Tetrahedron Vol. 41, No. 17, pp. 3529 to 3535, 1985
Printed in Great Britain.

0040-4020/85 $3.00 + .00
Pergamon Press Ltd.

DIASTEREOFACIAL SELECTIVITY IN AZOMETHINE YLIDE CYCLOADDITION REACTIONS DERIVED FROM CHIRAL α-CYANOAMINOSILANES

ALBERT PADWA,* YON-YIH CHEN, UGO CHIACCHIO and WILLIAM DENT
Department of Chemistry, Emory University, Atlanta, GA 30322, U.S.A.

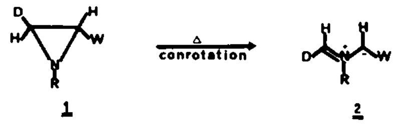
(*Received in Switzerland* 26 *October* 1984)

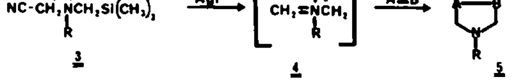
Abstract—A series of α-cyanoaminosilanes has been found to act as azomethine ylide equivalents. Treatment of these compounds with silver fluoride in the presence of electron deficient olefins gives substituted pyrrolidines in high yield. The extent of diastereoselectivity associated with the 1,3-dipolar cycloaddition of chiral azomethine ylides with several dipolarophiles has been studied. Reasonable levels of such diastereoselectivity have been found when optically active α-cyanoaminosilanes are employed as azomethine ylide equivalents. These compounds can be prepared in multigram quantities by treating the appropriate chiral amine with chlorotrimethylsilane followed by reaction of the resulting secondary amine with formaldehyde in the presence of potassium cyanide. It was found that N-benzyl-N-cyanomethyl-N-trimethylsilylmethylamine undergoes stereospecific cycloaddition with dimethyl fumarate and maleate. The stereospecificity of the reaction is consistent with a concerted cycloaddition reaction.

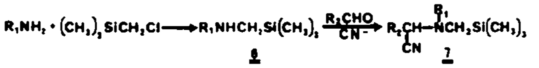
Asymmetric induction has become one of the cornerstones in modern synthetic methodology leading to a host of enantiomerically enriched compounds.[1,2] The use of chiral auxiliaries to induce biased stereochemical changes has allowed investigators to form a variety of C—X bonds with high enantioselectivity.[3,4] Recently, the asymmetric Diels–Alder reaction has received a great deal of attention.[5–9] Some of these 4+2-cycloadditions proceed with very high and sometimes near perfect diastereoselection.[10–12] In contrast to the well-documented asymmetric Diels–Alder reactions, asymmetric 1,3-dipolar cycloadditions have not been extensively explored. There are, however, several reports of stereoselective cycloadditions involving nitrones and nitrile oxides.[13–23] Nitrones which carry a chiral substituent on nitrogen often display high diastereoselectivity in dipolar cycloadditions with a variety of achiral dipolarophiles.[13–17] In certain cases, the reaction of chiral dipolarophiles with nitrones and nitrile oxides leads to reasonably high diastereoselectivity in the formation of the cycloadducts.[18–23] Since the N—O bonds of the cycloadducts are readily cleaved to produce acyclic molecules, the diastereoselectivity displayed in the cycloadditions serves as a means of controlling acyclic stereochemistry.[19,22] To the best of our knowledge there have been no reports concerning asymmetric 1,3-dipolar cycloadditions using azomethine ylides as dipoles. As a consequence of our interest in azomethine ylide chemistry,[24,25] we initiated a study designed to examine the extent to which an asymmetric center adjacent to the nitrogen atom of the dipole can control diastereoselective cycloadditions with achiral dipolarophiles. We report here the results of this study.

RESULTS AND DISCUSSION

The pyrrolidine ring is a frequently encountered structural unit of many synthetically challenging alkaloids.[26] Little attention has been given in alkaloid synthesis to one of the most conceptually simple ways of pyrrolidine formation, a 1,3-dipolar cycloaddition of an azomethine ylide with an olefin. This is not surprising since few methods exist for the preparation of nonstabilized azomethine ylides.[27–38] Although ring opening of aziridines to azomethine ylides works well when the substituent groups are capable of stabilizing the dipole centers,[39] the ring cleavage fails completely when simple alkyl substituents are used. We have recently discovered that α-cyanosilylamines 3 are useful and convenient synthons for azomethine ylides.[24] The development of this strategy was based on literature reports that cyanomethylamines can function as convenient iminium ion precursors.[40,41] The propensity of silicon to transfer to a silylphile when bound to an electronegative carbon[42] strongly inferred that the treatment of α-cyanosilylamines with silver fluoride will generate azomethine ylides. This prediction has indeed proven valid. Since tertiary N-(cyanomethyl)amines can be prepared from virtually any aliphatic or aromatic secondary amine, the two-step sequence illustrated below provides a convenient method to generate a wide range of azomethine ylides.



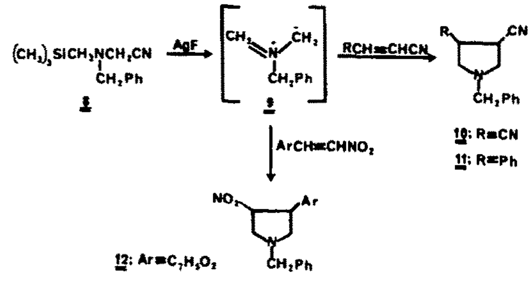




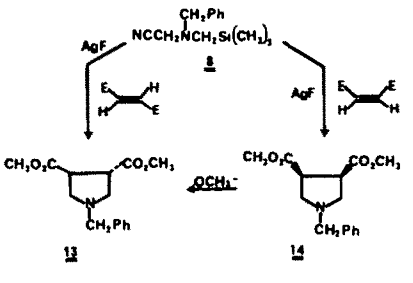
$$R_1NH_2 + (CH_3)_3SiCH_2Cl \longrightarrow \underset{\mathbf{6}}{R_1NHCH_2Si(CH_3)_3} \xrightarrow[CN^-]{R_2CHO} \underset{\mathbf{7}}{R_2\underset{CN}{CH}-\overset{R_1}{N}CH_2Si(CH_3)_3}$$

The high chemical yields and potential regiochemical control suggested that cycloaddition processes based upon the above strategy might be applied in the construction of a series of alkaloids. Prior to launching into the synthesis of complex molecular systems using these reagents, we have designed and executed model studies with a series of optically active silyl amines in order to probe the diastereoselectivity of the cycloaddition reaction.

In spite of its simplicity and its obvious potential as an azomethine ylide equivalent, N-benzyl α-cyanoaminosilane **8** could not be found in the literature. This reagent was conveniently prepared in multigram quantities by treating benzylamine with chloromethyltrimethylsilane followed by reaction of the resulting secondary amine with formaldehyde in the presence of potassium cyanide; NMR ($CDCl_3$, 90 MHz) δ 0.10 (9H, s), 2.02 (2H, s), 3.23 (2H, s), 3.51 (2H, s) and 7.20 (5H, s). A solution of **8** and fumaronitrile in acetonitrile was allowed to react in the dark with a slight excess of silver fluoride. Stirring was continued at 25° over the course of 10 hr. The black precipitate that formed was filtered, the solvent was removed under reduced pressure and the residue was subjected to silica gel chromatography to provide *trans*-3,4-dicyano-N-benzylpyrrolidine (**10**) in 69% yield. The azomethine ylide **9** derived from **8** could also be trapped with both cinnamonitrile and 1-nitro-2-(3,4-methylenedioxyphenyl)ethene in good yield.

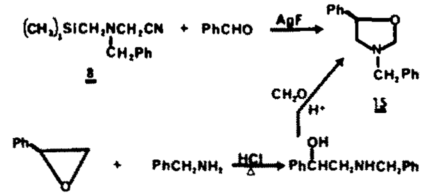


All octet-stabilized 1,3-dipoles examined so far in the literature have been shown to undergo stereospecific *cis* cycloaddition.[39] In order to determine whether the azomethine-ylide generated from the silver fluoride treatment of α-cyanosilylamine **8** behaves similarly, we have studied the reaction of **8** with *cis* and *trans* disubstituted dipolarophiles. It was found that the cycloaddition with dimethyl fumarate and maleate proceeds stereospecifically and yields pyrrolidines **13** and **14** in good yield. The *trans*-fumarate cycloadduct **13** showed NMR signals ($CDCl_3$, 360 MHz) at δ 2.79 (dd, 2H, J = 9.3 and 5.9 Hz), 2.91 (t, 2H, J = 9.3 Hz), 3.45 (dd, 2H, J = 9.3 and 5.9 Hz), 3.61 (s, 2H), 3.70 (s, 6H) and 7.25 (s, 5H). The *cis*-maleate cycloadduct **14** exhibited a set of signals at 2.73 (m, 2H), 3.16 (m, 2H), 3.32 (m, 2H), 3.65 (m, 8H) and 7.3 (m, 5H). Additional information which supports the stereochemical assignments was obtained from some base-catalyzed epimerization experiments. The *cis*-maleate adduct **14** was found to isomerize to the thermodynamically more stable fumarate adduct on treatment with sodium methoxide in methanol. The stereospecificity of the reaction is most consistent with the involvement of an azomethine ylide which undergoes concerted cycloaddition across the dipolarophiles' π-bond.

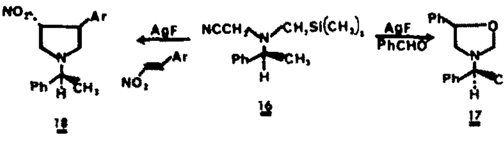


All attempts to obtain a cycloadduct from the reaction of **8** with non-activated olefins (i.e. cyclohexene, 1-octene, etc.) failed. Our inability to isolate a 1,3-cycloadduct with these systems is perfectly consistent with the principles of frontier MO theory.[43] Azomethine ylides generally react with electron deficient alkenes, since such a pair of addends possesses a narrow dipole HOMO–dipolarophile LUMO gap.[44]

1,3-Dipolar cycloaddition of azomethine ylides to heteromultiple bonds is a widely applicable and convenient route to a variety of heterocycles.[39] Aromatic aldehydes react with azomethine ylides derived from aroylaziridines to give oxazolidines in high yield.[45,46] The observed regioselectivity is due to the dipole HO-controlled addition reaction. Specific addition across the carbonyl group occurs with α,β-unsaturated aldehydes, illustrating the high dipolarophilic activity of the carbonyl group compared with the carbon–carbon double bond.[46] We have found that α-cyanoaminosilane **8** reacts smoothly with benzaldehyde in the presence of silver fluoride to give N-benzyl-5-phenyloxazolidine (**15**) in high yield. The structure of oxazolidine **15** was verified by comparison with an authentic sample prepared from the reaction of styrene oxide, benzylamine and paraformaldehyde.

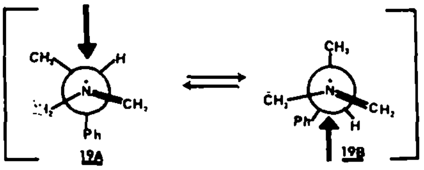


Our first indication that some diastereoselectivity could be achieved in these cycloadditions was gleaned from the reactions of *R*(+)-N-(1-phenylethyl)-N-cyanomethyl-N-trimethylsilylmethylamine (**16**). Optically active α-cyanoamino silane **16** was prepared by treating *R*(+)-α-methylbenzylamine with chloromethyltrimethylsilane followed by reaction of the resulting secondary amine with formaldehyde in the presence of potassium cyanide. The identity of **16** was determined by its straightforward spectral characteristics [NMR (90 MHz) δ 1.33 (d, 3H, J = 6.0 Hz), 2.02 (d, 1H, J = 15.0 Hz), 2.14 (d, 1H, J = 15.0 Hz), 3.38 (d, 1H, J = 18.0 Hz), 3.55 (d, 1H, J = 18.0 Hz), 3.60 (q, 1H, J = 6.0 Hz) and 7.30 (s, 5H)]. When benzaldehyde was used as the dipolarophile, a 1 : 1 mixture of diastereomeric oxazolidines (**17**) resulted. On the other hand, the ratio of diastereomeric cycloadducts (**18**) formed in the reaction of **16** with 1-nitro-2-(3,4-methylenedioxyphenyl)ethene was 3 : 2 as determined

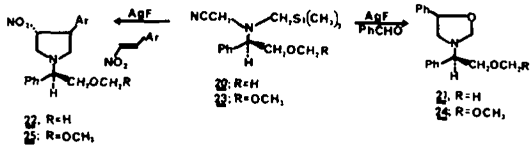


by proton NMR spectroscopy (360 MHz) (see Experimental).

Diastereofacial selectivity in dipolar cycloadditions can generally be rationalized by assuming that a Felkin model transition state is adopted during the cycloaddition.[47] Azomethine ylide **19** derived from cyanoaminosilane **16** can adopt either of two conformations (i.e. **19A** or **19B**). With conformation **19A**, the preferred direction of dipolarophile approach is onto the face of the azomethine ylide anti to the phenyl group. Anti attack onto conformation **19B** would result in the selective approach of the dipolarophile onto the opposite face of the dipole. Houk and co-workers[48] and Anh and Eisenstein[49] have concluded that anti approach is generally favored due to the lack of unfavorable nonbonded orbital interactions in the transition state. Since the groups attached to the nitrogen atom of ylide **19** differ little in their size or electronic make-up, it is not surprising to find that the extent of diastereoselection is small.



Since selectivity should increase as the size and electronic character of one of the groups attached to the chiral center is increased, we decided to explore diastereoselective azomethine ylide cycloadditions in a more thorough manner. The successful execution of high diastereoselectivity would be extremely valuable for the synthesis of a wide range of alkaloids. The next system we studied involved the preparation and cycloaddition chemistry of *R*(−)-N-(1-phenyl-2-methoxyethyl) - N - cyanomethyl - N - trimethylsilyl - methylamine (**20**). Treatment of this material with silver fluoride in the presence of benzaldehyde produced a 3:2 mixture of diastereomeric cycloadducts (**21**).



Reasonable diastereoselectivity was encountered from the reaction of **20** with 1-nitro-2-(3,4-methylenedioxyphenyl)ethene. In this case, the azomethine ylide derived from **20** gave rise to a 4:1 mixture of diastereomeric cycloadducts (**22**). The degree of diastereoselection does not seem to be influenced by the nature of the substituent group attached to the O atom. For example, when optically active α-cyanoaminosilane **23** was used as the azomethine ylide precursor, an 80:20 mixture of diastereomeric cycloadducts (i.e **25**) also resulted. When benzaldehyde was used as the dipolarophile, however, a 1:1 mixture of diastereomers (**24**) was formed.

Although the present study is limited to the reactions with only two dipolarophiles, the diastereoselectivity observed with some of the systems is encouraging. While it would appear difficult to develop a general and predictive transition state picture which can precisely accommodate diastereoselectivity in azomethine ylide cycloaddition processes, the reasonable stereoselectivity found in several of these reactions can potentially be put to synthetic use. The cycloaddition reactions of optically active α-cyanoaminosilanes derived from amino sugars is currently underway. Utilization of this chemistry in the context of alkaloid synthesis is also being explored and will be reported on at a later date.

EXPERIMENTAL

All m.ps and b.ps are uncorrected. Elemental analyses were performed by Atlantic Microlabs, Atlanta, Georgia. IR absorption spectra were determined on a Perkin–Elmer 467 IR spectrophotometer. UV absorption spectra were measured with a Cary Model 14 recording spectrophotometer, using 1 cm matched cells. PMR spectra were determined at 90 MHz using a Varian EM-390 spectrometer. Mass spectra were determined with a Finnegan 4000 mass spectrometer at an ionizing voltage of 70 eV.

Preparation of N - *benzyl* - N - *cyanomethyl* - N - *trimethylsilylmethylamine* (**8**). A soln containing 12.58 g of chloromethyltrimethylsilane and 33.10 g of benzylamine was heated with stirring at 200° for 2.5 hr. At the end of this time 0.1 N NaOH was added to the mixture in order to hydrolyse the white organic salt which had formed. The mixture was extracted with ether and the organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. The residue was distilled under reduced pressure (5 mmHg) and the fraction corresponding to N-benzyl-N-trimethylsilylmethylamine which boiled at 89–90° was collected; 10.60 g (53%); NMR ($CDCl_3$, 90 MHz) δ 0.10 (s, 9H), 2.00 (s, 2H), 3.78 (s, 2H), and 7.28 (s, 5H).

To a soln containing 5.00 g of the above compound was added 25.8 ml of 1.0 N HCl which caused a white ppt to form. To the mixture was added 14 ml of THF, 2.10 g of KCN and 2.48 ml of a 37% aqueous formaldehyde soln. The mixture was allowed to stir overnight and was then extracted with ether and washed with water. The ether layer was dried over $MgSO_4$ and concentrated under reduced pressure to give 5.63 g (94%) of **8** as a clear oil; IR (neat) 3004, 2990, 2900, 2800, 1500, 1460, 1430, 1370, 1330, 1250, 1100, 850, 745, and 700 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 0.10 (s, 9H), 2.02 (s, 2H), 3.51 (s, 2H) and 7.20 (s, 5H); *m/e* 232 (M^+), 141, 91, and 78; ^{13}C-NMR ($CDCl_3$, 50 MHz) δ 0.04, 45.0, 46.6, 61.4, 127.7, 128.6, 128.9 and 137. (Found: C, 67.24; H, 8.73; N, 12.04. Calc for $C_{13}H_{20}N_2Si$: C, 67.19; H, 8.67; N, 12.05%.)

Cycloaddition of N - *benzyl* - N - *cyanomethyl* - N - *trimethylsilylmethylamine* (**8**) *with fumaronitrile*. A soln containing 500 mg of **8**, 300 mg of fumaronitrile and 180 mg of AgF in 10 ml of acetonitrile was allowed to stir overnight in the dark. At the end of this time the mixture was passed through a Celite column and the residue was chromatographed on a silica gel column using a 10% EtOAc–hexane mixture as the eluent. The major fraction contained *trans*-**10** as a clear oil (71%); IR (neat) 3080, 3040, 2970, 2930, 2820, 2250, 1740, 1500, 1480, 1455, 1390, 1360, 1270, 1215, 1190, 1070, 920, 890, 745, and 700 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 2.7–3.0 (m, 4H), 3.15–3.35 (m, 2H), 3.64 (s, 2H) and 7.30 (s, 5H); *m/e* 211 (M^+), 91, 81, and 70. (Found: C, 73.88; H, 6.33; N, 19.56. Calc for $C_{13}H_{13}N_3$: C, 73.91; H, 6.20; N, 19.89%.)

Cycloaddition of N - *benzyl* - N - *cyanomethyl* - N - *trimethylsilylmethylamine* (**8**) *with cinnamonitrile*. A soln containing 500 mg of **8**, 290 mg of cinnamonitrile, and 290 mg of AgF in 10 ml of acetonitrile was allowed to stir for 10 hr in the dark. The mixture was diluted with $CHCl_3$, filtered through Celite, and concentrated under reduced pressure. The residue was chromatographed on a silica gel column using a 25% EtOAc–hexane mixture as the eluent. The major fraction (33%) contained *trans*-**11** as a clear oil; IR (neat) 3080, 3045, 2980, 2930, 2810, 2250, 1610, 1500, 1470, 1460, 1375, 1350, 1270, 1215, 1150, 1080, 1030, 915, 890, 760, 740, and 700 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 2.60–3.20 (m, 5H), 3.50–3.70 (m, 1H), 3.67 (s, 2H), and 7.2–7.4 (m, 10H). (Found: C, 82.23; H, 6.99; N, 10.55. Calc for $C_{18}H_{18}N_2$: C, 82.41; H, 6.92; N, 10.68%.)

Cycloaddition of N - *benzyl* - N - *cyanomethyl* - N - *trimethylsilylmethylamine* (**8**) *with* 1 - *nitro* - 2 - (3,4 - *methylenedioxyphenyl)ethene.* A soln containing 470 mg of **8**, 390 mg of 1-nitro-2-(3,4-methylenedioxyphenyl)ethene and 260 mg of AgF in 6 ml of acetonitrile was allowed to stir in the dark for 10 hr. The mixture was diluted with $CHCl_3$, filtered through Celite and concentrated under reduced pressure. The residue was chromatographed on a silica gel column using a 10% EtOAc–hexane mixture as the eluent. The major fraction (50%) contained **12** as a yellow oil; IR (neat) 3000, 2940, 2900, 1610, 1525, 1490, 1460, 1360, 1250, 1200, 1060, 1000, 850, 740, and 700 cm^{-1}; NMR ($CDCl_3$, 360 MHz) δ 2.66 (dd, 1H, J = 9.0 and 7.2 Hz), 3.12 (dd, 1H, J = 10.8 and 7.9 Hz), 3.23 (dd, 1H, J = 9.0 and 8.3 Hz), 3.35 (dd, 1H, J = 10.8 and 4.3 Hz), 3.69 (d, 1H, J = 13.0 Hz), 3.74 (d, 1H, J = 13.0 Hz), 3.92 (td, 1H, J = 7.6 and 5.4 Hz), 4.87 (ddd, 1H, J = 7.6, 5.4 and 4.7 Hz), 5.95 (s, 2H), 7.2–7.4 (m, 8H); *m/e* 326 (M^+), 262, 231, 169, 135, 91 and 77. (Found: C, 66.40; H, 5.56; N, 8.47. Calc for $C_{18}H_{18}N_2O_4$: C, 66.25; H, 5.56; N, 8.58%.)

Cycloaddition of N - *benzyl* - N - *cyanomethyl* - N - *trimethylsilylmethylamine* (**8**) *with dimethyl fumarate.* A soln containing 500 mg of **8**, 320 mg of dimethyl fumarate and 290 mg of AgF in 10 ml of acetonitrile was allowed to stir for 10 hr in the dark. The mixture was diluted with $CHCl_3$, filtered through Celite, and concentrated under reduced pressure. The residue was chromatographed on a silica gel column using a 10% EtOAc–hexane mixture as the eluent. The major fraction contained *trans*-**13** as a clear oil (71%); IR (neat) 3000, 2940, 2900, 2800, 1730, 1480, 1460, 1440, 1425, 1350, 1200, 1060, 1020, 930, 855, 745, and 700 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 2.79 (dd, 2H, J = 9.3 and 5.9 Hz), 2.91 (t, 2H, J = 9.3 Hz), 3.45 (dd, 2H, J = 9.3 and 5.9 Hz), 3.61 (s, 2H), 3.70 (s, 6H) and 7.25 (s, 5H); *m/e* 277 (M^+), 227, 226, 186, and 91. (Found: C, 64.88; H, 7.02; N, 4.78. Calc for $C_{15}H_{19}NO_4$: C, 64.97; H, 6.91; N, 5.05%.)

Cycloaddition of N - *benzyl* - N - *cyanomethyl* - N - *trimethylsilylmethylamine* (**8**) *with dimethyl maleate.* A soln containing 500 mg of **8**, 320 mg of dimethyl maleate and 290 mg of AgF in 10 ml of acetonitrile was allowed to stir in the dark for 10 hr. The mixture was diluted with $CHCl_3$, filtered through Celite, and concentrated under reduced pressure. The residue was chromatographed on a silica gel column using a 10% EtOAc–hexane mixture as the eluent. The major fraction (45%) contained *cis*-**14** as a clear oil; IR (neat) 3000, 2940, 2900, 2800, 1730, 1480, 1470, 1460, 1425, 1350, 1200, 1060, 1020, 1000, 970, 850, 740, and 700 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 2.60–2.85 (m, 2H), 3.05–3.40 (m, 4H), 3.66 (s, 8H), and 7.27 (s, 5H). (Found: C, 64.95; H, 6.87; N, 5.03. Calc for $C_{15}H_{19}NO_4$: C, 64.97; H, 6.91; N, 5.05%.)

Cycloaddition of N - *benzyl* - N - *cyanomethyl* - N - *trimethylsilylmethylamine* (**8**) *with benzaldehyde.* A soln containing 200 mg of **8**, 0.09 ml of benzaldehyde, and 120 mg of AgF in 5 ml of acetonitrile was allowed to stir in the dark for 10 hr. The mixture was diluted with $CHCl_3$, filtered through Celite, and concentrated under reduced pressure. The residue was subjected to flash chromatography using a 10% EtOAc–hexane mixture as the eluent. The major fraction (50%) isolated contained **15** as a clear oil; IR (neat) 3100, 2850, 2700, 1590, 1490, 1440, 1340, 1300, 1140, 1060, 1020, 1000, 900, 860, 740, and 700 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 2.82 (dd, 1H, J = 12.0 and 8.0 Hz), 3.45 (dd, 1H, J = 12.0 and 7.0 Hz), 3.81 (s, 2H), 4.60 (s, 2H), 5.15 (dd, 1H, J = 8.0 and 7.0 Hz); *m/e* 239 (M^+), 133, 132, 120, 110, 91, and 77. (Found: C, 80.22; H, 7.21; N, 5.79. Calc for $C_{16}H_{17}NO$: C, 80.30; H, 7.16; N, 5.86%.)

The structure of **15** was further verified by an independent synthesis. A mixture containing 9.8 ml of styrene oxide, 10.2 g of benzylamine, and 0.7 g of benzylamine hydrochloride was stirred at room temp for 48 hr. The resulting residue was filtered and washed with ligroin to give a white solid. This material was recrystallized twice from ligroin to give 7.2 g (63%) of a white crystalline solid whose structure was assigned as N-benzyl-2-hydroxy-2-phenylethylamine on the basis of its spectral data; m.p. 100–101°; IR (KBr) 3350, 3020, 2980, 2940, 1610, 1590, 1490, 1480, 1440, 1360, 1280, 1240, 1150, 1100, 1040, 900, 840, 770, and 700 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 2.3 (br s, 2H), 2.65 (dd, 1H, J = 14.0 and 9.0 Hz), 2.85 (dd, 1H, J = 14.0 and 4.0 Hz), 3.80 (s, 2H), 4.70 (dd, 1H, J = 9.0 and 4.0 Hz) and 7.25 (s, 10H). The above material was heated with 0.4 g of paraformaldehyde and a trace of benzylamine hydrochloride in 10 ml of benzene for 24 hr. The solution was cooled and poured into water and extracted with ether. The ethereal extracts were washed with water, a sat NaCl aq, dried over $MgSO_4$ and concentrated under reduced pressure to give 0.8 g (80%) of a clear oil whose structure was identical to that obtained from the reaction of **8** with AgF in the presence of benzaldehyde.

Preparation of R(+)-N-(1-*phenylethyl*)-N-*cyanomethyl*-N-*trimethylsilylmethylamine* (**16**). A soln containing 2.42 g of trimethylsilylchloromethane and 7.36 g of *R*(+)-α-methylbenzylamine was heated at 190° for 2 hr. At the end of this time 20 ml of a 5% NaOH aq was added and the mixture was extracted with ether. The organic layer was dried over $MgSO_4$ and was concentrated under reduced pressure to give a clear oil. This material was chromatographed on a silica gel column using a 10% EtOAc–hexane mixture as the eluent. The major fraction contained 2.44 g (60%) of *R*(+)-N-(1-phenylethyltrimethylsilylmethyl)amine: IR (neat) 3340, 3080, 3040, 2960, 2900, 2780, 1600, 1500, 1450, 1370, 1250, 1120, 920, 880, 760, 700 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 1.30 (d, 3H, J = 6.0 Hz), 1.32 (s, 1H), 1.87 (s, 2H), 3.63 (q, 1H, J = 6.0 Hz) and 7.3 (s, 5H); *m/e* 207 (M^+), 192, 167, 149, 105, 103, 102, 91 and 77.

To a stirred soln containing 2.7 g of the above compound in 30 ml of a 1 N HCl was added 10 ml of THF, 1.3 g of KCN, and 16.2 ml of a 37% aqueous formalin soln. The resulting mixture was stirred for 12 hr and at the end of this time 20 ml of a 5% NaOH aq was added and the mixture was extracted with ether. The organic layer was dried over $MgSO_4$ and was concentrated under reduced pressure to give a clear oil. This material was chromatographed on a silica gel column using a 10% EtOAc–hexane mixture as the eluent. The first fraction contained pure *R*(+)-**16** as a clear liquid (1.72 g, 70%); IR (neat) 3070, 3040, 2960, 2900, 2850, 2795, 2240, 1600, 1500, 1455, 1430, 1250, 1140, 850, 770, 700 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 1.33 (d, 3H, J = 6.0 Hz), 2.02 (d, 1H, J = 15.0 Hz), 2.14 (d, 1H, J = 15.0 Hz), 3.38 (d, 1H, J = 18.0 Hz), 3.55 (d, 1H, J = 18.0 Hz), 3.60 (q, 1H, J = 6.0 Hz) and 7.30 (s, 5H); *m/e* 246 (M^+), 231, 209, 174, 147, 141, 105, 103, 79 and 77. (Found: C, 68.15; H, 8.75; N, 11.26. Calc for $C_{14}H_{22}N_2Si$: C, 68.24; H, 9.00; N, 11.37%.)

Cycloaddition of R(+) - N - (1 - *phenylethyl*) - N - *cyanomethyl* - N - *trimethylsilylmethylamine* (**16**) *with* 1 - *nitro* - 2 - (3,4 - *methylenedioxyphenyl)ethene.* A soln containing 570 mg of **16**, 447 mg of 1-nitro-2-(3,4-methylenedioxyphenyl)-ethene and 290 mg of AgF in 10 ml of acetonitrile was allowed to stir at 25° for 36 hr. At the end of this time the mixture was passed through a Celite column and the residue was chromatographed on a silica gel column using a 10% EtOAc–hexane mixture as the eluent. The major fraction contained 392 mg of **18** as a yellow oil (50%): IR (neat) 3040, 3020, 2980, 2900, 2800, 1610, 1550, 1510, 1485, 1450, 1370, 1250, 1040, 980, 880, 820, 770, 700 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 1.38 (d, 3H, J = 6.5 Hz), 2.55 (m, 1H), 2.99–3.40 (m, 4H), 3.6–4.0 (m, 1H), 4.7–4.9 (m, 1H), 5.95 (s, 2H), 6.70–6.86 (m, 3H) and 7.35 (s, 5H); *m/e* 340 (M^+), 325, 294, 161, 149, 135, 131, 105, 103 and 77. The 360 MHz NMR spectrum ($CDCl_3$) shows the presence of two diastereomers in a 3:2 ratio: δ 1.41 (d, 3H, J = 6.50 Hz, 40% of diastereomer A), 1.42 (d, 3H, J = 6.50 Hz, 60% of diastereomer B), 2.5 (dd, J = 9.20 and 7.41 Hz), 2.70 (dd, J = 9.31 and 6.73 Hz), 3.07 (dd, J = 9.90 and 7.84 Hz), 3.23 (dd, J = 10.90 and 4.23 Hz), 3.30–3.40 (m, 2H), 3.83–3.90 (m, 1H), 4.81–4.88 (m, 1H), 5.95 (s, 2H, 40% of diastereomer A), 5.96 (s, 2H, 60% of diastereomer B), and 7.35 (m, 5H). (Found C, 66.81; H, 5.73; N, 8.20. Calc for $C_{19}H_{20}N_2O_4$: C, 67.04; H, 5.92; N, 8.23%.)

Cycloaddition of R(+) - N - (1 - *phenylethyl*) - N - *cyanomethyl* - N - *trimethylsilylmethylamine* (**16**) *with benzaldehyde*. A soln containing 570 mg of **16**, 245 mg of benzaldehyde and 290 mg of AgF in 10 ml of acetonitrile was stirred for 36 hr at room temp. At the end of this time the mixture was passed through a Celite column and the residue was chromatographed on a silica gel column using a 10% EtOAc–hexane mixture as the eluent. The major fraction contained 350 mg of **17** as a clear oil (60%); IR (neat) 3080, 3045, 2990, 2940, 2880, 2800, 1600, 1500, 1450, 1380, 1360, 1310, 1220, 1180, 1080, 1060, 970, 910, 760, 700 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 1.36 (d, 3H, J = 6.0 Hz), 2.61 (dd, 1H, J = 12.0 and 9.0 Hz), 3.20–3.60 (m, 2H), 4.40–4.60 (m, 2H), 5.03 (t, 1H, J = 6.0 Hz), 7.33 (s, 10H); *m/e* 253 (M^+), 149, 147 and 105. The 360 MHz NMR spectrum ($CDCl_3$) shows two diastereomers in a 1 : 1 ratio: 1.40 (d, 3H, J = 6.4 Hz, 50% of diastereomer A), 1.41 (d, 3H, J = 6.4 Hz, 50% of diastereomer B), 2.65 (dd, J = 9.0 and 8.9 Hz), 3.30 (dd, J = 10.3 and 6.6 Hz), 3.36 (dd, J = 10.3 and 6.6 Hz), 3.50–3.60 (m, 1H), 4.45 (d, J = 8.7 Hz), 4.47 (d, J = 8.3 Hz), 4.55 (d, J = 8.3 Hz), 4.59 (d, J = 8.7 Hz), 5.10 (m, 1H), 7.22–7.45 (m, 10H). (Found C, 80.39; H, 7.48; N, 5.34. Calc for $C_{17}H_{19}NO$: C, 80.57; H, 7.56; N, 5.53%.)

Preparation of R(−) - N - (1 - *phenyl* - 2 - *methoxyethyl*) - N - *cyanomethyl* - N - *trimethylsilylmethylamine* (**20**). A soln containing 2.52 g of *R*(−)-1-amino-1-phenyl-2-methoxyethane[50] in 15 ml of acetonitrile and 4.1 g of trimethylsilyl iodide was stirred at 90° for 12 hr. At the end of this time 20 ml of a 5% NaOH aq was added and the mixture was extracted with ether. The organic layer was dried over $MgSO_4$ and was concentrated under reduced pressure to give a clear oil. This material was chromatographed on a silica gel column using a 10% EtOAc–hexane mixture as the eluent. The first fraction contained 3.13 g of *R*(−)-N-(1-phenyl-2-methoxyethyl)-N-trimethylsilylmethylamine (80%): IR (neat) 3360, 3080, 3040, 2970, 2900, 2840, 2780, 1600, 1500, 1450, 1350, 1250, 1200, 1160, 980, 870, 750, and 700 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 1.66 (brs, 1H), 1.86 (s, 2H), 3.40 (s, 3H), 3.43 (d, 2H, J = 6.0 Hz), 3.81 (dd, 1H, J = 9.0 and 6.0 Hz) and 7.33 (s, 5H); *m/e* 237 (M^+), 192, 149, 135, 134, 103 and 77.

To a soln containing 560 mg of the above compound in 10 ml of a 1.0 N HCl was added 6 ml of THF, 304 mg of KCN and 1.1 ml of a 37% aqueous formalin soln. The resulting mixture was stirred for 12 hr and at the end of this time 20 ml of a 5% NaOH aq was added and the mixture was extracted with ether. The organic layer was dried over $MgSO_4$ and was concentrated under reduced pressure to give a clear oil. This material was chromatographed on a silica gel column using a 10% EtOAc–hexane mixture as the eluent. The major fraction contained 542 mg of *R*(−)-**20** (83%): IR (neat) 3080, 3050, 2970, 2910, 2840, 2250, 1600, 1500, 1450, 1430, 1260, 1200, 1100, 860, 770, and 710 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 1.75 (d, 1H, J = 14.0 Hz), 1.99 (d, 1H, J = 14.0 Hz), 3.33 (s, 3H), 3.45–3.85 (m, 5H) and 7.36 (s, 5H); *m/e* 276 (M^+), 231, 135, 128, 105, 103 and 77. (Found: C, 64.88; H, 8.69; N, 10.04. Calc for $C_{15}H_{24}N_2OSi$: C, 65.17; H, 8.75; N, 10.13%.)

Cycloaddition of R(−) - N - (1 - *phenyl* - 2 - *methoxyethyl*) - N - *cyanomethyl* - N - *trimethylsilylmethylamine* (**20**) *with* 1 - *nitro* - 2 - (3,4 - *methylenedioxyphenyl*)*ethene*. A soln containing 637 mg of **20**, 447 mg of 1-nitro-2-(3,4-methylenedioxyphenyl)-ethene and 290 mg of AgF in 10 ml of acetonitrile was stirred for 36 hr at room temp. At the end of this time the mixture was passed through a Celite column and the residue was chromatographed on a silica gel column using a 10% EtOAc–hexane mixture as the eluent. The major fraction contained 256 mg (30%) of a yellow oil which was identified as **22** on the basis of the following spectral data: IR (neat) 3070, 3040, 2990, 2940, 2900, 2820, 1640, 1510, 1495, 1450, 1250, 1155, 1040, 940, 810, 770, and 710 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 2.66 (m, 1H), 3.12 (m, 1H), 3.33 (s, 3H), 3.41–3.92 (m, 6H), 4.83 (m, 1H), 5.80 (s, 2H), 6.69–6.76 (m, 3H), 7.35 (s, 5H); *m/e* (30 eV) 370 (M^+), 325, 207, 204, 160, 161, 149, 119, 105, 103, 96, 91 and 77. The 360 MHz NMR spectrum ($CDCl_3$) shows the presence of two diastereomers in a 4 : 1 ratio: 2.60–2.70 (m, 1H), 3.10–3.20 (m, 1H), 3.25–3.30 (m, 1H), 3.305 (s, 3H, 20% of diastereomer A), 3.313 (s, 3H, 80% of diastereomer B), 3.40 (t, 1H, J = 2.0 Hz), 3.50–3.55 (m, 2H), 3.70–3.80 (m, 1H), 3.85–3.95 (m, 1H), 4.80–4.85 (m, 1H), 5.945 (s, 2H, 20% diastereomer A), 5.955 (s, 2H, 80% of diastereomer B), 6.70–6.80 (m, 3H), 7.23–7.35 (m, 5H). (Found: C, 64.93; H, 5.81; N, 7.72. Calc for $C_{20}H_{22}N_2O_5$: C, 64.85; H, 5.99; N, 7.56%.)

Cycloaddition of R(−) - N - (1 - *phenyl* - 2 - *methoxyethyl*) - N - *cyanomethyl* - N - *trimethylsilylmethylamine* (**20**) *with benzaldehyde*. A soln containing 637 mg of **20**, 245 mg of benzaldehyde and 290 mg of AgF in 10 ml of acetonitrile was stirred at room temp for 32 hr. At the end of this time the mixture was passed through a Celite column and the residue was chromatographed on a silica gel column using a 10% EtOAc–hexane mixture as the eluent. The major fraction contained 213 mg of a clear oil (40%) which was identified as **21** on the basis of following spectral data: IR (neat) 3095, 3070, 3060, 2980, 2930, 2890, 2820, 1600, 1498, 1455, 1350, 1120, 970, 760, and 710 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 2.52–2.79 (m, 1H), 3.33 (s, 3H), 3.40–3.90 (m, 4H), 4.48–4.69 (m, 2H), 4.90–5.08 (m, 1H), 7.32 (brs, 10H); *m/e* 283 (M^+), 281, 238, 208, 164, 147, 140, 117, 105, 103, 91, 77. The 360 MHz NMR spectrum ($CDCl_3$) shows the presence of two diastereomers in a 3 : 2 ratio: δ 2.61 (dd, J = 10.5 and 8.0 Hz), 2.73 (dd, J = 10.5 and 8.0 Hz), 3.30 (s, 3H, 60% of diastereomer A), 3.32 (s, 3H, 40% of diastereomer B), 3.40–3.55 (m, 2H), 3.65–3.75 (m, 2H), 4.51 (m, 1H), 4.63 (m, 1H), 4.95–5.05 (m, 1H), 7.22–7.40 (m, 10H). (Found: C, 76.18; H, 7.52; N, 4.71. Calc for $C_{18}H_{21}NO_2$: C, 76.29; H, 7.47; N, 4.94%.)

Preparation of R(−) - N - (1 - *phenyl* - 2 - *methoxyethoxyethyl*) - N - *cyanomethyl* - N - *trimethylamine* (**23**). A soln containing 2.96 g of *R*(−)-1-amino-1-phenyl-2-(2-methoxyethoxy)ethane[50] in 15 ml of acetonitrile and 4.1 g of trimethylsilyl iodide was stirred at 90° for 12 hr. At the end of this time 20 ml of a 5% NaOH aq was added and the mixture was extracted with ether. The organic layer was dried over $MgSO_4$ and was concentrated under reduced pressure to give a clear oil. This material was chromatographed on a silica gel column using a 10% EtOAc–hexane mixture as the eluent. The first fraction contained 3.2 g of *R*(−)-N-(1-phenyl-2-methoxyethoxyethyl)-N-trimethylsilylmethylamine (75%): IR (neat) 3350, 3020, 3070, 2960, 2900, 2820, 2780, 1600, 1500, 1460, 1310, 1250, 1200, 1110, 860, 760, and 710 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 1.72 (s, 1H), 1.86 (s, 2H), 3.44 (s, 3H), 3.50–3.90 (m, 7H) and 7.39 (s, 5H); *m/e* 281 (M^+), 279, 192, 149, 140, 122, 109, 105, 104, 103, 101, 79 and 77.

To a stirred soln containing 663 mg of the above compound in 10 ml of a 1.0 N HCl was added 6 ml of THF, 304 mg of KCN and 1.1 ml of a 37% aqueous formalin soln. The resulting mixture was stirred at room temp for 12 hr. At the end of this time 20 ml of a 5% NaOH aq was added and the mixture was extracted with ether. The organic layer was dried over $MgSO_4$ and was concentrated under reduced pressure to give a clear oil. This material was chromatographed on a silica gel column using a 10% EtOAc–hexane mixture as the eluent. The major fraction contained 604 mg of *R*(−)-**23** (80%): IR (neat) 3075, 3060, 2960, 2900, 2830, 2240, 1600, 1500, 1455, 1430, 1410, 1250, 1200, 1140, 1100, 860, 840, 770, and 710 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 2.07 (d, 1H, J = 15.0 Hz), 2.17 (d, 1H, J = 15.0 Hz), 3.38 (s, 3H), 3.40–3.70 (m, 9H) and 7.34 (s, 5H); *m/e* 320 (M^+), 278, 262, 231, 105, 104, 103, 91 and 77. (Found: C, 63.65; H, 8.74; N, 8.51. Calc for $C_{17}H_{28}N_2O_2Si$: C, 63.71; H, 8.81; N, 8.74%.)

Cycloaddition of R(−) - N - (1 - *phenyl* - 2 - *methoxyethoxyethyl*) - N - *cyanomethyl* - N - *trimethylsilylmethylamine* (**23**) *with* 1 - *nitro* - 2 - (3,4 - *dimethylendioxyphenyl*)*ethene*. A soln containing 370 mg of **23**, 224 mg of 1-nitro-2-(3,4-dimethylendioxyphenyl)ethene and 145 mg of AgF in 10 ml of acetonitrile was stirred at room temp for 32 hr. At the end of this time the mixture was passed through a Celite column and the residue was chromatographed on a silica gel column using a 10% EtOAc–hexane mixture as the eluent. The major fraction contained 96 mg of a yellow oil (20%) which was identified as **25** on the basis of the following spectral data: IR (neat) 3060, 3000, 2900, 2820, 1550, 1500, 1450, 1360, 1250, 1100, 1040, 930, 810, 770, and 700 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 2.80 (dd, 1H, J = 11.0 and 8.0 Hz), 3.15 (m, 1H), 3.41 (s, 3H), 3.51–3.82 (m, 10H), 4.84–5.00 (m, 1H), 6.02 (s, 2H), 6.69–6.76 (m, 3H), 7.40 (s, 5H); *m/e* (40 eV) 414 (M^+), 325, 278, 161, 148, 131, 118, 105, 91 and 77. The 360 MHz NMR ($CDCl_3$) shows the presence of two diastereomers in a 4:1 ratio: 2.63–2.70 (m, 1H), 3.10–3.20 (m, 1H), 3.23 (s, 3H, 80% of diastereomer A), 3.33 (s, 3H, 20% of diastereomer B), 3.25–3.35 (m, 1H), 3.40–3.60 (m, 6H), 3.89–3.90 (m, 2H), 4.80–4.90 (m, 1H), 5.94 (s, 2H, 80% of diastereomer A), 5.95 (s, 2H, 20% of diastereomer B), 6.72–6.83 (m, 3H), 7.25–7.45 (m, 5H). (Found: C, 63.81; H, 6.27; N, 6.58. Calc for $C_{22}H_{26}N_2O_6$: C, 63.75; H, 6.32; N, 6.76%.)

Cycloaddition of R(−) - N - (1 - *phenyl* - 2 - *methoxyethoxyethyl*) - N - *cyanomethyl* - N - *trimethylsilylmethylamine* (**25**) *with benzaldehyde.* A soln containing 370 mg of **25**, 125 mg of benzaldehyde and 145 mg of AgF in 10 ml of acetonitrile was stirred at room temp for 32 hr. At the end of this time the mixture was passed through a Celite column and the residue was chromatographed on a silica gel column using a 10% EtOAc–hexane mixture as the eluent. The major fraction contained 87 mg of a clear oil (23%) which was identified as **24** on the basis of following spectral data: IR (neat) 3080, 3050, 2940, 2900, 2830, 1500, 1460, 1210, 1110, 1040, 770, and 710 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 2.60–2.92 (m, 1H), 3.42 (s, 3H), 3.51–3.92 (m, 8H), 4.50–4.70 (m, 2H), 4.95–5.20 (m, 1H), 7.33 (brs, 10H); *m/e* (40 eV) 323 (M^+), 238, 208, 159, 149, 123, 122, 108, 106, 105, 104, 103, 91 and 77. The 360 MHz NMR spectrum ($CDCl_3$) shows the presence of two diastereomers in a 1:1 ratio: 2.58 (dd, J = 10.4 and 8.0 Hz), 2.76 (dd, J = 10.4 and 8.0 Hz), 3.33 (s, 3H, 50% of diastereomer A), 3.36 (s, 3H, 50% of diastereomer B), 3.45–3.90 (m, 8H), 4.54 (dd, J = 12.6 and 4.0 Hz), 4.66 (dd, J = 12.6 and 4.0 Hz), 4.95–5.07 (m, 1H), 7.25–7.48 (m, 10H). (Found: C, 73.18; H, 7.78; N, 4.23. Calc for $C_{20}H_{25}NO_3$: C, 73.36; H, 7.70; N, 4.28%.)

Acknowledgement—We gratefully acknowledge support of this work by the National Institutes of Health. A.P. wishes to thank the organic faculty at the University of Würzburg for their gracious hospitality during his stay at the Institute as an Alexander von Humboldt Senior Awardee. We are also grateful for a NATO Fellowship administered by CNR (Rome) to one of us (U.C.). Use of the high field NMR spectrometer used in these studies was made possible through a NSF equipment grant.

REFERENCES

[1] J. D. Morrison (Editor), *Asymmetric Synthesis—a Multivolume Treatise*. Academic Press, New York (1984).

[2] R. Scheffold (Editor), *Modern Synthetic Methods*. Verlag Sauerlander, Frankfurt (1979).

[3] J. Scott and D. Valentine, *Synthesis* 329 (1978).

[4] J. W Apsimon and R. P. Segun, *Tetrahedron* **35**, 2797 (1979).

[5] Y. J. Mori, *J. Synth. Org. Chem. Japan* **40**, 321 (1982).

[6] S. Masamune, L. A. Reed, J. T. Davis and W. Choy, *J. Org. Chem.* **48**, 4441 (1983).

[7] W. Oppolzer, *Diastereo and Enantioselective Cycloaddition of the Ene Reactions in Organic Synthesis*, 4th Int. Conf. on Organic Synthesis, Tokyo (1982).

[8] W. Oppolzer, M. Kurth, D. Reichlin and F. Moffatt, *Tetrahedron Lett.* 2545 (1981).

[9] E. J. Corey and H. E. Ensley, *J. Am. Chem. Soc.* **97**, 6908 (1975).

[10] B. M. Trost, D. O'Krongly and J. Belletire, *J. Am. Chem. Soc.* **102**, 7595 (1980).

[11] W. Oppolzer, C. Chapuis, G. M. Dao, D. Reichlin and T. Godel, *Tetrahedron Lett.* 4781 (1982).

[12] W. Choy, L. A. Reed and S. Masamune, *J. Org. Chem.* **48**, 1137 (1983).

[13] P. M. Wovkulich and M. R. Uskokovic, *J. Am. Chem. Soc.* **103**, 3956 (1981).

[14] C. Belzecki and I. Panfil, *J. Org. Chem.* **44**, 1212 (1979).

[15] A. Vasella, *Helv. Chim. Acta* **60**, 1273 (1977).

[16] T. Koizumi, H. Hirai and E. Yoshii, *J. Org. Chem.* **47**, 4004 (1982).

[17] A. Vasella and R. Voeffray, *Helv. Chim. Acta* **65**, 1134 (1982).

[18] P. DeShong and J. M. Leginus, *J. Am. Chem. Soc.* **105**, 1686 (1983).

[19] A. P. Kozikowski and Y. Y. Chen, *Tetrahedron Lett.* 2081 (1982); A. P. Kozikowski and A. K. Ghosh, *J. Am. Chem. Soc.* **104**, 5788 (1982); A. P. Kozikowski and Y. Y. Chen, *J. Org. Chem.* **46**, 5248 (1981); A. P. Kozikowski and H. Ishida, *J. Am. Chem. Soc.* **102**, 4265 (1980); A. P. Kozikowski and P. D. Stein, *J. Am. Chem. Soc.* **104**, 4023 (1982); A. P. Kozikowski and A. K. Ghosh, *J. Org. Chem.* **49**, 2762 (1984).

[20] A. A. Hagedorn, B. J. Miller and J. O. Nagy, *Tetrahedron Lett.* 229 (1980).

[21] P. A. Wade, M. K. Pillay and S. M. Singh, *Tetrahedron Lett.* 4563 (1982).

[22] V. Jäger, R. Schohe and E. F. Paulus, *Tetrahedron Lett.* 5501 (1983).

[23] K. N. Houk, S. R. Moses, Y. D. Wu, N. G. Rondan, V. Jäger, R. Schohe and F. R. Fronczek, *J. Am. Chem. Soc.* **106**, 3880 (1984).

[24] A. Padwa and Y. Y. Chen, *Tetrahedron Lett.* 3447 (1983).

[25] A. Padwa, G. Haffmanns and M. Tomas, *Tetrahedron Lett.* 4303 (1983).

[26] *The Alkaloids—Specialist Periodical Reports*, The Royal Society, London.

[27] E. Vedejs and G. R. Martinez, *J. Am. Chem. Soc.* **101**, 6452 (1979); **102**, 7993 (1980).

[28] K. Achiwa and M. Sekiya, *Tetrahedron Lett.* 2589 (1982); *Heterocycles* **20**, 167 (1983); *Chem. Lett.* 1213 (1981).

[29] T. Livinghouse and R. Smith, *J. Chem. Soc. Chem. Commun.* 210 (1983); *J. Org. Chem.* **48**, 1554 (1983).

[30] K. Achiwa, T. Motoyama and M. Sekiya, *Chem. Pharm. Bull.* **31**, 3939 (1983).

[31] Y. Terao, N. Imai, K. Achiwa and M. Sekiya, *Chem. Pharm. Bull.* **30**, 3167 (1982).

[32] O. Tsuge, S. Kanemasa, S. Kuraoka and S. Takenaka, *Chem. Lett.* 279 (1984); 281 (1984).

[33] O. Tsuge, S. Kanemasa, A. Hatada and K. Matsuda, *Chem. Lett.* 801 (1984).

[34] O. Tsuge and K. Ueno, *Heterocycles* **20**, 2133 (1983).

[35] R. Grigg, L. D. Basanagoudar, D. A. Kennedy, J. F. Malone and S. Thianpatanagul, *Tetrahedron Lett.* 2803 (1982).

[36] R. Grigg, H. Q. N. Gunaratne and J. Kemp, *Tetrahedron Lett.* 99 (1984).

[37] R. Grigg, M. F. Aly, V. Sridharan and S. Thianpatanagul, *J. Chem. Soc. Chem. Commun.* 182 (1984).

[38] R. Grigg and S. Thianpatanagul, *J. Chem. Soc. Chem. Commun.* 180 (1984).

[39] J. W. Lown, 1,3-*Dipolar Cycloaddition Chemistry* (Edited by A. Padwa), Vol. 1, pp. 653–732. Wiley, New York (1984).

[40] D. S Grierson, M. Harris and H. P. Husson, *J. Am. Chem. Soc.* **102**, 1064 (1980).

[41] L. E. Overman and E. J. Jacobsen, *Tetrahedron Lett.* 2741 (1982).

[42] E. W. Colvin, *Chem. Soc. Rev.* **7**, 15 (1978); T. H. Chan and I. Fleming, *Synthesis* 761 (1979).

[43] I. Fleming, *Frontier Orbitals and Organic Chemical Reactions*. Wiley, New York (1976).

[44] K. N. Houk, J. Sims, C. R. Watts and L. J. Luskus, *J. Am. Chem. Soc.* **95**, 7301 (1973).

[45] J. W. Lown and M. H. Akhtar, *Can. J. Chem.* **50**, 2236 (1972); G. Dallas, J. W. Lown and J. P. Moser, *J. Chem. Soc. Chem. Commun.* 278 (1970); *J. Chem. Soc.* (C) 2383 (1970); *Can. J. Chem.* **48**, 89 (1970).

[46] F. Texier and R. Carrie, *C. R. Acad. Sci. Ser. T* **269**, 709 (1969).

[47] M. Cherest, H. Felkin and N. Prudent, *Tetrahedron Lett.* 2199 (1968); M. Cherest and H. Felkin, *Ibid.* 2205 (1968).

[48] P. Caramella, N. G. Rondan, M. N. Paddon-Row and K. N. Houk, *J. Am. Chem. Soc.* **103**, 2438 (1981); N. G. Rondan, M. N. Paddon-Row, P. Caramella, J. Mareda, P. H. Mueller and K. N. Houk, *J. Am. Chem. Soc.* **104**, 4974 (1982); K. N. Houk, S. R. Moses, Y. D. Wu, N. G. Rondan, V. Jäger, R. Schohe and F. R. Fronczek, *J. Am. Chem. Soc.* **106**, 3880 (1984).

[49] N. T. Anh and O. Eisenstein, *Nouv. J. Chim.* **1**, 61 (1977).

[50] A. I. Meyers, G. S. Poindexter and Z. Brich, *J. Org. Chem.* **43**, 892 (1978).