Tetrahedron. Vol. 29, pp. 1503 to 1506. Pergamon Press 1973 Printed in Great Britain

STRUCTURE AND REACTIVITY OF α,β-UNSATURATED ETHERS—XIV[1]

PROTONATION OF *cis*- AND *trans*-1-ETHOXYBUTA-1,3-DIENES

T. OKUYAMA, T. SAKAGAMI and T. FUENO
Faculty of Engineering Science, Osaka University, Toyonaka, Osaka 560, Japan

(*Received in Japan* 30 *November* 1972; *Received in the UK for publication* 23 *January* 1973)

Abstract—The acid-catalysed hydrolysis and alcohol addition of *cis*- and *trans*-1-ethoxybuta-1,3-dienes have been investigated. It was found by product analyses with deuterium incorporation experiments that in both the reactions the *cis* isomer protonates at the 2-position as well as at the 4-position while the *trans* isomer protonates exclusively at the 4-position. The kinetic experiments showed that the *trans* isomer is much more reactive than the *cis* isomer. The possible origin of the observations is discussed.

INTRODUCTION

The protonation of conjugated dienols and their ethers has recently attracted attention because of structure dependence of the site.[2-5] Rogers and Sattar[2a,b] observed that the competitive α-protonation as well as γ-protonation occurs on alicyclic dienol ethers of cisoid structure while transoid ethers protonate solely at the γ-carbon. Heap and Whitham[4] reported the α-protonation of cyclic dienols. However, an acyclic analog, 1-methoxybuta-1,3-diene, was found to protonate exclusively at the γ-position.[2c,6] On the other hand, Morrison and Kurowsky[3] obtained evidence for the α-protonation of hexa-2,4-dien-2-ol during the study on the acid-catalysed dehydration of hex-3-en-2,5-diol.

Thus, the α-protonation is possible for dienols of a certain structure, although it is different from the general pattern of electrophilic additions to conjugated dienes where the γ-attack usually leads to a stable allylic-cation intermediate.[7]

In the present communication, extensive investigations on the protonation of 1-ethoxybuta-1,3-diene are presented focusing attention on the effects of a geometrical structure. It was found that the *cis* isomer protonates at C-2 as well as at C-4 while the *trans* isomer protonates exclusively at C-4. Kinetic studies showed that the *trans* ether is much more reactive than its *cis* isomer. The reaction mechanisms of the acid-catalysed hydrolysis and alcohol addition will be discussed.

RESULTS

Hydrolysis of cis- *and* trans-1-*ethoxybuta*-1,3-*dienes* (**1c** *and* **1t**). The acid-catalysed hydrolysis of both **1c** and **1t** gave crotonaldehyde **2** and ethanol in 80% aqueous dioxane. Yields of **2** were *ca* 97% by VPC of the product extracts with n-pentane both from **1c** and **1t**. During the reaction, no isomerization from either **1c** or **1t** to the other was observed.

$$\underset{\textbf{1c and 1t}}{CH_2{=}CH{-}CH{=}CH{-}O{-}Et} \xrightarrow{H_3O^+} \underset{\textbf{2}}{Me{-}CH{=}CH{-}CHO} + EtOH \qquad (1)$$

Hydrolysis of the ethers obeys the first-order kinetics in over 80% conversion as is shown in Fig 1. The pseudo-first order rate constants were $1{\cdot}45 \times 10^{-4}$ and $2{\cdot}08 \times 10^{-3}\,sec^{-1}$ for **1c** and **1t**, respectively, in 0·2 M HCl-80% aqueous dioxane at 25·0°. The *trans* isomer **1t** is 14·3 times as reactive as **1c**.

In order to decide the site of protonation, the reaction was undertaken in acidic deuterium medium. For the convenience of product isolation, aqueous diglyme (2/5 by volume) was used as a solvent. The reaction was allowed to proceed for

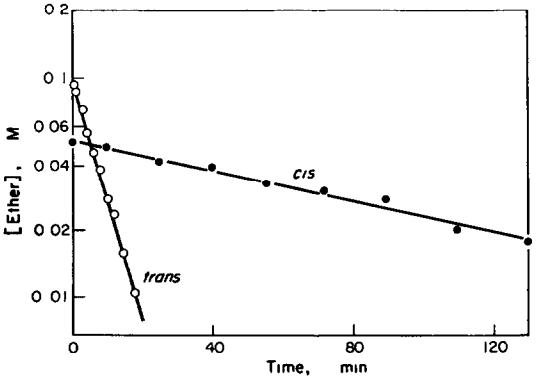


Fig 1. First-order plots for the hydrolysis of **1c** (●) and **1t** (○); [HCl] = 0·2 M in 80% aqueous dioxane, 25°C.

Table 1. Relative area of NMR peaks of crotonaldehyde produced in deuterium medium

	From 1t			From 1c + 1t[a]		
	2-H[b]	3-H[c]	4-H[d]	2-H[b]	3-H[c]	4-H[d]
	1·83	1·84	3·80	2·91	3·21	6·41
	1·82	1·82	3·83	2·91	3·09	6·40
	1·84	1·81	3·82	2·94	3·01	6·38
Av.	$1·83_0$	$1·82_3$	$3·81_7$	$2·91_7$	$3·10_3$	$6·39_7$
	1·00	(1·00)[e]	2·09	0·94	(1·00)[e]	2·06

[a] 1c/1t = 1·00/2·07.
[b] δ 6·23.
[c] δ 6·87.
[d] δ 2·03.
[e] Ref.

ca 20 hr in 0·1 N DCl. Deuterium distribution in the product **2** was determined by NMR spectroscopy. Relative integral areas of protons found in the product **2** are given in Table 1 and deuterium distribution was calculated as follows.

$$\mathbf{1t} \longrightarrow \underset{0.91}{CH_2D}—\underset{0.00}{CH}=\underset{0.00}{CH}—CHO$$

$$\mathbf{1c} \longrightarrow \underset{1.0}{CH_2D}—\underset{0.0}{CH}=\underset{0.19}{CD}—CHO$$

Deuterium was found only at C-4 of **2** produced from the *trans* isomer **1t**, while it was found both at C-4 and C-2 of the product **2** from the *cis* isomer **1c**. It was ascertained that crotonaldehyde does not exchange proton at C-2 with solvent deuterium under the same conditions.

Alcohol additions. The acid-catalysed addition of ethanol to **1c** and **1t** was carried out at 25·0° in ethanol containing 0·085 M hydrochloric acid. The reaction of **1t** for *ca* 10 min gave a 4,1-adduct **3** and a small amount of diadduct **4** accompanied by some oligomers in accord with the results of Kubler.[6] In prolonged reactions, **3** was completely converted to **4**. The yield of **4** was 77% on the basis of **1t**.

Under the same conditions, **1c** gave a 2,1-adduct **5** in 16% yield as well as **3** and **4** (18% yield together) and oligomers (60% yield). The 2,1-adduct **5** is stable in the above acidic medium in contrast to the considerable amenability of **3**. The results indicate the competitive α-protonation of **1c** in spite of the exclusive γ-protonation of **1t**.

Kinetic studies were undertaken under the same conditions as above. The isomerization from either isomer to the other was not observed. The pseudo-first order rate constant for the disappearance of **1t** was $1·2 \times 10^{-2}$ sec^{-1} and that for appearance of **4** was $1·0 \times 10^{-4}$ sec^{-1}. The reference reaction of the authentic sample of **3** under the same conditions showed that the rate for the disappearance of **3** agrees, within experimental error, with that for the formation of **4** from **1t**. The rate constant for the disappearance of **1c** was found to be $2·8 \times 10^{-4}$ sec^{-1}, 1/43 times smaller than **1t**.

DISCUSSION

α-Protonation of **1c**. From the product analysis of acid-catalysed ethanol addition (finding of **5**), the occurrence of competitive α-protonation of **1c** is obvious. This is the first direct observation of α-protonation of acyclic conjugated dienes.

In the acid-catalysed hydrolysis in the deuterium medium, deuterium was found at C-2 of the product from **1c**, which is quite convincing evidence of the α-protonation of **1c**.* A primary product in this case should be but-3-en-1-al **6**, which might give **2** through the reaction sequence:

$$\mathbf{1c} \xrightarrow{D^+} CH_2{=}CH{-}CHD{-}\overset{+}{C}H{-}OEt \longrightarrow \underset{\mathbf{6}}{CH_2{=}CH{-}CHD{-}CHO}$$

$$\rightleftharpoons \underset{\mathbf{7}}{CH_2{=}CH{-}CD{=}CH{-}OD} \xrightarrow{D^+} CH_2D{-}\overset{+}{C}H{\cdots}CD{\cdots}CH{-}OD \longrightarrow \underset{\mathbf{2}}{CH_2D{-}CH{=}CD{-}CHO} \quad (3)$$

However, **6** was not detected in any mixture of the hydrolysis. An alternative possibility for **1c** to lead to **2** (eq. 4) is not completely excluded in spite of the failure to find **1t** in the mixture, because **1t** is much more reactive than **1c** in acidic media as was kinetically shown. Nevertheless, it is highly un-

*The failure of Rogers *et al.*[2c] in observing α-protonation of a butadienol ether must be due to the exclusive *trans* structure of their substrate and/or to the instability of **6**.

$$\begin{array}{lll} \mathbf{1t} \longrightarrow & \underset{\mathbf{3}}{Me{-}CH{=}CH{-}CH(OEt)_2} \longrightarrow & \underset{\mathbf{4}}{MeCH(OEt)CH_2{-}CH(OEt)_2} \\ & \searrow \quad \text{Oligomers} & \\ \mathbf{1c} \longrightarrow & \underset{\mathbf{5}}{CH_2{=}CH{-}CH_2{-}CH(OEt)_2} & \end{array} \quad (2)$$

likely since the acetal of **6** was isolated in the reaction of **1c** with acidic alcohol.

$$\mathbf{1c} \xrightarrow{D^+} CH_2{=}CH{-}CHD{-}\overset{+}{C}H{-}OC_2H_5$$

$$\xrightarrow{-H^+} \mathbf{1t} \longrightarrow \longrightarrow \underset{\mathbf{2}}{CH_2D{-}CH{=}CD{-}CHO} \qquad (4)$$

According to the scheme 3, possible chances for deuterium to incorporate at C-2 of **1c** are two-fold, the first protonation step and the following reversible enolization between **6** and **7**. In the enolization step, **6** might lose a part of D incorporated in the first step. The relative possibility to lose D as compared with H from C-2 of **6** is estimated to be *ca* 1/4.[8] The D-H scrambling at C-2 of **6** under the same reaction conditions was examined with use of diethyl acetal of **6**.* This acetal **5** is easily hydrolysed through transient **6** to give crotonaldehyde according to the sequence;

$$\underset{\mathbf{5}}{CH_2{=}CH{-}CH_2{-}CH(OEt)_2}$$

$$\xrightarrow[-C_2H_5OD]{+D^+} CH_2{=}CH{-}CH_2{-}\overset{+}{C}H{-}OEt$$

$$\longrightarrow \underset{\mathbf{6}}{CH_2{=}CH{-}CH_2{-}CHO}$$

$$\rightleftharpoons \underset{\mathbf{7}}{CH_2{=}CH{-}CH{=}CH{-}OD}$$

$$\longrightarrow \longrightarrow \underset{\mathbf{2}}{CH_2D{-}CH{=}CD{-}CHO} \qquad (5)$$

Observed deuterium distribution in the deuteriolysis product of **5** was

$$\mathbf{5} \longrightarrow \underset{1{\cdot}02}{CH_2D}\text{—}\underset{0{\cdot}00}{CH}\text{=}\underset{0{\cdot}28}{CD}\text{—}CHO$$

The only chance of D-incorporation at C-2 is in the reversible enolization step of the above sequence. Therefore, the extent of D-H exchange at C-2 by enolization of **6** during the reaction is estimated as about 30%. With these estimations, the α-protonation of **1c** in the first step is evaluated to occur in *ca* 22%.

The relative primary protonation at C-2 and C-4 of **1c** in acidic alcohol is not straightforward because of the substantial amount of oligomer formation. The oligomers are very likely to be formed from the 4,1-adduct **3** rather than from the 2,1-adduct **5** since the latter is stable under the reaction conditions. Thus, the α-protonation occurs in > 16%, probably to a similar extent to that in the hydrolysis.

Alcohol additions. It was found that the rate of the formation of the diadduct **4** from **1t** is the same as that of the disappearance of authentic **3**. The 4,1-adduct **3** was actually isolated from the reaction. Thus, the formation of **4** from **1t** is obviously via **3** as can be seen in Eq. 2. The earlier suggestion[7] that **4** is formed by successive 4,3- and 2,1-additions of alcohol to **1** proved to be wrong.

The great amenability of **3** in acidic alcohol as compared with **5** seems worth noting. A possible source of decay through double-bond protonation will not explain the difference of the reactivity between **3** and **5**.

$$\underset{\mathbf{3}}{Me{-}CH{=}CH{-}CH(OEt)_2}$$

$$\overset{H^+}{\rightleftharpoons} Me{-}CH{=}CH{-}\overset{H}{\underset{|}{\overset{|}{\overset{+}{O}}}}{-}Et \quad (O{-}Et)$$

$$\rightleftharpoons Me{-}\overset{\delta+}{C}H \cdots CH \cdots \overset{\delta+}{C}H{-}OEt + EtOH$$

$$\longrightarrow [Me{-}\underset{OEt}{CH}{-}CH{=}CH{-}OEt]$$

$$\xrightarrow{EtOH} \underset{\mathbf{4}}{Me{-}\underset{OEt}{CH}{-}CH_2{-}CH(OEt)_2} \qquad (6)$$

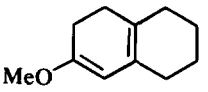
It is well known that the alcohol exchange of acetals occurs easily in acidic alcohol. An intermediate allylic cation from **3** has two amenable carbons C-1 and C-3 (See eq. 6). An ethanol attack at C-1 results in a reverse reaction, *i.e.* alcohol exchange. On the other hand, the same attack at C-3 gives an enol ether which easily reacts with ethanol to give **4** (decay of **3**). However, the corresponding cationic intermediate from **5**, $CH_2{=}CH{-}CH_2{-}\overset{+}{C}H{-}OEt$, leads only to the starting material, thus seemingly stable.

Effects of geometrical isomerism. It was found that the *trans* isomer **1t** is more reactive than its *cis* isomer **1c** by factors of 14·3 and 43 for the reactions in aqueous and alcoholic media, respectively. On the other hand, **1t** is thermochemically more stable than **1c** by 0·93 kcal/mole in the liquid phase.[9] That is, the less stable isomer **1c** is less reactive, which means that the transition state for the reaction of **1c** is much less stable than that of **1t**.

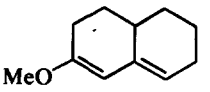
It was also found that the α-protonation can occur only on **1c**, the less stable isomer. This striking feature is much the same as that found for alicyclic dienol ethers.[2] Namely, the less stable cisoid isomers like **8** can protonate at the α-carbon,

*Attempts to prepare authentic **6** were unsuccessful.

while the stable transoid isomers like **9** protonate exclusively at the γ-carbon.



8



9

This prominent contrast in orientation was explained[2b] in terms of Hammond's postulate.[10] That is, in protonation of high-energy species, the transition state must resemble the starting substrates, *i.e.* be less-bonding, and thus the charge density largely determines the position of protonation. On the other hand, low-energy species react through the transition state resembling the products and their stability determines the protonation site. As a result, the stable conjugated dienol derivatives protonate at the γ-position giving the stable products and the unstable dienol derivatives can protonate at the α-position, where the electron density is higher than the γ-position.[2b]

This argument seems to be applicable to interpret the present observations concerning site of protonation of **1c** and **1t**. In the case of less stable **1c**, the importance of charge density in determining the protonation site leads to the α-protonation. However, when the charge-density factor is less important, the γ-protonation predominates. This appears also to explain the relative reactivity of **1c** and **1t**. The lower reactivity of **1c** is attributed to its transition state which is less-bonding and hence less stable as compared with **1t**.

The same argument regarding the protonation site was also applied to explain the α-protonation of dienolate anions, which are considered to be high-energy species.[3,4]

One of the present authors and his coworkers have recently reported the cationic polymerization of **1c** and **1t**.[11] They found that **1t** is 8·7 times as reactive as **1c** and that the polymerization of **1c** proceeds partly through α-attack of a polymeric cation while **1t** polymerizes exclusively through the γ-attack. Thus, the problem of attacked site seems not to be limited to the protonation but to be more general in electrophilic additions to dienol derivatives. Extensive investigations on other electrophilic additions seem to be necessary.

EXPERIMENTAL

NMR spectra were recorded with use of JNM-4H-100.* For preparative and analytical VPC, a Shimadzu Model GC-2C and a Model 4APT gas chromatographs were used respectively.

Materials. **1c** and **1t** were obtained as described previously;[11] **3** was prepared according to Claisen,[12] b.p. 49°/17 mmHg (lit.[13] 48–49°/21 mmHg); **5** was prepared from ethyl vinyl ether and diethyl acetal by the method of Hattori,[14] b.p. 140–142° (lit.[14] 142·0°); **4** was synthesized according to Meier,[15] b.p. 75–77°/12 mmHg (lit.[15] 85–86°/18 mmHg); deuterium oxide (E. Merck) was 99·75% pure; diglyme was dried and distilled from calcium hydride; Dioxane was refluxed overnight over Na and distilled; EtOH was dried and distilled over CaO; Toluene, chlorobenzene, and n-pentane were used after distillation.

Hydrolysis of **1c** *and* **1t**. The acid-catalysed hydrolysis was carried out in 80% aqueous dioxane containing 0·2 M HCl.

Kinetic measurements were undertaken at 25·0° by a VPC technique using toluene as internal standard in the same way as described before.[16]

Deuterium chloride catalyzed hydrolysis. The ethers were hydrolysed in deuterium oxide-diglyme (2/5 by volume) containing 0·1 M deuterium chloride (deuterium purity > 99 5%). The formed crotonaldehyde was extracted with n-pentane, purified by preparative VPC and analysed by NMR spectroscopy. Relative areas of proton peaks were calculated from integral curves.

Alcohol additions. The acidic EtOH was obtained by introducing dry HCl (passed through conc H_2SO_4). Acid concentration was 0·085 M and contained 0·650% (w/v) water by Karl Fisher titration in MeOH. An appropriate amount (0·3 ml) of the substrate was dissolved in 10 ml of the acidic EtOH and the products were extracted with n-pentane and isolated by fractional distillation or preparative VPC. The distillation residue under 2 mmHg was denoted as oligomers.

Kinetic experiments were carried out at 25° by VPC analysis using chlorobenzene as internal standard.

*The authors wish to thank Mr. Y. Terawaki for recording NMR spectra.

REFERENCES

[1]For Part XIII of this series, see, T. Okuyama and T. Fueno, *J. Polymer Sci.* A-1, **9**, 629 (1971)
[2a]N. A. J. Rogers and A. Sattar, *Tetrahedron Letters* 1311 (1964); [b]*Ibid.* 1471 (1965); [c]T. N. Huckerby, N. A. J. Rogers and A. Sattar, *Ibid.* 1113 (1967)
[3]S. Malhotra and H. Ringold, *J. Am Chem. Soc.* **87**, 3228 (1965)
[4]N Heap and G. A. Whitham, *J. Chem Soc.* (B), 164 (1966)
[5]H. Morrison and S. R. Kurowsky, *Chem. Comm.* 1098 (1967)
[6]D. G. Kubler, *J. Org. Chem.* **27**, 791 (1962)
[7]P. B. D. de la Mare and R. Bolton, *Electrophilic Additions to Unsaturated Systems*, Chapter 12. Elsevier, London (1966)
[8]K. B. Wiberg, *Chem. Rev.* **55**, 713 (1955); F. A. Long and D. Watson, *J. Chem. Soc.* 2019 (1958)
[9]T. Okuyama, T. Fueno and J. Furukawa, *Tetrahedron* **25**, 5409 (1969)
[10]G. S. Hammond, *J Am. Chem Soc* **77**, 334 (1955)
[11]T. Fueno, T. Tsunetsugu, K. Arimoto and J. Furukawa, *J. Polymer Sci.* A-1, **9**, 163 (1971)
[12]T. Claisen, *Ber. Dtsch Chem. Ges* **31**, 1016 (1898); **40**, 3903 (1907)
[13]S. M. McElvain, R. L. Clarke and G. D. Tones, *J. Am. Chem Soc.* **64**, 1966 (1942)
[14]S. Hattori, *J. Soc. Org. Synth. Chem. Japan* **19**, 453 (1961)
[15]G. Meier, *Ber. Dtsch. Chem. Ges* **76**, 1016 (1943)
[16]T. Okuyama, T. Fueno, H. Nakatsuji and J. Furukawa, *J Am. Chem. Soc.* **89**, 5826 (1967)