Tetrahedron Vol. 39, No. 18, pp. 2995 to 2998, 1983
Printed in Great Britain

0040-4020/83 $3.00 + 00

BOROXAZOLIDONES AS SIMULTANEOUS PROTECTION OF THE AMINO AND CARBOXYL GROUP IN α-AMINO ACIDS

G. H. L. NEFKENS and B. ZWANENBURG*
Department of Organic Chemistry, University of Nijmegen, Toernooiveld, 6525 ED NIJMEGEN, The Netherlands

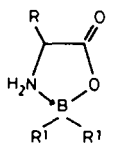
(*Received in UK 17 September 1982*)

Abstract—The synthesis of boroxazolidones **1** form a variety of α-amino acids is given. These compounds **1** show a strong intramolecular coordination between B and the amino group. These heterocycles can serve as protected α-amino acids in which the α-amino and the carboxyl function are simultaneously blocked, while the side chain remains free for further reactions. The boroxazolidines were reconverted into α-amino acids under mild acid conditions. Using this methodology aspartic acid was converted into β-benzyl aspartate and glutamic acid into γ-benzyl glutamate.

In effecting an efficient conversion of functional groups present in the side chain of α-amino acids an appropriate, preferably simultaneous, protection of the α-amino and the carboxyl function is highly desirable. For the dibasic amino acids ornithine and lysine Cu(II) complexes have been used for this purpose, e.g. during the synthesis of ω-acyl derivatives.[1,2]

However, in most cases the applicability of Cu complexes is limited due to their low solubiltiy. 5-Oxazolidinone derivatives which can be prepared from N-protected α-amino acids and paraformaldehyde have been employed as dual protection of the α-amino and α-carboxyl group in the synthesis of β-aspartyl and γ-glutamyl peptides. The protecting oxazolidinone ring can readily be removed by alkaline hydrolysis[3] or by catalytic hydrogenolysis.[3] However, it should be noted that the CO group in these oxazolidinones still has an appreciable reactivity towards amines.[3,4]

The aim of the present study is to investigate the synthetic utility of the zwitterionic boron amino acids complexes with the general structure **1**, for the simultaneous protection of the α-amino and α-carboxyl group. Compounds of this nature occur in the chemical literature under various names, viz as boroxazolidones[5] and as esters[6] or mixed anhydrides[7-9] of amino acids and di-alkyl (or aryl) borinic acid. We prefer to designate these compounds as heterocycles in accordance with Chemical Abstracts.

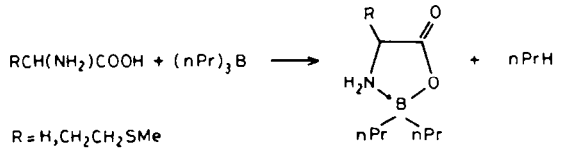


1

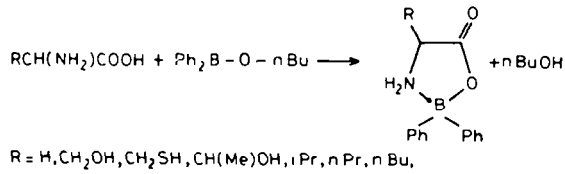
The synthesis of boroxazolidones was reported for the first time by Lang *et al.*[5] by reaction of glycine and methionine with tri-n-propylborane in refluxing xylene (Scheme 1).

A different route was described by a group of Chinese authors[7] who treated various amino acids with n-butyl diphenylborinate (Scheme 2).

The same approach was reported by Skoog[8] for the preparation of the heterocycles **1** (R^1 = Ph) from glycine,



Scheme 1.



Scheme 2.

alanine and leucine. Baum[9] reacted the comercially available sodium tetraphenylborate with an amino acid chlorohydrate in refluxing aqueous solution. This conversion probably proceeds via the *in situ* generated triphenylborane which then reacts according to Scheme 1. In this manner B,B-diphenylboroxazolidones were obtained from glycine, alanine, phenylalanine, proline, cysteine and tyrosine.

An improvement of the method depicted in Scheme 1 was reported by Köster and Rothgery[6] who used triethylborane in acetonitrile as the solvent and diethylboryl pivalate as accelerator. As α-amino acids they studied glycine, alanine, phenylalanine and sarcosine (N-methylglycine).

B,B-Difluoroboroxazolidones[10] were obtained from the reaction of *N*-alkyl α-amino acids with borontrifluoride etherate. Heterocycles of type **1** having two H atoms at B were prepared from N,N-dimethyl α-amino acids and the complex of trimethyl amine and jodoborane.[11]

The heterocyclic nature of the compounds was clearly established by an X-ray analysis[12] of the product **1** derived from proline and diphenylborinic acid. As consequence of the strong intramolecular N–B coordination the B atom has the tetrahedral configuration.

It should be noted that, although various boroxazolidones have been prepared, their chemical behaviour hardly has received attention. This paper describes a

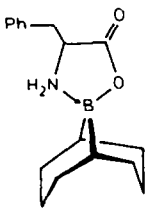
slightly modified synthesis of boroxazolidones from a variety of α-amino acids, particularly those having an additional functional group in the side chain.

RESULTS

Synthesis and properties of boroxazolidones derived from glycine, phenylalanine and tryptophane. Finely powdered dry glycine and phenylalanine both gave upon treatment with a slight excess of a one molar solution of triethylborane (Et_3B) in tetrahydrofuran (THF) products which are identical in all respects with the boroxazolidones **1** having R = H, R^1 = Et and R = $PhCH_2$, R^1 = Et, respectively, reported by Köster *et al.*[6] In fact our method closely resembles that described by Köster *et al.*,[6] however, we found no need for adding an accelerator.

B,B-Diphenylboroxazolidone **1c** could conveniently be prepared from L-phenylalanine and triphenylborane in THF solution. The required borane was obtained according to the method of Wittig[13] by pyrolysis of dimethylammonium tetraphenylborate.

Tryptophane could also be converted into the corresponding heterocyclic **1d** using the experimental conditions indicated above. The yields and m.p. of the respective boroxazolidones **1** are recorded in the Table. L-Phenylalanine also reacted smoothly with 9-borabicyclo[3.3.1]nonane (9-BBN) in THF to give the boroaxazolidone **2** in high yield.



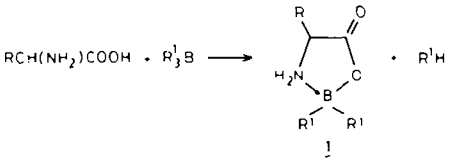
The product **1a** was subjected to some electrophilic and nucleophilic reactions in order to establish the merits of the heterocyclic systems as protecting group for amino acids. By heating **1a** with one equiv of benzylamine in refluxing toluene starting material could be recovered almost quantitatively. Treatment of **1a** with 2,4,6-trichlorophenyl N-(benzyloxy-carbonyl)glycidate in THF at 50° in the presence of one equiv of triethylamine did not lead to any acylated product. these experiments indicate a low reactivity of the CO as well as of the N atom of the boroaxzolidones.

It is of importance that boroxazolidones can be reconverted into the corresponding amino acids under mild conditions. By dissolving **1a** and **1b** in ethyl acetate and passing dry gaseous hydrogen chloride or hydrogen bromide over this solution, resulted in a practically quantitative precipitate of the amino acid halohydrate. It is also possible to recover the amino acids from **1a** and **1b** by treatment of these heterocycles with 4N HCl at 40°, or even by refluxing the compounds over night in pure methanol. It is remarkable, however, that the heterocycles **1a** and **1b** can be dissolved in acetic acid or even trifluoroacetic acid without noteable decomposition.

The B,B-diphenylboroaxazolidone **1c** is much more stable towards hydrolysis than the diethyl analogue as it is stable in refluxing water[7,9,12].

Boroxazolidones derived from aspartic and glutamic acid. Treatment of finely divided L-aspartic acid and L-glutamic acid with Et_3B in THF results in both cases in B containing compounds in high yields (Table 1). The structures of these materials need detailed attention as either of the carboxyl group can be involved in the reaction with Et_3B. Intramolecular coordination of B with the amino group then can lead to different types of heterocycles, viz the 5-membered boroxazolidones **1e, f** or the larger heterocyclic rings **3a, b**. These latter rings are quite feasible as Köster *et al.*[6] reported the formation

Table 1.

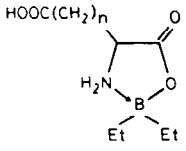


1

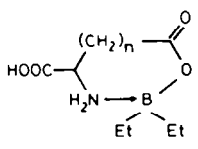
nr.	R	R^1	m.p. (°C)	%
1a	H	Et	174 (a)	~100
1b	$PhCh_2$	Et	174 (b)	80
1c	$PhCh_2$	Ph	230 (c)	70
1d	3-indolylmethyl	Et	134	50
1e	$HOOCCH_2$	Et	166-168	~100
1f	$HOOCCH_2CH_2$	Et	oil (d)	~100
1g	$HOOCCH_2$	Ph	115 (e)	60
1h	$HOOCCH_2CH_2$	Ph	218	50
1i	$HSCH_2$	Et	90	~100
1j	$PhCH_2SCH_2$	Et	109-110	90
1k	$HSCH_2$	Ph	232 (f)	65
1l	$ClH \cdot H_2N(CH_2)_4$	Et	98-99 (e)	60

(a) lit.[6] 160-161°
(b) lit.[6] 175°
(c) lit.[9] reports for the product derived from racemic phenylalanine: 219°
(d) solidifies slowly on standing or on treatment with a little diisopropyl ether, m.p. 110°
(f) lit.[9] 210°
(e) contains one mole of DMSO of crystallisation.

of a 6-membered B-heterocycle from β-alanine and Et_3B. On the case of γ-amino-butyric acid these authors proposed the coordination of the γ-amino group with B to a 7-membered ring. However, in view of the deviating solubility properties of thes product a polymeric structure seems more likely.



1e (n = 1)
1f (n = 2)



3a (n = 1)
3b (n = 2)

In order to elucidate the structures of the products obtained from aspartic and glutamic acid the extra carboxyl groups in the B containing materials were derivatized as benzyl ester by treatment with dicyclohexylamine followed by benzylbromide in dimethyl formamide. After reconversion of the thus-obtained B-heterocycles into the amino acids by treatment with hydrogen bromide in ethyl acetate, followed by neutralisation with Et_3N, β-benzyl L-aspartate and γ-benzyl L-glutamate were obtained, respectively. These benzyl esters were identical with authentic samples prepared by unambigeous routes.[14] These results clearly demonstrate that with aspartic and glutamic acid the 5-membered boroxazolidones **1e** and **1f** have been formed exclusively.

In a similar fashion as described in the previous section the B,B-diphenyl B heterocycles **1g** and **1h** were obtained from aspartic and glutamic acid, respectively, upon treatment with Ph_3B. The 5-membered ring structure is also adopted in these cases in analogy with the B,B-diethyl derivatives and in view of the mechanism of formation (Discussion).

The free carboxyl groups in the boroxazolidones **1e** and **1f** could readily be converted into the corresponding *p*-nitrophenyl esters by treatment with *p*-nitrophenol and dicyclohexylcarbodiimide. These activated esters may be considered as suitable starting materials for making β-aspartyl and γ-glutamyl peptides.

Boroxazolidones from cysteine. By treatment of L-cysteine with Et_3B in THF smooth formation of a B containing product took place. In order to establish its structure the product was treated with one equiv of dicyclohexylamine followed by one equiv of benzylbromide in DMF. The thus-formed compound was identical to the one (**1j**) produced by the reaction of S-benzyl cysteine[15] with Et_3B in THF. Hence, the reaction of cysteine with Et_3B leads to the 5-membered boroheterocycle **1i**. Cysteine gave with Ph_3B the corresponding heterocycle **1k**.

Boroxazolidone from lysine. Lysine hydrochloride suspended in DMF gave upon treatment with Et_3B in THF the product **1l** in moderate yield. The compound was assigned the 5-membered boroxazolidone structure as coordination of B with the ε-amino function in a 9-membered ring seems highly unlikely. The terminal aminogroup in **1l** can be converted[16] into the 2,4-dinitrophenylamino group by treatment with base and subsequently with 2,4-dinitrofluorobenzene. The corresponding ε-derivatized lysine hydrochloride was then obtained by solvolysis with hydrogen chloride in methanol.

DISCUSSION

The results obtained with the various amino acids clearly demonstrate the exclusive formation of 5-membered boroxazolidones by reaction of Et_3B with the α-amino and α-carboxyl group, even when competing functions for ring-formation are present in the substrate. A plausible mechanism for this exclusive formation of the 5-membered ring heterocycles is pictured in Scheme 3.

The amino acid in its zwitterionic form first reacts with Et_3B at the carboxylate group to form borate **4**. Intramolecular protonolysis of this borate then leads to hydrocarbon and the heterocycle possessing a strong coordination between N and B. Support for the proposed borate **4** is that stable borates of a similar type have been isolated and characterized from amino acids (glycine, alanine and phenylalanine) and boron tri-fluoride $[RCH(NH_3)COOB\ F_3]$.[17]

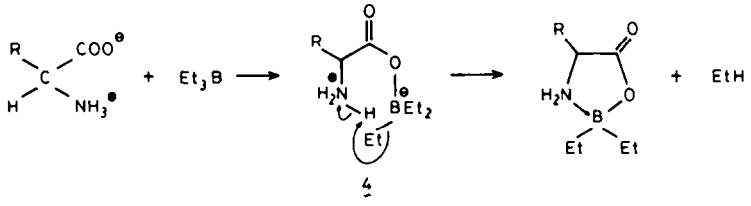
The boroxazolidones derived from α-amino acids and Et_3B are soluble in a variety of solvents, they are stable under basic conditions and they can be reconverted into α-amino acids using very mild acidic reagents. Therefore, these boroheterocycles are suitable for the simultaneous protection of the α-amino and α-carboxyl group in α-amino acids. The B,B-diphenyl derivatives, that are obtained from α-amino acids and Ph_3B, are much more stable towards solvolysis and therefore less suitable for the double protection purpose.

Further exploration and search for synthetic applications of these boroxazolidones are currently under active investigation in our laboratory.

EXPERIMENTAL

IR spectra were taken on a Perkin–Elmer 257 grating spectrometer. NMR spectra were recorded on a Varian EM 390 using TMS as internal standard. All m.ps are uncorrected.

Boroxazolidones **1** (General procedures). Finely ground L-amino acid (10 mmoles) was suspended in THF (5–10 ml), then a 1M soln of triethylborane (12 mmole) in THF (12 ml) was added and the mixture was stirred until the amino acid had dissolved. The reaction time strongly depends on the effectiveness of the grinding, with finely powdered amino acid the reaction is completed within 5–30 min. The soln was then filtered, if necessary and concentrated to dryness. The residue was treated with either toluene or cyclohexane, the product was collected by filtration



4

Scheme 3.

and washed with cyclohexane or diisopropyl ether. With lysine hydrochloride the amino acid was suspended in DMF (10 mmole in 100 ml). The reaction was accelerated by a small flow of N_2. Dissolution in this case required about 24–48 hr. Product **11** was recrystallized from dimethylsulfoxide–ethyl acetate.

The B,B-diphenyl derivatives were obtained from Ph_3B (prepared according to Ref. 13) and finely powdered amino acid in either THF, DMSO or DMF as the solvent and at temp of 100–115°. After dissolution of the amino acids, the solvent was removed and the residue crystallized from acetonitrile or acetonitrile–diisopropyl ether. For product **2** derived from phenyl alanine and 9-BBN the procedure as described for Et_3B was used (yield 90%, m.p. 190°).

Spectral data: **1a**; IR ν_{max}^{KBr} 3300, 3230, 3140 (N–H), 1700 (C=O) cm^{-1}; NMR (d_6-DMSO) δ 0.3–0.8 (m, 10H, B-CH_2CH_3), 3.52 (t, 2H, CH_2CO), 5.72 (broad signal, 2H, NH_2). **1b**: IR ν_{max}^{KBr} 3280, 3205, 3060 (N–H), 1705 (C=O) cm^{-1}; NMR (d_6-DMSO) δ 0.3–1.0 (m, 10H, B-CH_2CH_3), 3.3 (m, 2H, CH_2Ph), 4.1 (m, 1H, >CHCO), 4.8 (broad signal, 1H, N–H), 6.15 (broad signal, 1H, NH), 7.3 (s, 5H, Ph); $[\alpha]_D^{20} = -86.2$ (C = 1, DMF). **1c**: IR ν_{max}^{KBr} 3250, 3190, 3100 (N–H), 1715 (C=O) cm^{-1}; NMR (d_6-DMSO) δ 3.1 (m, 2H, CH_2Ph), 3.73 (m, 1H, >CHCO), 6.8 (broad signal, 2H, NH_2), 7.1–7.6 (m, 15H, Ph); $[\alpha]_D^{20} = -29.2$ (C = 1, DMF). **1d**: IR ν_{max}^{KBr} 3315, 3205 (N–H), 1690 (C=O) cm^{-1}; NMR (d_6-DMSO) δ 0.2–0.9 (m, 10H, BCH_2CH_3), 3.2 (m, 2H, CH_2), 3.85 (m, 1H, CH) 5.1 and 6.5 (broad t, 2×1H, NH_2), 6.9–7.6 (m, 5H, arom. pr.), 10.85 (s, 1H, N–H); $[\alpha]_D^{20} = -99.1$ (C = 1, DMF). **1e**: IR ν_{max}^{KBr} 3300, 3220 (N–H), 1700 (br, C=O) cm^{-1}; NMR (d_6-DMSO) δ 0.2–0.9 (m, 10H, B-CH_2CH_3), 2.7 (d, 2H, CH_2), 3.8 (m, 1H, CH), 5.62 and 6.4 (br. t, 2×1H, NH_2), 8.2 (s, 1H, COOH); $[\alpha]^{D20} + 79.2$ (C = 1, DMF). **1f**: IR ν_{max}^{KBr} 3200 (br., OH, NH), 1715 (C=O) cm^{-1}; NMR (d_6-DMSO) δ 0.2–0.8 (m, 10H, B-CH_2CH_3), 1.9 (m, 2H, >$CHCH_2$), 2.42 (t, 2H, -CH_2COOH), 3.5 (m, 1H, CH), 5.6 and 6.45 (br.t, 2×1H, N–H). $[\alpha]_D^{20} - 17.3$ (C = 1, DMF). **1g**: IR ν_{max}^{KBr} 3140 (br, NH, OH), 1730 (C=O) cm^{-1}; NMR (d_6-DMSO) δ 2.75 (d, 2H, CH_2), 3.78 (m, 1H, CH), 6.8 (br.t, 2H, NH_2), 7.1–7.6 (m, 10H, Ph), 12.5 (br.s, 1H, COOH), the product contained 1 mole of DMSO of crystallisation: δ 2.5 (6H). $[\alpha]_D^{20} + 15.2$ (C = 1, DMF). **1h**: IR ν_{max}^{KBr} 3100 (broad, N–H and O–H), 1710 (C=O) cm^{-1}; NMR (d_6-DMSO) δ 2.0 (m, 2H, >$CHCH_2$), 2.5 (m, 2H, CH_2COOH), 3.6 (br.m, 1H, CH), 6.76 (br.t, 2H, NH_2), 7.1–7.6 (m, 10H, Ph), 12.1 (br.s, 1H, COOH). $[\alpha]_D^{20} - 7.9$ (C = 1, DMF). When the product is prepared in DMF the crystals contain adherent solvent. **1i**: IR ν_{max}^{KBr} 3230, 3180, 3030 (N–H), 1700 (C=O) cm^{-1}; NMR (d_6-DMSO) δ 0.2–0.9 (m, 10H, B-CH_2CH_3), 1.5 (q, 1H, SH), 2.5–3.6 (m, 2H, CH_2), 4.2 (m, 1H, CH), 4.75 and 6.0 (br.t, 2×1H, NH_2); $[\alpha]_D^{20} - 4.8$ (C = 1, DMF). **1j**: NMR ($CDCl_3$) δ 0.2–0.9 (m, 10H, B-CH_2CH_3), 2.8–3.4 (4d, 2H, CH_2CH), 3.70 (s, 2H, CH_2Ph), 3.95 (m, 1H, CH), 4.4 and 5.6 (br.t, 2×1H, NH_2), 7.3 (s, 5H, Ph). **1k**: IR ν_{max}^{KBr} 3180, 3100 (N–H), 2560 (S–H), 1740 (C=O) cm^{-1}; NMR (d_6-DMSO) δ 2.8 (m, 3H, -CH_2SH), δ 3.8 (m, 1H, CH), 6.8 (br.t, 2H, NH_2), 7.2–7.7 (m, 10H, Ph); $[\alpha]_D^{20} - 118.5$ (C = 0.5, DMF). **1l**: IR ν_{max}^{KBr} 3000 (NH_3, $^+NH_3$), 1690 (C=O) cm^{-1}; NMR (d_6-DMSO) δ 0.2–0.9 (2m, 10H, B-CH_2CH_3), 1.4–2.0 (br.m, 6H, $(CH_2)_3CH$), 2.8 (t, 2H, $CH_2NH_3^+$), 3.45 (br.m, 1H, CH), 5.78 and 6.60 (br.t, 2×1H, NH_2), 8.15 (br.m, 3H, NH_3^+); the compound contained one mole of adherent DMSO, δ 2.57 (6H); $[\alpha]_D^{20} - 17.1$ (C = 1, DMF). **2**: IR ν_{max}^{KBr} 3340, 3200 (N–H), 1730 (C=O) cm^{-1}; NMR (d_6-DMSO) δ 0.5 (m, 2H, CHBCH), 1.65 (m, 12H, cyclooctane prot.), 3.1 (m, 2H, CH_2Ph), 3.8 (m, 1H, CHCO), 5.75 and 6.40 (br.m, 2×1H, NH_2), 7.2 (s, 5H, Ph); $[\alpha]_D^{20} - 87.9$ (C = 1, DMF).

β-Benzyl aspartate and γ-benzyl glutamate. Compound **11** (10 mmole) was dissolved in DMF (10 ml) and dicyclohexylamine (10 mmole) was added. The mixture was heated to 60–70° and then benzylbromide (10 mmole) was added. After heating for 5 min the mixture was cooled, dicyclohexylammonium bromide was filtered off and the filtrate concentrated *in vacuo*. The residue was dissolved in EtOAc, then washed with water, well dried on $MgSO_4$. After some concentration HCl-gas was passed over the soln affording β-benzyl aspartate as the hydrochloride. This salt was dissolved in water and β-benzyl aspartate was precipitated by neutralisation with triethylamine. Yield 62%, m.p. 218–219°, lit. [14b]222°. $[\alpha]_D^{20} + 7.73$ (C = 1, ACOH), lit. [14a,b] + 7.65. NMR (d_6-DMSO) of **1** with R = CH_2COOCH_2Ph, R^1 = Et: δ 0.2–0.9 (m, 10H, B-CH_2CH_3), 2.9 (d, 2H, -CH_2CH), 3.9 (m, 1H, >CHCO), 5.2 (s, 2H, CH_2Ph), 5.8 and 6.6 (br.t, 2×1H, NH_2), 7.4 (s, 5H, Ph).

β-Benzyl glutamate was prepared from **1f** in the same manner. Yield 65%, m.p. 175°, $[\alpha]_D^{20} + 20.18$ (C = 1, AcOH). Rotation and spectra were identical with those of an authentic sample.[14c]

p-Nitrophenyl esters of **1e** *and* **1f**. A soln of **1e**, prepared *in situ* from aspartic acid (10 mmole) and Et_3B (*vide supra*) was treated with *p*-nitrophenol (15 mmole) in THF. At −20° dicyclohexylcarbodiimide was added under stirring. After 2 hr at −20° the temp was allowed to raise to +20°. After standing over night dicyclohexylurea was filtered off and the filtrate was concentrated. The remaining oil was treated with a little ether affording the crystalline *p*-nitrophenyl ester of **1e**, yield 86%, m.p. 120–121° (from AcOH/diisopropylether). NMR (d_6-DMSO) δ 0.2–0.9 (m, 10H, B-CH_2CH_3), 3.10 (d, 2H, CH_2), 3.9 (m, 1H, CH), 5.9 and 6.7 (br.t, 2×1H, NH_2), 7.5 and 8.4 (ABq, 4H, C_6H_4).

In the same manner the *p*-nitrophenyl ester of **1f** was obtained in 75% yield, m.p. 127–128° (from AcOH/iPr_2O). NMR (d_6-DMSO) δ 0.2–0.9 (m, 10H, B-CH_2CH_3), 1.8–2.4 (m, 2H, CH_2CH), 2.85 (t, 2H, -CH_2CO), 3.6 (m, 1H, CH), 5.8 and 6.5 (br.t, 2×1H, NH_2), 7.4 and 8.3 (ABq, 4H, C_6H_4).

REFERENCES

[1] A. C. Kurtz, *J. Biol. Chem.* **122**, 477 (1938).
[2] A. Neuberger and F. Sanger, *Biochem. J.* **37**, 515 (1943), **38**, 125 (1944).
[3] M. Itoh, *Chem. Pharm. Bull.* **17**, 1679 (1969).
[4] F. Michael and S. Thomas, *Chem. Ber.* **90**, 2906 (1957); F. Michael and H. Haneke, *Ibid.* **92**, 309 (1959); **95**, 1009 (1962); F. Michael and W. Meckstroth, *Ibid.* **92**, 1675 (1959).
[5] K. Lang, K. Nuetzel and F. Schubert, *Ger. Pat.* 1.130.445 (May 1962), *Chem. Abstr.* **58**, 1488a (1963).
[6] R. Köster and E. Rothgery, *Liebigs Ann. Chem.* 112 (1974).
[7] Shih-Hua Tung, Kuo-Min Chang, Shih-Lu Tah, Chia-Chun Liu and Shih-Lin Chang, K'O Hsueh T'ung Pao **17**, 414 (1966), *Chem. Abstr.* **66**, 37990m (1967).
[8] I. H. Skoog, *J. Org. Chem.* **29**, 492 (1964).
[9] G. Baum, *J. Organomet Chem.* **22**, 269 (1970).
[10] J. Halström, E. Nebelin and E. J. Pedersen, *J. Chem. Res.* (S), 80 (1978).
[11] N. E. Miller, *Inorg. Chem.* **13**, 1459 (1974).
[12] S. J. Rettig and J. Trotter, *Can. J. Chem.* **55**, 958 (1977).
[13] G. Wittig and P. Roff, *Liebigs Ann. Chem.* **573**, 195 (1951).
[14a] D. Ben-Ishai and A. Berger, *J. Org. Chem.* **17**, 1564 (1952); [b] M. Goodman, L. B. Jacobsberg and N. S. Choi, *Israel J. Chem.* **9**, 125 (1971); [c] St. Guttman and R. A. Boissonnas, *Helv. Chim. Acta* **41**, 1852 (1958).
[15] A sample of this compound was kindly provided by Dr. G. I. Tesser (University of Nijmegen).
[16] This experiment was carried out by J. Zwikker and E. Vlietstra, University of Utrecht (The Netherlands).
[17] M. Nakatani, Y. Takahashi, A. Ouchi and K. Watanuki, *Sci. Papers. Coll. Chem. Educ. Univ. Tokyo* **22**, 37 (1972).