# Chemistry of Tetra-alkoxyethenes. Part V.[1] Thermal Cycloadditions with Carbonyl Compounds

By **Pieter H. J. Ooms, Hans W. Scheeren,** and **Rutger J. F. Nivard,*** Department of Organic Chemistry, Catholic University, Toernooiveld, Nijmegen, The Netherlands

Heating tetra-alkoxyethenes with α-oxo-nitriles leads to cycloaddition products, *viz.* 3,3,4,4-tetra-alkoxyoxetan-2-carbonitriles (16), which can be converted into 2,2-dialkoxy-3-cyano-3-hydroxy-carboxylic esters (17) by aceto-lysis, and subsequently into α-acyl-αα-dialkoxyacetates (18) by treatment with alkali.

IN contrast with the photochemical formation of oxetans from olefins and carbonyl compounds, often referred to as the Büchi–Paterno reaction,[2] thermal $[_\pi2 + _\pi2]$ cycloadditions between these compounds have been observed relatively seldom. Simple olefins having allylic hydrogen atoms generally yield products of the 'ene' reaction (Scheme 1) when heated with carbonyl compounds.[3] However, cycloaddition products, *i.e.* oxetans (Scheme 2), have been isolated when strongly electrophilic carbonyl compounds like mesoxalonitrile[4] and perfluorocyclobutanone[5] were used.
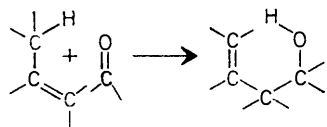
SCHEME 1
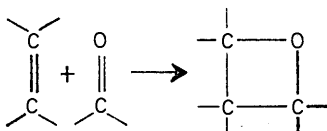
SCHEME 2

Various types of product have been obtained from electron-rich ethenes and carbonyl compounds, depend-ing on the structure of the reagents. Enamines (1) possessing a β-hydrogen atom (Scheme 3; R^2 and/or R^3 = H) gave compounds[6] (3), analogous to the so-called Stork products, which arise on reaction with electron-poor olefins.[7] β-Alkylated enamines, *e.g.* 2-methyl-1-morpholinopropene, yield[8] 1 : 2 adducts (5) on reaction with chloral, whereas with formaldehyde the presumed dipolar intermediates (2) rearrange into β-amino-aldehydes (4).

In the reaction of the symmetrically substituted and extremely nucleophilic tetra-aminoethene 1,1′,3,3′-tetra-phenylbi-imidazolidin-2-ylidene (6) with aromatic aldehydes, the zwitterionic intermediate (7) splits off a carbene, giving a 2-acyl-1,3-diphenylimidazolidine (8) as the end-product.[9-11] As a consequence of the high basicity of (6), other carbonyl compounds, *e.g.* aceto-phenone, give products (9) formed *via* α-carbanions[10] (Scheme 4).

In a reaction between 1,1-dimethoxyethene (10) and a carbonyl compound, the existence of an oxetan (11) in the solution has been demonstrated recently.[12] In general, working up of the reaction mixture leads to elimination of an alcohol, providing, however, an αβ-unsaturated ester (13) as the end-product[13] (Scheme 5).

In view of these results and as a continuation of our studies on cycloadditions of electron-rich tetra-alkoxy-

[1] P. H. J. Ooms, J. W. Scheeren, and R. J. F. Nivard, Part IV, *Synthesis*, 1975, 662; Part III, *ibid.*, p. 639.

[2] N. J. Turro, *Pure Appl. Chem.*, 1971, **27**, 679.

[3] H. M. R. Hoffmann, *Angew. Chem.*, 1969, **81**, 597; *Angew. Chem. Internat. Edn.*, 1969, **8**, 556.

[4] O. A. Achmatowicz and M.Leplawy, *Roczniki Chem.*, 1959, **33**, 1349, 1371 (*Chem. Abs.*, 1960, **54**, 13,056a).

[5] D. C. England, *J. Amer. Chem. Soc.*, 1961, **83**, 2205.

[6] L. Birkofer, S. M. Kim, and H. D. Engels, *Chem. Ber.*, 1962, **95**, 1495.

[7] P. H. J. Ooms, J. W. Scheeren, and R. J. F. Nivard, *Synthesis*, 1975, 260.

[8] K. C. Brannock, R. D. Burpitt, H. E. Davis, H. S. Pridgen, and J. G. Thweatt, *J. Org. Chem.*, 1964, **29**, 2579.
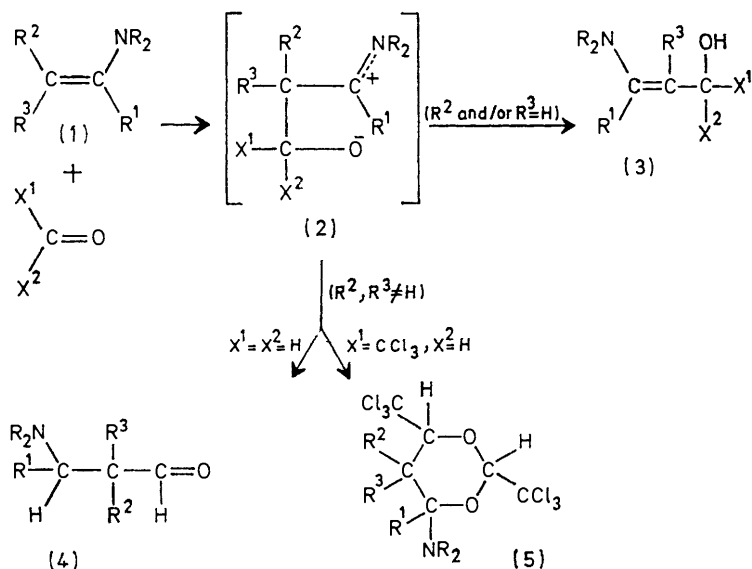
[9] J. Hocker and R. Merten, *Angew. Chem.*, 1972, **84**, 1022; *Angew. Chem. Internat. Edn.*, 1972, **11**, 964.

[10] H. W. Wanzlick and H. J. Kleiner, *Chem. Ber.*, 1963, **96**, 3024.
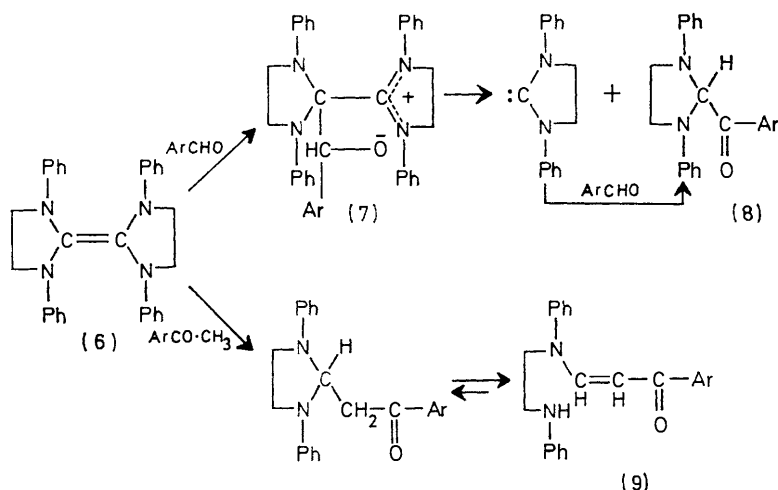
[11] B. Lachmann, H. Steinmaus, and H. W. Wanzlick, *Tetrahedron*, 1971, **27**, 4085.

[12] T. H. Koch, J. Olesen, and J. Foy, *J. Org. Chem.*, 1975, **40**, 117.

[13] S. M. McElvain, E. R. Degginger, and J. D. Behun, *J. Amer. Chem. Soc.*, 1954, **76**, 5736.
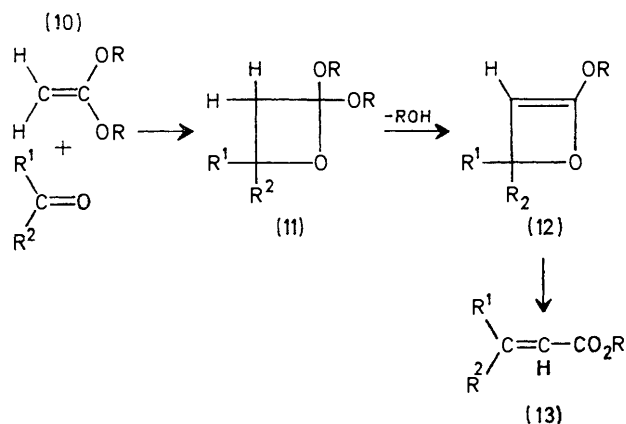
Scheme 3

Scheme 4

ethenes (14) with electron-poor olefins,[7] we have investigated the reactivity of these tetrasubstituted keten acetals with electron-deficient carbonyl compounds. Products of [2 + 2] cycloaddition, *viz.* 3,3,4,4-tetra-alkoxyoxetan-2-carbonitriles (16), were isolated in good yields on heating a tetra-alkoxyethene (14) with an α-oxo-nitrile (15), neat or in acetonitrile solution (Scheme 6).

The results (Table 1) show that the reaction velocity strongly depends on the nature of the carbonyl compound. With $R^2 = p\text{-}NO_2\cdot C_6H_4$ the reaction proceeds smoothly at room temperature; with $R^2 = p\text{-}MeC_6H_4$ prolonged heating is necessary for completion; and with $R^2 = p\text{-}MeO\cdot C_6H_4$ the reaction is too slow to be of use. Pyruvonitrile (15; $R^2 = Me$) and chloral gave no oxetans with compounds (14); the actual products were not identified in these cases. βγ-Unsaturated α-oxo-nitriles gave [4 + 2]cycloaddition products with tetra-alkoxyethenes, *e.g.* 2-oxo-4-phenylbut-3-enonitrile
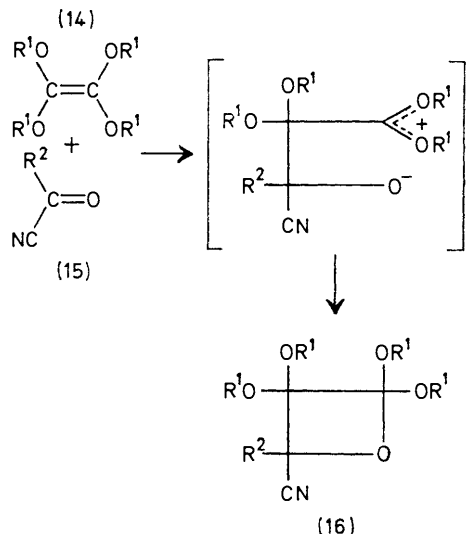
afforded 2,2,3,3-tetra-alkoxy-4-phenyl-3,4-dihydro-2*H*-pyran-6-carbonitriles (Table 2). An analogous formation

Scheme 5

of six-membered ring compounds was found with β-acyl-β-cyanostyrenes.[7,14]

The tetra-alkoxyoxetancarbonitriles (16) are as stable towards bases as acyclic and strainless orthoesters. No

(14)

Scheme 6

traces of decomposition products were detected after heating under reflux in piperidine or in a solution of sodium methoxide in 1,2-dimethoxyethane. Acetolysis in glacial acetic acid under reflux for 1 h led to cyano-hydrins of αα-dialkoxy-β-oxo-esters (17) (Table 3), which

mixture of the products (17) and (18). Efforts to synthesize tetra-alkoxyazetidinecarbonitriles in an analogous manner from tetra-alkoxyethenes and cyano-imines [$R^2C(CN)=NR^2$] were unsuccessful; the reactivity of the latter was apparently too low.
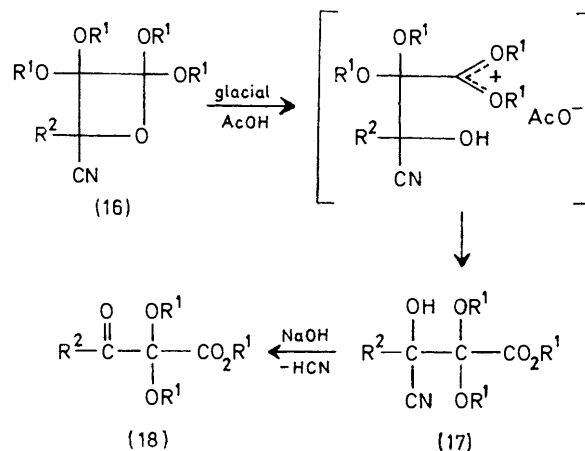
Scheme 7

EXPERIMENTAL

All products were characterized by their m.p.s, mass spectra, and from i.r. data (KBr pellets).

Synthesis of the α-Oxo-nitriles. Compounds not commercially available were prepared according to literature procedures.[15-17]

3,3,4,4-*Tetra-alkoxyoxetan-2-carbonitriles* (16) (Table 1).—

TABLE 1

3,3,4,4-Tetra-alkoxyoxetan-2-carbonitriles (16) from tetra-alkoxyethenes and α-oxo-nitriles

R^1	R^2	Yield (%)	M.p. (°C)	m/e	$\nu_{max}./cm^{-1}$	Formula	Analyses (%) ‡			Time (h); temp (°C)
							C	H	N	
Me	p-O₂NC₆H₄	40	141	309 (M − CH₃), 293 (M − OCH₃), 234 [M − CO(OCH₃)₂]	2 240,* 984,† 948	C₁₄H₁₆N₂O₇	51.85 51.3	4.95 4.8	8.65 8.6	1; 25
Me	p-ClC₆H₄	85	117	284/282 (M − OCH₃), 223/221 [M − CO(OCH₃)₂]	2 238,* 991,† 955	C₁₄H₁₆ClNO₅	53.6 53.6	5.15 5.2	4.45 4.35	10; 100
Me	Ph	90	50	248 (M − OCH₃), 189 [M − CO(OCH₃)₂]	2 240,* 990,† 958	C₁₄H₁₇NO₅	60.2 60.2	6.15 6.2	5.0 4.9	30; 100
Me	p-MeC₆H₄	75	77	262 (M − OCH₃), 203 [M − CO(OCH₃)₂]	2 238,* 992,† 955	C₁₅H₁₉NO₅	61.45 61.2	6.55 6.6	4.8 4.7	200; 100
Et	p-ClC₆H₄	82	62	371/369 (M), 326/324 (M − OC₂H₅), 253/251 [M − CO(OC₂H₅)₂]	2 235,* 997,† 957	C₁₈H₂₄ClNO₅	58.45 58.7	6.55 6.4	3.8 3.75	15; 100
Et	Ph	80	54	335 (M), 290 (M − OC₂H₅), 217 [M − CO(OC₂H₅)₂]	2 237,* 991,† 960	C₁₈H₂₅NO₅	64.45 64.9	7.5 7.5	4.2 4.2	40; 100
Et	p-MeC₆H₄	70	(Oil)	304 (M − OC₂H₅), 231 [M − CO(OC₂H₅)₂]	2 238,* 995,† 957					250; 100

* C≡N. † C−O Stretching vibrations for oxetans are reported (ref. 4 and F. Nerdel, P. Weyerstahl, and K. Lucas, *Tetrahedron Letters*, 1968, 5751) at *ca.* 980 cm⁻¹. ‡ Upper values required; lower values found.

eliminate hydrogen cyanide on treatment with aqueous sodium hydroxide (Scheme 7; Table 4). From compound (16; $R^1 = p$-MeC₆H₄) the cyanohydrin could not be isolated, owing to spontaneous loss of HCN during the acetolysis.

Hydrolysis of compounds (16) also takes place on heating under reflux for 1 h in dioxan–water, to give a

A mixture of an α-oxo-nitrile (0.01 mol) and a tetra-alkoxyethene (0.02 mol) was heated at 100 °C for the time indicated in Table 1. With 2-(p-nitrophenyl)glyoxylo-nitrile only 0.015 mol of the tetra-alkoxyethene was used, and the reaction was performed at room temperature, with dry acetonitrile (5 ml) as solvent. After completion of the

[14] P. H. J. Ooms, L. P. C. Delbressine, J. W. Scheeren, and R. J. F. Nivard, *J.C.S. Perkin I*, in the press.

[15] T. S. Oakwood and C. A. Weisgerber, *Org. Synth.*, Coll. Vol. III, ed. E. C. Horning *et al.*, Wiley, New York, 1955, p. 112.
[16] A. Dornow and H. Grabhöfer, *Chem. Ber.*, 1958, **91**, 1824.
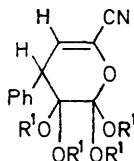[17] L. Claissen and E. Moritz, *Ber.*, 1880, **13**, 2124.

reaction the excess of tetra-alkoxyethene and the solvent were evaporated off *in vacuo*, and the residual oil was crystallized, usually from carbon tetrachloride. The product (16; R^1 = Et, R^2 = p-MeC$_6$H$_4$) was an oil, purified by bulb-to-bulb distillation at 100 °C and 0.1 Torr.

under reflux for 1 h. The mixture was evaporated *in vacuo* and the residual oil was crystallized from carbon tetrachloride–light petroleum.

In the acetolysis of (16; R^2 = p-MeC$_6$H$_4$), the cyanohydrin (17) could not be isolated as it loses HCN spon-

TABLE 2

2,2,3,3-Tetra-alkoxy-4-phenyl-3,4-dihydro-2H-pyran-6-carbonitriles from tetra-alkoxyethenes and 2-oxo-4-phenylbut-3-enonitrile

| | Yield | M.p. | | | | | Analyses (%) * | | | Time (h); |
R^1	(%)	(°C)	m/e	$\nu_{max.}$/cm^{-1}	Formula		C	H	N	temp. (°C)
Me	82	95	305 (M), 290 (M − CH$_3$), 274 (M − OCH$_3$)	2 230,† 1 650 ‡	C$_{16}$H$_{19}$NO$_5$		62.95	6.25	4.6	3; 100
							63.2	6.3	4.6	
Et	90	(Oil)	361 (M), 332 (M − CH$_3$), 316 (M − OCH$_3$)	2 230,† 1 655 ‡	C$_{20}$H$_{27}$NO$_5$		66.45	7.55	3.9	3; 100
							66.3	7.4	3.85	

* Upper values required; lower values found. † C≡N. ‡ C=C–O.

TABLE 3

2,2-Dialkoxy-3-cyano-3-hydroxypropionic esters (17) by acetolysis of 3,3,4,4-tetra-alkoxyoxetan-2-carbonitriles (16)

| | | Yield | M.p. | | | | Analyses (%) * | | |
R^1	R^2	(%)	(°C)	m/e	$\nu_{max.}$/cm^{-1}	Formula	C	H	N
Me	p-ClC$_6$H$_4$	92	76	270/268 (M − OCH$_3$), 242/240 (M − CO$_2$CH$_3$), 215/213 (M − CO$_2$CH$_3$ − HCN)	3 450 † 2 239 ‡ 1 745 §	C$_{13}$H$_{14}$ClNO$_5$	52.1 52.1	4.7 4.7	4.65 4.7
Me	Ph	90	64	234 (M − OCH$_3$), 206 (M − CO$_2$CH$_3$), 179 (M − CO$_2$CH$_3$ − HCN)	3 468 † 2 237 ‡ 1 750 §	C$_{13}$H$_{15}$NO$_5$	58.85 58.8	5.7 5.8	5.3 5.25
Et	p-ClC$_6$H$_4$	88	77	298/296 (M − OC$_2$H$_5$), 270/268 (M − CO$_2$C$_2$H$_5$), 243/241 (M − CO$_2$C$_2$H$_5$ − HCN)	3 378 † 2 232 ‡ 1 736 §	C$_{16}$H$_{20}$ClNO$_5$	56.25 55.9	5.9 5.95	4.1 4.1
Et	Ph	87	59	262 (M − OC$_2$H$_5$), 234 (M − CO$_2$C$_2$H$_5$), 207 (M − CO$_2$C$_2$H$_5$ − HCN)	3 410 † 2 232 ‡ 1 735 §	C$_{16}$H$_{21}$NO$_5$	62.55 62.3	6.9 6.65	4.55 4.6

* Upper values required; lower values found. † OH. ‡ C≡N. § C=O.

TABLE 4

α,α-Dialkoxy-α-aroylacetic esters (18) from 2,2-dialkoxy-3-cyano-3-hydroxypropionic esters (17)

| | | Yield | M.p. | | | | Analyses (%) * | |
R^1	R^2	(%)	(°C)	m/e	$\nu_{C:O}$/cm^{-1}	Formula	C	H
Me	p-ClC$_6$H$_4$	80	(Oil)	274/272 (M), 243/241 (M − OCH$_3$), 215/213 (M − CO$_2$CH$_3$)	1 755 1 700	C$_{12}$H$_{13}$ClO$_5$	52.85 52.7	4.8 4.8
Me	Ph	75	(Oil) ^{a}	238 (M), 207 (M − OCH$_3$), 179 (M − CO$_2$CH$_3$)	1 761 1 701	C$_{12}$H$_{14}$O$_5$	60.5 60.0	5.9 5.9
Me	p-MeC$_6$H$_4$	85	40 ^{b}	252 (M), 221 (M − OCH$_3$), 193 (M − CO$_2$CH$_3$)	1 760 1 702	C$_{13}$H$_{16}$O$_5$	61.9 61.3	6.4 6.4
Et	p-ClC$_6$H$_4$	88	52	271/269 (M − OC$_2$H$_5$), 243/241 (M − CO$_2$C$_2$H$_5$)	1 758 1 710	C$_{15}$H$_{19}$ClO$_5$	57.25 57.0	6.1 6.0
Et	Ph	90	(Oil)	280 (M), 235 (M − OC$_2$H$_5$), 207 (M − CO$_2$C$_2$H$_5$)	1 757 1 710	C$_{15}$H$_{20}$O$_5$	64.25 64.0	7.2 7.2

^{a} Synthesized previously by the reaction of benzoyl chloride with tetramethoxyethene (R. W. Hoffmann and J. Schneider, *Chem. Ber.*, 1966, **99**, 1899). ^{b} Obtained directly on acetolysis of the parent oxetan (16).

* Upper values required; lower values found.

2,2,3,3-Tetra-alkoxy-4-phenyl-3,4-dihydro-2H-pyran-6-carbonitriles (Table 2).—The same procedure was followed as in the preparation of oxetans.

2,2-Dialkoxy-3-cyano-3-hydroxypropionic Esters (17) (Table 3).—A solution of a tetra-alkoxyoxetancarbonitrile (16) (0.01 mol) in glacial acetic acid (25 ml) was heated

taneously, leaving an αα-dialkoxy-α-(p-methylbenzoyl)-acetic ester (18) (see Table 4).

αα-Dialkoxy-α-aroylacetic Esters (18) (Table 4).—The cyanohydrin (17) was dissolved in ether (5 ml) and added to M-sodium hydroxide (5 ml). The layers were separated after stirring for 1 h at room temperature, and the aqueous

layer was extracted twice with ether. The combined extracts were extracted with saturated sodium chloride solution until neutral, dried (Na_2SO_4), filtered, and evaporated *in vacuo* to leave the ester (18) as an oil. The compounds slowly solidified and were recrystallized from methanol.