Pergamon

Tetrahedron Letters, Vol. 38, No. 45, pp. 7867-7870, 1997

0040-4039/97 $17.00 + 0.00

PII: S0040-4039(97)10149-6

Solvent Free Protection of Carbonyl Group under Microwave Irradiation

Bertrand Pério[a], Marie-Joelle Dozias[b], Patrick Jacquault[b] and Jack Hamelin[a]*.

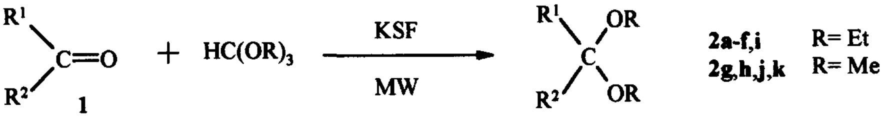
[a] Laboratoire de Synthèse et Electrosynthèse Organiques 3, CNRS et Université Rennes 1,
Campus de Beaulieu 35042 Rennes, France.

[b] Prolabo, 54 rue Roger Salengro, 94126 Fontenay sous Bois, France.

Abstract : Protection of aldehydes and ketones as acetals or dioxolanes catalysed by PTSA or KSF clay was readily achieved from orthoformates, 1,2-ethanediol or 2,2-dimethyl-1,3-dioxolane without solvent under microwave irradiation. © 1997 Elsevier Science Ltd.

Acetal formation is the most widely used protecting method for aldehydes and ketones[1]. This transformation is usually catalysed by Brönsted acids[2]. Nevertheless, some transition metal complexes have been used as Lewis acid catalysts[3] and a significant number of papers reports the efficiency of clays as acidic solid supports[4]. Some other methods use silyl reagents[5] or inorganic catalysts ($FeCl_3$, $TiCl_4$)[6]. Five main types of reagent have been used to protect aldehydes and ketones: alcohols[7], diols[8], orthoesters[9] even acetals[10] and scarcely oxiranes[11]. Owing to our current work on synthesis in dry media with microwave activation[12], we decided to study the protection of various aldehydes and ketones by reacting orthoesters, 1,2-ethanediol and 2,2-dimethyl-1,3-dioxolane without solvent in the presence of acid catalysts under microwave irradiation. The Prolabo (Synthewave® 402)[13] microwave oven allows to irradiate under two modes : either an assigned power with continuous measure of the resulting temperature (by an IR captor) or an assigned temperature with continuous adjustment of the irradiation power. The general procedure is as follow : the carbonyl compound (10 mmol.) was introduced in the reactor of a Synthewave® 402 single mode apparatus followed by the acidic catalyst, *para*-toluene sulfonic acid (PTSA) 10% or montmorillonite clay KSF 1g (10 mmol.) and the reagent (methyl or ethyl orthoformate, 2 eq.; 1,2-ethanediol, 2 eq.; or 2,2-dimethyl-1,3-dioxolane, 3eq.) After irradiation, the product is filtered or washed by a solution of $NaHCO_3$ to remove the catalyst and the product is purified by distillation or recristalization. The results obtained with these various reagents are summarized in the following tables.

Fax: 02-99-28-63-74; e-mail: Jack.Hamelin@univ-rennes1.fr



1a: $R^1 = C_6H_5(CH_2)_2$; $R^2 = H$
1b: $R^1 = nC_3H_7$; $R^2 = H$
1c: $R^1 = C_6H_5CH{=}CH$; $R^2 = H$
1d: $R^1 = C_6H_5$; $R^2 = H$
1e: $R^1 = 4\text{-}NO_2C_6H_5$; $R^2 = H$
1f: R^1 = 3,4-methylenedioxyphenyl; $R^2 = H$

1g: $R^1 = C_6H_5$; $R^2 = CH_3$
1h: $R^1 = C_6H_5$; $R^2 = C_6H_5$
1i: R^1,R^2 = cyclohexyl
1j: $R^1 = C_6H_5CH{=}CH$; $R^2 = CH_3$
1k: R^1 = *iso*butyl; $R^2 = CH_3$

Scheme 1

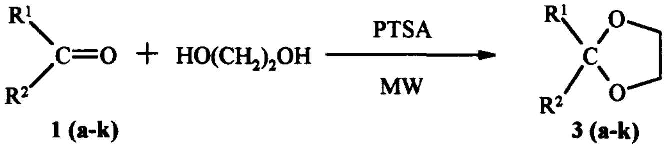
Table 1: Acetal Synthesis from Orthoesters.

Product	**2a**	**2b**	**2c**	**2d**	**2e**	**2f**	**2g**	**2h**	**2i**	**2j**	**2k**
Temp. (°C)[a]	80	65	75	60	90[b]	70	70[b]	135	75	70[b]	70[b]
Time (min.)	2	2	1	2	2	2	10	1,5	2	10	10
% completion[c]	100	100	100	100	100	100	90	0	100	0	90
% Yield[d]	93	91	74	86	97	95	82	0	91	0	73

[a] temperature reached at a power of 150 W. [b] temperature assigned for the experiment and monitored by the computer.
[c] completion estimated by ^1H NMR. [d] isolated product, purified by distillation or recrystallization.

Some of these acetals have been already prepared with a large excess of orthoformate over K10[3d] or with a mixture of orthoformate and alcohol over KSF[4a].

Then we studied the formation of dioxolanes directly from 1,2-ethanediol catalysed by PTSA.



Scheme 2

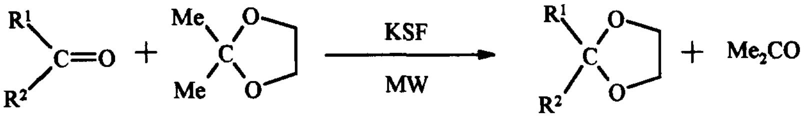
Table 2: Synthesis of Dioxolanes from 1,2-ethanediol.

Product	**3a**	**3b**	**3c**	**3d**	**3e**	**3f**	**3g**	**3h**	**3i**	**3j**	**3k**
Temp. (°C)[a]	110	100	100	120[b]	120	120	120	120	120	120	100
Time (min.)	30	10	10	30	30	30	30	30	30	30	30
% completion	100	0	30	63	100	75	20	0	85	22	15
% Yield	78	0[c]	23[c]	51	93	59	13	0	72	17[c]	9

[a] unless otherwise stated the temperature is monitored with a maximum emitted power of 120 W. [b] maximum power 150 W.
[c] polymerization of the mixture.

In this case we can see that, depending on the carbonyl compound, the yields may be good (**1a**, **1e**, **1i**) or poor for less reactive or polymerizable compounds (**1b**, **1c**, **1j**, **1k**).

Then we studied the protection by dioxolane exchange with 2,2-dimethyl-1,3-dioxolane (DMD).



1 (a-k) (DMD) **3 (a-k)**

Scheme 3

As may be seen in Table 3 this procedure is the best one to prepare dioxolanes in good yields and very short time (10 to 30 minutes), the best catalyst being montmorillonite clay KSF.

Table 3: Dioxolane Exchange.

Product	**3a**	**3b**	**3c**	**3d**	**3e**	**3f**	**3g**	**3h**	**3i**	**3j**	**3k**
Temp. (°C)[a]	80[b]	105	120[b]	135	120[b]	120[b]	120[b]	120[b]	110	110	110
Time (min.)	10	15	15	15	10	15	15	30	15	30	30
% completion	100	100	100	100	100	100	95	45	100	90	100
% Yield	82	88	85	88	95	93	87	38	92	82	93

[a] unless otherwise stated the maximum power is 120 W. [b] monitored temperature.

It is noteworthy that in this case even benzophenone **1h** which is known to be unreactive[3c,9a] may be protected.

Finally we choose some examples to compare classical heating in an oil bath (OB) previously set at the temperature monitored in the microwave oven (MW). The results are summarized in Table 4.

Table 4: Classical or Microwave Heating with DMD (3 eq.).

Product	MW Temp (°C) Time (min.)	Oil Bath Temp. (°C) Time (min.)	% completion MW / OB	**3** % Yield MW / OB
1d	135[a] / 15	130[b] / 15	100 / 90	88 / 77
1g	120[c] / 15	130 / 15	95 / 35	95 / 31
1h	120[c] / 30	130 / 30	47 / 35	38 / 29

[a] temperature for 120 W emitted power. [b] temperature of the oil bath. [c] monitored temperature.

It may be concluded that the best way to prepare dioxolanes is the exchange method and the best activation process is microwave irradiation.

Acknowledgements : One of us (B.P.) wishes to thank Agence de l'Environnement et de la Maîtrise de l'Energie and Prolabo for a research fellowship.

References

1. a) Greene, T.W.; Wuts, P.G.M. *Protective Groups in Organic Synthesis*; John Wiley and Sons, Inc.: New York, **1991**, pp. 188-191. b) Kocienski, P.J. *Protecting Groups*; Thieme, **1994**, pp. 156-170
2. a) Verevkin, S.P.; Dogan, B.; Hädrich, J.; Beckhaus, H.D.; Rüchardt, C. *J. Prakt. Chem.* **1995**, *337*, 93-98. b) Byrne, B.; Wengenroth, K.J. *Synthesis* **1986**, *10*, 870-871
3. a) Lipschutz, B.H.; Pollart, D.; Monforte, J.; Kotsuki, H. *Tetrahedron Lett.* **1985**, *26*, 705-708. b) Hoffman, R.V. *Tetrahedron Lett.* **1974**, *28*, 2415-2416. c) Ott, J.; Ramos Tombo, G.M.; Schmid, B.; Venanzi, L.M.; Wang, G.; Ward, T.R. *Tetrahedron Lett.* **1989**, *30*, 6151-6154
4. a) Cabrera, A.; Vazquez, D.; Velasco, L.; Salmon, M. *J. Mol. Catal.* **1992**, *75*, 101-107. b) Kamitori, Y.; Hojo, M.; Masuda, R.; Yoshida, T. *Tetrahedron Lett.* **1985**, *26*, 4767-4770. c) Li, T.S.; Li, S.H.; Li, J.T.; Li, H.Z. *J. Chem. Res. (S)* **1997**, 26-27. d) Taylor, E.C.; Chiang, C.S. *Synthesis* **1977**, 467
5. a) Tsunoda, T.; Suzuki, M.; Noyori, R. *Tetrahedron Lett.* **1980**, *21*, 1357-1358. b) Kim, S.; Kim, Y.G.; Kim, D. *Tetrahedron Lett.* **1992**, *33*, 2565-2566. c) Lillie, B.M.; Avery, M.A. *Tetrahedron Lett.* **1994**, *35*, 969-972
6. a) Moghaddam, F.M.; Sharifi, A. *Synth. Commun.* **1995**, *25*, 2457-2461. b) Lu, T.; Yang, J.; Sheu, L. *J. Org. Chem.* **1995**, *60*, 2931-2934
7. a) Thuy, V.M.; Maitte, P. *Bull. Soc. Chim. Fr.* **1975**, 2558-2560. b) Gora, J.; Smigielski, K.; Kula, J. *Synthesis* **1986**, *7*, 586-588
8. a) Tamai, Y.; Hagiwara, H.; Uda, H. *J. Chem. Soc., Perkin Trans. 1* **1986**, 1311-1315. b) Chavez, F.; Suarez, S.; Diaz, M.A. *Synth. Commun.* **1994**, *24*, 2325-2329. c) Kumar, T.P.; Reddy, K.R.; Reddy, R.S. *J. Chem. Res. (S)* **1994**, 394-395. d) Patney, H.K. *Tetrahedron Lett.* **1991**, *32*, 413-416. e) Dauben, W.G.; Gerdes, J.M.; Look, G.C. *J. Org. Chem.* **1986**, *51*, 4964-4970
9. a) Ishihara, K.; Karumi, Y.; Kubota, M.; Yamamoto, H. *Synlett* **1996**, 839-841. b) Patwardhan, S.A.; Dev, S. *Synthesis* **1974**, 348-349
10. a) Dauben, J.; Löken, B.; Ringold, H.J. *J. Am. Chem. Soc.* **1954**, *76*, 1359. b) Barton, D.H.R.; Darres, C.C.; Magnus, P.D. *J. Chem. Soc., Chem. Commun.* **1975**, 432-433. c) Bauduin, G.; Pietrasanta, Y. *Tetrahedron* **1973**, *29*, 4225-4231. d) Smith, A.B.; Mewshaw, R. *J. Org. Chem.* **1984**, *49*, 3685-3689. e) Pilar Bosch, M.; Camps, F.; Coll, J.; Guerrero, A.; Tatsuoka, T.; Meinwald, J. *J. Org. Chem.*, **1986**, *51*, 773-784. f) Paquette, L.A.; Sauer, D.R.; Cleary, D.G.; Kinsella, M.A.; Blackwell, C.M.; Anderson, L.G. *J. Am. Chem. Soc.* **1192**, *114*, 7375-7387
11. a) Torok, D.S.; Figueroa, J.J.; Scott, W.J. *J. Org. Chem.* **1993**, *58*, 7274-7276. b) Nagata, T.; Takai, T.; Yamada, T.; Imagawa, K.; Mukaiyama, T. *Bull. Chem. Soc. Jpn.* **1994**, *67*, 2614-2616
12. Jolivet-Fouchet, S.; Hamelin, J.; Texier-Boullet, F.; Toupet, L.; Jacquault, P. *Tetrahedron* **1997**, submitted, and references cited
13. Commarnot, R.; Didenot, R.; Gardais, J.F.; Fr Demande, 2560529 (Cl. B01J19/12), 06 Sept. 1985, Appl. 84/3,496, 02 Mar. 1984 (*Chem. Abstr.*, **1986**, *105*: 17442e). Temperature measured by an IR captor : Prolabo, Fr. Pat. 62241D, 14669Fr, 23 Dec. 1991

(*Received in France* 16 *July* 1997; *accepted* 12 *September* 1997)