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CARBAMATE MEDIATED FUNCTIONALIZATION OF UNSATURATED ALCOHOLS II. REGIO- AND STEREO-SELECTIVE SYNTHESIS OF 1,3-SYN AND 1,2-ANTI AMINO ALCOHOL DERIVATIVES VIA IODOCARBAMATION

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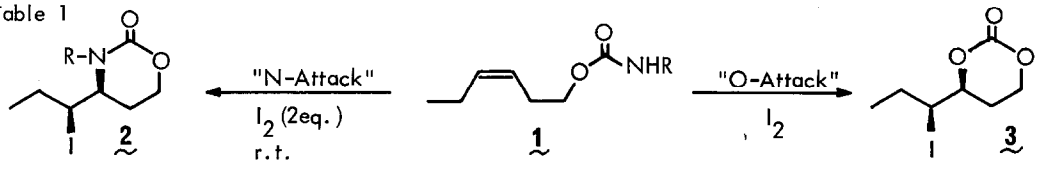
Abstract: A regio- and stereo-selective introduction of nitrogen functions to double bonds of acyclic, allylic and homoallylic alcohols was achieved via iodocyclization of the corresponding N-sulfonylated O-carbamates.

Iodofunctionalization of homoallylic O-carbamates has been recently utilized for a diastereoselective synthethes of acyclic 1,3-syn diols[2]. Because of the ambident nature[3], O-carbamate would cyclize with its nitrogen, if it is properly modified by N-substitution. We report herein the realization of such cyclizations using N-sulfonylated carbamates. The result would provide a stereoselective route to 1,2-anti and 1,3-syn amino alcohol systems[4].

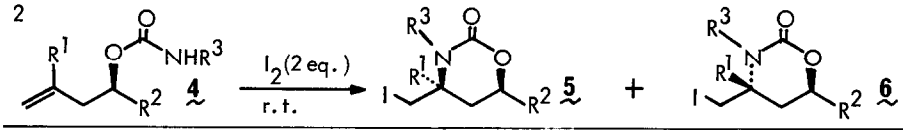
In the search of proper N-substituent (N-R) to effect the cyclization of homoallylic carbamate at nitrogen-site, we found that those with R=H (1a)[2], CH_2Ph, Ph, $COCCl_3$, and $COCF_3$ cyclized only by oxygen when treated with I_2 in the presence of bases[2]. By use of sulfonyl group, however, nitrogen-attack (to give 2) became predominant or exclusive (Table 1)[5,6]. Modification of arylsulfonyl group[6] did not essentially alter the chemical yield and diastereoselectivity, cyclic carbamates 5, 1,3-syn amino alcohol derivatives, being formed preferentially as shown in Table 2[7]. The same reaction of N-sulfonylated allylic carbamates 7[6] furnished the oxazolidinones, 8 and 9, as shown in Table 3[7]: 7c showed a moderate diastereoselectivity favoring 8c (4,5-cis), i.e. 1,2-anti amino alcohol derivative.

Table 1



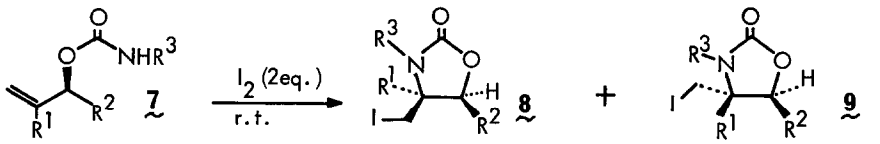
Substrate	Solvent	Base	Reaction Time	Isolated Yield 2	3
1a, R=H[2]	Ether	aq. $NaHCO_3$	3 h	0%	64%
1b, R=SO_3CH_3	Ether	aq. $NaHCO_3$	1.2	22	16
1c, R=$SO_3CH_2CCl_3$	Ether	aq. $NaHCO_3$	0.3	67	10
1d, R=Ts	CCl_4	aq. $NaHCO_3$	1.5	75	7
1d	CCl_4	K_2CO_3	7.5	64	0

Table 2



Substrate	Solvent	Base	Time	5/6	Yield (5+6)
4a, R^1=CH_3, R^2=H, R^3=Ts	CCl_4	aq. $NaHCO_3$	1 h	—	71%
4b, R^1=H, R^2=CH_3, R^3=Ts	Ether	K_2CO_3	1	5.2:1	59
4c, R^1=H, R^2=CH_3, R^3=SO_2Ph	Ether	K_2CO_3	1	6.2:1	68
4d, R^1=H, R^2=CH_3, R^3=SO_2-C$_6$H$_4$	Ether	K_2CO_3	1	5.5:1	52

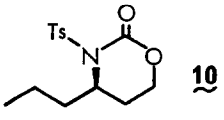
Table 3



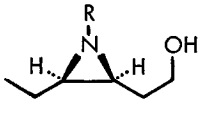
Substrate	Solvent	Base	Time	8/9	Yield (8+9)
7a, R^1=CH_3, R^2=H, R^3=Ts	Ether	K_2CO_3	0.5 h	—	67%
7b, R^1=CH_3, R^2=H, R^3=SO_2Ph	Ether	K_2CO_3	0.5	—	74
7c, R^1=H, R^2=CH_3, R^3=Ts	Ether	K_2CO_3	1.3	2.7:1	78
7c	Ether	K_2CO_3	1.5 (-25°C)	3.4:1	52

The present iodocyclocarbamation appears to be kinetically controlled, because i) the ratio of 8c and 9c was not affected in the reaction of 7c from 1.3 hr to 18 hrs and ii) no change from 8c to 9c was observed when the former was placed under the iodocarbamation condition.

This methodology should be useful for functionalization of unsaturated alcohols. For example, deiodination of 2d was readily realized by n-Bu_3SnH/cat. AIBN (C_6H_6, 60°C, 1.5 h, 88%) to afford the protected 1,3-amino alcohol (10). Treatment of 2c and 2d with K_2CO_3 in MeOH (r.t., 1 hr) gave N-protected aziridines, 11 and 12 in 90% yields, respectively.



10



11, R=$SO_3CH_2CCl_3$

12, R=Ts

References and Notes

1) Present address: Department of Chemistry, Tohoku University, Sendai 980, Japan.
2) Part 1: M. Hirama and M. Uei, Tetrahedron Lett., 23, 5307 (1982).
3) F.L. Scott, R.E. Glick and S. Winsterin, Experientia, 13, 183 (1957).
4) Similar strategy for constructing amino alcohol systems via halocyclization of trichloroacetimidate has recently been reported by two groups: G. Cardillo, M. Orena, G. Porzi and S. Sandri, J. Chem. Soc., Chem. Comm., 1308 (1982); H.W. Pauls and B. Fraser-Reid, J. Org. Chem., 48, 1392 (1983).
5) Recently similar nucleophilic attack by nitrogen was realized in halocyclization of N-sulfonylated β,γ-unsaturated amide: A.J. Biloski, R.D. Wood and B. Ganem, J. Am. Chem. Soc., 104, 3233 (1982).
6) All N-substituted carbamates except 1b were prepared by mixing the corresponding alcohol with the requisite N-substituted isocyanate. 1b was obtained by heating cis-3-hexen-1-ol with methyl N-(2,4,6-tribromophenoxycarbonyl)sulfamate, which was readily synthesized by the consecutive addition of 2,3,6-tribromophenol and MeOH to chlorosulfonyl isocyanate.
7) The stereochemical assignment of the diastereomers was based on detailed 360 MHz ^{1}H-NMR study including NOE measurement.

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