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STEREOSELECTIVITY OF A POLYMER SUPPORTED REACTION

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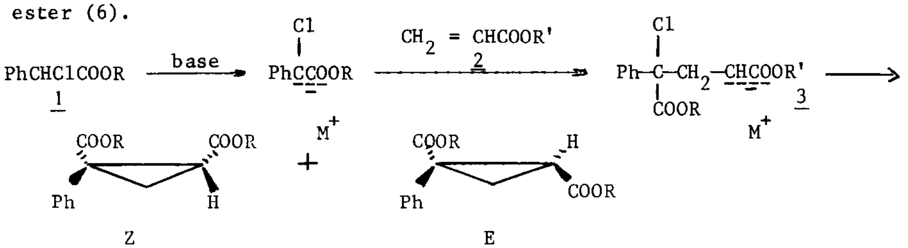
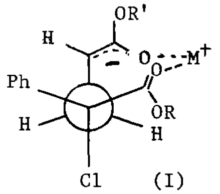
Abstract : the substitution of Cl by $PhCH_2 - CO_2 -$ *and* $CH_2 = CH - CO_2 -$ *in a soluble chloromethylated polystyrene leads to polymer supported esters which were used for the preparation of cyclopropyl derivatives. For the first time at our knowledge, a reaction was performed between two functionalized polymers. The polymer backbone effect on the reaction with one or two bound reagents is not large, and it depends on the temperature.*

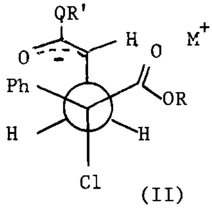
Insoluble polymer supports such as Merrifield resins were widely used in organic synthesis (1-3). Differences between the reactivity of polymer reagents and analogous small molecules were observed before (4-5). However, to our knowledge, a polymer effect on the stereoselectivity of a reaction with supported reagents was not yet studied. For this purpose, we chose to study the stereoselectivity of the cyclopropane formation from an α halo- ster and an acrylic ester (6).



The stereochemistry determining step is the cyclization of the intermediate 3 (7), the formation of which is irreversible (8). There are two favoured conformations of the carbanionic intermediate 3 (I) and (II), which lead respectively to Z and E isomers.



(I)



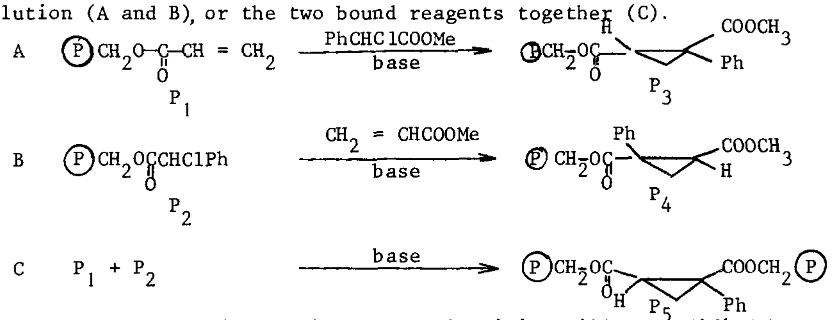
(II)

The Z/E ratio depends on solvent nature, association degree between anionic species and cations, and steric interactions (7) :

- the decrease of solvent polarity and donor number, or the cationic bridge formation with metal cation such as Li^+ in conformation (I), favours the Z isomer.

- steric strains between two big carbalkoxy groups are minimized in the conformation (II) which leads to E isomer.

In order to show up the polymer effect we bound acrylic or phenylchloracetic group on a polymer (P_1 or P_2), and we condensed either one of these two bound reagents with the other one in solution (A and B), or the two bound reagents together (C).



It may be expected that the stereoselectivity will be modified because of steric interactions due to the chain backbone and, in the neighbourhood of the reagents, to a polar environment quite different from the pure solvent (5).

Reactions on polymer

We used first a partly chloromethylated soluble polymer : ⓅCH_2Cl: 34.10^{-3} equiv.Cl/g Such a polymer allowed us to follow the different steps of functionalization to obtain P_1 and P_2, by ^1H-NMR and ^{13}C-NMR spectroscopy. Thus, it is possible to see side reactions which give by-products or reticulation of the polymer, and to avoid them by convenient conditions.

The condensations were performed with two cations, Li^+ and K^+, in the same solvent, THF, and with the same cation K^+, in various solvents : THF/DMSO (3%), THF/DMSO (3%)/ DMF (40%).

The choice of the bases was determined by their compatibilities with these solvent mixtures (9).

In order to avoid the acrylic ester polymerization by anionic initiators (10) and the self condensation of the phenylchloracetic anion, one condenses the preformed anion with the acrylic derivative at -60°C by the way A and at -5°C by the ways B or C. (11).
(3%)/DMF (40%). The cyclopropanes are cleaved from the polymers, P_3 P_4 and P_5, by reduction with $LiAlH_4$ in THF. A mixture of hydroxylated polymer, ⓅCH_2OH, and cyclopropanic diols is obtained. The Z/E ratio is determined by G.L.C after acylation.

Reactions with low molecular weight reagents

The condensations from PhCHClCOOMe and CH_2 = CHCOOMe are carried out in the same conditions of solvent, base and temperature as from polymer reagents.

Results and discussion :

Temperature effect.

In the table, we see that the stereoselectivities obtained from P_1 at -60°C and P_2 at -5°C with K^+ as cation are different (12). We showed on one example (THF-DMSO (3%)-Ph_3CK) that, at -5°C, P_1 and P_2 gave the same result. Thus, the observed differences are not due to the nature of the bound reagent.

There is no temperature effect with the monomers.

We can conclude that the observed differences of stereoselectivity with the temperature are only due to the polymer backbone.

We think that they are probably a consequence of a variation of the entropy value : at a low temperature the polymer mobility is lessened and, in the cyclization step, this fact favours intermediate 3 the most organized around the cation, which leads to Z isomer. When the cation is Li^+, the temperature effect disappears because this small cation is sufficient to orientate the cyclization by itself.

Steric effect

The same stereoselectivity is observed either from one bound reagent (P_1 or P_2) and the other one in solution, or from the two bound reagents (P_1+P_2). It seems that, in the cyclization transition state, no steric interaction exits between either the carbalkoxygroup bound to the polymer (R' = CH_2Ⓟ, R = CH_3) and the phenyl group in the conformation (II), or the two carbalkoxy groups bound to the polymer (R = R' = CH_2Ⓟ) in the conformation (I). We think that , from a chloromethylated polymer, the functional group is too far from the polymer backbone to induce a steric hindrance very different of the monomer one.

Cation and solvents effects

Cation effect is similar with bound and no bound reagents : the Z/E ratio decreases from Li^+ to K^+, and with solvation of K^+ by good electron donor solvents.
It is observed that with K^+ the Z/E ratio is always slightly higher with bound reagents even in a highly polar medium.

It seems that the polymer contributes to the effective medium polarity around the bound reagents,by decreasing it. It has a similar behaviour as toluene in the case of monomers

Z/E RATIO FOR BOUND AND NO BOUND REAGENTS

Reagents (13)	Ph_3CLi THF	t.buOK Toluène	$[Me_3Si]_2NK$ THF	Ph_3CK THF/DMSO (3%)**	Ph_3CK THF/DMSO (3%)/ DMF(40%)
Ⓟ$CH_2OCOCH = CH_2$ P_1 at -60°	95/5		81/19	65/35 53/47 *	55/45
Ⓟ$CH_2OCOCHClPh$ P_2 at - 5°C	95/5		74/26	54/46	48/52
P_1 + P_2 at -5°C				55/45	49/51
Monomers -60°				61/39	39/61
Monomers -5°				59/41	39/61
Monomers 20°	95/5	74/26	67/33	60/40	41/59

* The reaction is performed at -5°C.
** % in volumes.

Conclusion

This preliminary study with a partly chloromethylated soluble polymer allowed us to show that no steric effect occurred even by condensing the two bound reagents together. Elsewhere, the polymer induces a temperature effect and a solvent effect. The influence of the polymer is the greatest one at low temperature . On a soluble polymer, these effects are small and we hope to precise and to increase them by using cross-linked polymers and by changing the polymer backbone.

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9) In THF we used Ph_3CLi and $[Me_3Si]_2NK$ instead of Ph_3CK. The preparation of this last base involves the use of one molar equivalent of DMSO at least, whereas $[Me_3Si]_2NK$ can be obtained in pure THF.

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12) The results are reproductible : the error in each isomer ratio is about 1 to 2%.

13) a) Chloromethylated polystyrene is obtained from styrene (0,52mole), vinylbenzylchloride (0,30mole), azobis-isobutyronitrile (0,0061mole), in toluene. The monomers represent 20% by weight of the reaction mixture.
$(ClCH_2 - C_6H_4 - \overset{|}{C}H - CH_2)_x \quad (C_6H_5 - \overset{|}{C}H - CH_2)_y$: $x = 1$, $y = 1,4$
Cl : 12,03% or $3,4 \times 10^{-3}$ equiv/g.
b) Microanalytical results show that functionalization of ⓅCH_2Cl to P_1 and P_2 is quantitative.
c) Osmometric M_n values : ⓅCH_2Cl: 16000 ± 400; Ⓟ$CH_2O - CO - CH = CH_2$: 25250 ± 250;
Ⓟ$CH_2O - CO - CHCl - Ph$: 17250

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