compounds. The SSCC agrees well with the dihedral angle found from the Williamson—Johnson curve [6]. The dihedral angles for compounds of the Aa and Ab series that were found in this manner suggest that the angle 4-H—$C_{(4)}$—$C_{(5)}$—5-H of Aa is about two times less than the analogous angle of Ab. This is consistent with a large distortion of the oxazolidine ring of Ab compared with Aa. The single exception is 9, which has the bulkiest aromatic substituent on $C_{(2)}$. It was found that $^3J_{(4,5)}$ of 9Aa (4.18 Hz) is almost two times less than that of 9Ab (8.22 Hz). Apparently steric interactions of the substituent on $C_{(2)}$ in 9Aa with the 4-CH_3 and 5-Ph groups significantly distort the ring (angle 4-H—$C_{(4)}$—$C_{(5)}$—5-H is $\sim 50 \pm 3°$). However, the same interactions of the substituent in the 2-position of 9Ab with the N—Me group flatten the five-membered ring (angle 4-H—$C_{(4)}$—$C_{(5)}$—5-H is $\sim 30 \pm 3°$). With respect to the Ba—Bb series, the comparative conformations of these isomers cannot be judged from the PMR spectra owing to a lack of data for the Bb isomer.

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SYNTHESIS OF *N*-BENZYLOXYCARBONYL-*N*-METHYLAMINOACIDS FROM OXAZOLIDINE-5-ONE DERIVATIVES

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Hydrogenolysis of 3-benzyloxycarbonyloxazolidine-5-one and 3-benzyloxycarbonyl-4-benzyloxazolidine-5-one by Et_3SiH in the presence of F_3CCO_2H is demonstrated to be a convenient method for preparing substituted N-methylaminoacids. In contrast with catalytic hydrogenation on Pd/C catalyst, the benzyloxycarbonyl is not removed and the methyl is not lost using this method.

Natural antibiotics such as actinomycins, etamycins, enniamtins, and others containing the *N*-methylaminoacid residue are widely used for modifying biologically active peptides [1, 2]. Synthetic analogs of oxytocin and vasopressin [3], bradykinin [4], gramicidin [5], and other peptides also contain *N*-methylaminoacids. Heterocyclic derivatives of 1,3-oxazolidine-5-one and pyrroline-2-one [6] are synthesized using *N*-methylaminoacids.

Many synthetic methods for synthesizing *N*-methylaminoacids have been developed (see a previous monograph [7]). A promising method for preparing *N*-substituted-*N*-methylaminoacids is the hydrogenolysis of the corresponding derivatives of 5-oxazolidinones by Et_3SiH in F_3CCO_2H [8]. This method was used to synthesize *N*-methyl-*N*-(9-fluorenylmethyloxycarbonyl)aminoacids, mainly lysine derivatives.

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TABLE 1. Conditions and Hydrogenolysis with Et_3SiH in the Presence of F_3CCO_2H for I, II, and VI

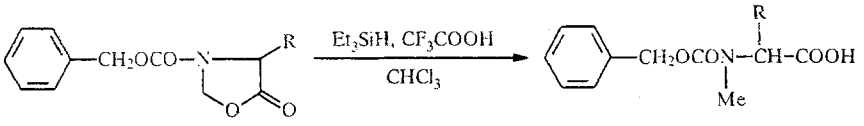
Starting compound	Starting compound: Et_3SiH, mole*	Reaction time, h	Number of expts.	Reaction product**	Yield, %
I	1 : 2,69	26	2	III A	38
II	1 : 2,69	27	1	IV B	43
II	1 : 2,69	27	3	IV A	76
II	1 : 2,68	27,2	2	IV C	64
II	1 : 4,39	24	1	IV A	52
II	1 : 1,8	24	1	IV A	68
VI	1 : 2,68	27	1	V A	Not detected

*The concentration of starting compound in F_3CCO_2H:$CHCl_3$ (1:1) is 0.115 m*M*.

**A is the DCHA salt; B, Na; C, Li.

We studied hydrogenolysis of 3-benzyloxycarbonyloxazolidine-5-one (I) and 3-benzyloxycarbonyl-4-benzyloxazolidine-5-one (II) by Et_3SiH in the presence of F_3CCO_2H. It was found that the reaction produces *N*-benzyloxycarbonylsarcosine (III) and *N*-benzyloxycarbonyl-*N*-methylphenylalanine (IV).

The ratio II:Et_3SiH was varied from 1:2.7 to 1:4.4 (Table 1).



I, II III, IV

I, III R=H; II, IV R=CH_2Ph

The average hydrogenolysis yield for II with a 1:2.7 molar ratio of starting compound to Et_3SiH is 76%. Increasing the amount of Et_3SiH in the ratio to 4.39 reduces the yield to 52%. The yield of IV also depends on the method of isolation. Under the studied conditions, the yield of the Na salt is 42%; of the dicyclohexylammonium (DCHA) salt, 76%; of the Li salt, 64%.

The ability to synthesize *N-tert*-butyloxycarbonyl-*N*-methylphenylalanine (V) by hydrogenolysis of 3-*tert*-butyloxycarbonyl-4-benzyloxazolidine-5-one (VI) was also checked. However, the *Boc*-protected acid was not observed. Hydrogenolysis of I was carried out by an analogous method, resulting in the isolation in 38% yield of *N*-benzyloxycarbonylsarcosine.

Thus, only the hydrolysis of the ring and reduction of the hydroxymethyl group to methyl without involvement of the *N*-protecting group occur during hydrogenolysis of *N*-benzyloxy-protected 4-benzyloxazolidine-5-ones. However, catalytic hydrogenolysis of the aforementioned starting compounds on Pd/C catalysts is accompanied by hydrogenolysis of the *N*-protecting benzyloxycarbonyl group [9, 10]. Moreover, a side reaction involving cleavage of the resulting N–CH_3 group to form the free aminoacid occurs during catalytic hydrogenolysis [10].

EXPERIMENTAL

Analysis employed liquid chromatography on a DuPont 830 chromatograph equipped with a UV spectrophotometer and a column (4.6×150 mm) packed with Zorbax C_8 sorbent. The detection wavelength was 215 or 220 nm. The optical pathlength of the cuvette was 1 mm. The sample volume was 10-50 μl. The concentration was 1-2 mg/ml. The eluent for compounds IV and V was 30% CH_3CN and 70% 0.02 *M* NH_4Ac at pH 5.0. Chromatographic analysis of III was carried out

using a DuPont 850 chromatograph, Silasorb SPN C_{18} sorbent, and 0.5% tetrabutylammonium phosphate eluent at pH 3. The NMR spectrum was recorded on a Bruker WM-360 spectrometer in DMSO-D_6 with TMS internal standard.

Elemental analyses for C, H, and N agreed with those calculated.

The starting oxazolidine-5-ones are prepared in high yield by condensation of *N*-substituted aminoacids with formaldehyde in the presence of formic or *p*-toluenesulfonic acids [7].

General Method for Preparing *N*-Methylaminoacids from *N*-Substituted Oxazolidine-5-ones. A mixture of benzyloxycarbonyl-protected oxazolidine-5-one, $CHCl_3$, and F_3CCO_2H is treated with Et_3SiH and stirred at 20°C (see Table 1). After the reaction was finished the solvent and unreacted Et_3SiH were vacuum distilled. The F_3CCO_2H and Et_3SiH were more completely removed by dissolving the oily residue in CH_2Cl_2 and again vacuum distilling the solvent. The resulting oily liquid was freed of traces of F_3CCO_2H by washing and stirring with distilled water (3×20 ml). The water was decanted. The oil was dried over P_2O_5, dissolved in a small amount of ether, and treated with dicyclohexylamine in equimolar amounts. Petroleum ether was added to the resulting solution, which was stored at 5 °C for 24 h. The residue was filtered off and crystallized from *n*-hexane. Yield of Z-Sar·DCHA, 38%.

Z-L-MePhOH·DCHA. The data are: mp 118 °C, lit. [11] 118 °C; $[\alpha]_D^{15} = -19.6°$ (c = 1, ethanol). The PMR spectrum is consistent with *cis-trans*-isomers (A and B) at the amide bond in a 1:1 ratio. PMR spectrum: 7.1-7.4 (10H, m, C_6H_5); 5.00, 4.93 (d, ^2J = 13.2 Hz, CH_2O) B; 4.85 (s, CH_2O) A; 4.65 (doublet of doublets, ^3J = 5.4, 11.5 Hz, $-C_B^{\alpha}H$); 4.56 (d. of d., ^3J = 4.0, 11.5 Hz, $-C_A^{\alpha}H$); 3.76, 2.80 (d. of d., ^2J = 14.0 Hz, $-C_A^{\beta}H_2$); 3.78, 2.83 (d. of d., ^2J = 14.0 Hz, $C_B^{\beta}H_2$); 4.85 (s, $-N_A-CH_3$); 4.93 (s, N_B-CH_3). PMR spectrum of DCHA (ppm): 2.92 (2H, N—CH); 1.94 (4H); 1.69 (4H), 1.58 (2H); 1.0-1.3 (10H). Yield 85%.

Z-L-MePhONa. $[\alpha]_D^{20} = -64.3°$ (c = 1, H_2O), mp 222.4-223 °C.

Z-L-MePhOLi. $[\alpha]_D^{20} = -25.7°$ (c = 1, ethanol), mp 127-129 °C.

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