J. Org. Chem. 1993, 58, 5880-5882

Synthesis and Reactivity of Dioxycarbenium Ions from Epoxy Esters and Cationic Zirconium Complexes

Peter Wipf* and Wenjing Xu

Department of Chemistry, University of Pittsburgh, Pittsburgh, Pennsylvania 15260

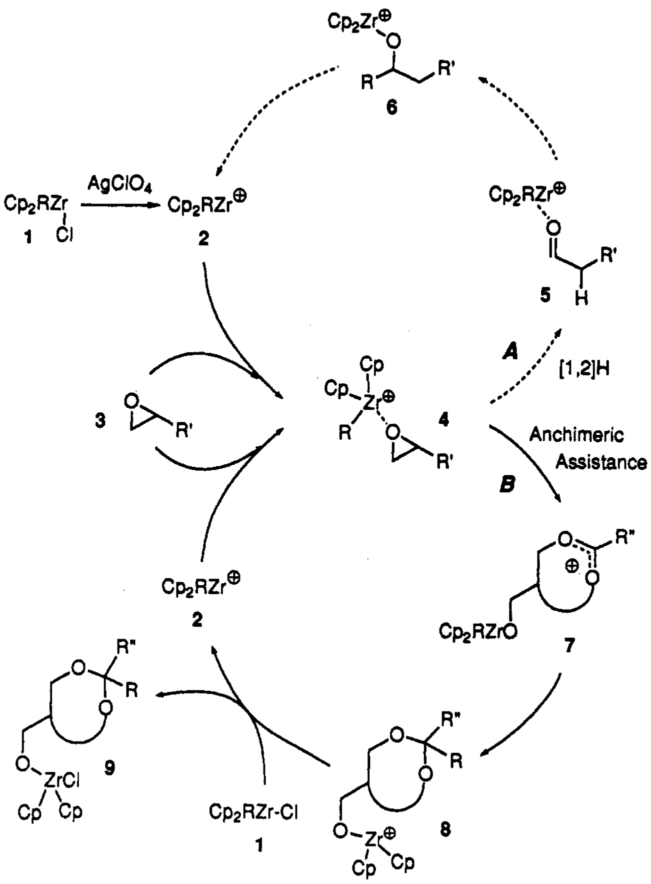
Received June 22, 1993[●]

Summary: Rearrangement of epoxy esters in the presence of $Cp_2Zr(R)^+$ or $Cp_2Zr(Cl)^+$ results in synthetically useful dioxycarbenium intermediates. Acetals, ortho esters, and tetrahydrofurans are prepared by ligand transfer from zirconium, intramolecular trapping, or further rearrangement reactions.

Recently we reported a novel tandem epoxide rearrangement–carbonyl addition reaction of epoxides.[1] After the generation of the Lewis-acidic Cp_2RZr^+ (**2**)[2] by catalytic chloride abstraction from organozirconocene **1**,[3] an epoxide rearrangement is followed by a nucleophilic attack on the resulting aldehyde **5** (Scheme I, pathway A). In the presence of an intramolecular Lewis base, however, we envisioned that the intermediate-activated epoxide **4** could be trapped before the [1,2]H shift takes place. Neighboring-group participation of an ester carbonyl substituent, for example, leads to a cyclic dioxycarbenium ion **7** (pathway B). At this stage, ligand transfer from the zirconocene moiety, followed by intermolecular chloride abstraction, would generate acetal **9** and close the catalytic cycle.

Di- and trialkoxycarbenium ions have found widespread use as versatile electrophiles for formation of C,C-bonds.[4] Since the stabilized carbocation **7** in pathway B is formed in situ under mild, neutral reaction conditions, many synthetic transformations with electron-rich olefins and C,H-acidic systems are feasible. Therefore, we decided to investigate the rearrangement of epoxy esters with cationic organozirconocenes **2** and the reactivity profile of the proposed intermediate dialkoxycarbenium ions **7**.

Scheme I



Treatment of fumarate **10** with in situ prepared hexenylzirconocene **11** in CH_2Cl_2 in the presence of 5 mol % silver perchlorate led after 7 h at 22 °C to the formation of acetal **12** in 56% yield (Table I, entry 1). Similarly, succinate **13** provided a 49% yield of acetal **14** after 4 h at rt. Interestingly, both of these acetals were isolated as single diastereomers. As a consequence of the suprafacial vinyl group transfer in the dialkoxycarbenium intermediates, only the *syn*-isomers are formed (Scheme II).[5] Treatment of **14** with traces of anhydrous HCl in $CDCl_3$ in the NMR tube led to a mixture of isomeric 6- and 5-ring acetals (**29**, **14'**). The exclusive formation of **14** in the former sequence is therefore clearly the result of kinetic rather than thermodynamic control.

Acetal hydrolysis of **14** in aqueous acetone provided keto ester **30** in quantitative yield (Scheme II). Formally, the epoxy moiety assumes the role of a specific activating group in the reaction of carbonyl compounds with organozirconocenes and mediates the mild conversion of esters to α,β-unsaturated ketones.[6] The intermediate acetals are potentially useful tools for asymmetric synthesis.[7]

With acetals **12** and **14**, no isomerization of the dioxolane stereochemistry was observed under the reaction conditions. The more labile crotonate and benzoate derivatives **16** and **18**, however, were obtained in 84% and 70% yield as 4:1 mixtures of diastereomers after 2-h reaction time from the corresponding epoxy esters **15** and **17** (Table I, entries 3 and 4). Any increase in the reaction time led to a further drop in the diastereoselectivity. This slow epimerization of the acetal centers can be avoided by

---

[●] Abstract published in *Advance ACS Abstracts*, September 15, 1993.

[1] Wipf, P.; Xu, W. *J. Org. Chem.* **1993**, *58*, 825.

[2] For a recent review on the chemistry of cationic metallocene compounds of group 4 transition elements, see: Jordan, R. F. *Adv. Organomet. Chem.* **1991**, *32*, 325.

[3] Matsumoto, T.; Katsuki, M.; Suzuki, K. *Tetrahedron Lett.* **1988**, *29*, 6935.

[4] For reviews, see: (a) Pindur, U. In *The chemistry of acid derivatives*; Patai, S., Ed.; Wiley: Chichester, 1992; Vol. 2, Part 2; pp 967–1030. (b) Pindur, U.; Müller, J.; Flo, C.; Witzel, H. *Chem. Soc. Rev.* **1987**, *16*, 75. (c) DeWolfe, R. H. *Carboxylic Ortho Acid Derivatives*; Academic Press: New York, 1970.

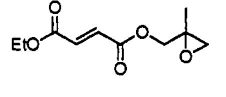
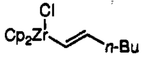
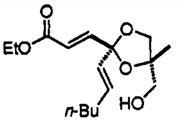
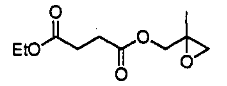
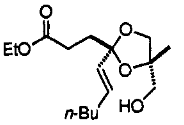
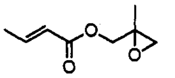
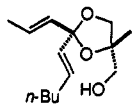
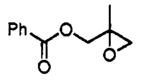
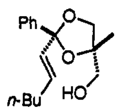
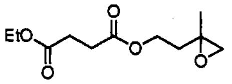
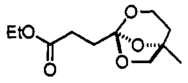
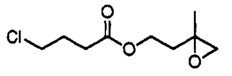
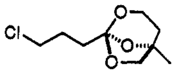
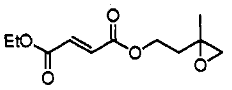
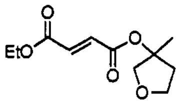
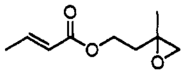
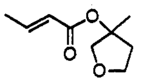
[5] The stereochemistry of **12** and **14** was assigned based upon 1 D NOE experiments; a complete listing of NOE data is given in the supplementary material.

[6] For the Cu(I)-catalyzed preparation of ketones from acyl chlorides and organozirconocenes, see: Wipf, P.; Xu, W. *Synlett* **1992**, 718.

[7] The use of enantiomerically enriched epoxy ester **13** leads to optically active acetal **14**: Wipf, P.; Xu, W. Unpublished results. For a recent review of the chemistry of chiral acetals, see: Alexakis, A.; Mangeney, P. *Tetrahedron Asymmetry* **1990**, *1*, 477.

0022-3263/93/1958-5880$04.00/0

Table I. Rearrangement of Epoxy Esters with Organozirconocenes in the Presence of Catalytic (5 mol %) Silver Perchlorate[8]

entry	epoxy ester structure	epoxy ester no.	zirconocene[a] structure	zirconocene[a] no.	product structure	product no.	yield[b] (%)
1		10		11		12	56
2		13		11		14	49
3		15		11		16	84[c]
4		17		11		18	70[c]
5		19		11		20	96
6		19	Cp_2ZrCl_2	21[d]		20	96
7		22		21[d]		23	93
8		24		21[d]		25	75
9		26		21[d]		27	78

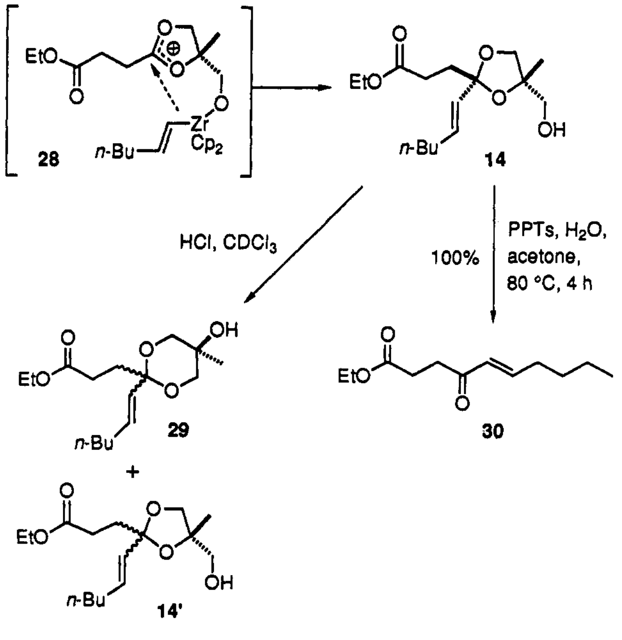
[a] Alkenylzirconocenes were prepared in situ by hydrozirconation[9] of 1-hexyne with Schwartz'[10] reagent. [b] Yields are not optimized and are based on epoxy ester and chromatographically purified product. [c] Isolated as a 4:1 mixture of diastereomers if the reaction is stopped after 2 h at rt. [d] 0.10 equiv of Cp_2ZrCl_2 and 0.01 equiv of $AgClO_4$ were used.

lowering the reaction temperature. Crotonate **15**, for example, provided acetal **16** as a single isomer in 42% yield after 5 h at 0 °C.

Bicyclic ortho esters are formed in quantitative yields in the rearrangement of the chain-extended epoxy esters **19** and **22** (Table I, entries 5–7). No transfer of the hexenyl substituent from zirconium to the dialkoxycarbenium intermediate from succinate **19** was observed. The formation of the bicyclo[3.2.1] ring system by ring closure of the zirconium alkoxide seems to be considerably more facile than the formation of the corresponding bicyclo[2.2.1] ortho ester from carbenium ion **28**.[11] This reaction can also be mediated catalytically by zirconocene dichloride. Ortho esters **20** and **23** were formed in 96% and 93% yield within 15 min at rt in the presence of 0.10 equiv of Cp_2ZrCl_2 and 0.01 equiv of $AgClO_4$ (entries 6 and 7). The catalytic variant is especially useful for the protection of carboxylic acids as ortho esters. Mechanistically, this procedure is related to Corey's BF_3-catalyzed rearrangement of acyloxetanes to 2,6,7-trioxabicyclo[2.2.2]octanes (OBO esters).[12]

Interestingly, the rearrangement of the α,β-unsaturated epoxy esters **24** and **26** with catalytic Cp_2ZrCl_2 and $AgClO_4$

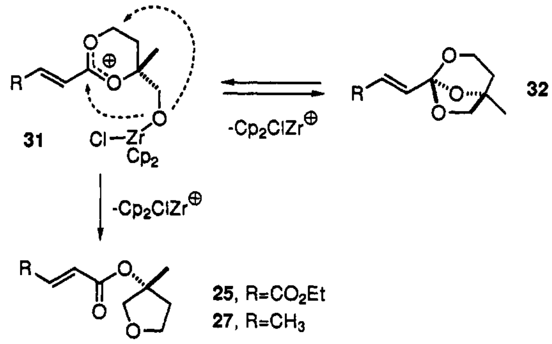
Scheme II



did not lead to the corresponding ortho esters but provided tetrahydrofurans **25** and **27**, respectively (Table I, entries 8 and 9). Presumably, as a consequence of the greater stability of the delocalized dialkoxycarbenium ion **31**, an equilibrium with ortho ester **32** is established (Scheme III). Irreversible attack of the alkoxide at the C,O-bond in **31** provides tetrahydrofurans.[13,14]

In conclusion, we have demonstrated novel rearrangements of synthetically readily available epoxy esters and cationic zirconocene complexes. Neighboring group participation of the ester in the zirconium-mediated oxirane opening leads to dialkoxycarbenium ion intermediates. Depending on the ring size of the carbenium ion, selective transfer of alkenyl or alkoxy ligands from zirconium provides diastereomerically pure dioxolanes or bicyclic ortho esters, respectively. With highly stabilized allylic dialkoxycarbenium ions or in the presence of strong Lewis acids, a further rearrangement of the ortho ester to the tetrahydrofuran ring system occurs. The conversion of epoxy esters into ortho esters and tetrahydrofurans is catalytic in zirconocene dichloride and silver perchlorate, which makes the preparation of these synthetically useful systems by cationic zirconium chemistry especially attractive.

Scheme III



Supplementary Material Available: Experimental procedures and compound characterization data (5 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

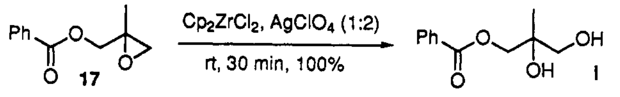
---

(8) **Typical Procedures. (2S,4S),(2R,4R)-2-[2-(Ethoxycarbonyl)-ethenyl]-2[1-(*E*)-hexenyl]-4-(hydroxymethyl)-4-methyl-1,3-dioxolane (12).** A mixture of 100 mg (1.22 mmol, 1.2 equiv) of 1-hexyne and 313 mg (1.22 mmol, 1.2 equiv) of $Cp_2Zr(H)Cl$ in 4 mL of CH_2Cl_2 was stirred at 20 °C for 10 min. To the resulting yellow reaction mixture was added a solution of 217 mg (1.02 mmol) of fumarate **10** in 4 mL of CH_2Cl_2 followed by 11 mg (0.05 mmol, 0.05 equiv) of $AgClO_4$. After being stirred at 20 °C for 7 h, the mixture was poured into saturated aqueous $NaHCO_3$ solution and extracted with EtOAc (3×). The combined organic layers were dried (Na_2SO_4), filtered over SiO_2, and concentrated *in vacuo*. The oily residue was purified by silica gel chromatography (EtOAc/hexanes (1:4)) to give 56 mg (26%) of starting material **10** and 170 mg (56%) of acetal **12** as a colorless oil: ^1H NMR δ 6.83 (d, 1 H, J = 15.8 Hz), 6.12 (d, 1 H, J = 15.8 Hz), 5.89 (dt, 1 H, J = 15.6, 6.8 Hz), 5.51 (dt, 1 H, J = 15.6, 1.2 Hz), 4.21 (q, 2 H, J = 7.1 Hz), 4.03 (d, 1 H, J = 8.4 Hz), 3.65 (d, 1 H, J = 8.4 Hz), 3.58–3.45 (m, 2 H), 2.09–2.02 (m, 2 H), 1.85 (t, 1 H, J = 6.1 Hz), 1.40–1.23 (m, 10 H), 0.88 (t, 3 H, J = 7.1 Hz); ^{13}C NMR δ 166.4, 146.4, 134.7, 128.5, 121.5, 107.0, 82.7, 71.7, 67.3, 60.8, 31.8, 30.9, 22.7, 22.3, 21.5, 14.3, 14.0; MS (EI) m/z (rel intensity) 298 (M^+, 2), 267 (50), 253 (20), 225 (100), 199 (30), 137 (40), 130 (30), 111 (25), 71 (20), 55 (30); HRMS (EI) m/z calcd for $C_{15}H_{23}O_4$ (M – CH_2OH) 267.1596, found 267.1607. **(1R,5S)-(1S,5R)-1-[2-(Ethoxycarbonyl)ethyl]-5-methyl-2,7,8-trioxobicyclo[3.2.1]octane (20).** A solution of 230 mg (1.0 mmol, 1.0 equiv) of succinate **19** in 8 mL of CH_2Cl_2 was treated at 20 °C with 29 mg (0.10 mmol, 0.10 equiv) of Cp_2ZrCl_2 and 2 mg (0.01 mmol, 0.01 equiv) of $AgClO_4$. The reaction mixture was stirred at 20 °C for 15 min, poured into saturated aqueous $NaHCO_3$, and extracted with EtOAc (3×). The combined organic layers were dried (Na_2SO_4), filtered through SiO_2, and concentrated *in vacuo*. The oily residue was purified by silica gel chromatography (EtOAc/hexanes, (1:4)) to give 220 mg (96%) of **20** as a colorless oil: ^1H NMR δ 4.11 (q, 2 H, J = 7.1 Hz), 4.07 (dd, 1 H, J = 11.3, 4.1 Hz), 4.01 (d, 1 H, J = 7.1 Hz), 3.85 (dd, 1 H, J = 11.3, 6.6 Hz), 3.48 (dd, 1 H, J = 7.1, 2.2 Hz), 2.49–2.44 (m, 2 H), 2.20–2.15 (m, 2 H), 2.07–1.96 (m, 1 H), 1.43 (dd, 1 H, J = 13.3, 4.3 Hz), 1.35 (s, 3 H), 1.23 (t, 3 H, J = 7.1 Hz); ^{13}C NMR δ 173.2, 120.1, 78.8, 74.0, 60.4, 59.2, 33.8, 30.7, 28.9, 22.0, 14.3; MS (EI) m/z (relative intensity) 185 ($[M - OEt]^+$, 10), 147 (8), 129 (85), 101 (100), 85 (40), 55 (20), 43 (30); HRMS (EI) m/z calcd for $C_9H_{13}O_4$ (M – OEt) 185.0814, found 185.0814.

(9) Labinger, J. A. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I. Eds.; Pergamon: Oxford, 1991; Vol. 8; pp 667–702.

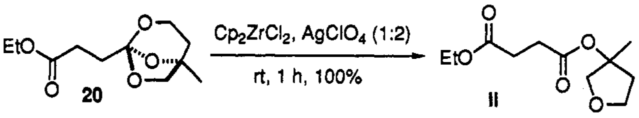
(10) (a) Schwartz, J.; Labinger, J. A. *Angew Chem., Int. Ed. Engl.* **1976**, *15*, 333. (b) Wailes, P. C.; Weigold, H. *J. Organomet. Chem.* **1970**, *24*, 405.

(11) Treatment of benzoate **17** with 1 equiv of Cp_2ZrCl_2 and 2 equiv of $AgClO_4$ (which, presumably, generates the highly Lewis acidic Cp_2Zr^{2+}, cf. Suzuki, K.; Maeta, H.; Matsumoto, T. *Tetrahedron Lett.* **1989**, *30*, 4853) resulted in the formation of diol **i** in quantitative yield after hydrolytic workup. The same product was observed upon treatment of **17** with $BF_3 \cdot OEt_2$.



(12) Corey, E. J.; Raju, N. *Tetrahedron Lett.* **1983**, *24*, 5571.

(13) This hypothesis is supported by the following experiment: Treatment of ortho ester **20** with 1.0 equiv of Cp_2ZrCl_2 and 2.0 equiv of $AgClO_4$ provides tetrahydrofuran **ii** in quantitative yield in 1 h at rt:



(14) For mechanistic studies on a related Lewis acid catalyzed rearrangement, see: Coxon, J. M.; Hartshorn, M. P.; Swallow, W. H. *J. Org. Chem.* **1974**, *39*, 1142.