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High-pressure Ammonolysis of Lactones to Hydroxyamides†

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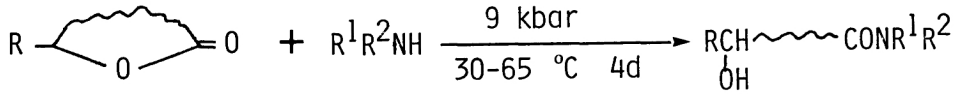
The preparation of hydroxyamides from a variety of lactones and amines has been achieved at 9 kbar and 30 °C or 65 °C. The yields of hydroxyamides were excellent to moderate.

Although one of the most convenient and simplest methods for preparing hydroxyamides would consist in direct nucleophilic ring opening of lactones with amines, this conversion is generally limited to reasonably highly nucleophilic amines. Especially, the reactions of γ-substituted-γ-butyrolactones with amines were reported to be sluggish,[1] and even β-butyrolactone, a strained four membered lactone, did not react with 4-nitroaniline in refluxing acetonitrile.[2]



We now report that alkyl-, aryl-, and aralkylamines react with a variety of lactones in excellent to moderate yields in the kirobar region at room to moderate temperature producing the corresponding hydroxyamides. The results are summarized in Table 1.[3] Neither an inert atmosphere nor dry solvents are required, nor the hydrolysis procedure employed in the method using alkylaluminium amide reagents that often led to recyclization to starting lactones.[4] It is surprising that the reaction of γ-valerolactone with benzyl amine took place quantitatively at 9 kbar (entry 7) since some starting lactone was always recovered under the vigorous conditions at 190 °C for several days at 1 bar that resulted in much decomposition.[1] Furthermore, γ-butyrolactone and γ-valerolactone did react with aniline at 9 kbar and 65 °C to give the corresponding hydroxyamides albeit in moderate yields (entries 3 and 6); aniline, with a pKa of 4.69, is 10^6 times less basic than primary alkylamines and therefore reported to be inert to γ-valerolactone even upon heating to 180 °C.[1] The reaction of β-butyrolactone with 4-nitroaniline,[2] an extremely unreactive amine, further illustrates the utility and generality of the method (entry 14).

In conclusion, the direct aminolysis of lactones is highly accelerated by application of pressure (pressure effect: see footnote c) for entry 5), thus providing a powerful method for the preparation of hydroxyamides.

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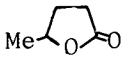
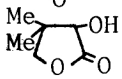
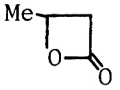
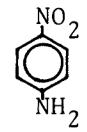
†This paper is dedicated to the late Professor Ryozo Goto, Kyoto University.

Table 1. Hydroxyamides from Lactones and Amines

Entry	Lactone	Amine	Product	Mp/°C	Temp/°C	Yield[a]/%
1			$HO(CH_2)_3CON$ 	oil	30	99[b]
2	〃	Et_2NH	$HO(CH_2)_3CONEt_2$	oil	30	100
3	〃	$PhNH_2$	$HO(CH_2)_3CONHPh$	69-70	65	47
4			$MeCH(OH)CH_2CH_2CON$ 	oil	30	95[b]
5	〃	Et_2NH	$MeCH(OH)CH_2CH_2CONEt_2$	oil	30	95[c]
6	〃	$PhNH_2$	$MeCH(OH)CH_2CH_2CONHPh$	88-89	65	39
7	〃	$PhCH_2NH_2$	$MeCH(OH)CH_2CH_2CONHCH_2Ph$	oil	30	100[b]
8	$n\text{-}C_6H_{13}$ 		$n\text{-}C_6H_{13}CH(OH)CH_2CH_2CON$ 	oil	30	96
9		〃	$HOCH_2C(Me)_2CH(OH)CON$ 	79-80	30	59
10		〃	$HO(CH_2)_4CON$ 	oil	30	96[b]
11	〃	Et_2NH	$HO(CH_2)_4CONEt_2$	oil	30	94
12	〃	$PhNH_2$	$HO(CH_2)_4CONHPh$	67-68	55	94
13			$HO(CH_2)_5CON$  $HO(CH_2)_5CO_2(CH_2)_5CON$	oil oil	30	86 3
14			$MeCH(OH)CH_2CONHC_6H_4NO_2\text{-}p$ $MeCHCH_2CO_2H$ $NHC_6H_4NO_2\text{-}p$	142-143 88-91	30	40 60

a) Isolated yield. b) No reaction at 1 bar and 80 °C for 5 h. c) 36% yield at 5 kbar.

References

1) J. B. Jones and J. M. Young, Can. J. Chem., 44, 1059 (1966); see also, N. H. Cromwell and K. E. Cook, J. Am. Chem. Soc., 80, 4573 (1958).
2) Y. Iwakura, K. Nagakubo, J. Aoki, and A. Yamada, Nippon Kagaku Zasshi, 75, 315 (1954).
3) Procedure: A mixture of the lactone (5 mmol) and the amine (10 mmol) was diluted with CH_3CN in an 8 ml Teflon capsule, which was then stored for 4 days at 9 kbar. After evaporation of the solvent and amine, the residue was chromatographed on silica gel. All spectral and analytical data were in accord with assigned structure.
4) T. Hirabayashi, K. Ito, S. Sakai, and Y. Ishii, J. Organomet. Chem., 25, 33 (1970).

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