, UK.

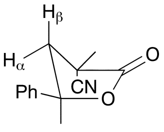
et al.[13] corresponds to that of **9g** given elsewhere.[9–12] Hashem and Shaban[11] claim to have obtained **8e** and **9e**, but their melting points do not accord with those of the present work or elsewhere.[17] Furthermore, they appear to have interchanged the melting points of **10h** and **11h**[17] compared with their authentic sample.[8]

Similarly, reaction of **5** with butadiene monoxide **2**, using standard conditions,[13] proceeds *via* **6f** and **7f**, the isolated products being identified as **8f** and **9f** by ^{1}H NMR spectroscopy[18] of the materials obtained after preparative HPLC. Zuidema *et al.*[13] claim to have obtained the diastereoisomers of **8f** which gave, on removal of the cyano group, **10i**. Comparison of their IR data with those of the present work suggests that Zuidema's samples of **8f** and **10i** are all mixtures of the 3- and 4-vinyl lactones.

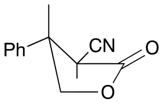
Both **8e** and **9e** would be expected to be a mixture of diastereoisomers. Careful examination of the ^{1}H NMR data[19] for **8e**, and comparison with published values for other substituted γ-lactones, indicates that the major diastereoisomer is *cis*-2-cyano-4-phenyl-γ-butyrolactone **12**, the ratio of **12** to **13** being 70:30 by HPLC. Isomers **12** and **13** were separated by HPLC, but subsequent examination by HPLC and NMR spectroscopy showed the samples to have reverted back to the equilibrium mixture. In the case of **9e**, the ratio of diastereoisomers is 85:15 by HPLC, thought to be the **14** and **15** isomers respectively.



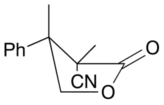
12



13



14



15

In both these cases (**8e** and **9e**) the C*H*CN hydrogen is labile as observed in D_2O experiments using NMR spectroscopy, and thus the ratios of diastereoisomers probably represent their equilibrium mixtures.

Taking the results of the present work into account, there is firm evidence for attack by malonate ion **3** at both epoxide carbon atoms in **1** and **2**. Similarly, cyanoacetate ion **5** reacts at both epoxy sites of **1** and **2**. In all the cases studied here the major products have been the result of attack on the more substituted carbon of the epoxide, giving predominantly the 3-phenyl and 3-vinyl products. Since simple alkyl mono-substituted epoxides undergo nucleophilic attack under these conditions exclusively at the primary carbon atom, this is evidence for the participation of the conjugative effect in the ring opening of these epoxides.

Experimental

Reaction of butadiene monoxide with malonate was carried out in the manner described in ref. 3; reactions of styrene oxide and butadiene monoxide with cyanoacetate were carried out according to ref. 13.

We are grateful to the board of the Malaysian Rubber Producers' Research Association for permission to publish this work, and to M. J. R. Loadman and A. D. Edwards for NMR and HPLC analyses.

Received, 10th November 1997; Accepted, 22nd January 1998
Paper E/7/08062J

References and notes

1 R. E. Parker and N. S. Isaacs, *Chem. Rev.*, 1959, **59**, 737.
2 J. G. Buchanan and H. Z. Sable, in *Selective Organic Transformations*, ed. B. S. Thyagarajan, Interscience, New York, 1972, vol. 2, p. 1.
3 R. R. Russell and C. A. VanderWerf, *J. Am. Chem. Soc.*, 1947, **69**, 11.
4 G. Van Zyl and E. E. van Tamelen, *J. Am. Chem. Soc.*, 1950, **72**, 1357.
5 C. K. Ingold, in *Structure and Mechanism in Organic Chemistry*, Cornell University Press, 1953, p. 342.
6 A. Rosowsky, in *Heterocyclic Compounds with Three- and Four-membered Rings, Part 1*, ed. A. Weissberger, Interscience, New York, 1964, ch. 1.
7 E. L. Eliel, in *Steric Effects in Organic Chemistry*, ed. M. S. Newman, Wiley, New York, 1956, pp. 106–114.
8 C. H. DePuy, F. W. Breitbeil and K. L. Eilers, *J. Org. Chem.*, 1964, **29**, 2810.
9 P. M. G. Bavin, D. P. Hansell and R. G. W. Spickett, *J. Chem. Soc.*, 1964, 4535.
10 S. A. M. Tayyeb Hussain, W. D. Ollis, C. Smith and J. F. Stoddart, *J. Chem. Soc., Perkin Trans. 1*, 1975, 1480.
11 A. I. Hashem and M. E. Shaban, *Indian J. Chem., Sect. B*, 1981, **20**, 807.
12 T. Jakobiec, *Diss. Pharm. Pharmacol.*, 1971, **23**(4), 401.
13 G. D. Zuidema, P. L. Cook and G. Van Zyl, *J. Am. Chem. Soc.*, 1953, **75**, 294.
14 **10i**: 2.4 (2 H, m, H^2); 2.4–1.9 (2 H, m, H^3); 4.82 (1 H, m, H^4); 5.1–5.5 (2 H, m, vinyl CH_2); 5.7–6.1 (1 H, m, vinyl CH). **11i**: 2.4 (2 H, m, H^2); 3.2 (1 H, sextuplet, H^3); 3.92–4.36 (2 H, dq, H^4); 5.1–5.3 (2 H, m, vinyl CH_2); 5.6–6.1 (1 H, dq, vinyl CH).
15 **8e**: 7.3 (5 H, C_6H_5): 5.85 (0.22 H, PhC*H*—O); 5.6 (0.55 H); 4.35 (0.9 H); 2.2–3.2 (2, 5 H). **9e**: 7.3 (5 H, C_6H_5); 4–5 (3 H, m).
16 R. M. Adams and C. A. VanderWerf, *J. Am. Chem. Soc.*, 1950, **72**, 4368.
17 **8e**: mp 131.4–132.5 °C (113–115,[11] diastereoisomers 93–94 and 133–134 °C[13]). **9e**: mp 93.4–94.0 °C (93–95,[12] 126–128 °C[11]). **10h**: mp (45–46,[11] 37–38,[8] 36–37 °C[9]). **11h**: mp (37–38,[11] 45–46,[8] 49–50,[12] 47–48 °C[9]).
18 **8f**: 5.6–6.0 ($CH{=}CH_2$); 5.2–5.5 ($CH{=}CH_2$); 4.8–5.0 (CH—O); 3.5–4.0 (CHCN); 2.0–3.0 (CH_2). **9f**: 5.0–6.0 ($CH{=}CH_2$); 3.5–4.5 (CHCN and CH_2—O); 3.0–4.0 ($CHCH_2$).
19 **12**: 5.5–6.0 (dd, $J^{3\alpha-4,3\beta-4}$, 5.4, 10.9 PhCH); 4.2–4.6 (dd, $J^{3\alpha-2,3\beta-2}$, 8.3, 12.0, CNCH, D_2O exchangeable); 3.1–3.5 (m, $H^{3\alpha}$); 2.5–3.0 (m, $H^{3\beta}$). **13**: 5.8–6.0 (dd, $J^{3\alpha-4,3\beta-4}$, 8.0, 7.0, PhCH); 4.2–4.4 (dd, $J^{3\alpha-2,3\beta-2}$, 9.0, 10.0, CNCH). Assignments confirmed by decoupling experiments.