

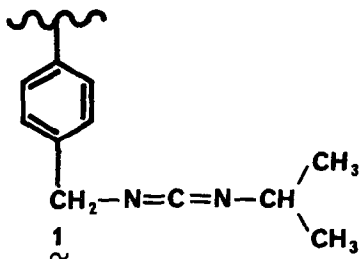
POLYMERIC REAGENTS II. PREPARATION OF KETONES AND ALDEHYDES
UTILIZING AN INSOLUBLE CARBODIIMIDE

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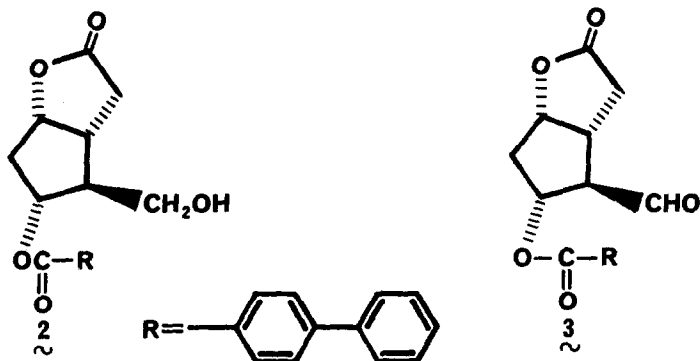
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The preceding paper² described the synthesis of a carbodiimide linked to a crosslinked polystyrene matrix (1). In this article the use of the reagent in the Moffatt³ oxidation is reported.



The Moffatt oxidation appeared to provide a test of the usefulness and applicability of our polymeric carbodiimide to organic synthesis. This oxidation technique has proven to be an extremely versatile method that is particularly useful in dealing with highly sensitive compounds⁴. Oxidation of a range of alcohols to aldehydes and ketones is shown in the table. It should be noted that even the labile prostaglandin intermediate⁵ 2 is converted readily to the desired aldehyde 3.



Oxidation of Alcohols Using Polymeric Carbodiimide 1

Alcohol ^a	Reaction Time (Hrs)	GC ^c	Y I E L D %		Isolated Carbonyl Product
			2,4DNP (Crude)	2,4DNP (Pure)	
Cyclohexanol	3-5	85	79	66 ^d	---
Heptyl Aldehyde	2-3	97	80	68 ^e	---
Benzyl Alcohol	2	95	88	82 ^f	---
Geraniol	3	63	--	--	---
PG Alcohol 2	3	--	--	--	91 ^g
PG Alcohol 2	7 ^b	--	--	--	89 ^g
4-Phenylcyclohexanol	5	--	--	--	67 ^g
4-Phenylcyclohexanol	16 ^b	--	--	--	67 ^g

(a) Reactions were carried out using 1 mmole of alcohol, \geq 2 mmole of carbodiimide, 16 μ l of orthophosphoric acid as catalyst, and 2:1 ϕ H-DMSO solvent at ambient temperature.

(b) Pure DMSO as solvent.

(c) Yields based on comparison with the internal standard (triglyme or DMF).

(d) mp 162°; lit^{7a} mp 162°.

(e) mp 108°; lit^{7b} mp 108°.

(f) mp 245-6°; lit^{7b} mp 237°.

(g) Isolated as the solid.

Using this method the products are free from contamination by ureas, a major purification problem in the general synthetic method. Although the advent of water soluble carbodiimides⁶ has partially solved that problem, the isolation of water soluble oxidation products still causes some difficulties. The present method should be universally applicable to substrates of varying physical properties.

The preceding table presents the scope of this method to date. Although some steps were taken to maximize yields, further refinements are possible. In general, orthophosphoric acid functioned as a superior catalyst. Use of trifluoroacetic acid-pyridine resulted in competitive formation of trifluoroacetates of the starting alcohols, especially in the case of benzyl alcohol. It should also be noted that reaction times were generally longer in pure DMSO than in the mixed solvent containing benzene. Since the yields are the same in the two cases studied, this rate change merely reflects the capacity of the solvents to swell the polymer and the resultant changes in diffusion rate of the substrate to the active sites in the beads. In several cases the polymeric reagent was regenerated generally with some loss of activity². The following example is illustrative of the method:

Oxidation of Alcohol 2 to Aldehyde 3. - The alcohol 2 (359 mg, 1.0 mmole) and 1.44 g (minimum of 2 mmoles) of carbodiimide were stirred in 12 ml of 2:1 benzene-dimethylsulfoxide for 20 minutes to cause swelling of the polymer beads. Then 16 μ l of orthophosphoric acid was added and stirring at ambient temperature was continued for 3 hours at which time tlc analysis (silica gel; 2:1 benzene-ethyl acetate) indicated that the oxidation was complete. The beads were filtered and washed with benzene-ethyl acetate and the combined filtrates were concentrated (aspirator pressure) to 5 ml. Dilution with 50 ml of water and stirring precipitated the aldehyde 3 which, after vacuum drying, amounted to 327 mg (91.2%). This material was identical in all respects (nmr, ir, and tlc) to aldehyde prepared by existing methods⁶.

References

- 1) ALZA Postdoctoral Fellow 1971-72.
- 2) N. M. Weinshenker and C.-M. Shen, preceding paper in this Journal.
- 3) For leading references see: "Reagents for Organic Synthesis," Fieser and Fieser, John Wiley and Sons, Inc., New York, 1967, Vol. I, pp. 303-307.
- 4) For example see: N. M. Weinshenker and F. D. Greene, J. Amer. Chem. Soc., 90, 506 (1968).
- 5) E. J. Corey, S. M. Albonico, V. Koelliker, T. K. Shaaf, and R. K. Varma, ibid., 93, 1491 (1971).
- 6) See "Reagents for Organic Synthesis," Vol. I, Fieser and Fieser, John Wiley and Sons, Inc., New York, 1967, p. 274.
- 7) "Semimicro Qualitative Organic Analysis," Second Edition, Cheronis and Entrikin, Interscience Publishers, Inc., New York, 1961. a) p. 633, b) p. 582.