Tetrahedron Letters No. 31, pp 2925 - 2928. 0040-4039/79/0729-2925$02.00/0

CHEMISTRY OF KETENE ACETALS II[1]. A SIMPLE ROUTE TO 2,2-DIALKOXYTETRAHYDROFURANS, γ-BUTYROLACTONES, 2-(5H)-FURANONES AND 2-ALKOXY-4,5-DIHYDROFURANS

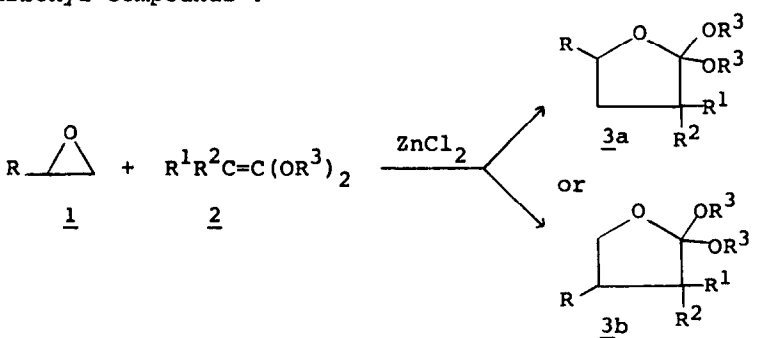
J.W. Scheeren, F.J.M. Dahmen and C.G. Bakker

Department of Organic Chemistry, Catholic University, Toernooiveld, 6525 ED Nijmegen, The Netherlands

Summary - 2,2-Dialkoxytetrahydrofurans 3 (a,b) have been synthesized from epoxides 1 and ketene acetals 2 using $ZnCl_2$ as a catalyst. By simple reactions compounds 3 were converted into γ-butyrolactones 5, 2-(5H)-furanones 7 and 2-alkoxy-4,5-dihydrofurans 8.

Recently simple, cyclic orthoesters (3; R = R^1 = R^2 = H) have been applied successfully in syntheses of biologically active compounds. Stereoselective Claisen rearrangements via such orthoesters (R^3 = allylic) gave useful intermediates in the preparation of calciferols[2]. Other naturally occurring compounds have been obtained by condensation of 3 with carbon acids[3]. Up to now, the compounds 3 were generally prepared in a two step procedure from γ-butyrolactones according to Meerwein[4].

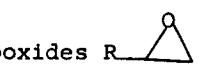
We found a single-step and rather general entry to these cyclic orthoesters by heating easy available epoxides (1) with ketene acetals (2) in the presence of $ZnCl_2$ (Scheme 1). The reaction does not proceed without the catalyst, but ketene acetals have a remarkably low tendency to polymerise under the influence of $ZnCl_2$, as was previously observed in cycloadditions of 2 with carbonyl compounds[1].



(1)

In the common procedure 0.1 mol of 1 was supplied with 1 mol% $ZnCl_2$ and then mixed with 0.15 mol of 2 (0.08 mol when R = Ph). The mixture was heated to the temperature and for the time given in Table 1. After addition of pentane, containing 5 g of triethylamine, it was filtered and distilled. All products gave satisfying NMR and MS data (M^+ and $M-OCH_3$). Some representative results given in the Table show that the regioselectivity of the reaction is determined by the ketene acetal as well as the epoxide used. Tetramethoxyethene (TME), the most electron-rich ketene acetal, attacks the epoxide always at the less hindered carbon atom. This route is also followed by other ketene acetals, when the epoxide used cannot be opened to a stabilized dipolar intermediate ($R = CH_2Cl$). Styrene oxide (R = Ph) seems to add, however, as a dipolar reagent ($PhCH^+-CH_2-O^-$), formed by acid-catalysed ring opening, to all ketene acetals except TME.

Table 1

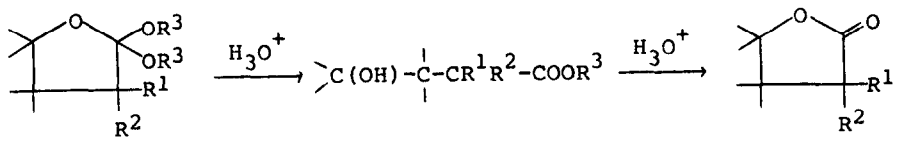
Synthesis of 2,2-dimethoxytetrahydrofurans 3a,b from epoxides  and ketene acetals $R^1R^2C=C(OMe)_2$

R	R^1	R^2	reaction temp.(°C)	reaction time(hrs)	product	b.p./mmHg	yield(%)[a]
H	Me	H	80[b,c]	8	3	100°/15	50
CH_2Cl	Me	H	120[b]	2	3a	62-64°/2[e]	60
CH_2Cl	OMe	OMe	120[b]	3	3a	88-90°/1.5	40
C_6H_5	Me	H	80[b]	5	3b	64-66°/0.2[e]	60
C_6H_5	Cl	H	60[d]	24	3b	115°/0.5[e]	50
C_6H_5	Me	Me	80[d]	3	3b		50[f]
C_6H_5	OMe	OMe	85[d]	48	3a	108-110°/0.3	60

a: Destillation is accompanied by loss of product due to polymerisation.
b: Heated without solvent.
c: Heated in an autoclave.
d: Heated in acetonitrile (30% solution)
e: *Cis-trans* mixture.
f: Calculated from the NMR spectrum; the product could not be distilled.

Steric factors have a strong influence on the reactivity of the epoxide. Epoxides of cyclohexene, β,β-dicyanostyrene and cinnamic acid methyl ester gave no conversion.

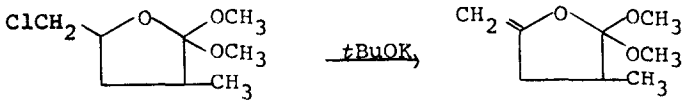
Proton-catalysed hydrolysis of the products 3 gives γ-hydroxy esters 4 after short reaction times at low acid concentration, and γ-butyrolactones 5 after prolonged reaction times at higher acid concentration (Scheme 2; *cf.* ref. 4b).



(2)

3 4 5

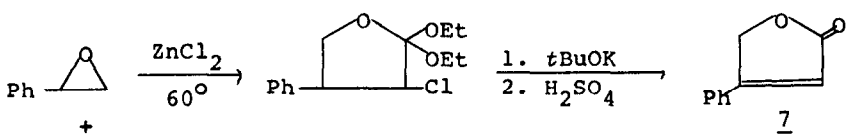
Cyclic orthoesters having R = CH_2Cl can be converted into 5-methylenetetrahydrofurans 6 (Scheme 3). Treatment of 0.04 mol of 3a (R = CH_2Cl, R^1 = R^3 = CH_3, R^2 = H) in 50 ml of diethyl ether with 0.07 mol of *t*BuOK for 3 hrs at room temperature gave after filtration and distillation 2,2'-dimethoxy-3-methyl-5-methylenetetrahydrofuran in 65% yield; b.p. 50°/15 mm, NMR (60 MHz, $CDCl_3$): δ 4.20-4.30 (m, 1H, HC=), 3.75-3.85 (m, 1H, HC=), 3.33 (s, 6H, OCH_3), 2.06-2.95 (m, 3H, H_2C and HC), 1.03 (d, 3H, C-CH_3, J = 6 Hz).



(3)

3a (R = CH_2Cl) 6

Cyclic orthoesters obtained from α-chloroketene acetals (2, R^1 = Cl) can be used in the synthesis of butenolides 7. As the orthoesters can be used without previous purification, the preparation of 7 can be performed as a one pot synthesis. In this way β-phenyl-$\Delta^{\alpha,\beta}$-butenolide was obtained in 55% yield according to Scheme 4; the intermediate 3b (R = Ph, R^1 = Cl, R^2 = H, R^3 = Et), prepared as described before, was heated without previous distillation with *t*BuOK (30% excess) in THF for 1 hr. The solvent was removed *in vacuo*, diethyl ether was added, the ethereal solution was filtered and concentrated, and then added to concentrated H_2SO_4 at 0°. After 15 minutes the mixture was poured onto ice. The butenolide was isolated by extraction with ether and crystallisation from CCl_4; m.p. 93-94° (lit.[5] 93°); NMR (60 MHz, CCl_4): δ 7.37 (s, 5H), 6.24-6.30 (m, 1H, HC=), 5.17 (d, 2H, CH_2O, J = 1 Hz).

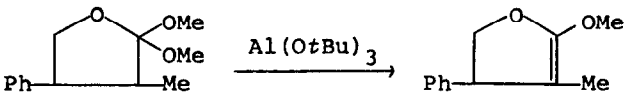


(4)

+

$HCCl{=}C(OEt)_2$

Elimination of alcohol from compounds 3 with aluminium *t*.butoxide, as described for analogous tetrahydropyrans[6] was demonstrated with 3b (R = Ph, R^1 = H, R^2 = R^3 = Me) (Scheme 5).

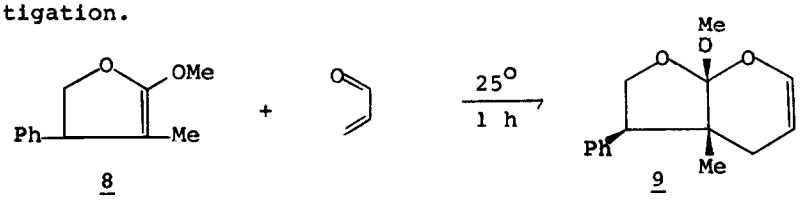


(5)

8

With commercial butoxide the reaction fails[2], giving a γ-butyrolactone (5). However, freshly prepared aluminium *t*.butoxide (free from hydroxyl groups) gave good results.

It was anticipated that the product 8, being a ketene acetal, should be a reactive partner in cycloadditions with electron-poor π-systems. Indeed, with acrylic aldehyde the product (9) was obtained in 1 hr at room temperature (Scheme 6). Further exploration of the chemistry of compounds 8 is under investigation.



8 9

(6)

ACKNOWLEDGEMENT

We wish to thank Prof.Dr. R.J.F. Nivard for helpful discussions and Mr. R. Hofstraat for technical assistance.

REFERENCES

1. Part I is: H.W. Scheeren, R.W.M. Aben, P.H.J. Ooms and R.J.F. Nivard, J. Org. Chem. 42, 3128 (1977).
2. C.B. Chapleo, P. Hallett, B. Lythgoe, I. Waterhouse and P.W. Wright, J.C.S. Perkin I, 1211 (1977); R.J. Cave, B. Lythgoe, D.A. Metcalfe and I. Waterhouse, J.C.S. Perkin I, 1218 (1977).
3. T. Tsujikawa, Y. Nakagawa, K. Tsukamura and K. Masuda, Chem. Pharm. Bull. 25, 2775 (1977).
4. a. Meerwein, P. Borner, O. Fuchs, H.J. Hasse, H. Schrodt and J. Spille, Chem. Ber. 89, 2060 (1956); b. see also: P. Deslongchamps, R. Chênevert, R.J. Taillefer, C. Moreau and J.K. Saunders, Can. J. Chem. 53, 1601 (1975).
5. E.R. Blaut and R.C. Elderfield, J. Org. Chem. 8, 34 (1943).
6. S.M. McElvain and G.R. McKay Jr., J. Amer. Chem. Soc. 77, 5601 (1955).

(Received in UK 22 May 1979)