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One Pot Synthesis of *N*-Derivatized 2-Oxazolidinones from Amino Alcohol Carbamates

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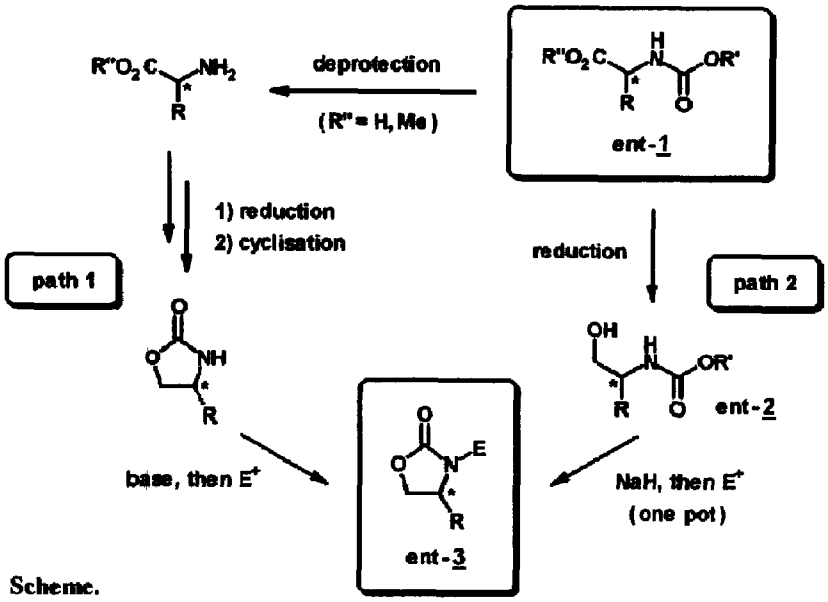
Abstract: A one pot protocol for the synthesis of *N*-derivatized 2-oxazolidinones from amino alcohol carbamates is described. The method is exceptionally useful if the parent amino acids are prepared in their enantiopure forms via enzymatic resolution of the racemic carbamate esters.

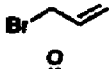
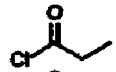
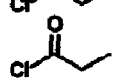
Introduction. 2-oxazolidinones[1] can be prepared from other heterocyclic compounds (mostly epoxides) and from β-difunctional compounds. An important method belonging to the last category is the generation of 2-oxazolidinones from β-amino alcohols, which are usually prepared from the corresponding amino acids,[2] often via carbamate intermediates. This procedure gives easy access to enantiopure 2-oxazolidinones if the parent amino acids are easily (or even commercially) available in enantiopure form. Usually, *N*-derivatized 2-oxazolidinones are prepared using a two[2b,c] or even three[2a,d] step process consisting of reduction, intermolecular 2-oxazolidinone formation and *N*-derivatization (scheme, path 1). However, unusual amino acids, e.g. vinyl glycine, which are often easier obtainable as racemates,[3] can be converted to the enantiopure forms via enzymatic resolution of the ester carbamates using esterases.[4] The products of these enzymatic resolutions still contain a carbamate moiety (**1**). These carbamates can be converted directly to *N*-derivatized 2-oxazolidinones **3** via chemoselective reduction (**1** → **2**) and treatment with base, followed by addition of an electrophile in one pot (scheme, path 2), which is shorter than path 1. In addition, possible racemization during deprotection is avoided.

Results and Discussion. In the context of our efforts to use vinyl glycine derivatives as chiral building blocks in the synthesis of heterocycles[5] we first developed an one pot protocol for the conversion of Cbz-protected vinyl glycinol **2** (R = vinyl, R' = benzyl), prepared from racemic Cbz-protected vinyl glycine methyl ester via enzymatic resolution and reduction,[6] to *N*-derivatized 4-vinyl-2-oxazolidinones **3** using sodium hydride followed by an electrophile in etheral solvents (table; entries 1, 2). The generality of the process was then demonstrated by preparation of some other *N*-derivatized 2-oxazolidinones[7] in good yields using the same procedure[9,10] (table).



Scheme.

Table. *N*-Derivatized 2-Oxazolidinones Produced via One Pot Reaction

Entry	Solvent[a]	R	R'	Electrophile	Yield [%][b]
1	THF		Bn		72
2	DME		Bn		92
3	DME		Bn		89
4	DME		^{t}Bu		81
5	DME		Bn		76
6	DME		Bn		71

[a] THF: tetrahydrofuran, DME: 1,2-dimethoxyethane

[b] yield of isolated, purified product

In order to optimize the method, the influences of solvent (table; entries 1, 2), carbamate moiety (table; entries 3, 4) and electrophile (table; entries 3, 5) were investigated. We found, that DME was superior to THF as the solvent and the Cbz protecting group gave a better yield than the Boc group. Finally, both allyl bromide and propionyl chloride proved to be suitable electrophiles, although the latter gave a lower yield, probably due to side reactions under the standard reaction conditions used in this study (see below).

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REFERENCES AND NOTES

1. For important applications of 2-oxazolidinones see: (a) Coppola, G.M.; Schuster, H.F. *Asymmetric Synthesis. Construction of Chiral Molecules using Amino Acids*; Wiley Interscience: New York. 1987 (b) Evans, D.A. *Aldrichimica Acta* **1982**, *15*, 23 (c) Evans, D.A.; Ennis, M.D.; Mathre, D.J. *J. Am. Chem. Soc.* **1982**, *104*, 1737 (d) Evans, D.A.; Ennis, M.D.; Le, T.; Mandel, N.; Mandel, G. *J. Am. Chem. Soc.* **1984**, *106*, 1154 (e) Evans, D.A.; Ellman, J.A., Dorow, R.L. *Tetrahedron Lett.* **1987**, *28*, 1123 (f) Evans, D.A.; Britton, T.C.; Dorow, R.L.; Dellaria, J.F. *J. Am. Chem. Soc.* **1986**, *108*, 6395 (g) Evans, D.A.; Morrisey, M.M.; Dorow, R.L. *J. Am. Chem. Soc.* **1985**, *107*, 4346 (h) Heathcock, C.H. *Aldrichimica Acta* **1990**, *23*, 99 (i) Ertan, R.; Tuncbilek, M. *FABAD Farm. Bilimler Derg.* **1991**, *16*, 31 (j) Dyen, M.E.; Swern, D. *Chem. Rev.* **1967**, *67*, 197 (k) Pankratov, V.A.; Frenkel, Ts.M.; Fainlaib, A.M. *Russ. Chem. Rev.* **1983**, *52*, 576 (l) Atobe, I.; Takata, T.; Endo, T. *J. Polym. Sci., Part A: Polym. Chem.* **1993**, *31*, 1543.
2. For example see: (a) Gage, J.R.; Evans, D.A. *Org. Synth.* **1990**, *68*, 77 (b) Correa, A.; Denis, J.-N.; Greene, A.E. *Synth. Commun.* **1991**, *21*, 1 (c) Pridgen, L.N.; Prol, J. *J. Org. Chem.* **1989**, *54*, 3233 (d) Evans, D.A.; Sjogren, E.B. *Tetrahedron Lett.* **1985**, *26*, 3783.
3. For example compare: (a) Meffre, P.; Vo-Quang, L.; Vo-Quang, Y.; Le Goffic, F. *Synth. Commun.* **1989**, *19*, 3457 (b) *Eur. Pat. Appl.* 559927 A1, *CA* **1994**, *120*, P 271176f.
4. (a) Williams, R.M. *Synthesis of Optically Active α-Amino Acids*; Pergamon Press: Oxford. 1989; p. 257 (b) Chen, S.-T.; Chen, S.-Y.; Hsiao, S.-C.; Wang, K.-T. *Biotechnol. Lett.* **1991**, *13*, 773.
5. Huwe, C.M. *Diploma Thesis*, Technische Universität Berlin, 1993.
6. To be published in detail elsewhere.
7. All synthesized compounds gave satisfactory spectroscopic data (^{1}H-NMR, ^{13}C-NMR, MS, IR).
8. Kano, S.; Yuasa, Y.; Yokomatsu, T.; Shibuya, S. *J. Org. Chem.* **1988**, *53*, 3865.
9. Experimental procedures: The substrates (table; entries 3-6) were synthesized by adaption of published procedures from commercially available L-alaninol (Lancaster) and D-phenylglycinol (Fluka).[8] The products[10] (table; entries 1-6) were synthesized according to the following general procedure: 1.90 mmol of NaH (80%, suspension in paraffine) were placed in a dried, two necked flask under argon, washed twice with 2 ml of dry pentane and suspended in 16 ml of dry DME (table;

entries 2-6) or THF (table; entry 1). 1.26 mmol of amino alcohol carbamate, dissolved in 5 ml of dry solvent (DME or THF, see above), were added dropwise at room temperature. After stirring at room temperature for 24 h, 6.30 mmol of allyl bromide (table; entries 1-4) or propionyl chloride (table; entries 5, 6) were added and stirring continued at room temperature for 24 h. Aqueous work-up with methylene chloride and flash chromatography on silica gave the products stated (table).

10. Spectroscopic data of selected products: (*R*)-1-Allyl-4-vinyl-2-oxazolidinone (table; entries 1, 2; yellowish oil): ^{1}H-NMR (400 MHz, $CDCl_3$): δ [ppm] = 3.51 (brdd, 1H, J=7.5/15.5 Hz, NCH_2), 3.97 (dd, 1H, J=7/8.5 Hz, OCH_2), 4.12 (dddd, 1H, J=1.5/1.5/4.5/15.5 Hz, NCH_2), 4.23 (ddd, 1H, J=7/8/8.5 Hz, NCH), 4.44 (dd, 1H, J=8.5/8.5 Hz, OCH_2), 5.19 (brd, 1H, J=17 Hz, CH_2-CH=C<u>H</u>$_2$), 5.22 (brd, 1H, J=10 Hz, CH_2CH=C<u>H</u>$_2$), 5.33 (brd, 1H, J=17 Hz, CHCH=C<u>H</u>$_2$), 5.36 (brd, 1H, J=10.5 Hz, CHCH=C<u>H</u>$_2$), 5.69 (ddd, 1H, J=8/10.5/17 Hz, CHC<u>H</u>=CH_2), 5.74 (dddd, 1H, J=4.5/7.5/10/17 Hz, CH_2C<u>H</u>=CH_2). ^{13}C-NMR (50.3 MHz, $CDCl_3$): δ [ppm] = 44.2 (CH_2, NCH_2 or OCH_2), 58.3 (CH, NCH), 66.9 (CH_2, NCH_2 or OCH_2), 118.4 (CH_2, CH=<u>C</u>H$_2$), 121.1 (CH_2, CH=<u>C</u>H$_2$), 131.5 (CH, <u>C</u>H=CH_2), 134.3 (CH, <u>C</u>H=CH_2), 157.5 (C_q, C=O). MS (EI, 70eV): m/z = 154 (2%), 153 (M^+, 18%), 152 (3%), 138 (4%), 126 (11%), 124 (5%), 112 (12%), 108 (6%), 94 (9%), 92 (4%), 82 (10%), 80 (8%), 68 (13%), 67 (10%), 56 (5%), 55 (34%), 54 (100%). HR-MS: $C_8H_{11}NO_2$ (M^+) calcd 153.0790, found 153.0790. IR (CCl_4): 1/ν [cm^{-1}] = 930 (m), 991 (w), 1061 (s), 1132 (w), 1195 (w), 1222 (w), 1248 (w), 1405 (s), 1427 (m), 1437 (m), 1765 (vs), 2856 (w), 2927 (m), 2964 (w), 3086 (w). $[\alpha]_D^{25}$ (c = 2.1, $CHCl_3$) = + 93.0°. (*S*)-1-Allyl-4-isopropyl-2-oxazolidinone (table; entries 3, 4; yellowish oil): ^{1}H-NMR (200 MHz, $CDCl_3$): δ [ppm] = 0.85 (d, 3H, J=7 Hz, CH(C<u>H</u>$_3$)$_2$), 0.87 (d, 3H, J=7 Hz, CH(C<u>H</u>$_3$)$_2$), 2.04 (dtt, 1H, J=3.5/7/7 Hz, C<u>H</u>(CH$_3$)$_2$), 3.51 (brdd, 1H, J=8/16 Hz, NCH_2), 3.73 (ddd, 1H, J=3.5/6/9 Hz, NCH), 4.06 (dd, 1H, J=6/9 Hz, OCH_2), 4.14-4.27 (m, 2H, NCH_2 and OCH_2), 5.22 (brd, 1H, J=10.5 Hz, CH=C<u>H</u>$_2$), 5.23 (brd, 1H, J=17 Hz, CH=C<u>H</u>$_2$), 5.76 (m, 1H, C<u>H</u>=CH_2). ^{13}C-NMR (50.3 MHz, $CDCl_3$): δ [ppm] = 14.0 (CH_3, CH(<u>C</u>H$_3$)$_2$), 17.4 (CH_3, CH(<u>C</u>H$_3$)$_2$), 27.0 (CH, <u>C</u>H(CH$_3$)$_2$), 44.5 (CH_2, NCH_2 or OCH_2), 58.4 (CH, NCH), 62.6 (CH_2, NCH_2 or OCH_2), 118.3 (CH_2, CH=<u>C</u>H$_2$), 131.9 (CH, <u>C</u>H=CH_2), 158.1 (C_q, C=O). MS (EI, 70eV): m/z = 169 (M^+, 10%), 126 (100%), 98 (14%), 86 (3%), 82 (3%), 70 (2%), 68 (2%), 56 (6%), 55 (11%), 54 (12%). HR-MS: $C_9H_{15}NO_2$ (M^+) calcd 169.1103, found 169.1103. IR (CCl_4): 1/ν [cm^{-1}] = 928 (m), 994 (w), 1055 (s), 1072 (s), 1119 (m), 1134 (w), 1198 (w), 1242 (s), 1341 (w), 1371 (w), 1394 (s), 1414 (s), 1485 (m), 1764 (vs), 2876 (w), 2915 (m), 2929 (m), 2966 (s), 3084 (w). $[\alpha]_D^{25}$ (c = 2.1, $CHCl_3$) = - 32.1°.

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