Anionic Activation on Solid Inorganic Supports: Malonic Ester Syntheses

By GEORGES BRAM and TAUQIR FILLEBEEN-KHAN
(*Groupe de Recherches No.* 12, *C.N.R.S.*, 2—8, *rue Henri-Dunant*, 94320 *Thiais, France*)

Summary Malonic ester anions are generated on 'basic' inorganic solid supports (alumina and silica gels) where they undergo either intra- or inter-molecular alkylations selectively and in high yield.

SOLID inorganic supports have been increasingly used in synthetic organic chemistry recently.[1] Reactions on such supports often involve milder conditions, easier work-up, and higher selectivity than analogous reactions in solution, but they have been mainly limited to oxidations,[1–3] reductions,[4,5] eliminations,[1,6] and additions.[7] Recently Keinan and Mazur[8] have reported the conversion of a nitro group into a carbonyl group (Nef reaction) on 'basic'[8] silica gel; thus they have suggested that it is possible, by adsorption of a nitro compound, to generate a nitronate anion which leads to a carbonyl derivative.

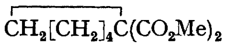
Until now, there have been very few reports of anionic activation on solid inorganic supports leading to C–C bond formation.[9] We therefore studied anionic condensations on solid inorganic supports and intermolecular (Table 1) and intramolecular (Table 2) malonic ester syntheses on alumina and silica gels which had been made 'basic' using Mazur's method.[8] The simplicity of the experimental procedure is illustrated by the following typical example (expt. 2): 1·30 g of the malonic ester (**1**) was mixed with 30 g of 'basic' alumina (containing 1 equiv. of MeONa per kg of alumina) followed by the addition of 2·88 g of 1,5-dibromopentane (**2**). The reactants adsorbed on the solid support were mixed thoroughly for *ca.* 2 min and left at room temperature for 72 h with occasional shaking. Elution with CH_2Cl_2 gave 43% (v.p.c.) of the product (**3**) and unchanged starting materials were also recovered.

It is significant that when the same reaction was carried out in the absence of sodium methoxide, no products could be detected after 3 days. Therefore it is appropriate to assume that malonic ester anions are generated on the basic support and subsequently react with the electrophile.

$CH_2(CO_2Me)_2$
(**1**)

$Br[CH_2]_5Br$
(**2**)

$Br[CH_2]_5CH(CO_2Me)_2$
(**3**)


$CH_2[CH_2]_4C(CO_2Me)_2$
(**4**)

$(MeCO_2)_2CH[CH_2]_5CH(CO_2Me)_2$
(**5**)

TABLE 1. Intermolecular condensation of (**1**) + (**2**)

Expt.	Support	Base/ Support (mol/kg)	Reactants/ Base (mol ratios)	Time days	% (**3**)	Yield (**4**)
1	Al_2O_3[a]	1	1:1:1	2	27	—
2	,,	1	1:1:3	3	43	—
3	,,	1·7	1:1:13	8	—	27
4	SiO_2[b]	1·5	1:1:5	12	28	—
5	SiO_2[c]	1·7	1:1:5·6	13	52	—
6	SiO_2[d]	1·5	1:1:5	13	—	—

[a] Aluminium oxide 90 (Merck), 70—230 mesh. [b] Silica 'Spherosil' XOA 400 (Rhône–Poulenc), >350 mesh. [c] Silica 'Spherosil' XOB 030 (Rhône–Poulenc), 70—150 mesh,. [d] Silica gel 60 (Merck), 70—230 mesh.

These reactions not only give very good yields of product but also have the advantage of being highly selective in comparison with the analogous reactions in solution; thus the condensation of (**1**) and (**2**) on 'basic' alumina (Merck) or 'Spherosil' silica gels (Rhone–Poulenc) leads exclusively to the product (**3**) (Table 1, expts. 1, 2, 4, 5) without any trace of the by-products (**4**) and (**5**) which are formed when the reaction is carried out in solution[10]). However, (Table 1, expt. 3) if the ratio MeONa/alumina is increased, only the cyclised product (**4**) is observed, *i.e.* a double condensation takes place. Similarly, when (**3**) is allowed to react on 'basic' alumina (Table 2, expt. 9) the cyclised product (**4**) is obtained in quantitative yield (yields of 50—69% have been reported for this reaction in solution[10–12]). The specificity of support is of interest; alumina appears to be the preferred support for the intramolecular cyclisation (**3**) → (**4**) whereas for the inter-

TABLE 2. Intramolecular condensation of (**3**)

Expt.	Support	Base/ Support (mol/kg)	Reactant/ Base (mol ratios)	Time days	% Yield (**4**)
7	Al_2O_3^{a}	0·4	1:0·5	2	7
8	,,	0·4	1:1	3	14
9	,,	1	1:4	1	100
10	SiO_2^{b}	1·5	1:4	4	5
11	SiO_2^{d}	1·5	1:4	8	4

[a,b,d] See footnotes, Table 1.

molecular condensation (**1**) + (**2**) → (**3**) some 'Spherosil' silica gels give results comparable to those obtained on alumina.

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[1] G. H. Posner, *Angew. Chem. Internat. Edn.*, 1978, **17**, 487 and references therein.

[2] E. Santaniello, F. Ponti, and A. Manzocchi, *Synthesis*, 1978, 534 and references therein.

[3] J. San Filippo and Chueng-Ing Chern, *J. Org. Chem.*, 1977, **42**, 2182.

[4] E. Santaniello, F. Ponti, and A. Manzocchi, *Synthesis*, 1978, 891.

[5] N. Y. Fung, P. de Mayo, J. H. Schauble, and A. C. Weedon, *J. Org. Chem.*, 1978, **43**, 3977.

[6] E. Keinan and Y. Mazur, *J. Org. Chem.*, 1978, **43**, 1020.

[7] P. A. Risbood and D. M. Ruthven, *J. Amer. Chem. Soc.*, 1978, **100**, 4919.

[8] E. Keinan and Y. Mazur, *J. Amer. Chem. Soc.*, 1977, **99**, 3861.

[9] (a) S. L. Regen and C. Koteel, *J. Amer. Chem. Soc.*, 1977, **99**, 3837; (b) J. H. Clark, *J.C.S. Chem. Comm.*, 1978, 789; (c) for use of polymeric organic solid supports for anionic activation see G. Gelbard and S. Colonna, *Synthesis*, 1977, 113, and S. Colonna, A. Re, G. Gelbard, and E. Cesarotti, *J.C.S. Perkin II*, 1979 in the press.

[10] V. P. Golmov, *J. Gen. Chem.* (*U.S.S.R.*), 1952, **22**, 1993.

[11] J. I. G. Cadogan, D. H. Hey, and S. H. Ong, *J. Chem. Soc.*, 1965, 1932.

[12] G. Nee, Thesis, Paris, 1978.