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Substrate-Specific Rearrangement and Acetonidation of Epoxy-Ethers Catalyzed by Tetracyanoethylene

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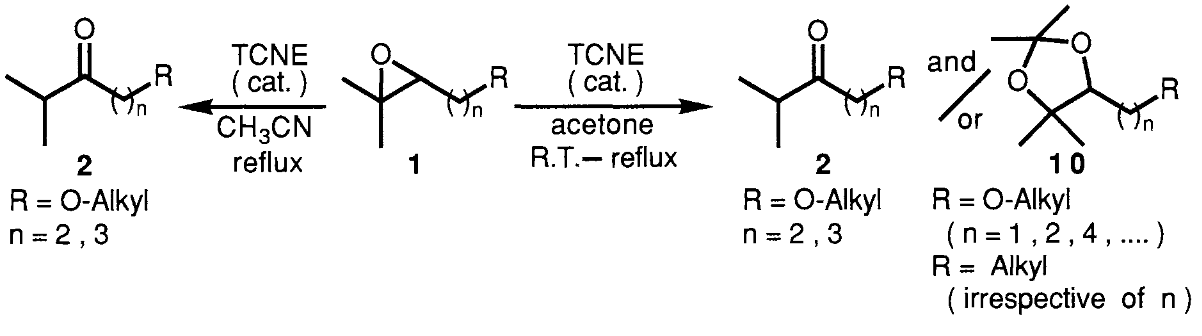
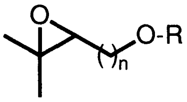
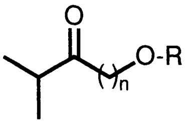
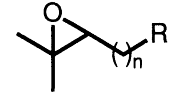
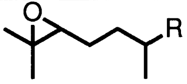
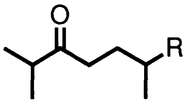
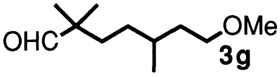
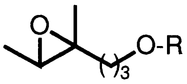
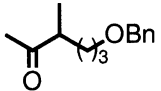
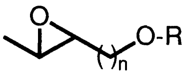
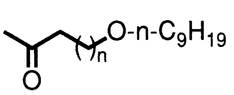
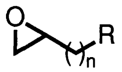
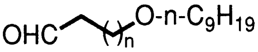
Rearrangement of epoxy-ethers providing carbonyl compounds was catalyzed by tetracyanoethylene (TCNE) in acetonitrile under the preferential anchimetric assistance of intramolecular etheric oxygen function in the 5-exo mode for the 1,2-disubstituted epoxide unit and in the quaternary 5-exo, 5-endo, and 6-endo mode for the trisubstituted type. In acetone, epoxy-ethers favored by neighboring group participation were led to carbonyl compounds and the other epoxides furnished acetonides.

Epoxides are versatile intermediates in organic synthesis due to susceptibility of a vast array of chemo-, regio-, and stereoselective transformations with concomitant ring-opening.[1)] Among the epoxide-transformations, rearrangement of epoxides to carbonyl compounds has been extensively studied and reviewed.[1a)] Most commonly, the rearrangement has been effected by use of protic[2a)] and Lewis acid,[2b)] and in a few cases promoted by lithium bromide,[2c)] zero-valent transition metals,[2d)] and electrolysis.[2e)] Acetalization of epoxides with carbonyl compounds has been caried out usually by Lewis acid catalysis,[3)] although an appreciable extent of polymerization of epoxide and/or acetal is usually inevitable as side reaction. During examinations of chemical function of tetracyanoethylene (TCNE),[4)] which is a powerful and the simplest one-electron acceptor, we have found novel catalytic properties of TCNE in the transformation of epoxides. We wish to disclose a mild catalysis of TCNE in substrate-specific epoxide-ketone rearrangement and acetonidation of epoxy-ethers.



A trisubstituted epoxy-ether (**1a**$_3$) was heated for 6 h under reflux with 0.2 equiv. of TCNE in acetonitrile (CH_3CN) to give a ketone (**2a**$_3$)[5)] as a sole product in 70% yield. Interestingly, under the same conditions epoxides (**1a**$_1$) and (**1c**$_4$) underwent no reaction or gave a little amount (6% yield) of a ketone (**2c**$_4$) with a large amount of recovery of the epoxide (**1c**$_4$), respectively, although epoxides (**1a**$_2$) was rearranged to the corresponding ketone (**2a**$_2$) in 75% yield. Neither an epoxide (**1d**) nor an epoxy-ether (**1g**) reacted with TCNE in CH_3CN and even in isopropyl ether under reflux, and complete recovery of the starting epoxides resulted. In contrast to TCNE-catalysis, the reaction of **1g** in benzene was promoted by BF_3-Et_2O,[1a)] one of the most commonly used Lewis acid for epoxy-ketone isomerization, to give indiscriminately a ketone (**2g**) (68%) together with the isomeric aldehyde (**3g**). Based on these observations, we envisioned that location of intramolecular etheric oxygen is important for the epoxide-ketone rearrangement assisted by TCNE. A variety of epoxides of different types of substitution, with and without the etheric oxygen function, and of various length of carbon chain between the etheric oxygen and epoxide unit were screened in the conditions.The results are summarized in Table 1.

Table 1. Substrate-Specific Rearrangement of Epoxy-Ethers Catalyzed by TCNE (0.2 equiv.) in CH_3CN at reflux temperature

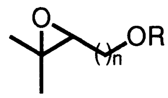
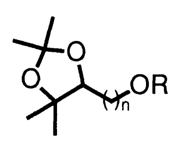
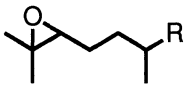
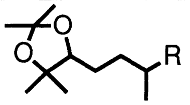
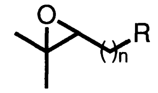
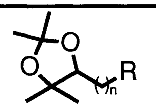
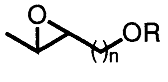
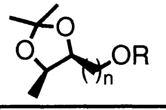
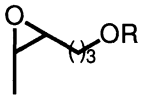
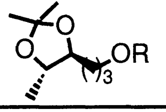
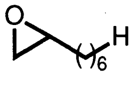
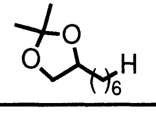
Epoxide				Reaction time / h	Product (Carbonyl compound)		Yield / %
	$\mathbf{1a_1}$	R = Bn	n = 1	6			---[a)]
	$\mathbf{1a_2}$	R = Bn	n = 2	4		$\mathbf{2a_2}$	75
	$\mathbf{1b_2}$	R = n-C_9H_{19}	n = 2	2.5		$\mathbf{2b_2}$	72
	$\mathbf{1a_3}$	R = Bn	n = 3	6		$\mathbf{2a_3}$	70
	$\mathbf{1b_3}$	R = n-C_9H_{19}	n = 3	3		$\mathbf{2b_3}$	84
	$\mathbf{1c_4}$	R = Me	n = 4	6		$\mathbf{2c_4}$	6 (SM 51)[c)]
	**1d**	R = Ph	n = 2	6			---[a, b)]
	1e	R = H	n = 8	6			---[a)]
	**1f**	R = OMe		6		**2f**	75
	1g	R = CH_2CH_2OMe		6			---[a ,b)]
				12 *		**2g**	68 , **3g** 28
		* (BF_3-Et_2O (0.1 equiv.) C_6H_6 , R.T.)				**3g**	
	**4a**	R = Bn		6		**5a**	81
	4h	R = Ac		3			---[a)]
	$\mathbf{T\text{-}6b_1}$	R = n-C_9H_{19}	n = 1	5.5			---[a)]
	$\mathbf{T\text{-}6b_2}$	R = n-C_9H_{19}	n = 2	7			---[a)]
	$\mathbf{T\text{-}6b_3}$	R = n-C_9H_{19}	n = 3	2		$\mathbf{7b_3}$	75
	$\mathbf{C\text{-}6b_3}$	(cis-isomer)		2		$\mathbf{7b_3}$	80
	$\mathbf{T\text{-}6b_4}$	R = n-C_9H_{19}	n = 4	6		$\mathbf{7b_4}$	20 (SM 65)[c)]
	$\mathbf{T\text{-}6i_5}$	R = n-Pr	n = 5	6			---[a)]
	$\mathbf{8b_3}$	R = O-n-C_9H_{19}	n = 3	6		$\mathbf{9b_3}$	61
	$\mathbf{8b_4}$	R = O-n-C_9H_{19}	n = 4	6.5		$\mathbf{9b_4}$	37 (SM 48)[c)]
	8e	R = H	n = 6				---[a)]

a) The starting material was recovered in 70% to quantitative yields.
b) The starting material was recovered unchanged also on refluxing in isopropyl ether.
c) The starting material was recovered in the % yield indicated.

Results indicated that epoxide-ketone rearrangement took place only with epoxides which bear the etheric oxygen function at the position of appropriate carbon chain length between 2 and 4, and that the others were recovered unchanged. Particularly for 1,2-disubstituted epoxides, the appropriate carbonchain length for the rearrangement appeared to be restricted to 3 and 4, and both *trans*-(**T-6b$_3$**) and *cis*-1-alkoxy-4-hexeneoxide (**C-6b$_3$**) were regioselectively rearranged to the methyl ketone (**7b$_3$**) in high yields irrespectively of the stereochemistry of substrate epoxides. With trisubstituted epoxy-ethers, rearrangement to ketones proceeded efficiently and regioselectively for only epoxides in which the etheric oxygen reaches at the quaternary terminus of oxirane ring in the 5-exo, 5-endo or 6-endo mode.[6)] Assistance from the etheric oxygen should be essential because the acetate (**4h**) underwent no reaction while the corresponding benzyl ether (**4a**) furnished exclusively a methyl ketone (**5a**) in high yield. Based on these observations, remarkable anchimetric assistance[7)] of neighboring etheric oxygen function appeared to be involved and reflected on the stability of the transition state for TCNE-catalyzed and highly regioselective rearrangement of epoxy-ethers, although plausible mecahnism concerning the interaction between TCNE and epoxide (coordination or electron transfer from epoxide) is still ambiguous.

Recently, 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ) and ceric ammonium nitrate (CAN) which are the representative one-electron oxidants were reported to catalyze alcoholysis and thiolysis of epoxides.[8)] Brief examinations of DDQ and CAN revealed that these reagents also catalyzed the rearrangement of a trisubstituted epoxy-ether ($\mathbf{1b_2}$) providing in appreciable yields (54-60% yield) the same ketone ($\mathbf{2b_2}$) that obtained with TCNE. DDQ and CAN, however, were not so mild and selective as catalyst and promoted other type of reactions simultaneously when these reagent were applied to epoxides of types bearing no etheric oxygen functionalities such as 2-methyl-2-undeceneoxide (**1e**), which gave complex mixtures of products along with the ketone (**2e**) (18-19% yield) and variable recovery of the starting material on treatment with 0.2 equiv. of DDQ or CAN in refluxing CH3CN for 3-5 h.

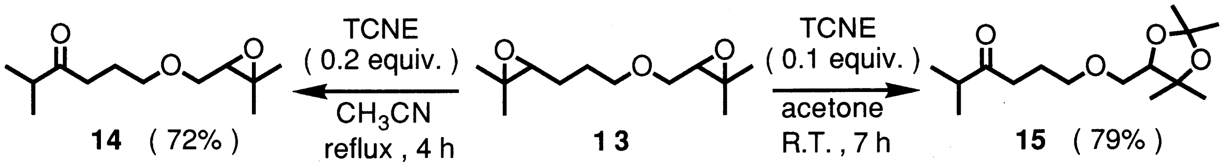
Table 2. Substrate-Specific Rearrangement and Acetonidation of Epoxy-Ethers Catalyzed by TCNE (0.1 - 0.2 equiv.) in Acetone

Epoxide				Reaction conditions Temp and Time / h			Product, Yield / %	
							acetonide	ketone
	$\mathbf{1a_1}$	R = Bn	n = 1	R.T.	11		$\mathbf{10a_1}$ 84	
	$\mathbf{1b_2}$	R = n-C_9H_{19}	n = 2	R.T.	3		$\mathbf{10b_2}$ 44	$\mathbf{2b_2}$ 42
	$\mathbf{1b_3}$	R = n-C_9H_{19}	n = 3	R.T.	5			$\mathbf{2b_3}$ 89
				reflux	0.5			$\mathbf{2b_3}$ 97
	$\mathbf{1c_4}$	R = Me	n = 4	R.T.	5		$\mathbf{10c_4}$ 73	$\mathbf{2c_4}$ 2
	**1g**	R = CH_2CH_2OMe		R.T.	5		**10g** 85	
	1j	R = CH_2CH_2OH		R.T.	4		**10j** 65	
	**1d**	R = Ph	n = 2	R.T.	12		**10d** 87	
	1e	R = H	n = 8	R.T.	6		**10e** 87	
	$\mathbf{T\text{-}6b_1}$	R = n-C_9H_{19}	n = 1	R.T.	48		$\mathbf{Er\text{-}11b_1}$ 72 (SM 13%)[a)]	
	$\mathbf{T\text{-}6h_3}$	R = Ac	n = 3	reflux	20		$\mathbf{Er\text{-}11h_3}$ 80	
	$\mathbf{C\text{-}6b_3}$	R = n-C_9H_{19}		reflux	4			$\mathbf{2b_3}$ 82
	$\mathbf{C\text{-}6h_3}$	R = Ac		reflux	3		$\mathbf{Tr\text{-}11h_3}$ 80	
	**8e**			reflux	6		**12e** 60 (SM 15%)[a)]	

a) The starting material was recovered in the % yield indicated.

In examination of reaction conditions for the epoxy-ketone rearrangement using TCNE-catalyst , we found that the reaction proceeds in acetone at the ambient temperature to refluxing conditions more smoothly than in CH_3CN, and that acetonides were obtained in high yields from the epoxides which hardly acquire any neighboring group participation mentioned above and have no etheric oxygen function in the molecule. The results are summarized in Table 2. The trisubstituted epoxide (**1b$_2$**) bearing an alkoxyethyl group at the less substituted terminus of oxirane appears to be on the border line and provided both a ketone (**2b$_2$**) and an acetonide (**10b$_2$**) in nearly parallel extent. Stereospecific anti-opening of epoxide in the acetonidation described is so obvious that a *cis*- (**C-6h$_3$**) and *trans*-epoxide (**T-6h$_3$**) gave exclusively the *threo*- (**Tr-11h$_3$**) and *erythro*-acetonide (**Er-11h$_3$**), respectively.$^{9)}$

Reactions of the unsymmetrical diepoxy-ether (**13**) are illustrative of the high specificity of the TCNE-catalysis to the substrate-structure. Thus, the diepoxy-ether (**13**) was led exclusively to the epoxy-ketone (**14**) (72%) in refluxing CH_3CN and produced, on the other hand, preferentially the ketone-acetonide (**15**) (79%) in acetone at the room temperature.



14 (72%) **13** **15** (79%)

References

1) a) J.G. Smith, *Synthesis*, **1984**, 629; b) A.S. Rao, S.K. Paknikar, and J.G. Kirtane, *Tetrahedron*, **39**, 2323 (1983).
2) a) K. Uneyama, A. Isimura, K. Fujii, and S. Torii, *Tetrahedron Lett.*, **24**, 2857 (1983); b)S.Nagahara, K. Maruoka, and H. Yamamoto, *Chem. Lett.*, **1992**, 1193; K. Maruoka, T. Ooi, and H. Yamamoto, *J. Am. Chem. Soc.*, **111**, 6431 (1989); c) B. Rickborn and R.M. Gerkin, *ibid.*, **93**, 1693 (1971); d) M. Suzuki, A. Watanabe, and R. Noyori, *ibid.*, **102**, 2095 (1980); A. Miyashita, T. Shimada, A. Sugawara, and H. Nohira, *Chem. Lett.*, **1986**, 1323; e) J. Delaunay, A. Lebouc, A. Tallec, and J. Simonet, *J. Chem. Soc., Chem. Commun.*, **1982**, 387.
3) F.A.J. Meskens, *Synthesis*, **1981**, 501; S-B. Lee, T. Takata, and T. Endo, *Chem. Lett.*, **1990**, 2019 and references cited therein.
4) A.J. Fatiadi, *Synthesis*, **1986**, 249; **1987**, 959.
5) All new compounds were fully characterized by spectroscopy (IR, ^{1}H-NMR, and/or MS).
6) J.E. Baldwin, *J. Chem. Soc., Chem. Commun.*, **1976**, 734.
7) G. A. Molander and J.P. Haar, Jr., *J. Am. Chem. Soc.*, **113**, 3608 (1991); P-C. Boldt, M.H.M.G. Schumacher-Wandersleb, and M.G. Peter, *Tetrahedron Lett.*, **32**, 1413 (1991); B. Capon, *Quart. Rev.*, **18**, 45 (1964).
8) N. Iranpoor and I.M. Baltork, *Tetrahedron Lett.*, **31**, 735 (1990); N. Iranpoor, I.M. Baltork, and F.S. Zardaloo, *Tetrahedron*, **47**, 9861 (1991) and references cited therein.
9) Structures for these acetonides (**Tr-11h$_3$**) and (**Er-11h$_3$**) were deduced on the basis of the fact that **Tr-11h$_3$** and **Er-11h$_3$** were obtained stereospecifically also with catalytic amount of BF_3-Et_2O from **C-6h$_3$** and **T-6h$_3$**, respectively, and characterized by favorable comparison of the chemical shifts (d) and the coupling constants (J) for the C(4)-H and C(5)-H of dioxolane skeleton in ^{1}H-NMR (d 3.53, 3.72 ppm; J 8.30 Hz for threo-(**Tr-11h$_3$**) and d 4.04, 4.25 ppm; J 6.34 Hz for erythro-(**Er-11h$_3$**) to the reported data of those for analogous acetonides structurally defined: B.N. Blackett, J.M. Coxon, M.P. Hartshorn, A.L. Lewis, G.R. Little, and G.J. Wright, *Tetrahedron*, **26**, 1311 (1970); R.P. Hanzlik and M. Leinwetter, *J. Org. Chem.*, **43**, 438 (1978); R.W. Hoffmann and W. Ladner, *Chem. Ber.*, **116**, 1631 (1983).

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