A New α-Amino Acid Synthesis *via* an Acetimidate Rearrangement

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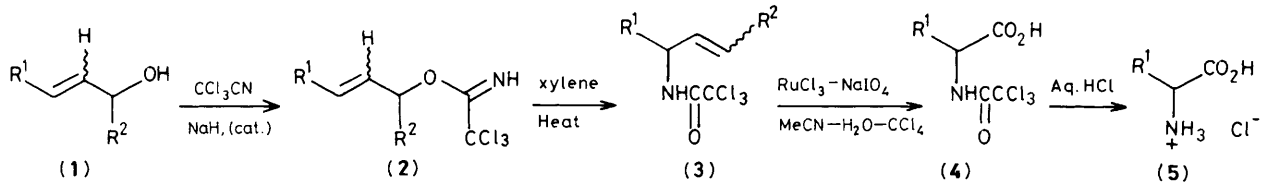
A new efficient synthesis of α-amino acids from allyl alcohol derivatives *via* an acetimidate rearrangement has been developed.

Although a wide range of methods is available for the synthesis of α-amino acids,[1] there are very few examples employing the cleavage of an alkene for the construction of the carboxy moiety[2] probably because of the reactivity of the amine moiety under the oxidative conditions used. We describe herein a new synthesis of α-amino acids using just such a reaction to obtain the carboxy group in the presence of a protected amine group. A key stage of the present synthesis is the well-established [3,3]sigmatropic rearrangement of a trichloroacetimidate[3] of an allylic alcohol. This produces an alkene with a primary amine group, in an appropriate position and in a protected form, suitable for the synthesis of an α-amino acid.

According to the established procedure,[3b,4] the allyl alcohols (**1a**—**g**) were condensed with trichloroacetonitrile [NaH(cat.)] to give the corresponding trichloroacetimidates (**2a**—**g**) which were used without purification. Compounds (**2a**—**g**) thus obtained were heated in refluxing xylene overnight to give, in acceptable overall yields, the corresponding rearranged compounds (**3a**—**g**)† which have a trichloroacetamide group at the allylic position.

Oxidation of the alkenes (**3a**—**g**) [$RuCl_3$ (cat.), $NaIO_4$ (5 mol. equiv.), $MeCN$–CCl_4 (aq.)][5] at ambient temperature furnished the carboxylic acids (**4a**—**g**), in good yields without affecting the trichloroacetamide moiety. The compounds, (**4**),

† All new compounds exhibited satisfactory analytical (combustion and/or high resolution mass spectrum) and spectroscopic (i.r., ^1H n.m.r., and mass) data.



			(3) Yield from (1) (%)	(3) M.p. (°C)	(4) Yield (%)	(4) M.p. (°C)
	R^1	R^2				
a	H	H	50	30.5—31.5	77	132—133
b	Me	H	75	39.5—41	84	162
c	$PhCH_2OCH_2$	H	53	Semi-solid	83	91.5—92.5
d	Bu^t	H	63	52—53	80	104—105
e	Ph	H	62	44—46	72	165.5—166
f	$PhCH_2$	H	62	53—54	60	126—127
g	$-[CH_2]_3-$		69	84.5—85	60	135—136

were identical with authentic materials prepared from the corresponding α-amino acids by acylation with hexachloroacetone.[6] It is worthy of note that an ω-carboxylic α-amino acid may be obtained in one stage using the cyclic substrate (**1g**). However the trichloroacetimidate prepared from cyclopent-2-enol did not afford the corresponding trichloroacetamide under the same conditions. Treatment of (**4a—g**) with 1 M HCl at refluxing temperature left the corresponding α-amino acid hydrochlorides (**5a—g**), in good yields after azeotropic removal of volatile material from the reaction mixture under reduced pressure. Under these conditions the benzyl group of compound (**5c**) could be removed to give the primary alcohol group although a longer reaction time (45 h) was required.

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References

1 J. H. Jones, 'Comprehensive Organic Chemistry', eds. D. H. R. Barton and W. D. Ollis, Pergamon, Oxford, 1979, vol. 2, p. 815; I. T. Harrison and S. Harrison, 'Compendium of Organic Synthetic Methods,' Wiley, New York, 1974, vol. II, p. 248; L. S. Hegedus and L. Wade, *ibid.*, 1977, vol. III, p. 345; L. G. Wade, Jr., *ibid.*, 1980, vol. IV, p. 352.
2 R. C. Kelly, I. Schletter, S. J. Stein, and W. Wierenga, *J. Am. Chem. Soc.*, 1979, **101**, 1054; P. Casara, C. Danzin, B. W. Metcalf, and M. J. Jung, *J. Chem. Soc., Chem. Commun.*, 1982, 1190.
3 (a) L. E. Overman, *J. Am. Chem. Soc.*, 1974, **96**, 597; 1976, **98**, 2901; (b) L. A. Clizbe and L. E. Overman, *Org. Synth.*, 1978, **58**, 4.
4 F. Cramer, K. Pawelzik, and H. J. Baldauf, *Chem. Ber.*, 1958, **91**, 1049.
5 P. H. J. Carlsen, T. Katsuki, V. S. Martin, and K. B. Sharpless, *J. Org. Chem.*, 1981, **46**, 3936.
6 C. A. Panetta and T. G. Casanova, *J. Org. Chem.*, 1970, **35**, 2423.