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Ortho Esters and Dialkoxycarbenium Ions: Reactivity, Stability, Structure, and New Synthetic Applications

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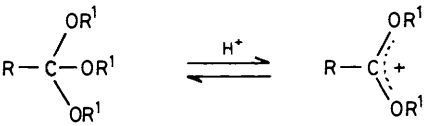
1 Introduction

The high synthetic potential of ortho esters[1,2] and dialkoxycarbenium ions[3] is reflected in their use as versatile electrophiles in preparative chemistry for the synthesis of selectively protected diketones, acylated heterocycles, and heterocyclic ring systems.[1-7] As numerous reactions of ortho esters (I) take place in the presence of proton or Lewis acids with *in situ* generation of dialkoxy- or trialkoxycarbenium ions, a knowledge of the reactivities and structural features of this class of compounds is of considerable interest for the interpretation of their modes of reaction. In the present review, therefore, the mechanism and kinetics of the heterolysis of ortho esters and, hence, the structures and reactivities of the di- or trialkoxycarbenium ions (II) generated from them will be summarized. In the last section, some new synthetic applications of these electrophiles will be discussed.



(I) (II)

R = Alkyl, aryl, OR
R^1 = Alkyl

2 Mechanism of the Proton-catalysed Ortho Ester Heterolysis

The ortho esters (I) can be considered as relatively soft *O*-bases.[2] As such, they react with Lewis acids such as BF_3, $SbCl_5$,[8] or PF_5,[9] as well as with Brönsted acids

[1] R. H. DeWolfe, 'Carboxylic Acid Derivatives', Academic Press, New York, London, 1970.
[2] E. H. Cordes in 'The Chemistry of Carboxylic Acids and Esters', ed. S. Patai, Wiley-Interscience, London, 1969.
[3] H. Perst, 'Oxonium Ions in Organic Chemistry', Verlag Chemie, Weinheim, Academic Press, New York, 1971.
[4] E. Akgün, U. Pindur, and J. Müller, *J. Heterocyclic Chem.*, 1983, **20**, 1303; J. Müller, *Thesis*, University of Würzburg, 1986.
[5] U. Pindur and C. Flo, *Monatsh. Chem.*, 1986, **117**, 375.
[6] U. Pindur, C. Flo, E. Akgün, and M. Tunali, *Liebigs Ann. Chem.*, 1986, 1621.
[7] U. Pindur, L. Pfeuffer, and C. Flo, *Chem.-Ztg.*, 1986, **101**, 307.
[8] H. Meerwein, K. Bodenbenner, P. Borner, F. Kunert, and K. Wunderlich, *Liebigs Ann. Chem.*, 1960, **632**, 38.
[9] G. A. Olah, J. A. Olah, and J. J. Svoboda, *Synthesis*, 1973, 490.

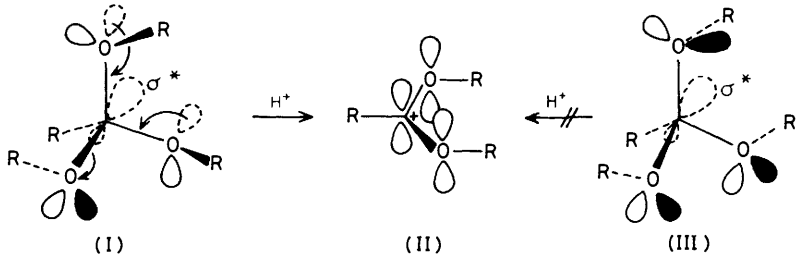


Figure 1 *Stereoelectronic control of the ortho ester cleavage*[13,14]

(H_2SO_4–SO_3, trifluoroacetic acid,[10] or HBF_4[11]) in anhydrous media to form the corresponding di- or trialkoxycarbenium ions (II).[12] In general, the heterolytic ortho ester cleavage proceeds under stereoelectronic control,[13,14] *i.e.* it only takes place relatively rapidly when, in a defined conformation, the free electron pairs on the remaining heteroatoms have antiperiplanar orientations with respect to the leaving group (Figure 1).

In conformation (I), the overlapping of the free electron pairs with the antibonding σ* orbital of the leaving group 'OR' reaches a maximum so that the starting orbitals can undergo transformation to the product orbitals in (II) with a minimal structural change. In this way, an optimal relative stabilization of the transition state in the route from (I) to (II) is reached. In a (hypothetical) fixed conformation (III), however, a stereoelectronic barrier to the heterolysis giving (II) exists. With the aid of the 'antiperiplanar lone pair hypothesis',[14] the unusual reluctance of some conformationally relatively fixed ortho esters to undergo acid hydrolysis[15,16] and the product distribution obtained on hydrolysis of mixed cyclic ortho esters[17] can, among others, be explained well. A stereoelectronic effect, which is only meaningful in comparison to other systems, on the rate of formation of cations from sterically unhindered, conformationally flexible, aliphatic and aromatic ortho esters is most certainly only of minor significance. In these cases the sterically optimal conformation can be achieved 'almost always' as a result of the rapid rotation about the C–O bond.

3 Stability and Structure of the Di- and Trialkoxycarbenium Ions

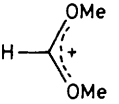
The fact that di- and trialkoxycarbenium ions are also smoothly accessible by

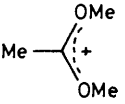
[10] B. G. Ramsay and R. W. Taft, *J. Am. Chem. Soc.*, 1966, **88**, 3058.
[11] A. Gerlach, *Thesis*, University of Marburg, 1969.
[12] H. Meerwein, *Angew. Chem.*, 1955, **67**, 374.
[13] S. Chandrasekhar, A. J. Kirby, and R. J. Martin, *J. Chem. Soc., Perkin Trans. 2*, 1983, 1619.
[14] P. Deslongchamps, 'Stereoelectronic Effects in Organic Chemistry', Pergamon Press, Oxford, 1983; P. Deslongchamps, *Tetrahedron*, 1975, **31**, 2463.
[15] R. A. McClelland and P. W. K. Lam, *Can. J. Chem.*, 1984, **62**, 1068.
[16] O. Bouad, G. Lamaty, and C. Moreau, *J. Chem. Soc., Chem. Commun.*, 1978, 678; O. Bouad, G. Lamaty, C. Moreau, O. Pomares, P. Deslongchamps, and L. Ruest, *Can. J. Chem.*, 1980, **58**, 567; P. W. K. Lam and R. A. McClelland, *J. Chem. Soc., Chem. Commun.*, 1980, 883.
[17] P. Deslongchamps, *Tetrahedron*, 1975, **31**, 2463.

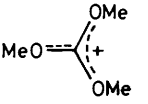
Table 1 *Relative energies of stabilization (SE) of alkoxycarbenium ions according to ref.*[19]

Ion	Me^+	$MeOCH_2^+$	$(MeO)_2CH^+$	$(MeO)_3C^+$
SE (kJ mol^{-1} ± 12.5)	0	276	356	377
(kcal mol^{-1} ± 3)	(0)	(66)	(85)	(90)

Table 2 *Enthalpies of formation* $[\Delta H_f(R^+)]$ *of dialkoxycarbenium ions in the gas phase derived from the determination of the appearance potentials* (R^+) *of the corresponding ortho esters*[19]

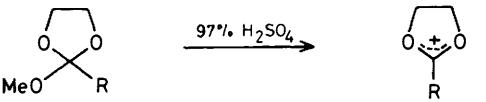






$\Delta H_f(R^+)$	kJ mol^{-1}	469	548	285
	(kcal mol^{-1})	(112)	(131)	(68)

Table 3 *Enthalpies of formation* (ΔH_{R+}) *of* 1,3-*dioxolan*-2-*ylium ions in solution.*



R		H	Me	Ph
ΔH_{R+}	kJ mol^{-1}	−91.7	−105.9	−122.6
	(kcal mol^{-1})	(−21.9)	(−25.3)	(−29.3)

The enthalpies of formation are calculated from the difference between the enthalpy of formation measured in 97% H_2SO_4 (ΔH_s,H_2SO_4) and the enthalpy of formation measured in CCl_4 (ΔH_s,CCl_4):

$$\Delta H_{R+} = \Delta H_s,H_2SO_4 - \Delta H_s,CCl_4$$

This correction takes the heat of solution used up by the dissolution of the non-ionized substrate in H_2SO_4 into account.

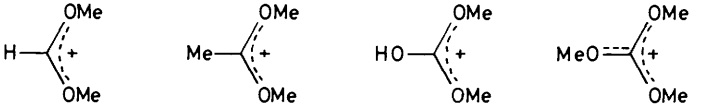
alkoxide transfer with the acceptor trityl cation[18] proves their high thermodynamic stability. Taft and co-workers[19] have determined the relative energies of stabilization [SE(kJ mol^{-1})] of some carboxonium ions (the corresponding methoxy-substituted methanes were precursors) by measuring their appearance potentials in a mass spectrometer. As expected, the energy of stabilization increased with the increasing number of groups with donor characteristics on the charge-bearing carbon atom.

Correspondingly, the enthalpies of formation $[\Delta H_f(R^+)]$ of dialkoxycarbenium ions, generated from structurally closely related precursors, should decrease on going from left to right (Table 2).

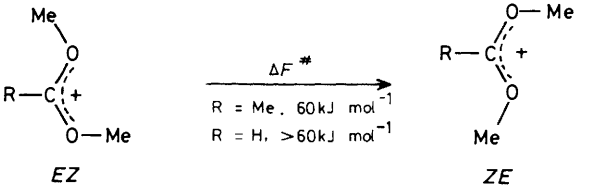
This, at least in the gas phase, is not the case.[19] Measurements in the condensed phase for the formation of the structurally related 1,3-dioxolan-2-ylium (1,3-

[18] H. Meerwein, V. Hederich, H. Morschel, and K. Wunderlich, *Liebigs Ann. Chem.*, 1960, **635**, 1.
[19] R. H. Martin, F. W. Lampe, and R. W. Taft, *J. Am. Chem. Soc.*, 1966, **88**, 1353.

Table 4 ^{1}H *n.m.r. resonances of methoxy groups in methoxycarbenium ions (solvent:* H_2SO_4—SO_3, *reference: TMS) according to refs.* 3 *and* 10



δ (ppm)	5.20	4.95	4.90	5.0—5.1



Scheme 1 *Rotational isomerization of dimethoxycarbenium ions*

dioxolenium) ions show an increase in the thermodynamic stability with increasing donor characteristics of the substituents at the *pro*-acyl carbon atom.[20]

^{1}H n.m.r. chemical shift data suggest that this stability order in solution is also valid for the open-chain representatives. The ^{1}H-resonances of the *O*-methyl protons of methoxycarbenium ions appear at higher fields in correlation with the strength of the charge delocalization[10] (see Table 4). An increasing charge delocalization should, as a rule, be accompanied by an increasing thermodynamic stability.

A satisfactory explanation for the deviating spectroscopic behaviour of the C_3-symmetrical cation in this series has not been found to date.[3] Consideration of the trimethoxycarbenium ion as a so-called 'Y-aromatic'[21,22] could possibly provide a key to the interpretation.

Dialkoxycarbenium ions exist as rotational isomers. For example, in the ^{1}H n.m.r. spectrum of methyldimethoxycarbenium tetrafluoroborate at less than 14 °C, two *O*-methyl resonances are observed.[10] The barrier to rotation about the partial C–O double bond ($\Delta F^{\neq}$) was determined to be 60 kJ mol^{-1} (14.3 kcal mol^{-1}) at 14 °C by coalescence measurements[23] (Scheme 1).

In the case of R = H, as expected, $\Delta F^{\neq}$ is higher (double signal at room temperature[10]). The existence of a further rotational isomer (*E*/*E*), as postulated by Borch,[24] could not be observed by other authors[25,26] under comparable

[20] R. H. Martin, C. A. Chambers, Y. Chiang, C. S. Hillock, A. J. Kresge, and J. W. Larsen, *J. Org. Chem.*, 1984, **49**, 2622.
[21] P. Gund, *J. Chem. Educ.*, 1972, **49**, 100.
[22] R. West and J. Nin in 'Nonbenzoid Aromatics', ed. J. P. Snyder, Academic Press, New York, 1969.
[23] R. K. Lustgarten, M. Brookhart, and S. Winstein, *Tetrahedron Lett.*, 1971, 141.
[24] R. F. Borch, *J. Am. Chem. Soc.*, 1968, **90**, 5303.
[25] Ch. H. von Dusseau, S. E. Schaafsma, H. Steinberg, and T. J. de Boer, *Tetrahedron Lett.*, 1969, 467.
[26] M. Sundaralingam and A. K. Chwang in 'Carbonium Ions', Vol. V, ed. G. A. Olah and P. v. R. Schleyer, Interscience, New York, 1976.

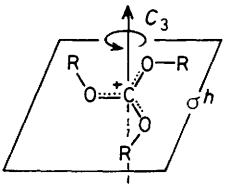


Figure 2 *Conformation of the trialkoxycarbenium ions*

conditions. Only a single, sterically favourable conformation with C_{3h}-symmetry can be formulated for the trialkoxycarbenium ions. Correspondingly, the ^1H n.m.r. spectra only show one signal for all three alkoxy groups, even at -60 °C (Figure 2).[10]

The ^{13}C n.m.r. spectra of the alkoxycarbenium ions provide information on the relation of the π-electron density at the cationic centre. Thus, as expected, the following order is found for the resonance position of the central carbon atom in acyclic representatives (CD_3NO_2, δ-scale):

199.0	185.1	178.5	167.3	
$H–C(OEt)_2^+$	$Me–C(OEt)_2^+$	$Ph–C(OMe)_2^+$	$(MeO)_3C^+$	BF_4^-

These shift data permit the assumption of an increase in the π-electron density at the carbenium centre on going from left to right.

From a comparison of the C···O valency vibrations in the i.r. spectra with those of the reference ions $MeCOO^-$ (π-bond order: 0.5) and CO_3^{2-} (π-bond order: 0.33), Taft and co-workers[10] postulated a π-bond proportion of 0.2—0.3 for dialkoxycarbenium ions.

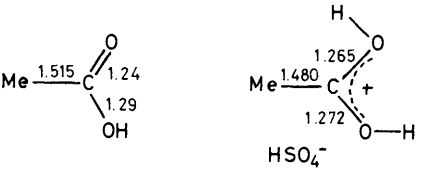


Figure 3 *Bond lengths (in Å) for acetic acid and the dihydroxymethylcarbenium ion*[26]

Reliable data on the internal bond coordinates are to be expected from *X*-ray diffraction studies. Unfortunately, these data are not yet available for acyclic di- and trialkoxycarbenium ions. The data determined for the dihydroxymethylcarbenium ion,[26] however, should be transferable to the system of interest here without any major deviations (Figure 3).

The C–O bond lengths of this cation are practically equal, the C–C bond length of 1.480 Å is noticeably shorter than that of acetic acid as a result of hyperconjugation between the methyl group and the sp^2-hybridized carboxonium

[27] L. Hevesi, S. Desauvage, B. Georges, G. Evrard, P. Blanpain, A. Michel, S. Harkema, and G. J. van Hummel, *J. Am. Chem. Soc.*, 1984, **106**, 3784.

Table 5 *Calculated bond lengths, π-bond orders, and barriers to rotation for various 2-substituted 1,3-dioxolan-2-ylium ions*[29]

R	C-2–O *bond length*	*π-bond order*	*barrier to rotation about the* C-2–R *bond* kJ mol^{-1}	(kcal mol^{-1})
H	1.313	0.650	—	—
Me	1.328	0.587	0.54	(0.013)
OH	1.328	0.540	35.6	(8.5)
NH_2	1.336	0.485	128.1	(30.6)

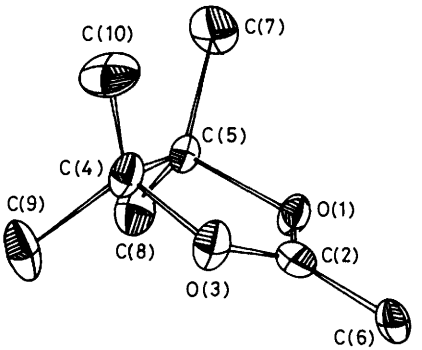


Figure 4 *Molecular structure of the 2,4,4,5,5-pentamethyl-1,3-dioxolan-2-ylium ion in the crystal state*[28]

carbon atom. The molecule is planar and the OH groups are *cis* and *trans* to the methyl group. The same geometry was recently found for the heteroanalogues, the bis(methylthio)- and bis(methylseleno)carbenium ions.[27]

Even in the 2,4,4,5,5-pentamethyl-1,3-dioxolan-2-ylium ion the dioxolan-2-ylium ring is, as demonstrated by an *X*-ray crystal structure analysis, completely planar (see Figure 4).[28] This structural result clearly shows how the high mesomeric energy of the π-system $(-O\cdots C\cdots O-)^+$ more than compensates for the sterically extremely unfavourable interaction between two *syn*-periplanar orientated pairs of methyl groups. The bond lengths between C-2 and the two oxygen atoms (1.28 and 1.24 Å) lie between the values for a C–O single bond in 1,3-dioxolanes (1.41 Å) and a double bond (1.22 Å).

Pittman and co-workers achieved similar, but not completely concordant, results from model calculations on 1,3-dioxolan-2-ylium ions.[29] These SCF–MO calculations according to the INDO approximation process (see Table 5) gave a π-

[28] H. Paulsen and R. Dammeyer, *Chem. Ber.*, 1973, **106**, 2324.
[29] C. U. Pittman, Jr., T. B. Patterson, and L. D. Kispert, *J. Org. Chem.*, 1973, **38**, 471.

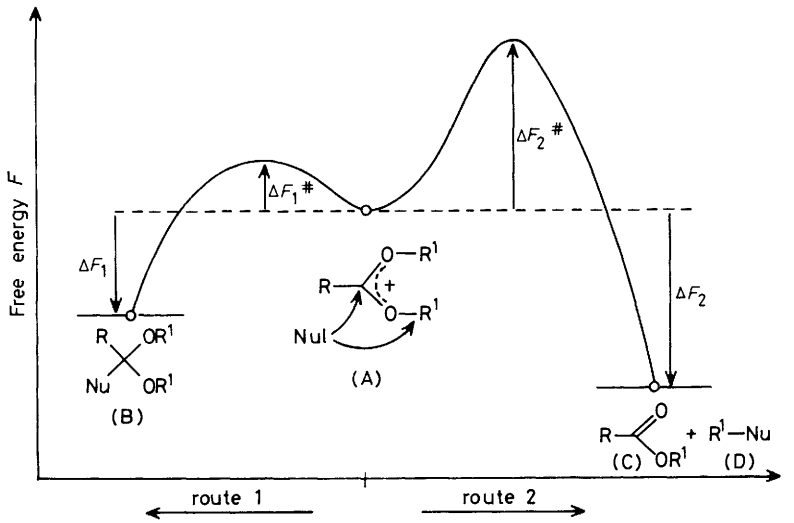


Figure 5 *Energy profile for the reaction of a dialkoxycarbenium ion with a nucleophile, according to ref.* 30

bond order of about 0.5—0.65 for the C-2–O bond, depending on the nature of the C-2 substituent.

Hevesi *et al.*[27] obtained even higher values of 0.7—0.8 by graphical extrapolation of the relationship bond length/π-bond order for acyclic carboxonium ions. Thus, both MO calculations and *X*-ray crystal structure data clearly illustrate the significant contribution of the oxonium resonance structure to the ground states of dialkoxycarbenium and 1,3-dioxolan-2-ylium ions.

4 Reaction Paths and Reactivity of Alkoxycarbenium Ions

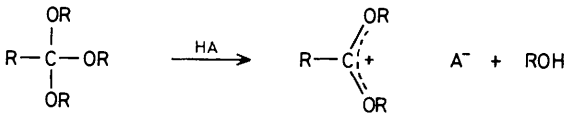
In principle, dialkoxycarbenium ions (A) can react with nucleophiles (Nu) in two ways depending on the reaction conditions: either in a kinetically controlled reaction to form saturated 1,1-dialkoxy compounds (B) or in a thermodynamically controlled reaction with alkylation of the nucleophile (D) to give carboxylic esters (C) (Figure 5).[30]

The preferred route and thus the product distribution depends mainly on the nature of the nucleophile, the stability of the ambident cation (A), the reaction temperature, the reaction time, and the solvent.

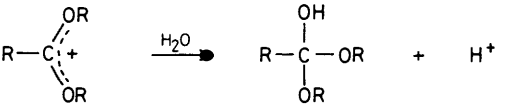
The combination 'hard nucleophile–energy-rich cation' (ΔF_1 is large) should lead preferentially to kinetically controlled products whereas the reaction of soft nucleophiles with energy-poor cations (ΔF_1 is small) should lead to thermodynamically controlled products. In fact, apart from a few exceptions,[31]

[30] S. Hünig, *Angew. Chem.*, 1964, **76**, 400; *Angew. Chem., Int. Ed. Engl.*, 1964, **3**, 548.
[31] C. U. Pittman, Jr., S. P. McManus, and J. W. Larsen, *Chem. Rev.*, 1972, **72**, 357.

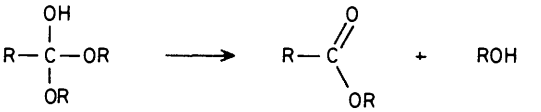
(I) Formation of the carboxonium ion



(II) Addition of the nucleophile H_2O



(III) Decomposition of the hemiortho ester



Scheme 2 *Mechanism of the ortho ester hydrolysis*

products from the kinetically controlled reaction (route 1) can only be isolated when strong nucleophiles such as EtO^- or CN^- are used. In the heteroaromatic series, for example, indoles, carbazoles, and pyrroles are also sufficiently nucleophilic to attack the carbenium ion centre.[5,6] Increases in the temperature and/or longer reaction times favour the thermodynamically controlled route 2.

Our studies on the a^1-acylating reactivity of acyclic ortho esters and di- or trialkoxycarbenium ions towards 2-methylindole have given the following orders of reactivity:

$$HC(OEt)_3 > MeC(OEt)_3 > PhC(OMe)_3 \gg (MeO)_4C;$$

$$HC(OEt)_2^+ > MeC(OEt)_2^+ > PhC(OMe)_2^+ \gg (MeO)_3C^+ \quad BF_4^-$$

As expected, trimethyl orthocarbonate as well as trimethoxycarbenium tetrafluoroborate represent the most unreactive a^1-electrophiles.

5 Kinetics and Mechanism of the Ortho Ester Hydrolysis

The influence of the structures of di- and trialkoxycarbenium ions on their reactivity towards nucleophiles has previously been studied exhaustively on the three component system ortho ester–H_2O–proton acid. From more recent studies on the kinetics and mechanism of the ortho ester hydrolysis, it can be deduced that this system is not well suited for the qualitative derivation of an order of reactivity of these cations. Today, it is generally accepted that the hydrolysis of ortho esters—as postulated earlier[32,33]—has to be formulated as a three-step mechanism (Scheme 2).[15,34]

[32] E. H. Cordes and H. G. Bull, *Chem. Rev.*, 1974, **74**, 581.
[33] T. H. Fife, *Acc. Chem. Res.*, 1972, **5**, 264.

The previously predominant opinion that step I, *i.e.* the cleavage of the C–O bond, is the rate-determining step of the ortho ester hydrolysis has now been replaced by a much more differentiated consideration.[14] Kresge *et al.*[35] showed that, for certain substrates and increasing pH values, step III dominates over step I as the rate-determining factor. Comparative, quantitative measurements of the hydrolysis kinetics of 2-alkoxy-1,3-dioxolanes and acyclic ortho esters have shown that the transition of the rate-determining step from I to III is, in the first instance, not dependent on the donor characteristics of the substituent at the *pro*-acyl carbon atom,[35,36] but that rather a solvation effect,[34] which stabilizes the intermediately formed hemiortho esters differently, is responsible. In the case of dioxolanes, entropy may also play a decisive role.

For certain ortho esters, the attack of water on the dialkoxycarbenium ion (step II) can also be rate-determining. This was demonstrated for the examples of trimethyl orthomesitoate[37] and conformationally fixed[16] ortho esters. In these cases, steric and stereoelectronic factors are decisive.

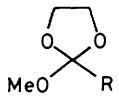
De Wolfe and Jensen[38] have measured the rates of hydrolysis of orthoformic, orthoacetic, orthobenzoic, and orthocarbonic esters. For acyclic ortho esters $R\text{–}C(OR^1)_3$, they found the following order (Table 6).

Table 6 *Relative rates of hydrolysis of ortho esters* (R^1 = *alkyl*) *according to ref.* 38

R	Me >	Et >	H >	Ph >	OEt
Relative rate of hydrolysis	38.5	24.3	1.00	0.62	0.17

For 1,3-dioxolanes, Kresge, Larsen *et al.*[20] obtained the following order (Table 7).

Table 7 *Relative rates of hydrolysis of* 1,3-*dioxolanes according to ref.* 20



R	Me >	Ph >	H
Relative rate of hydrolysis	125.7	30.8	1

These experimentally determined data clearly demonstrate that the thermodynamic and kinetic stabilities do not proceed in parallel. The fact that the rate of hydrolysis in the acyclic series was decreased by phenyl substitution was not understood for a long time. This is now explained in terms of the spatial structure of

[34] Y. Chiang, A. J. Kresge, M. O. Lahti, and D. P. Weeks, *J. Am. Chem. Soc.*, 1983, **105**, 6852.
[35] M. Ahmad, R. G. Bergstrom, M. J. Cashen, A. J. Kresge, R. A. McClelland, and M. F. Powell, *J. Am. Chem. Soc.*, 1977, **99**, 4827; M. Ahmed, R. G. Bergstrom, M. J. Cashen, Y. Chiang, A. J. Kresge, R. A. McClelland, and M. F. Powell, *J. Am. Chem. Soc.*, 1979, **101**, 2669; M. Ahmed, R. G. Bergstrom, M. J. Cashen, Y. Chiang, A. J. Kresge, R. A. McClelland, and M. F. Powell, *J. Am. Chem. Soc.*, 1982, **104**, 1156; R. A. Burt, Y. Chiang, A. J. Kresge, and M. A. McKinney, *J. Am. Chem. Soc.*, 1982, **104**, 3685.
[36] R. A. McClelland, S. Gedge, and J. Bohonek, *J. Org. Chem.*, 1981, **46**, 886.
[37] R. A. McClelland and M. Ahmed, *J. Am. Chem. Soc.*, 1978, **100**, 7027.
[38] R. H. DeWolfe and J. L. Jensen, *J. Am. Chem. Soc.*, 1974, **85**, 3264.

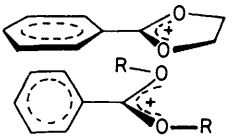


Figure 6 *Cyclic and acyclic phenyldialkoxycarbenium ions: spatial structures*

the cation. Based on comparative measurements of the hydrolysis kinetics of open-chain and cyclic orthobenzoic esters, Kresge and co-workers[39] deduced that in open-chain carboxonium ions, in contrast to the corresponding 1,3-dioxolan-2-ylium ions, the phenyl ring is twisted out of the carboxonium plane. This gives rise to a reduction of the (p-π)-conjugation and thus of the thermodynamic stability. Larsen and co-workers[40] have strengthened this theory (experimentally-determined structural evidence has not yet been reported) by measurements of the enthalpy of formation of methyl- and phenyl-substituted carboxonium ions. During studies on ortho ester hydrolyses in the cyclic series, it was noticed that the *in situ* generation of phenyl-substituted 1,3-dioxolan-2-ylium ion, although it is thermodynamically more stable by 16.5 kJ mol^{-1} (4 kcal mol^{-1}), occurs about four-times more slowly than the formation of the corresponding methyl-substituted ion (see Table 7).

As a possible explanation, it has been suggested[20] that, in the transition state of step I, which is similar to the substrate, the cation destabilizing $-$I effect of the phenyl group exceeds the stabilizing $+$M effect. This could also offer a plausible explanation for the striking sluggishness of the reactions of orthocarbonic esters, as we have also observed in our studies. Perhaps, however, for this reason step II takes up increasing importance as rate-determining step owing to the formation of the highly resonance-stabilized trialkoxycarbenium ion.

6 New Synthetic Applications of Ortho Esters and Dialkoxycarbenium Ions

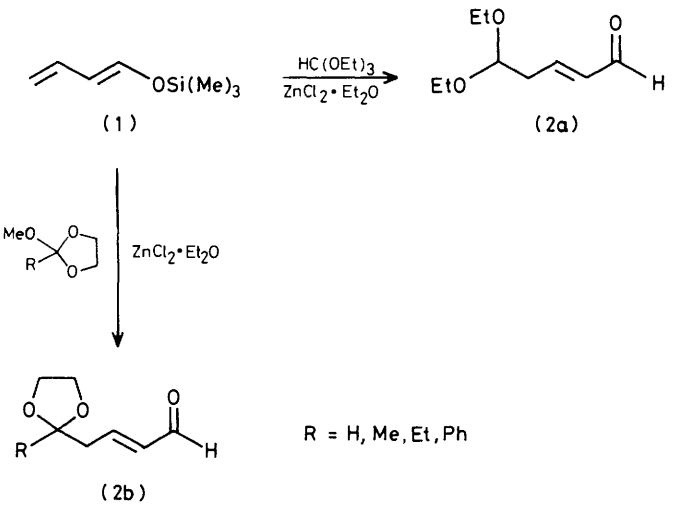
The synthetic potential of ortho esters and di- or trialkoxycarbenium ions as alkylating and acylating agents is so extensive[1-3,41] that only a few of the more recent preparative results can be mentioned here. In addition to the well-known applications as masking agents in the chemistry of carbonyl compounds[1] and for the synthesis of further carboxylic acid and alkoxy derivatives,[41] their use for the formation of carbon–carbon bonds is of major significance. These electrophiles also function as a^1-C synthons* for the construction of various heterocyclic ring systems[1] and serve as preparatively useful condensation reagents in reactions with

* a^1 is the notation for an acceptor synthon of the C–X series.

[39] Y. Chiang, A. J. Kresge, P. Salomaa, and C. I. Young, *J. Am. Chem. Soc.*, 1974, **96**, 4494.

[40] J. W. Larsen, P. A. Bouis, and C. A. Riddle, *J. Org. Chem.*, 1980, **45**, 4969.

[41] (*a*) W. Kantlehner, B. Funke, E. Haug, P. Speh, L. Kienitz, and T. Meier, *Synthesis*, 1977, 73. (*b*) G. Simchen, in Houben-Weyl, 'Methoden der Organischen Chemie', ed. J. Falbe, 4th Edn., Vol. E5, Georg Thieme Verlag, Stuttgart, New York, 1985.



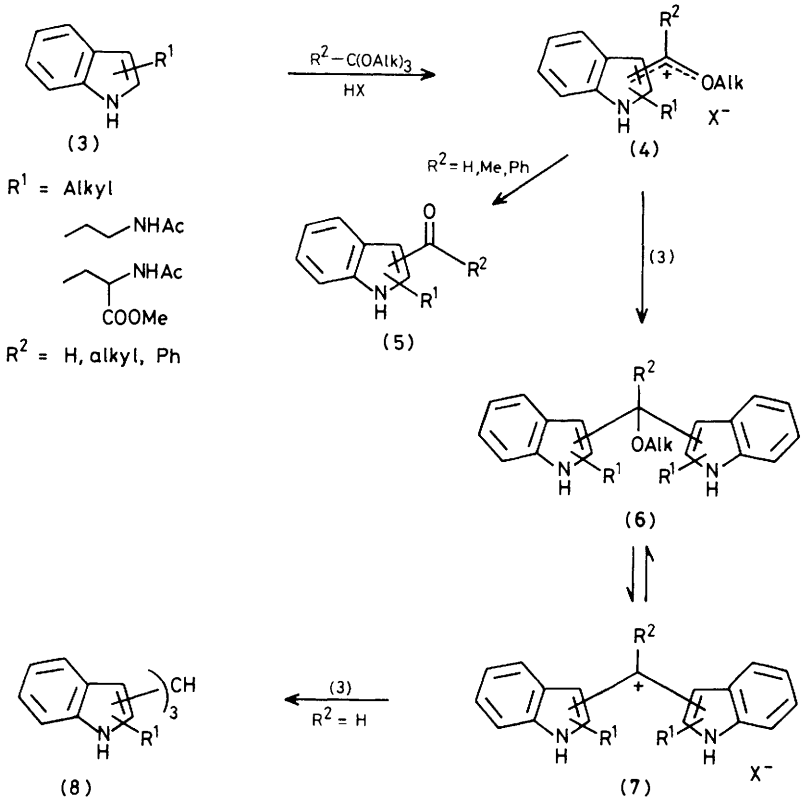
electron-rich olefins and *CH*-acid systems.[42] In particular, trialkyl orthoacetates have been employed successfully in the regio- and stereocontrolled formation of functionalized alkenes *via* the Claisen rearrangement.[43]

Acyclic and cyclic ortho esters as well as di- and trialkoxycarbenium tetrafluoroborates can be used successfully for the regiospecific acylation and alkylation of electron-rich π-systems (alkyl enol ethers, silyl enol ethers, enamines, indoles, carbazoles). Thus, for example, triethyl orthoformate or 2-methoxy-1,3-dioxolane reacts with the 1-trimethylsiloxy-1,3-butadiene (1) with high γ-selectivity to form the γ-protected 1,5-dicarbonyl compounds (2a) or (2b).[44]

The synthetic flexibility of this acylation variant is reflected in its wide scope of application: many simple silyl enol ethers, silyl ketene acetals, and enamines react with a high β-preference at the π-system with various acyclic and cyclic ortho esters under $TiCl_4$, $ZnCl_2$, or BF_3 catalysis.[45–49] See reference 41*b* for further new derivatization reactions with ortho esters.

Indoles (3) react as heterocyclic enamines with various acyclic ortho esters under proton catalysis and in dependence on the reaction conditions to form the

[42] O. Wolfbeis and H. Junek. *Tetrahedron Lett.*, 1973, 4905; O. Wolfbeis, *Z. Naturforsch.*, 1976, **31b**, 95.
[43] G. B. Benett, *Synthesis*, 1977, 589.
[44] E. Akgün and U. Pindur, *Synthesis*, 1984, 227.
[45] T. Mukaiyama, *Angew. Chem.*, 1977, **89**, 858; *Angew. Chem., Int. Ed. Engl.*, 1977, **16**, 817; T. Mukaiyama and M. Hayashi, *Chem. Lett.*, 1974, 15.
[46] E. Akgün and U. Pindur, *Liebigs. Ann. Chem.*, 1985, 2472.
[47] E. Akgün and U. Pindur, *Monatsh. Chem.*, 1984, **115**, 587.
[48] E. Akgün, M. Tunali, and U. Pindur, *Monatsh. Chem.*, in press.
[49] E. Akgün, M. Tunali, and U. Pindur, *Chem.-Ztg.*, 1986, **110**, 335.



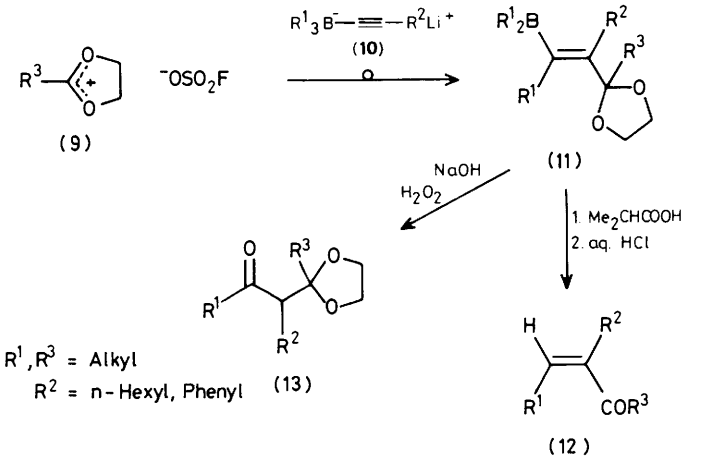
preparatively useful, functionalized indole derivatives (4)—(8).[4,50–53] Of these products the acylindoles (5) are of special interest as building blocks for alkaloid syntheses.[7] Cyclic ortho esters such as, for example, 2-alkoxy-1,3-dioxolanes also react to form compounds of the type (5).[54] Triethyl orthoacetate reacts as an a^1-C_2 synthon with 3-unsubstituted indoles to produce 3-vinylindole equivalents.[55,56]

4-Methoxyindole is regiospecifically functionalized at the 3-position by triethyl orthoformate to yield a tris(indolyl)methane of the type (8).[57] Whereas the parent

[50] J. Müller, L. Pfeuffer, and U. Pindur, *Monatsh. Chem.*, 1985, **116**, 365.
[51] U. Pindur and J. Müller, *J. Heterocyclic Chem.*, in press; U. Pindur and J. Müller, *J. Chem. Soc., Chem. Commun.*, submitted.
[52] U. Pindur and J. Müller, *Chimia*, 1985, **39**, 141.
[53] L. Pfeuffer, E. Sody, and U. Pindur, *Chem.-Ztg.*, in press.
[54] E. Akgün, M. Tunali, and U. Pindur, *Arch. Pharm. (Weinheim. Ger.)*, in press.
[55] U. Pindur and J. Müller, *Chem.-Ztg.*, 1984, **108**, 150.
[56] J. Müller, L. Pfeuffer, and U. Pindur, *Chem.-Ztg.*, 1985, **109**, 15.
[57] H. Witzel and U. Pindur, manuscript in preparation.

carbazole is preferentially dialkoxy-alkylated at N-9 on reaction with an excess of triethyl orthoformate, the analogous reaction with 4-methoxycarbazole results in regiospecific formylation at C-1. In the latter reaction, depending on the reaction conditions, carbazole derivatives analogous to compounds (6), (7), and (8) are formed as the subsequent products.[57] In the course of this functionalization method for heterocycles, we also studied the acylation and alkylation reactivity of the *per se* employed di- and trialkoxycarbenium tetrafluoroborates. Thus, for example, 3-unsubstituted indoles are regioselectively acylated or methoxycarbonylated at position 3 on reaction with $R–C(OAlk)_2^+\ BF_4^-$ (R = H, Me, Ph, OMe).[6] 3-Mono- and 2,3-disubstituted indoles react preferentially at N-1 with these ambident cations to form *N*-acyl-and *N*-alkylindoles.[6]

In the reactions of $R–C(OAlk)_2^+\ BF_4^-$ (R = H, Me, OMe) with carbazoles, in dependence of the structure of the carbazole, a wide spectrum of products are formed, among which, above all, the synthetically interesting, acylated and alkylated carbazoles are formed in good yields.[58] In these cases, $H–C(OEt)_2^+\ BF_4^-$ reacts as an a^1-C_1 synthon (formylation) and the thermodynamically more stable cations $Me–C(OEt)_2^+\ BF_4^-$ and $(MeO)_3C^+\ BF_4^-$ react as alkylating agents (*N*-alkylation).



Finally, a further, new variant for the preparation of functionalized ketones should be mentioned. The reactions of 2-alkyl-1,3-dioxolan-2-ylium fluorosulphonates (9) with alkynyltrialkylborates take place at the β-position of the alkynylborates (10). On hydrolytic work-up, these reactions give rise to (*Z*)-α,β-unsaturated ketones (12) whereas oxidative work-up results in the formation of specifically mono-protected 1,3-diketones (13).[59]

[58] U. Pindur and C. Flo, *Liebigs Ann. Chem.*, 1987, in press.
[59] A. Pelter and M. E. Colclough, *Tetrahedron Lett.*, 1986, **27**, 1935.