(benzene elution) to yield 0.61 g (31%) of a solid. The solid was recrystallized from benzene–hexanes to give 0.57 g (29%) of cyclophane **3**: mp 140–141.5 °C; ^{1}H NMR ($CDCl_3$) δ 6.94 (s, 4 H), 3.58 (s, 4 H), 2.33 (d, J = 20 Hz, 4 H), 1.65–0.95 (br, 8 H), and 0.45 (br t, 2 H); ν_{max} (KBr) 3200, 1500, 1460, 1445, 1410, 840, 830, and 715 cm^{-1}; mass spectrum, m/e 278 (M^+).

Anal. Calcd for $C_{16}H_{22}S_2$: C, 69.01; H, 7.96; S, 23.03. Found: C, 68.81; H, 8.14; S, 22.82.

X-ray Structural Analysis. $C_{12}H_{22}S_2$, M_r = 278.5, monoclinic space group $P2_1/c$, a = 11.749 (3), b = 7.959 (2), c = 16.097 (4) Å, β = 100.72 (1)°, V = 1479 A^3, Z = 4, d_{calcd} = 1.25 g cm^{-3}. The unit cell was obtained by a least–squares treatment of 14 reflections with 2θ values above 66°, using λ for Cu $K\alpha_1$ of 1.5404 Å. A θ–2θ scan using Ni-filtered Cu K_α (λ = 1.5418 Å) X-rays, 2° (1 min) scans, 10-s stationary backgrounds, and manual data collection procedures with a GE XRD-5 diffractometer gave 1628 observed reflections out of 1857 scanned to the limit of 110° in 2θ. The absorption correction (μ = 29.66 cm^{-1}) ranged from 0.66 to 0.91. The structure was solved by symbolic addition and Fourier methods. The final full-matrix least-squares refinement included positional and anisotropic thermal parameters for the C and S atoms and positional parameters for the H atoms; the standard deviation of an observation of unit weight was 0.73, the largest peak on the final difference map was 0.26 e/Å^3, the weighting scheme was without bias, and the final R was 0.055. Additonal derived parameters are contained in the supplementary material.

Acknowledgment. The mass spectrometer was obtained with the aid of a grant from the National Science Foundation.

Registry No. **1**, 623-25-6; *cis*-**2**, 78307-98-9; *cis*-**3**, 78307-99-0; *cis*-**4**, 15898-77-8; *cis*-**5**, 78328-73-1; *cis*-1,4-bis(hydroxymethyl)cyclohexane, 3236-47-3; *trans*-1,4-bis(hydroxymethyl)cyclohexane, 3236-48-4; **6**, 35541-78-7.

Supplementary Material Available: Tables I–VI listing crystal data, fractional coordinates, temperature factors, bond distances, bond angles, best planes data, and torsion angles for $C_{16}H_{22}S_2$ (6 pages). Ordering information is given on any current masthead page.

Communications

Acylations and Alkylations of an Ester Enolate in High Yield at Room Temperature on Polystyrene Supports[1]

Summary: Polymer-bound esters of 3-phenylpropanoic acid are converted to enolates at room temperature and acylated and alkylated in 73–87% isolated yields with little or no self-condensation of ester.

Sir: Insoluble polymeric supports enable separations of synthetic reaction mixtures by simple filtration.[2] They permit use of large excesses of reagents in peptide syntheses to drive the coupling reactions to completion[3] and provide easy separation of troublesome byproducts from reaction mixtures. Another advantage of polymeric supports sometimes cited is "site isolation" by which supposedly rigid polymer chains prevent polymer-bound species from reacting with one another, thus favoring either intramolecular reactions or reactions with reagents in solution rather than interchain reactions within the polymer matrix.[4] Numerous experiments have demonstrated that polymer chains in 1–2% cross-linked polystyrene are highly flexible, not rigid.[5-10] For synthetic purposes, however, one can achieve site isolation if polymer chain motion is slow enough to retard interchain reactions more than it retards the desired reaction. Kraus and Patchornik[11] avoided self-condensation of polymer-bound ester enolates and achieved acylation and alkylations of the enolates in low yields at 0–25 °C. Crowley and Rapoport[4d] did not obtain nine-membered rings by Dieckmann cyclization with diesters bound to 2% cross-linked polystyrene even when as little as 0.1 mmol/g of polymer-bound diester was used. The lifetimes for dimerization of polymer-bound benzyne[12] and for interchain reactions of polymer-bound amines and active esters[13] are on the order of minutes with use of 2% or 4% cross-linked polystyrene.

Chain mobility in cross-linked polystyrenes decreases as the degree of cross-linking increases and as the swelling of the polymer decreases.[5-10] Most attempts at site-isolation syntheses have employed conditions of high polymer chain mobility, lightly cross-linked (1–4% divinylbenzene) polystyrenes and good swelling solvents.[4-8,11-13] We describe here the generation, acylation, and alkylation at room temperature of an unhindered ester enolate supported on 10% and 20% cross-linked polystyrenes. Normally the generation of enolates from unhindered esters in solution is carried out at −78 °C because self-condensation of the ester predominates at higher temperature.[11,14]

The syntheses are outlined in Scheme I. By the same method Kraus and Patchornik[11] generated enolate **3** and

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(1) This research was supported by the U.S. Army Research Office.

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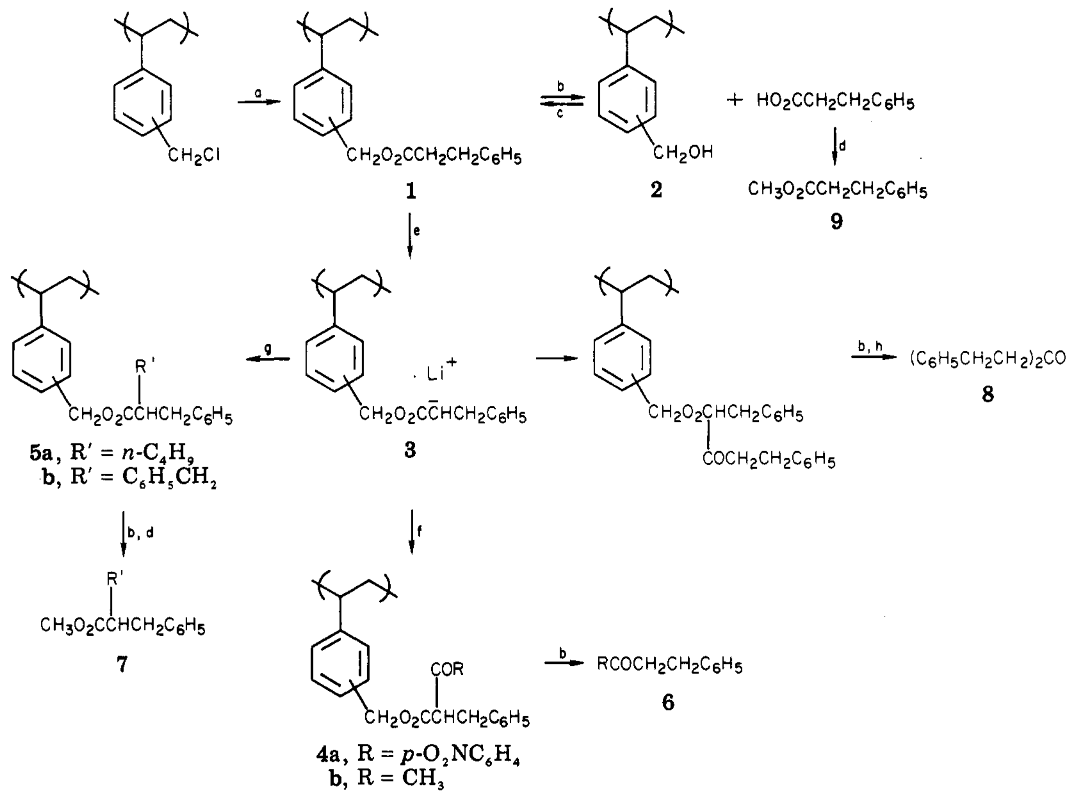
Scheme I[a]



[a] (a) $KO_2CCH_2CH_2C_6H_5$, o-C_6H_4, $(n\text{-}C_4H_9)_4NBr$, 95 °C. (b) i, KOH, $(n\text{-}C_4H_9)_4NOH$, THF, 75 °C; ii, HCl. (c), i, $(C_6H_5)_3CLi$, THF; ii, $ClCOCH_2CH_2H_6H_5$. (d) CH_2N_2. (e) $(C_6H_5)_3ClI$, THF, 25 °C. (f) RCOCl, THF. (g) R′Br, THF. (h) HCl, reflux.

trapped it with p-nitrobenzoyl chloride in up to 37% yield with ≤1% self-condensation, using a 2% cross-linked gel or a popcorn polystyrene support containing ≤0.15 mmol/g of polymer-bound ester. Much higher yields are obtained with 10% and 20% cross-linked copolymers synthesized in our laboratory. The suspension copolymerizations[15] employed 9–23 wt % (chloromethyl)styrenes (Dow, 60/40 meta/para) for 20 wt % divinylbenzene cross-linked macroporous polymers or 30.5 wt % (chloromethyl)styrenes for 10 wt % divinylbenzene cross-linked gel polymer. Polymer-bound esters 1 were prepared by a phase-transfer catalytic method[16] with potassium 3-phenylpropanoate and tetra-n-butylammonium bromide in o-dichlorobenzene at 95 °C. All of the chloromethyl groups were converted to benzyl esters in 4 days, but partial esterifications for 12–24 h led to much better yields in the subsequent enolate reactions. The degree of esterification of each sample was determined by hydrolysis of the ester with excess potassium hydroxide and tetra-n-butylammonium hydroxide in refluxing aqueous THF at 75 °C for 24 h. The recovered 3-phenylpropanoic acid was esterified with diazomethane and analyzed by gas chromatography. This hydrolysis procedure completely eliminated the IR bands at 1730 and 1235 cm^{-1} in the polymer, characteristic of polymer-bound ester.

Generation and trapping of enolate 3 were performed by swelling the polymer in THF at room temperature for 6 h, adding 1.5 molar equiv of (triphenylmethyl)lithium[17] in THF as quickly as possible by syringe to the vigorously stirred mixture, and adding 2.0 molar equiv of the acyl chloride or alkyl bromide 1 min later, after most of the red color due to (triphenylmethyl)lithium had disappeared. Esters 4 and 5 were hydrolyzed by the same phase-transfer catalysis procedure used on 1. The recovered β-keto acids were decarboxylated without isolation, and the recovered organic mixture was treated with diazomethane prior to GC analysis. In larger scale experiments the products were isolated by column chromatography on silica gel and identified by comparison of their ^1H NMR and IR spectra and GC retention times to those of authentic materials. In all experiments the acylated or alkylated product (6 or 7), self-condensation product (8), and methyl 3-phenylpropanoate (9) derived from unreacted ester accounted for ≥98% of the starting polymer-bound ester 1. Yields are given in Table I.

Results with the 10% cross-linked gel polymer should not be compared directly with results with the 20% cross-linked macroporous polymer because of the two polymers were esterified differently. The 10% cross-linked gel polymer originally contained 2.0 mmol/g of chloromethyl groups and was esterified to only 36% conversion. The 20% cross-linked macroporous polymer originally contained 1.10 mmol/g of chloromethyl groups and was esterified to 100% conversion. Effects of varied degrees of esterification of a 20% cross-linked macroporous polystyrene are shown in Table II. The higher the ester content of the polymer, the more self-condensation and the lower the conversion of ester to the p-nitrobenzoyl derivative. High conversion esterifications incorporate esters into sites that are unreactive during the short time allowed for enolate generation. Low conversion esterifications incorporatre esters only into sites where they react quickly with (triphenylmethyl)lithium and p-nitrobenzoyl chloride, allowing nearly quantitative enolate generation and acylation. Chlorine analyses of polymers recovered after enolate acylation indicate that the residual chloromethyl groups are inert to the enolate reaction conditions.

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Table I. Yields of Products from Acylation and Alkylation of Polymer-Bound Benzyl 3-Phenylpropanoate

polymer	RCOCl or RBr	product	% yield[a] 6 or 7	8	9
gel, 10% DVB[b]	p-$O_2NC_6H_4COCl$	**6a**	95 (85)	0	5
	CH_3COCl	**6b**	96 (87)	0	4
	n-C_4H_9Br	**7a**	97 (79)	0	2
	$C_6H_5CH_2Br$	**7b**	95 (73)	0	4
macroporous, 20% DVB[c]	p-$O_2NC_6H_4COCl$	**6a**	42 (40)	17	39
	CH_3COCl	**6b**	57	7	36
	n-C_4H_9Br	**7a**	63	1	36
	$C_6H_5CH_2Br$	**7b**	59	3	37

[a] Determined by GC from reactions using 5-10 g of polymer. Isolated yields from reactions using 25-50 g of polymer are in parentheses. [b] Polymer-bound ester, 0.67 mmol/g, was prepared from −200+400 mesh copolymer containing 2.00 mmol/g of chloromethyl groups. [c] Polymer-bound ester, 1.08 mmol/g, was prepared from −60+100 mesh copolymer containing 1.10 mmol/g of chloromethyl groups.

Table II. Effect of Degree of Esterification on Yields from Enolate Acylation with p-Nitrobenzoyl Chloride[a]

esterification time, days	mmol of ester/g	% yield[b] 6a	8	9
1	0.46	99	0	0
2	0.76	66	10	24
3	0.89	45	17	35
4	0.98	43	17	38

[a] Starting polymer was macroporous, −60+100 mesh, and contained 20 wt % divinylbenzene and 1.10 mmol/g of chloromethyl groups. [b] Determined by GC.

Table III. Recycling of 10% Cross-linked Gel Polymer for Ester Enolate Acylation with p-Nitrobenzoyl Chloride

cycle	mmol of ester/g	% yield of **6a**[a]
1	0.67	87
2	0.42	88
3	0.39	90

[a] Determined by GC and based on polymer-bound ester.

One batch of the recovered 10% cross-linked gel polymer from a p-nitrobenzoyl chloride acylation was recycled twice as follows. Recovered polymer was washed thoroughly and dried. The hydroxymethyl groups were reesterified by successive treatments with 1.5 molar equiv of (triphenylmethyl)lithium in THF at −40 °C and 4 molar equiv of 3-phenylpropanoyl chloride followed by warming to 25 °C for 24 h. Enolate generation and acylation were carried out by the usual method. Results are given in Table III.

Room temperature enolate generation and trapping give much more self-condensation when attempted without a polymer support or with polystyrenes cross-linked with only 2-6% divinylbenzene. Treatment of 0.11 M benzyl 3-phenylpropanoate in THF[18] under the same conditions used with polymer-bound ester gave 19% of acylated product **6a** and 58% of self-condensation product 8. A 6% cross-linked copolymer containing 0.68 mmol/g of polymer-bound ester **1** (from 1.00 mmol/g of chloromethyl groups) gave 52% of p-nitrobenzoyl derivative **6a**, 17% of self-condensation product 8, and 27% of unreacted ester **9** under the standard conditions.

Use of more highly cross-linked polystyrene and low conversion esterifications brings polymer-bound ester enolates into the realm of practical organic synthesis. Yields of acylation and alkylation products are nearly quantitative based on starting polymer-bound ester, and the effective concentrations of ester in the reaction mixtures are ~0.1 M, enabling 0.1 mol scale laboratory synthesis.[19] Performance of enolate chemistry with unhindered esters at room temperature instead of −78 °C avoids one major drawback to its large-scale application. Another major drawback, the use of expensive organolithium bases, still needs to be overcome.

Registry No. 6a, 54914-77-1; **6b**, 2550-26-7; **7a**, 78308-00-6; **7b**, 56964-65-9; **8**, 5396-91-8; **9**, 103-25-3.

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(18) The same effective concentration as in the polymer-supported reactions.

(19) Procedure: The polymer-bound 3-phenylpropanoic ester (175 g, 0.59 mmol/g, 100 mmol, 10% cross-linked polystyrene gel, −100+325 mesh) was stirred mechanically for 1 h in 500 mL of THF under nitrogen in a 2000-mL three-neck flask. A solution of 103 mmol of (triphenylmethyl)lithium,[17] prepared from equimolar amounts of triphenylmethane and n-butyllithium, in 500 mL of THF was added to the polymer mixture by syringe in a period of 3 min. After about 7 min the red color of the mixture had faded, and a solution of 220 mmol of p-nitrobenzoyl chloride in 50 mL of THF was added by syringe. The mixture was stirred for 12 h at room temperature. The polymer was separated by filtration through a fritted glass funnel and washed with 500 mL of THF/diethyl ether (3/1 v/v), 500 mL of THF/ethanol (3/1 v/v), and 500 mL of THF. Solvents were evaporated, and the residue was dried at 30 °C under vacuum. A mixture of the dried polymer, 500 mL of THF, 12 mL of 50% aqueous KOH, and 0.8 mL of tetra-n-butylammonium hydroxide (40% aqueous) was heated at reflux for 24 h. After cooling the polymer was filtered and washed with 500 mL of THF and 500 mL of ethanol. The combined filtrate was neutralized with 5 N HCl, acidified with 5 mL of concentrated HCl, and heated at reflux for 2 h. Solvents were evaporated, and the residue was chromatographed quickly over silica gel with CCl_4/C_6H_6 (9/1 v/v). The recovered 1-(4-nitrophenyl)-3-phenyl-1-propanone was crystallized from ethanol to give 20.1 g (79 mmol, 77%) of colorless plates, mp 73-75 °C uncorrected (lit.[20] mp 75-75 °C) whose ^1H NMR and IR spectra were identical with those of independently synthesized material.

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Friedel-Crafts Reactions of Ethyl Cyclopropanecarboxylate[1]

Summary: The reaction of ethyl cyclopropanecarboxylate with benzene in the presence of aluminum chloride gives 2-methyl-1-indanone in excellent yield.

Sir: The Friedel-Crafts reaction is one of the most useful methods for the formation of carbon bonds to aromatic

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(1) Taken in part from the MS thesis of Linwood W. Zoller, III, University of Georgia, 1980. Presented at the combined Southeast-Southwest Regional Meeting of the American Chemical Society, New Orleans, Dec 10-13, 1980; American Chemical Society: Washington, DC; Abstr. 478.