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ELECTRON-TRANSFER CHAIN ISOMERIZATION OF EPOXIDES INDUCED BY ONE-ELECTRON OXIDIZING AGENTS

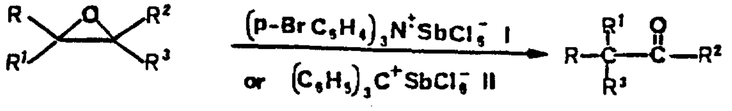
LUIGI LOPEZ*, LUIGINO TROISI

Centro C.N.R. "M.I.S.O.", Dipartimento di Chimica Università di Bari, via Amendola 173 -70126 Bari Italy

Abstract: One electron oxidizing agents have been employed to achieve the isomerization of epoxides to ketones.The reactions most likely proceed via a radical cation chain electron-transfer mechanism.

Recently, the electrochemical conversion of epoxides to ketones,[1,2] a procedure more convenient than the conventional acid-catalyzed reactions,[3] has been object of an intriguing debate on the actual mechanism operating in this process. Simonet *et al*[1] proposed, on the basis of cyclic voltammetric studies, an electron-transfer chain isomerization induced by the electrode, coming to the conclusion that the loss of an electron or the addition of a proton may have similar or identical effect in the rearrangement of epoxides. In contrast to this statement, Torii *et al*[2] suggested that similar electrochemical transformations could be due to an electrogenerated acid catalyzed reaction.[4] The inhibition to the isomerization observed in the presence of pyridine (1 equiv.) and/or in the electrolysis of epoxides carried out in acetonitrile (simply distilled once over P_2O_5) were the main chemical proofs that could account for such a mechanism not involving cation radicals as intermediates.[5,6]

In this context, as part of our continuing studies on the thermal and/or photochemical induced generation and evolution of cation radicals of different classes of organic substrates, [7,8] we report herein that tris-p-bromo-phenylammoniumyl-hexachloroantimonate $(p\text{-}BrC_6H_4)_3N^{+\cdot}\ SbCl_6^-$) **I** or trityl hexachloroantimonate $(C_6H_5)_3C^+\ SbCl_6^-$) **II**, well known one electron-oxidizing agents,[9] react at room temperature, under air atmosphere and/or oxygen-saturated methylene chloride solutions of several epoxides **1a-c**, 3-methoxy-3-(naphtyl)spiro[oxirane-2,2'-adamantane] **1d**, and β-ionone epoxide **1e**, easily synthesized by known procedures,[10, 11] to yield the corresponding carbonyl compounds **2a-c** (eq.1), different isomers **2d** or **4** from **1d** and a ring contraction isomer **2e** from **1e** (see text).



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1a R = R[1] = R[2] = R[3] = Phenyl

1b R = R[3] = H; R[2] = R[3] = Phenyl

1c R,R[1] = R[2], R[3] = Adamantyl

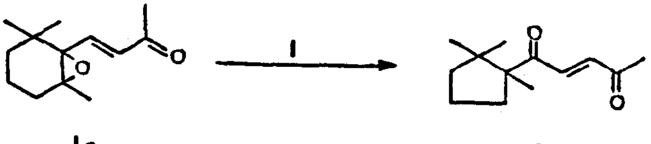
2a-c

The general procedure, attractively simple, is as follows: **1a-e** (0.119 mmol) are dissolved in dry methylene chloride (5 ml) and then **I** or **II** (0.01-0.02 mmol) are added. The progress of the reactions can be monitored by tlc, gc until completion (within the range 5min to 1h). The solvent is removed in vacuo and the reaction products isolated by column chromatography (silica gel, petroleum ether/ethyl ether 5/1 v/v). All products were identified by physical, spectral data (^{1}H, ^{13}C nmrs, ir, ms) and by comparison with commercial or synthesized pure samples[3a]

The success of this novel synthetic procedure for the isomerization of epoxides to ketones might be rationalized on the basis of the peculiar features of the reagents involved in this process. In fact, the powerful ammoniumyl salt oxidant (E^{red} = 1.17 V *vs* SCE)[12] can induce electron-transfer reactions on substrates **1a-e** with the formation of the corresponding cation radicals (**1a-e**$^{+\cdot}$) and neutral amine [(tris-p-bromophenyl) amine **3**].

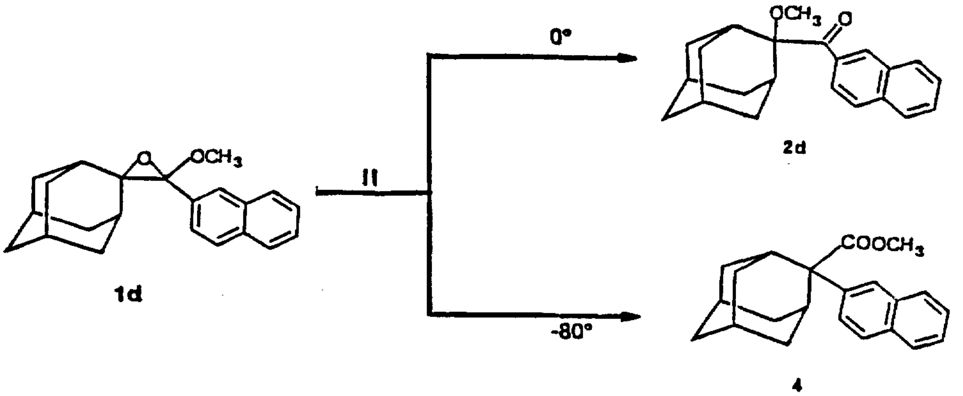
Although this first step is endoergonic,(epoxides such as **1a**, **1b**, **1d** show oxidation potentials in the range 1.9-2.1 V vs Ag/Ag^{+}),[13] the driving force of the process could be the following isomerization of the ring closed cation radicals into the corresponding ring opened ones. In a recent *ab initio* molecular orbital study on the structure and stability of ethylene oxide cation radical, with the charge almost exclusively located on the oxygen, it has been ascertained that the C--O bonds are relatively weak and they can easily be broken, so that the ring closed and its C···O ring opened isomer are separated by only a small energy barrier.[14] On the contrary the fission of the C···C bond requires more energy (105-120 KJ mol-1) but, when it occurs, the corresponding cation radical should be quite stable. By extension to our substrates, the fate of the presumed cation radicals (**1a-c**$^{+\cdot}$) could be the same with the generation of the corresponding ring opened cation radicals. The migration of a group, in relation to their aptitude, followed by the subsequent electron-transfer with the neutral substrates would afford the reaction products **2a-c**, as described by Simonet in the electrochemical process[1].

The chemical proofs that, in our conditions, could account for such a mechanism are the following: (a) the total isomerization of biadamantylidene oxide **1c** to spiro[adamantane-2,4'-homoadamantane-5'-one] **2c** is unprecedented. In fact, **1c** and **2c** are always in equilibrium even under acidic conditions.[3a] ; (b) the isomerization **1c**---**2c** is totally inhibited in the presence of catalytic amounts of 1,4-diazabicyclo[2,2,2] octane **DABCO** [E^{red}= 0.60 V *vs* SCE] and the inhibition could be due to a faster electron-transfer reaction between **I** and **DABCO** rather than to its basic behaviour;[15] (c) if the amount of added acid is calculated on the basis of the amount of the used oxidizing agent (assuming that loss of an electron corresponds to one equivalent of acid), the concentration of added acid is too low to cause the isomerization of **1a** in the time scale of our reactions; (d) similar reactions on B-ionone-oxide **1e**[16] with 0.015 mmoles of **I** lead, within 1h, to 1-(1,2,2-trimethylcyclopent-1-yl)-pent-2-ene-1,4-dione **2e** (90%)[17] (eq. 2).



1e **2e** 2

On the contrary, the same epoxide **1e** undergoes acid catalyzed ring contraction and enlargement together with the formation of several different reaction products in relation to the reaction conditions.[18b, 19] ; (e) similar reactions on **1d** with 0.02mmoles of **II** quantitatively lead to two different reaction products, namely **2d** or **4**, exclusively in relation to the reaction temperature (eq. 3).



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The products **2d, 4** have been easily isolated and fully characterized by physical and spectral data.[20] These latter unprecedented results, in our opinion, straightforwardly substantiate the involvement of a C···O ring opened cation radical , and at the same time, they show the different migratory aptitude of the groups R^2, R^3 in relation to the reaction conditions. In conclusion, although further detailed investigations in the area are warranted, we believe the preliminary results reported herein provide one more attractive procedure for the ring opening isomerization of epoxides.

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5) Pyridine and/or acetonitrile may react with cation radical intermediates inhibiting the subsequent reaction. See refs 6a,b.

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10) All the substrates have been synthesized by meta-chloroperbenzoic acid oxidation of the corresponding alkenes. For the sustrate **1d**, we have recently reported a new easy procedure by using, as oxidizing agent, trifluoromethyl-methyl dioxirane see ref.11.

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17) **2e** has been easily isolated by silica gel column chromatography (petroleum ether:ethyl ether 9:1 v:v) and the spectral data: ir, ^{1}H, ^{13}C nmrs, ms fit those reported by Ohloff and/or by Stevens in two different reports (see refs 18a,b).

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20) **4**: mp 164-165° (pentane); ^{1}H nmr ($CDCl_3$) δ 7.92-7.42 (m. 7H), 3.53 (s. 3H); ^{13}C nmr ($CDCl_3$) δ 175.7, 51.93 and consistent resonances for the the carbons of the naphtyl and adamantyl groups; ir ($CDCl_3$) 1720 cm^{-1}; ms (m/e) 320 (24 M^{+}), 261 (100) [Ad$>^{+}$—Nap]. All attempts to isolate a pure sample of **2d** fail since it subsides an easy conversion into the corresponding α-hydroxyketone, fully characterized by physical and spectral data, consistent with those previously reported on a similar α-hydroxyketone, see ref.11. Anyway, an instrumental detection of **2d** has been obtained by ^{1}H nmr spectroscopy, recording the spectrum directly on a crude reaction mixture carried out in deutherochloroform, showing a singlet at 3.48 ppm (OCH_3) and, above all, no broad resonance at 2.13 ppm characteristic of the OH group. A similar isomerization in different epoxyethers has been already observed by Stevens and co-workers (see refs 21).

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