

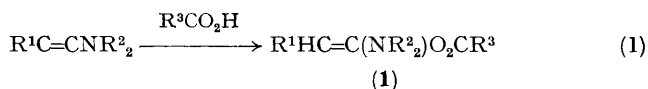
Synthesis and Reactions of an Insoluble Polymeric Yneamine

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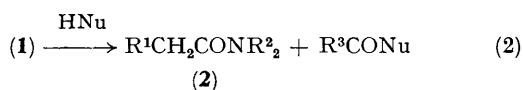
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Summary A resin-bound yneamine reacts with a carboxylic acid to form a stable intermediate which can be converted into anhydrides, amides, and esters at room temperature.

YNEAMINES¹ are presumed to react with carboxy-groups, *via* intermediate (1) [equation (1)], similarly to carbodiimides where the species analogous to (1) has been shown to be only transient during Merrifield synthesis.²



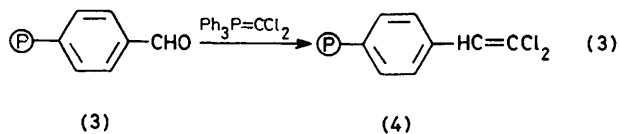
The synthesis of an insoluble polymeric yneamine reagent³ was undertaken to simplify separation of products from amide byproduct (2) [equation (2)]. Crosslinked (2%



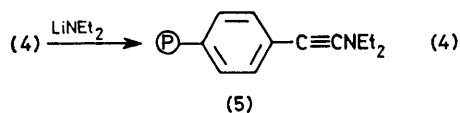
Nu = a, NR₂; b, OR; c, O₂CR.

divinylbenzene) polystyrene (Eastman) was washed,⁴ chloromethylated⁵ (1.98 mequiv. Cl/g), and oxidized⁶ by heating with dimethyl sulphoxide and NaHCO₃ at 150 °C to

give formylated resin (3) which contained no titratable chlorine. Reaction of a toluene suspension containing 8.75 mequiv. of (3) with dichloromethylene(triphenyl)phosphorane generated *in situ*⁷ gave (4) in 87% yield (Cl analysis)



[equation (3)]. Transformation to (5) (intense i.r. absorption at 2180 cm⁻¹) was accomplished in a conversion of 57% (N analysis) by adding 20 mequiv. (based on Cl content) of (4) to 40 mequiv. of lithium diethylamide in tetrahydrofuran (THF) [equation (4)].



Suspension of 1 mequiv. of (5) in CH₂Cl₂ and treatment with < 1 equiv. of benzoic acid shifted the characteristic i.r. absorption to 1720 cm⁻¹. Washing the resin exhaustively with dry CH₂Cl₂ did not alter the spectrum. Treatment of the washed resin with toluic acid gave the mixed anhydride of benzoic and toluic acids; with diethylamine or phenol, *NN*-diethylbenzamide or phenyl benzoate, respectively, was obtained.[†] After isolation of products, the i.r. absorption of the resin was observed at 1650 cm⁻¹, characteristic for the amide (2). These results constitute, to our knowledge, the first direct chemical evidence for the intermediacy of a stable, resin-bound species [which we surmise has structure (1)] in the activity of this kind of polymeric reagent.

Work is continuing to expand the application of this resin, particularly in the area of peptide synthesis⁸ as well as to develop an effective route for its regeneration.

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[†] The amount of intermediate (1) formed from any particular batch of resin varies and is accompanied by an amount of amide (2) corresponding to the amount of anhydride found in the CH₂Cl₂ wash. In general, the acid and resin are suspended in dry CH₂Cl₂ and stirred for 12 h. The resin is filtered and shaken with CH₂Cl₂ for 10 min (5 times). The washings are combined with the original filtrate, evaporated to dryness, and assayed for the presence of anhydride by n.m.r. spectroscopy (CDCl₃). The washed resin is suspended in CH₂Cl₂ and the nucleophile of choice is added and allowed to react for 1 h. In this way, 244 mg of benzoic acid added to 1.39 g of resin yielded 145 mg of material (after evaporation of CH₂Cl₂) of which 116 mg (51%) was anhydride. To the washed resin was added 77 mg of phenol to yield 16 mg (8.1%) of phenyl benzoate by n.m.r. spectroscopy. Similarly, from 73 mg of benzoic acid and 1.24 g of resin, followed by washing (10 mg of residue) and treatment with 65 mg of *p*-toluic acid, 60 mg (70% based on toluic acid) of mixed anhydride was obtained.

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³ For reviews of polymeric reagents see: 'Reactions on Polymers,' ed. J. A. Moore, Reidel Press, Boston, 1973; C. G. Overberger and K. N. Sannes, *Angew. Chem. Internat. Edn.*, 1974, **13**, 159; C. C. Leznoff, *Chem. Soc. Rev.*, 1974, **3**, 65; J. I. Crowley and H. Rapoport, *Accounts Chem. Res.*, 1976, **9**, 135.

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⁵ J. M. Stewart and J. D. Young, 'Solid Phase Peptide Synthesis,' Freeman, San Francisco, 1969, p. 27.

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⁸ H. G. Viehe, R. Fuks, and M. Reinstein, *Angew. Chem. Internat. Edn.*, 1964, **3**, 581; F. Weygand, W. Konig, R. Buijle, and H. G. Viehe, *Ber.*, 1965, **98**, 3632.

Addendum to p. 1046: The atomic co-ordinates for this work are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Rd., Cambridge CB2 1EW. Any request should be accompanied by the full literature citation for this communication.