A New Acetalisation Reagent: Ethyleneorthocarbonate

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Summary Diethylene orthocarbonate (**3**) converts ketones and aldehydes into their corresponding acetals in good yield at room temperature; it is particularly suitable for *ortho*-hydroxyaromatic aldehydes.

WHILST engaged on work directed towards the synthesis of tetracycline[1] we found that known procedures for the conversion of an aldehyde into its corresponding acetal were not satisfactory for the conversion of (**1**) into (**2**). The spiroacetal (**3**) appeared a promising reagent for transacetalisation reactions; our results, reported here, indicate this to be so.

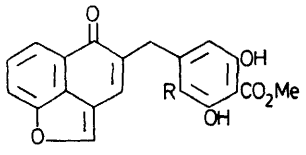
Diethylene orthocarbonate (**3**) is readily available *via* exchange with tetramethyl orthocarbonate[2]–ethylene gly-

TABLE[a]

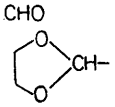
Reaction	Substrate (wt./g)		Amount of (3)/g	Catalyst[b]	Reaction time/h	Product	Yield/%
(a)	(4)	(1)	2·0	(A)	4	(5)[c]	82
(b)	(6)	(0·2)	0·4	(B)	8	(7)[d]	78
(c)	(9)	(0·2)	0·88	(A)	2—3	(10)	74
(d)	(11)	(0·2)	0·7	(B)	1	(12)[e]	79
(e)	(13)	(0·2)	0·7	(B)	1	(14)[f]	78
(f)	(15)	(0·2)	0·7	(A)	3	(16)	73
(g)	(17)	(0·2)	1·0	(B)	0·5	(18)[g]	71
(h)	(1)	(0·2)	1·0	(B)	1	(2)	80
(i)	(1)	(0·7)	1·1	(C)	4·5	(2)	95

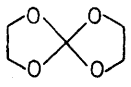
[a] Reactions were conducted in 1 ml of $CHCl_3$, except for reactions (a) (5 ml), (b) (2 ml), (h) (3 ml), and (i) (30 ml), and at room temperature, except for reaction (h) (reflux). [b] (A) = *p*-$MeC_6H_4SO_3H$ (100 mg); (B) = *p*-$MeC_6H_4SO_3H$ (20 mg); (C) = BF_3–Et_2O + H_2O (5% v/v) (35 ml) (anhydrous BF_3–Et_2O gave no reaction). [c] M. Gut, *J. Org. Chem.*, 1956, **21**, 1327. [d] G. B. Spero, J. L. Thompson, B. J. Magerlein, A. R. Henze, H. C. Murry, O. K. Sebek, and J. A. Hogg, *J. Amer. Chem. Soc.*, 1956, **78**, 6213. [e] H. Hibbert and M. Sturrock, *ibid.*, 1928, **50**, 3375. [f] H. E. Baumgarten, D. L. Pederson, and M. W. Hunt, *ibid.*, 1958, **80**, 1977. [g] G. Hesse and M. Förderrenther, *Ber.*, 1960, **93**, 1249.

col–toluene-*p*-sulphonic acid. More conveniently sodium glycolate reacted with CCl_3NO_2 to give compound (**3**) (33%). Other workers have recently described the use of thallium glycolates[3] and tin glycolates[4] to prepare (**3**).

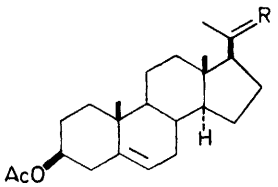


(1) R = CHO

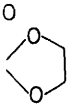
(2) R = 

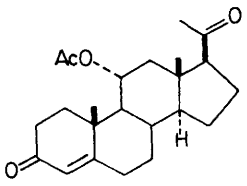


(3)



(4) R = O

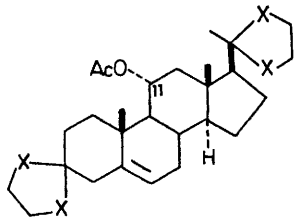
(5) R = 



(6) R = O

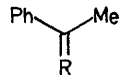
The reagent (**3**) is effective for transacetalisation using toluene-*p*-sulphonic acid catalysis (Table) or slightly wet BF_3–Et_2O. Benzophenone and 2,2,6,6-tetramethylcyclohexanone were not converted into their corresponding acetals under the conditions used for acetophenone.

The structure of the bis-acetal (**7**) of 11α-acetoxyprogesterone (**6**) was established by saponification of the 11α-acetate (MeONa–MeOH) and oxidation (CrO_3,2pyridine, CH_2Cl_2) to the known 11-keto compound,[5] thereby demonstrating the position of the Δ^5 double bond. The known tetrathio-orthocarbonate (**19**)[6] reacted with 11α-acetoxyprogesterone [Table; conditions as for (a)] to give the bis-dithioacetal (**8**) (75%) and could, no doubt, be applied in other cases.

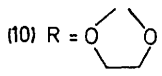


(7) X = O

(8) X = S



(9) R = O

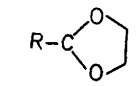
(10) R = 

R-CHO

(11) R = *p*-NO_2•C_6H_4

(13) R = *o*-NO_2•C_6H_4

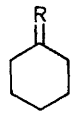
(15) R = *o*-HO•C_6H_4



(12) R = *p*-NO_2•C_6H_4

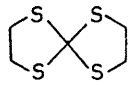
(14) R = *o*-NO_2•C_6H_4

(16) R = *o*-HO•C_6H_4



(17) R = O

(18) R = 



(19)

The diethylene orthocarbonate (**3**) reagent appears particularly useful in preparing *ortho*-hydroxy-acetals of aromatic aldehydes at room temperature under mild conditions.

All new compounds gave satisfactory spectral and microanalytical data.

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