Tetrahedron Letters No.12, pp. 809-812, 1971. Pergamon Press. Printed in Great Britain.

2-OXAZOLIDONES VIA THE LITHIUM BROMIDE CATALYZED REACTION OF ISOCYANATES WITH EPOXIDES IN HYDROCARBON SOLVENTS

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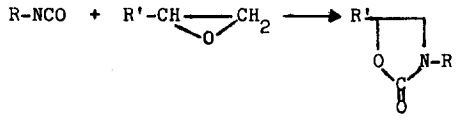
(Received in USA 17 February 1971; received in UK for publication 3 March 1971)

We wish to report an improved procedure for preparing N-substituted 2-oxazolidones (1) from organic isocyanates and epoxides via the use of a hydrocarbon-soluble adduct of lithium bromide and a phosphine oxide. The 1,3-cycloaddition of isocyanates to epoxides to form 2-oxazolidones



(1)

(1) has been known for some time.[1] The reaction has been carried out neat at elevated temperatures with or without catalysts bearing an anion suitable for epoxide ring opening. Aprotic, reactive solvents, such as DMF, have also been utilized to aid in moderating reaction temperatures and, more importantly, to solubilize the catalyst necessary for epoxide ring opening.[2]

We have found that lithium bromide solubilized in nonreactive solvents (benzene, xylene, etc.) by tributyl phosphine oxide as an adduct effects 2-oxazolidone formation from isocyanates and epoxides. The use of tributyl phosphine oxide as a solubilizing agent for certain lithium salts has been reported.[3] In addition to negating the need for high reaction temperatures and/or the use of polar reactive solvents, the current process is relatively rapid and specific usually providing for high yields of the desired 2-oxazolidone (1).

The reaction is effected by simply adding a solution of the reactants in the dried hydrocarbon solvent selected to a solution of the solubilized lithium bromide. The mode of addition of reactants was selected in order to minimize any side reactions such as carbodiimide formation

and/or rearrangement of the epoxide.* The lithium bromide adduct may be prepared in the reaction flask and dried by azeotropic removal of water, or an aliquot of a dried stock solution may be employed. An excess of the phosphine oxide, over and above that required for 1:1 adduct formation was found necessary to achieve complete solubility of the lithium salt. The phosphine oxide and lithium salt are present on the order of 3.5 and 2.5 mole % respectively of the reactants.

Table I summarizes results obtained using the hydrocarbon-soluble catalyst. In a number of cases, infrared spectra of reaction mixture aliquots were used to determine the relative completeness of the reaction as judged by the presence and/or intensity of the isocyanate and 2-oxazolidone carbonyl bands. Using this procedure, it was found that the reaction was complete in less than 15 minutes in refluxing xylene after rapid addition of reactants (Table I). In refluxing benzene (Table I) the reaction was essentially complete after a relatively slow addition, ca. 1.25 hrs. The reaction involving n-butyl isocyanate in refluxing xylene (Table I) was also fairly rapid. In all cases, the yield of 2-oxazolidone (1) was excellent. When styrene oxide was used as a coreactant, a good yield of the 2-oxazolidone (1) was realized - no attempt was made, however, to optimize reaction conditions. The hexamethylphosphoryl triamide (HMPT) soluble lithium bromide adduct was also shown to be an effective catalyst for 2-oxazolidone formation (Table I).

Methoxymethylene isocyanate (MMI) in toluene solution reacted with phenyl glycidyl ether in benzene (Table I) to give N-methoxymethylene-5-phenoxymethylene-2-oxazolidone (1, R=CH_3OCH_2-, R'=$PhOCH_2$-), m.p. 69.5 - 70.5°C [Anal. Calcd. for $C_{12}H_{15}NO_4$:C, 60.8; H, 6.4; N, 5.9, mol. wt. 237. Found: C, 60.6; H, 6.4; N, 6.1; mol. wt. 253 (determined in DMF by vapor pressure osmometry)]. As far as we have been able to determine, no N-methoxymethyl oxazolidones have been reported previously. The nmr spectral assignments for 1 (R=CH_3OCH_2-, R'=$PhOCH_2$-)(100 MHz in $CDCl_3$, TMS as internal standard) are given below. The disposition of the methine (H_A) and methylene protons (H_B and H_C) was in accord with that observed for other 5-isomeric 2-oxazolidones.[2] Of some interest is the observation that scale expansion to effect separation of signals due H_B and H_C also resulted in splitting of the signals attributed to H_D and H_E.

*Phosphine oxides are known to catalyze carbodiimide formation from isocyanates; in fact, when 2-oxazolidone formation was attempted with the phosphine oxide alone, infrared spectral analysis suggested the presence of a carbodiimide.

Table I

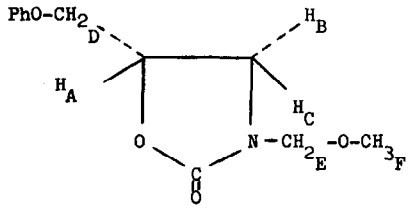
Preparation of 2-Oxazolidones (1) in Hydrocarbon Solvents Catalyzed by the Soluble Lithium Bromide Adduct.

R-NCO	R'-CH-CH_2O	Solvent	React. Temp., °C	React. Time, hrs.[a]	% Yield of (1)
p-$CH_3C_6H_4$-	$C_6H_5OCH_2$-	benzene	80	(0.75) 15	99
		benzene	80	(1.25)	90
		xylene	140	(<1 min) 0.25	95
		xylene[b]	140	(1.25) 0.25	92
		1,2,4-trimethyl benzene	155-160	(1) 6	98
$CH_3(CH_2)_3$		xylene	140	(1.5) 0.25	100
p-$CH_3C_6H_4$-	C_6H_5-	benzene	80	(1.5) 15	71
CH_3OCH_2-	$C_6H_5OCH_2$-	benzene/ toluene	80	(2) 1	62[c]

[a] Figures in ( ) represent addition time. The other figures signify additional heating periods.

[b] LiBr·HMPT catalyst. In all other cases the LiBr·Bu_3PO was employed.

[c] The modest yield may be a reflection on the purity of the MMI/toluene solution.



H_A = complex multiplet centered at 4.80 ppm

H_B = 3.62 (dd) ppm, J_{BC} = 8.5 cps.;

$J_{BA_{trans}}$ = 6.5 cps.

H_C = 3.77 (t) ppm, $J_{CA_{cis}}$ = J_{CB} = 8.5 cps.

H_D = 4.11 (dq) ppm, J_{DA} = 4.0 cps;

$J_{DD'}$ = 10.5 cps; $\Delta\delta_{DD'}$ = 5.80 cps.

H_E = 4.69 (q) ppm, $J_{EE'}$ = 10.75 cps;

$\Delta\delta_{EE'}$ = 5.80 cps.

H_F = 3.35 (s) ppm.

The nonequivalence of the H_D methylene protons is to be expected because of the adjacent asymmetric center, but the magnitude of the nonequivalence of the H_E protons was surprising. A temperature study was run on the 2-oxazolidone in o-dichlorobenzene. At 20°C the spectrum showed the H_E protons clearly split into an AB quartet ($J_{EE'}$ = 10.75 cps.; $\Delta\delta_{EE'}$ = 10.8 cps.). The H_D proton signals were composed of eight lines, showing splitting of an AB quartet (J_{AD} = 4.0 cps.; $J_{DD'}$ = 10.50 cps.; $\Delta\delta_{DD'}$ = 7.65 cps.). At 80°C, the H_D signal collapsed into a sharp doublet whie the H_E quartet persisted with an increase in the intensity of the central pair of lines and smaller chemical shift differences. At 100°C the H_E splitting was still present, but at 120°C it collapsed into a sharp singlet.

Further studies are necessary in order to ascertain whether the nonequivalence of the H_E protons is due to some conformational preference of the methoxyl group because of electronic interaction, or due to a long range effect of the asymmetric center.

The remaining 2-oxazolidones (1) were identified by m.p., mixture m.p. with authentic samples and infrared spectral analyses. In addition, nmr was used to establish the identity of the products as 5-isomeric 2-oxazolidones (1) in accordance with previously reported results.[2a]

REFERENCES

1. M. E. Dyer and D. Swern, Chem. Rev., 67, 197 (1967).

2. (a) J. E. Herweh, T. A. Foglia and D. Swern, J. Org. Chem., 33, 4029 (1968).

   (b) J. E. Herweh, J. Heterocyclic Chem., 5, 687 (1968).

3. B. Rickborn and R. M. Gerkin, J. Am. Chem. Soc., 90, 4193 (1968).