Tetrahedron Letters, Vol.29, No.18, pp 2261-2264, 1988 0040-4039/88 $3.00 + .00
Printed in Great Britain Pergamon Press plc

SILICA GEL FUNCTIONALIZED WITH AMINO GROUPS AS A NEW CATALYST FOR KNOEVENAGEL CONDENSATION UNDER HETEROGENEOUS CATALYSIS CONDITIONS

Enrico Angeletti, Carlo Canepa, Giovanni Martinetti,[1] and Paolo Venturello*
Istituto di Chimica Organica dell'Universita'
Via G. Bidone, 36 - 10125 Torino, Italy -

Knoevenagel condensation has been carried out under heterogeneous catalysis conditions using amino groups immobilized on silica gel: the results show that the catalytic support is recoverable without regeneration, and that the matrix probably participates to the catalysis mechanism.

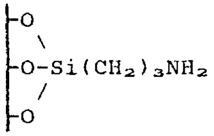
The Knoevenagel reaction[2] continues to be of importance in organic synthesis in order to convert carbonyl groups into alkenes under mild conditions.

Usually ammonia and ammonium salts, primary and secondary amines and their salts are used as catalysts in Knoevenagel condensation. Some works report the use of weak and strong ion exchange resins;[3] in the last years the use of insoluble catalysts, as Al_2O_3,[4] Al_2O_3-$AlPO_4$,[5] dopped Xonotlite,[6] and molecular sieves,[7] has been reported.

The use of insoluble catalysts allows easy work up of the reaction mixture, from which the products can be isolated by filtration, easy recovery of the catalyst and the conduction of the reaction under continuous flow, when the reaction is fast enough.[8]

We want to report here the use of a new catalyst for the Knoevenagel condensation, which allows to work in continuous flow conditions at room temperature.

The catalyst we used was silica gel functionalized with amino groups:

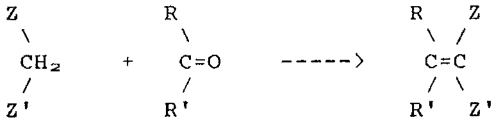


$$(\text{--O})_3Si(CH_2)_3NH_2$$

I

obtained by reaction of silica gel with (3-aminopropyl)- trimethoxysilane. The titer of the organofunctionalized silica gel was 0.79 mequiv. NH_2 g^{-1}, and was established from the weight increase.

The results obtained with different carbonyl compounds and different methylene active compounds according to equation 1 are reported in the Table.



$$\mathrm{Z(Z')CH_2} + \mathrm{RR'C{=}O} \longrightarrow \mathrm{RR'C{=}CZZ'} \tag{1}$$

Table. Knoevenagel Condensation with Amino Groups Immobilized on Silica Gel.

	Carbonyl Comp.	Methylene Active Comp.	Cat.	Conversion (%)[b]	Yield (%)[c]
1	Benzaldehyde	Ethyl acetoacetate	I	81	
2	Benzaldehyde	Acetylacetone	I	41	
3	Benzaldehyde	Ethyl cyanoacetate	I	100	98[d]
4	Benzaldehyde	Malononitrile	I	100	91[d]
5	Benzaldehyde	Malononitrile	I	100	90[e]
6	Anisaldehyde	Malononitrile	I	100	84[d]
7	Cinnamaldehyde	Ethyl acetoacetate[f]	I	75	72
8	Cinnamaldehyde	Malononitrile[f]	I	100	67
9	Cyclohexanone	Ethyl cyanoacetate	I	86	66
10	Benzaldehyde	Ethyl cyanoacetate[g]	I	100	96[d]
11	Benzaldehyde	Ethyl cyanoacetate[h]	SiO_2	0	

Experimental Conditions: catalyst, 10.0 g; carbonyl compound, 0.01 moles; methylene active compound, 0.01 moles; T = 25 °C; solvent, toluene, if not otherwise indicated. [b] Referred to the reacted carbonyl compound. [c] From the weight of the recovered reaction mixture, on the basis of the conversion, if not otherwise indicated. [d] Isolated product. [e] Referred to a catalytic bed used six times after the recovery from Entry 4. [f] No bis-addiction products were detected. [g] Reaction carried out with 5.0 g of catalyst I and 0.02 moles of the reagents. [h] Reaction carried out according to footnote[a], using unfunctionalized silica gel as a catalyst.

The reaction is performed in a vertical double jacket glass column (30 cm in length, 2 cm in diameter) thermostatted at 25 °C, that contains the catalytic support. The reagents mixture flows through the catalytic bed as in a liquid chromatographic process.[9] The product is collected at the column outlet and recovered after the evaporation of the solvent: the catalyst remains in the column, allowing to avoid separation from the reaction products. The catalytic support can be reused many times without regeneration, since it is still active even after several reactions.

The data show that: *a*) the obtained conversions are similar either to those reported for condensations in homogeneous conditions, or to those conducted in the absence of solvent with insoluble catalysts; *b*) even after many runs the activity of the catalyst remains unchanged (compare entries 4 and 5); *c*) no Michael addition product was detected neither in the case of cynnamaldehyde (entries 7 and 8); *d*) systems I is active also in catalytic amount (entry 10); *e*) with cyclohexanone the conversion resembles those obtained with aromatic aldehydes (entry 9); *f*) the unfunctionalized silica gel is not able to catalyze the condensation (entry 11).

We think that the catalytic process involves either the immobilized amino groups, or the residual silanolic groups on the silica gel surface. The former extract a proton from the methylene active compound, as in the classic mechanism of the Knoevenagel condensation, while the latter could activate the carbonyl group through a hydrogen bond -Si-OH···O=C, and also partially protonate the aldolic intermediate; in such a way the matrix would activate the dehydration.

The matrix influence is also proved by the low reactivity of acetylacetone (entry 2), that is not in accordance with the trend of the pK_a of the active methylene compounds used in this work.[10] It was actually reported that on a silica gel surface, acetylacetone is preferentially adsorbed in its enolic form,[11] which is unreactive in the condensation reaction.

Acknowledgments.

This work was supported by the Ministero della Pubblica Istruzione.

References and notes.

1. Abstracted from the Thesis dissertation of G. Martinetti. Universita di Torino, 1987.
2. For a review see: G. Jones, *Organic React.*, 1967, 15, 204.
3. (*a*) M. J. Astle and J. A. Zaslowsky, *Ind. Eng. Chem.*, 1952, 44, 2871; (*b*) M. J. Astle and W. C. Gergel, *J. Org. Chem.*, 1956, 21, 493; (*c*) M. J. Astle and F. P. Abbot, *J. Org. Chem.*, 1956, 21, 1228; (*d*) R. W. Heine, M. J. Astle, and J. R. Shelton, *J. Org. Chem.*, 1961, 26, 4874.
4. F. Texier-Boulett and A. Foucod, *Tetrahedron Lett.*, 1982, 4927.
5. J. A. Cabello, J. M. Campelo, A. Garcia, D. Luna, and J. M. Marinas, *J. Org. Chem.*, 1984, 49, 5195.
6. S. Chalais, P. Laszlo, and A. Mathy, *Tetrahedron Lett.*, 1985, 4453.
7. G. A. Taylor, *J. Chem. Soc., Perkin Trans.I,* 1981, 3132.
8. *(a)* P. Hodge, D. C. Sherrington, 'Polymer Supported Reaction in Organic Synthesis,' Wiley,Chichester, 1980; *(b)* A. Akelah and D. C. Sherrington, *Chem. Rev.*,1981, 81, 557; *Polymer*, 1983,24, 1369.
9. The reaction product begins to be collected ca. 5 min after the introduction of the reagents into the column, and ca. 250 ml of solvent are used for the complete recovery.
10. The pk_a of acetylacetone, ethyl cyanoacetate, ethyl acetoacetate, and malononitrile are, 9.0, >9, 10.7, and 11.2 respectively; from R. G. Pearson and R. L. Dillon, *J. Am. Chem. Soc.*, 1953, 75, 2439.
11. R. K. Iler, 'The Chemistry of Silica,' Wiley-Interscience, New York, 1979, p. 649, chap.6.

(Received in UK 12 February 1988)