Facile and highly selective monoacylation of symmetric diols adsorbed on silica gel with acetyl chloride

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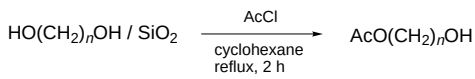
Monoacetylated alcohols of symmetric 1,*n*-diols are synthesized quantitatively by refluxing a suspension of the diols adsorbed on silica gel with acetylchloride.

The application of solid adsorbents such as alumina and silica gel as solid supports in organic synthesis affords a new procedure for selective reactions[1] involving oxidation,[2] alkylation,[3] condensation,[4] acetylation[5] and monomethyl esterification.[6] The significant potential of adsorbents is due to the milder reactions conditions and simpler work-up required and the selective organic transformations that they allow. It is important for organic chemists to develop methods that permit the selective protection or functionalization of one functional group of a bi- or multi-functional molecule. Monoprotection of polyols is achieved in some cases by carefully controlled reaction conditions,[7] continuous extraction,[8] the use of silica gel,[9] alumina,[10] phase-transfer catalysts[11] and insoluble polymer supports,[12] or *via* the formation of cyclic compounds.[13] Protection of hydroxy groups by acylation is common in organic syntheses and here we report the facile and highly selective monoacetylation of symmetric diols with acetyl chloride (AcCl) by use of silica gel.

Acetylation of symmetric diols adsorbed on silica gel was performed *via* the following method (adsorption method) (Scheme 1). Alcohols were adsorbed on silica gel (C-200, Wako Chemicals) as follows: 1 g of silica gel was added to a Et_2O solution of the alcohol; solvent was then eliminated under reduced pressure. The obtained solid (adsorption sample) and AcCl were introduced to 50–100 ml of cyclohexane and refluxed for 2 h. The reaction period of 2 h was sufficient for the reaction to reach completion. After the reaction the mixture was filtered and the solid was washed with distilled water and DMF. The washings plus the filtrate were concentrated, and the products were analyzed by GLC with higher hydrocarbons such as dodecane and heptadecane used as an internal standard. The products were spectrometrically identified *via* comparison with the authentic samples.



Scheme 1

The results of acetylation of symmetric diols are listed in Table 1. According to the adsorption method the monoacetylated products of 1,*n*-diols were quantitatively obtained, while in the case of cyclohexane-1,4-diol the products were obtained in lower yield. Even with a larger amount of decane-1,10-diol in the adsorption sample (3.2×10^{-3} mol g^{-1} SiO_2), the same result (quantitative monoacetylation) was observed. This adsorption method is insensitive to the amount of AcCl added, *e.g.* 2.5–20 equiv. of AcCl were effective for the quantitative formation of the monoacetylated alcohol of decane-1,10-diol.

The dependence of selectivity on reaction temperature was investigated in order to improve the selectivity in the reaction of cyclohexane-1,4-diol, which showed the lowest selectivity. Higher selectivity was observed with a decrease in the temperature. Selectivity was improved to 73% at 0 °C, and to 76% at 0 °C in hexane suspension (Table 2). Silica gel is considered to play a role as a protecting reagent for the counterpart hydroxy group of the symmetric diol, which is presumably adsorbed as a monomolecular layer on the surface of silica gel as in the case of the methylation of decan-1-ol on silica gel with CH_2N_2.[14] This explains why a large excess of AcCl yields only the monoacetylated alcohols of 1,*n*-diols. No further evidence has been obtained at the present time, however, this adsorption method should be applicable to the selective monoprotection or monofunctionalization of polyols.

Table 1 Monoacetylation of symmetric diols adsorbed on silica gel[a]

Substrate	Amount of AcCl[b] (in homogeneous reaction) (equiv.)	Yield (%)		Selectivity[c] (%)	Maximum yield in homogeneous reaction[d] (%)
		monoacetate	diacetate		
Butane-1,4-diol	9.0 (2.0)	99.5	0.0	100	52.3
Hexane-1,6-diol	5.0 (7.0)	99.5	0.0	100	58.6
Octane-1,8-diol	1.2 (7.0)	99.8	0.0	100	54.3
Decane-1,10-diol	2.5 (20.0)	99.8	0.0	100	56.5
Decane-1,10-diol[e]	2.5 (20.0)	98.3	1.7	98.3	56.5
Decane-1,10-diol[f]	3.0 (20.0)	99.0	1.0	99.0	56.5
Dodecane-1,12-diol	3.0 (3.0)	99.9	0.0	100	66.5
Hexadecane-1,16-diol	10.0 (5.0)	99.9	0.0	100	30.2
Cyclohexane-1,4-diol	4.0 (4.2)	29.9	40.8	42.7	32.6
trans-Cyclohexane-1,4-diol	4.0 (7.0)	39.9	30.1	50.1	43.1
Benzene-1,4-dimethanol	3.2 (3.0)	36.0	47.5	74.2	52.5

[a] Each experiment was carried out under reflux in cyclohexane for 2 h. Adsorption sample contains 3.2×10^{-4} mol g^{-1} SiO_2. [b] Minimum amount of AcCl. The same results were observed by the use of AcCl in the amount from the minimum to 20 equiv. [c] The value of [yield of the monoacetylated alcohol/(100 − intract diol)] × 100. [d] 2.5×10^{-2} M solution of diols in DMF in the presence of pyridine (1 equiv.). [e] Gas–solid phase reaction at room temperature in the bsence of cyclohexane solvent. [f] An adsorption sample containing 3.2×10^{-3} mol g^{-1} SiO_2 of the alcohol was used.

Table 2 Dependence of the monoacetylation of 1,4-cyclohexanediol on reaction temperature

	Yield (%)		
T/°C	monoacetate	diacetate	Selectivity[b] (%)
80.2 (reflux)	29.9	40.8	42.7
17.0	54.6	41.6	56.8
0.0	52.4	19.3	73.1
0.0[c]	61.4	19.4	76.0

[a] Adsorption sample of cyclohexane-1,4-diol (3.2×10^{-4} mol g^{-1} SiO_2) was used in cyclohexane suspension with 4.0 equiv. of AcCl. Other conditions as in the main text. [b] The value of [yield of the monoacetylated alcohol/(100 − intact diol)] × 100. [c] In hexane suspension.

Notes and References

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