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Tetracyanoethylene–Hydrogen Peroxide, a Mild Epoxidation System of Olefins

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A reagent combination system, tetracyanoethylene–30% hydrogen peroxide, was found to epoxidize olefins efficiently in acetonitrile at room temperature in a stereospecific manner with retention of the configuration of the double bond.

Key words epoxidation; tetracyanoethylene; hydrogen peroxide; epoxide

Epoxidation is one of the most important functionalizations of olefins.[1] *m*-Chloroperbenzoic acid (MCPBA) has been one of the most reliable and widely used reagents for this purpose, but in its pure form, it is both shock-sensitive and potentially explosive in the condensed phase.[2] Since aqueous hydrogen peroxide (H_2O_2) is easily available and not so hazardous, this has been used as the terminal oxidant for epoxidation of olefins.[3,4] In this context, we recently reported a combination of reagents, ethyl cyanoformate and 30% H_2O_2, as a mild epoxidizing system of olefins.[4h] We now wish to report another reagent system, tetracyanoethylene (TCNE) and 30% H_2O_2, which epoxidizes olefins in a stereospecific manner.

Bollyky and co-workers reported that TCNE, tetracyanoethylene oxide (TCNEO), and carbonyl cyanide ($(NC)_2CO$) give appreciable chemiluminescence when treated with alkaline H_2O_2 in the presence of fluorescers, such as 9,10-diphenylanthracene and rubrene.[5] They proposed a mechanism involving a cascade in which TCNE treated with alkaline H_2O_2 is transformed stepwise to TCNEO and then to carbonyl cyanide, which finally decomposes *via* peroxycyanoformic acid (NCC(O)OOH) and diperoxyoxalic acid (HOO(O)C–C(O)OOH) to cyanate, carbonate, and hydrogencarbonate with instantaneous release of energy needed to produce the singlet excited state of a fluorescer. We envisaged that the system, especially the intermediate peroxycyanoformic acid, might be useful as an epoxidizing agent of olefins.

cis-3-Hexen-1-ol (**1**) was submitted to Bollyky's conditions (TCNE (1 molar amount)/30% H_2O_2 (6 molar amounts)/KOH (powder, 6 molar amounts)/1,2-dimethoxyethane/room temperature) for 12 h, but was recovered unchanged. This result was ascribed to the fast decomposition of the oxidants peroxycyanoformic acid and diperoxyoxalic acid with alkaline H_2O_2.[5] Treatment of the olefin (**1**) under Bollyky's conditions without base (TCNE (1 molar amount)/30% H_2O_2 (4 molar amounts)/CH_3CN/room temperature/12 h) gave in high yield (95%) a single *cis*-epoxide (**2**),[6] which is identical with that obtained by oxidation of the olefin (**1**) with MCPBA. Complete recovery of the olefin was observed when the olefin (**1**) was exposed to the above conditions without TCNE. Results obtained from a variety of olefins including mono-, di-, and trisubstituted ones, and a 1,3-diene system with various functional groups and protecting groups are summarized in Table 1.

Yields of epoxidation of the 5-hydroxy-olefin (**12**) were generally poor and in one case, the isolable products from 5-methyl-4-hexen-1-ol (**12**) were a mixture of a tetrahydrofuran (**13**) and a tetrahydropyran derivative (**14**), which are usually formed by acid-catalyzed cyclization of the intermediary unstable hydroxy-epoxide (**15**).[7] Addition of an excess amount of sodium hydrogencarbonate powder to the reaction mixture improved the yield of epoxide (**15**). A trisubstituted olefin was epoxidized more rapidly than terminal olefin or 1,3-diene system,[8] although myrcene (**21**) had to be added to the oxidant 15 min after mixing TCNE and 30% H_2O_2 at room temperature in order to avoid formation of the Diels–Alder adduct[9] from myrcene and TCNE. With olefins (**23**, **25**) which contain an acid-sensitive group, *tert*-butyl ester or acetal, epoxidation proceeded smoothly in the presence of $NaHCO_3$. Oxidation of the sulfide portion of an olefin (**27**) took place with the present oxidizing system in preference to epoxidation of the olefin moiety. With menthone, no reaction took place under the same conditions, although a seven-membered lactone[10] was produced in 82% yield with MCPBA (CH_2Cl_2/room temperature/12 h). This fact indicated that the TCNE–H_2O_2 system does not induce Baeyer–Villiger oxidation.

According to Bollyky's mechanism for the reaction of TCNE with H_2O_2,[5] more than 0.5 mol of TCNE and 2.0 mol of H_2O_2 are necessary to produce 1.0 mol of peroxycyanoformic acid stoichiometrically, and both TCNEO and carbonyl cyanide were also expected to be useful for epoxidation in combination with H_2O_2. Table 2 shows the stoichiometry for the epoxidation of the unsaturated alcohol (**1**). The *cis*-epoxide (**2**) was obtained in 76% yield by treatment of the olefin (**1**) with 0.5 mol of TCNE and 2.0 mol of H_2O_2 at room temperature (entry 1), whereas no epoxidation of the olefin took place with equimolar amounts of TCNE and H_2O_2 (entry 2). Oxidation of the olefin (**1**) using 0.5 mol of TCNEO[11] and 1.5 mol of H_2O_2 afforded the epoxide (**2**) in 78% yield at room temperature (entry 4), and in 72% yield using 1.0 mol each of carbonyl cyanide[11a] and H_2O_2 at 0 °C (entry 5). These findings strongly suggested that the steps including addition followed by fragmentation of TCNEO with H_2O_2 to provide carbonyl cyanide appear to be much slower than the preceding and the following steps under

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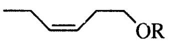
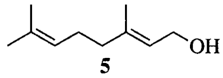
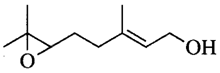
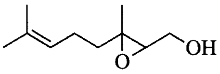
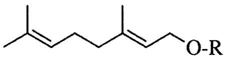
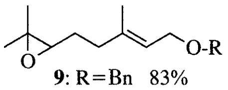
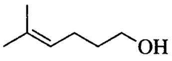
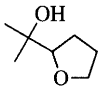
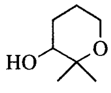
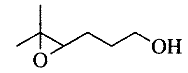
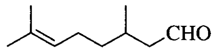
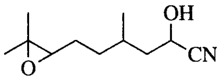
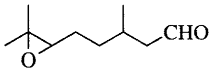
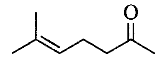
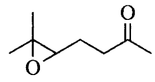
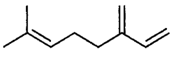
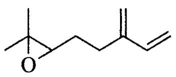
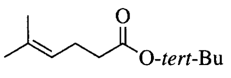
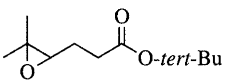
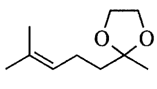
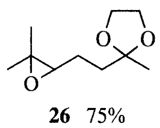
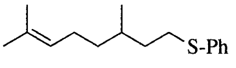
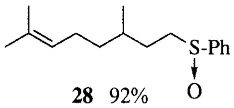
Table 1. Epoxidation of Various Olefins by TCNE–H_2O_2 System

$$\text{olefin} \xrightarrow[\text{CH}_3\text{CN, R.T.}]{\text{TCNE (1 mol)} \atop 30\%\ \text{H}_2\text{O}_2\ (4\ \text{mol})} \text{epoxide}$$

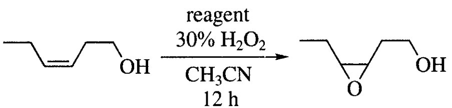
Substrate	Time (h)	Product/yield
 **1**: R=H **3**: R=Bn	12 12	 **2**: R=H 95% **4**: R=Bn 92%
 **5**	12	 **6** 44%  **7** 20%
 **8**: R=Bn **10**: R=Ac	12 12	 **9**: R=Bn 83% **11**: R=Ac 69%
 **12**	12	 **13** 13%  **14** 37%
12	12[a)]	 **15** 42%
 **16**	12	 **17** 85%
16	12[b)]	 **18** 82%
 **19**	12[a)]	 **20** 63%
 **21**	3	 **22** 90%
 **23**	6[a)]	 **24** 70%
 **25**	6[a)]	 **26** 75%
 **27**	3	 **28** 92%

a) $NaHCO_3$ (3 molar amounts) was added. *b)* The organic extract was washed with 3% NaOH in the work-up procedure. R.T. = room temperature.

the neutral condition, and the net oxidant in the present systems appeared to be peroxycyanoformic acid,[5)] although this is not certain.[12)]

Although particular care is necessary in large-scale operation in order to avoid hazards due to the toxicity of HCN generated in the reaction (see the experimental details), the present reagent system is facile and convenient for laboratory-scale epoxidation.

Table 2. Stoichiometry of the TCNE–H_2O_2 System in Epoxidation of *cis*-3-Hexen-1-ol (**1**) to the Epoxide (**2**)



1 **2**

Entry	Reagent (molar amount)	Molar amount of H_2O_2	Temp.	Yield (%)
1	TCNE (0.5)	2	R.T.	76
2	(1)	1	R.T.	0
3	(1)	3	R.T.	92
4	TCNEO (0.5)	1.5	R.T.	78
5	O=C(CN)$_2$ (1)	1	0 °C	72

R.T. = room temperature.

Experimental

General IR absorption spectra were recorded on a JASCO IRA-1 spectrometer. ^{1}H-NMR spectra were recorded on a JEOL JNM-GX-270 (270 MHz) and a JEOL JNM-EX-400 (400 MHz) spectrometer with $SiMe_4$ as an internal standard. Mass spectra (MS) and high-resolution MS (HRMS) were recorded on a JEOL JMS-SX102A spectrometer and are indicated at *m/z*. Products were purified by column chromatography on silica gel (Merck, Kieselgel 60, 70—230 mesh).

Materials Acetonitrile was distilled from CaH_2 and stored over Molecular Sieves. TCNE was purified by recrystallization from 1,2-dichloroethane. Compounds **1**, **5**, **16**, **19**, and **21** were all purchased from Tokyo Kasei (TIC) or Wako Pure Chemical Co., Ltd. Compounds **3**, **8**, **10**, **12**, and **25** were prepared by the reported methods.[13,14)]

***tert*-Butyl 5-Methyl-4-hexenoate (23)** **23** was prepared from *tert*-butyl acetate and 1-bromo-3-methyl-2-butene by the reported method.[15)] IR (neat): 1730 (C=O), 1360, 1140 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.44 (9H, s), 1.62 (3H, s), 1.68 (3H, s), 2.24 (4H, m), 5.08 (1H, m).

2,6-Dimethyl-8-phenylthio-2-octene (27) Triethylamine (0.76 ml, 5.5 mmol) and methanesulfonyl chloride (0.43 ml, 5.5 mmol) were added slowly to a solution of citronellol (780 mg, 5.0 mmol) in CH_2Cl_2 (10 ml) at 0 °C. The reaction mixture was stirred at 0 °C for 1 h, and the crude product was extracted with ether. The organic extract was washed with 3% HCl and saturated $NaHCO_3$, and dried over anhydrous $MgSO_4$, then the solvent was removed *in vacuo*, affording the crude mesylate of citronellol. Benzenethiol (0.80 ml, 7.8 mmol) was added to a solution of sodium ethoxide (150 mg, 65 mmol) in ethanol (20 ml) at room temperature. The mesylate prepared by the above procedure was added to the reaction mixture. The whole was stirred at room temperature for 3 h, and the crude product was extracted with ether. The organic extract was washed with saturated $NaHCO_3$ and brine, and dried over anhydrous $MgSO_4$, then the solvent was removed *in vacuo*. The crude product thus obtained was purified by silica gel column chromatography to give 2,6-dimethyl-8-phenylthio-2-octene (**27**) (530 mg, 43%) as a colorless oil. IR (neat): 1585, 1480, 1440, 1370, 1020, 730, 680 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.91 (3H, d, J=6.3 Hz), 1.23—1.71 (5H, m), 1.59 (3H, s), 1.68 (3H, s), 1.96 (2H, m), 2.92 (2H, m), 5.08 (1H, m), 7.13—7.34 (5H, m). HRMS (EI) Calcd for $C_{16}H_{24}S$ (M^+): 248.1589. Found: 248.1599.

General Procedure for Epoxidation of Olefins (1) with the TCNE–H_2O_2 System A 30% H_2O_2 solution (0.47 ml, 3.992 mmol) was added to a solution of TCNE (128 mg, 0.998 mmol) and *cis*-3-hexen-1-ol (**1**) (100 mg, 0.998 mmol) in CH_3CN (2 ml) at room temperature. The reaction mixture was stirred at room temperature for 12 h, then the crude product was extracted with ether. The organic extract was washed with brine, and dried over anhydrous $MgSO_4$, then the solvent was removed *in vacuo*. The crude product thus obtained was purified by silica gel column chromatography to give *cis*-3,4-epoxy-1-hexanol (**2**) (107 mg, 92%) as a colorless oil (Table 1). Reaction mixtures during large-scale operation must be handled carefully to avoid exposure to HCN, including treatment of aqueous washings of reaction mixtures with alkaline 5% NaOCl solution.

Compounds **17**, **18**, and **28** were obtained as inseparable mixture of diastereomers. Compounds **2**,[6] **4**,[16] **6**,[17] **7**,[18] **9**,[19] **11**,[20] **13**,[7] **14**,[7] **18**,[21] **20**,[22] **22**,[23] and **26**[24] were identified by comparison of their spectroscopic properties with those described in the literature. Compound **15** could not be isolated due to its instability, and was identified after derivation to the corresponding benzoate. The yield and reaction conditions of the epoxidation of olefins are shown in Table 1. Spectral data for new compounds are presented below.

4,5-Epoxy-5-methylhexyl Benzoate (Derivative of 15) IR (neat): 1720 (C=O), 1450, 1375, 1310, 1270, 1110, 1070, 1020, 710 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.28 (3H, s), 1.32 (3H, s), 1.68 (2H, m), 1.97 (2H, m), 2.80 (1H, t, $J=6.3$ Hz), 4.38 (2H, t, $J=6.6$ Hz), 7.40—7.59 (3H, m), 8.04 (2H, m). *Anal.* Calcd for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74. Found: C, 71.51; H, 7.84.

7,8-Epoxy-2-hydroxy-4,8-dimethylnonanenitrile (17) IR (neat): 3380 (OH), 2240 (CN), 1460, 1380, 1065 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.99 (3H, m), 1.29 (3H, s), 1.33 (3H, s), 1.41—2.03 (7H, m), 2.76 (1H, m), 3.66 (1H, m), 4.53 (1H, m).

***tert*-Butyl 4,5-Epoxy-5-methylhexanate (24)** IR (neat): 1730 (C=O), 1365, 1250, 1150 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.29 (3H, s), 1.31 (3H, s), 1.46 (9H, s), 1.65—1.94 (2H, m), 2.38 (2H, m), 2.76 (1H, dd, $J=7.3$, 5.1 Hz).

2,6-Dimethyl-8-phenylsulfinyl-2-octene (28) IR (neat): 1440, 1080, 1040 (S=O), 740, 695 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.88 (3H, m), 1.09—1.79 (5H, m), 1.57 (3H, s), 1.67 (3H, s), 1.93 (2H, m), 2.79 (2H, m), 5.04 (1H, m), 7.50 (3H, m), 7.61 (2H, m). HRMS (EI) Calcd for $C_{16}H_{24}OS$ (M^+): 264.1548. Found: 264.1536.

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