Tetrahedron Letters,Vol.23,No.11,pp 1159-1160,1982 0040-4039/82/111159-02$03.00/0
Printed in Great Britain

HIGHLY SELECTIVE ACYLATION OF AMINES AND ALCOHOLS BY POLY(3-ACYL-2-OXAZOLONE)

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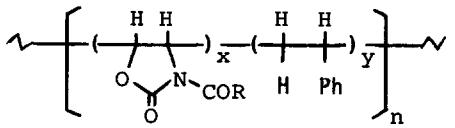
[Summary] : Poly(3-acyl-2-oxazolone) serves as a convenient reagent for highly chemo- and regioselective acylation of polyamines, amino-alcohols and polyalcohols.

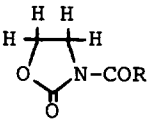
Insoluble polymeric reagents have been developed for a wide variety of chemical conversions[1] in catalytic or non-catalytic processes. Their usefulness in preparative aspects is obvious, in virtue of the product purification simplified by filtering the polymer away from the reaction mixture as well as many specific advantages widely exploited[2].

During the course of study on the telomerization of 2-oxazolones[3], we have found that homopolymers (1) derived from 3-acyl-2-oxazolones (4) still retain reactivity high enough to undergo a smooth acylation of the nucleophiles even under heterogeneous conditions and to serve as convenient protecting reagents. In this paper we wish to demonstrate high regio- and chemoselectivity performed in the acylation of amino-alcohols, amino-phenols, polyamines and polyalcohols.

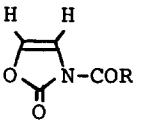
Homo- and copolymer (1 and 2)[4] with carbon-carbon backbone structure were readily obtainable as colorless powder, insoluble in most conventional solvents, by heating the corresponding monomers in the presence of benzoyl peroxide at 65-70° for several hours (1-5 hr).



(1) (y=0)
(2) (x:y=3:1)



(3)



(4)

Both polymeric reagents thus obtained were much more reactive toward amines in either heterogeneous or homogeneous media than the structural unit, 3-acyl-2-oxazolidinone (3), though they were not so reactve as the monomers (4) (Fig. 1). Such a considerable rate enhancement, viz. desirable "polymer effect", may be a consequence of steric repulsion imposed by the crowded functional groups. Among the solvent examined so far, tetrahydrofuran offers the most preferable heterogeneous medium in terms of high yields and simple work-up for the isolation of the products. Thus, various amines were acylated with the polymers in tetrahydrofuran at room temperature in yields heavily depending on the structural features (Table I). Acetylation of amines was also accomplished simply by passing the THF solutions through a column packed with the powdered polymer (5-10 eq) over a period of 1 hr at 40°. In this way, benzylamine was acetylated quantitatively.

Table I shows that the reaction rate among amines decreases in an order, comparable to those

of 2-oxazolone[5] and 2-thiazolidinethione derivatives[6]. Particularly interesting feature is a remarkable difference in yields between 1-adamantamine and 1-adamantanemethylamine or cyclohexylamine and dicyclohexylamine. Such selectivity leads to highly preferential acylation of less hindered amino functions of 2,6-dimethylpiperazine, 2-(ethylamino)ethylamine and spermidine (Table I). This type of polymers underwent an exclusive N-acylation of amino-alcohols and amino-phenols.

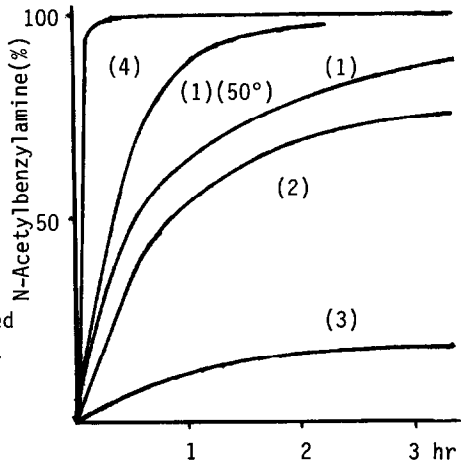


Fig. 1. Acetylation of benzylamine by reagents(1, 2, 3 and 4)(R=CH_3, 2eq.) in CH_3CN at room temperature.

Acylation of the alcohols with the polymers proceeded smoothly only in the presence of catalysts such as tertiary amine, the Lewis acids and fluoride ions, otherwise hydroxyl groups were completely unreactive. Acylation of 1,4-nonanediol resulted in an exclusive formation of primary alkyl ester, while phenylethyleneglycol showed less regioselectivity (Table I). Thus, this type of polymers may be expected as feasible reagents for regioselective protection of polyalcohols including carbohydrates.

Deacylated polymers recovered from the reaction could be regenerated by the conventional reagents (ex. Ac_2O-pyridine etc.) for repeated use without any significant loss of activity.

Table I. Acetylation by Polymeric Reagent (1, R=CH_3)(2 equiv.)[a]

Nucleophile	Isolated Yield	Nucleophile (Conditions)	Isolated Yield
$PhCH_2NH_2$	93 %	2,6-dimethylpiperazine	58[c] %
$Ph\text{-}NH_2$	10 (91)	$p\text{-}NH_2\text{-}PhCH_2CH_2NH_2$	81[b]
1-adamantanemethylamine	79 (85)	$HO\text{-}(CH_2)_5\text{-}NH_2$	92[b]
1-adamantamine	13 (41)	$p\text{-}HO\text{-}PhCH_2CH_2NH_2$ (DMF)	92[b]
cyclohexylamine	61	1,4-nonanediol (CH_3CN,18hr, + CsF)	58[d](85), 0[e](5)
dicyclohexylamine	0	$PhCH(OH)CH_2OH$ (CH_3CN, 8hr, + CsF)	47[d], 22[e], 9[f]
$CH_3CH_2NHCH_2CH_2NH_2$	80[b]	$p\text{-}HO\text{-}PhCH_2CH_2OH$($CH_3CN$,1.5hr, + CsF)	58[d], 22[e]
$H_2N(CH_2)_3NH(CH_2)_4NH_2$	93[b]		

a) The reactions were carried out in THF at room temperature for 6hr for a comparison, unless otherwise stated. Yields by (4) are given in parentheses. b) Primary amino functions were only affected. c) 4-Acetyl derivative. d) Primary alkyl ester. e) Diacetate. f) Secondary alkyl ester.

References and Notes

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4. Polymer (1) R=Me: mp>300°, $\overline{MW}$ 3500, IR 1710 cm^{-1}(Ac); R=Ph: mp 270°, $\overline{MW}$ 2300, IR 1691 cm^{-1}(Bz). Polymer (2) R=Me: mp>300°, $\overline{MW}$ 3400, IR 1708 cm^{-1}(Ac). Since most of the acyl groups retained is usable, 1.2equiv. of reagents is sufficient for acylation.
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(Received in Japan 8 December 1981)