(R_f 0.11) had been converted to a new product at R_f 0.30 (CAS, orange). Chromatography (1-mm SiO_2 chromatotron plate; 5% methanol in CH_2Cl_2) and concentration of the appropriate fractions gave 8 mg (59%) of (±)-N^a-methylkopsanone, which crystallized from pentane; mp 151–153.8 °C; UV (ethanol) λ_{max} 223, 256, 299 nm; IR (KBr) ν_{max} 2947, 2859, 1739, 1478, 1300, 1119, 891, 743 cm^{-1}; NMR ($CDCl_3$) δ 7.26 (dd, J = 0.7, 7.3 Hz, 1 H), 7.13 (td, J = 1.4, 7.6 Hz, 1 H), 6.75 (td, J = 0.7, 7.4 Hz, 1 H), 6.48 (d, J = 7.7 Hz, 1 H), 3.48 (t, J = 9.9 Hz, 1 H), 3.35 (d, J = 1.8 Hz, 1 H), 3.12 (dd, J = 4.8, 9.5 Hz, 1 H), 3.00–3.06 (m, 2 H), 2.78 (d, J = 10.9 Hz, 1 H), 2.60 (s, 3 H), 2.51–2.58 (m, 1 H), 2.05 (d, J = 14.7 Hz, 1 H), 1.70–1.78 (m, 2 H), 1.45–1.65 (m, 3 H), 1.21–1.40 (m, 4 H); mass spectrum, m/z (relative intensity) 321 (39), 320 (100), 277 (6), 264 (5), 242 (11), 210 (5), 169 (17), 129 (12), 109 (26), 69 (17), 55 (42).

(±)-Kopsanone (2, R = H; X = H_2). (±)-Kopsinine (15 mg, 0.044 mmol) was heated in methanol (0.5 mL) in a sealed tube at 210 °C. After 36 h TLC (SiO_2, 5% MeOH in CH_2Cl_2) showed that almost all of the (±)-kopsinine (R_f 0.20) had been converted to a single product with R_f 0.36 (CAS, orange). Chromatography (SiO_2, 1-mm chromatotron plate, 5% MeOH in CH_2Cl_2) afforded 12 mg (88%) of (±)-kopsanone, which crystallized from hexane as colorless crystals: mp 156–157 °C; UV (ethanol) λ_{max} 227, 249, 297 nm; IR (KBr) ν_{max} 3355, 2927, 2841, 1743, 1604, 1475, 1459, 1221, 1091, 759, 746 cm^{-1}; NMR ($CDCl_3$) δ 7.29 (d, J = 7.3 Hz, 1 H), 7.06 (t, J = 7.6 Hz, 1 H), 6.79 (t, J = 7.4 Hz, 1 H), 6.67 (d, J = 7.8 Hz, 1 H) 3.46–3.58 (m, 2 H), 3.37 (s, 1 H), 3.10–3.16 (m, 1 H), 3.02–3.06 (dd, J = 2.2, 7.5 Hz, 2 H), 2.69 (d, J = 10.8 Hz, 1 H), 2.57 (dd, J = 4.7, 10.4 Hz, 1 H), 2.03 (d, J = 15 Hz, 1 H), 1.48–1.87 (m, 5 H), 1.22–1.40 (m, 4 H); mass spectrum, m/z (relative intensity) 306 (100), 305 (81), 277 (8), 183 (18), 153 (20), 109 (25), 96 (17), 84 (34), 55 (24).

Acknowledgment. Support for this project, provided by the National Cancer Institute through National Institutes of Health Research Grant R01 CA 12010, is gratefully acknowledged. We thank Patricia Matson and Timothy Spitzer of our research group for mass spectra. We are greatly indebted to Prof. M. Hesse and Dr. A. Guggisberg of the University of Zurich for comparing spectra of natural kopsinine and pleiocarpine with those of our synthetic compounds.

Registry No. (±)-**1** (R = CH_3, X = H_2), 98737-04-3; (±)-**1** (R = H, X = H_2), 98737-06-5; (±)-**1** (R = CHO, X = H_2), 98737-07-6; (±)-**1** (R = CO_2CH_3, X = H_2), 98737-08-7; (±)-**2** (R = CH_3, X = H_2), 98759-80-9; (±)-**2** (R = H, X = H_2), 84960-64-5; **8**, 57584-86-8; (±)-**9**, 98736-98-2; (±)-**10**, 66859-22-1; **11**, 98759-97-8; (±)-**12**, 98759-74-1; (±)-**13**, 98736-99-3; (±)-**14**, 98737-00-9; (±)-**15**, 98737-01-0; (±)-**16**, 98759-98-9; (±)-**17**, 98737-02-1; (±)-**18**, 98737-03-2; (±)-**19**, 98776-94-4; (±)-**20**, 98759-76-3; (±)-**21**, 98759-77-4; (±)-**22**, 98759-75-2; (±)-**23**, 98777-02-7; (±)-**24**, 98776-95-5; (±)-**25**, 98737-05-4; (±)-epikopsinine, 98759-78-5; (±)-epiaspidofractine, 98759-79-6; 5-chloropentanal, 20074-80-0; benzeneselenenyl chloride, 5707-04-0; diethylamine, 109-89-7; phenyl vinyl sulfone, 5535-48-8.

Stereochemistry of Cyclic Dipeptides. Assignment of the Prochiral Methylenes of 1-Aminocyclopropane-1-carboxylic Acid

Ronald W. Woodard

Department of Medicinal Chemistry, College of Pharmacy, The University of Michigan, Ann Arbor, Michigan 48109-1065

Received July 8, 1985

The two enantiomeric methylene carbons of 1-aminocyclopropane-1-carboxcylic acid (ACC) were differentiated by an NMR study. Several amino acids such as L-alanine, D-alanine, and 2-aminoisobutyric acid as well as ACC were condensed with L- and/or D-phenylalanine to form their corresponding 2,5-diketopiperazines. The measurement of the ^1H NMR signal of these model compounds indicates that the benzyl in the 6-position of these diketopiperazines exerts a shielding effect on the β-carbon of the various amino acids causing an upfield shift in their ^1H resonances. Conversely, the shielding effect of the benzyl results in a downfield shift in the ^{13}C resonance. Although the assignment of the proton resonances of the ACC portion of cyclo[ACC-L-Phe] was more complex, a combination of homonuclear and heteronuclear experiments allowed the proton signals at δ 1.4 and 0.98 to be assigned to the trans methylene group, the one not being shielded by the 6-benzyl group (^{13}C, δ 17.02), and the proton signals at δ 0.74 and 0.36 to be assigned to the cis methylene (^{13}C, δ 19.46). This assignment allows for the nondestructive, nonisotopic diluting analysis of various biosynthetically derived deuterated ACC's formed from the corresponding deuterated *S*-adenosylmethionines.

Our studies on the mechanism of the biosynthesis of 1-aminocyclopropane-1-carboxylic acid (ACC) from *S*-adenosyl-L-methionine (SAM) by 1-aminocyclopropane-1-carboxylic acid synthase[1-3] and our interest in the synthesis of regio- and stereospecifically deuterium-labeled 1-aminocyclopropane-1-carboxylic acid[4] for the study of the mechanism of the biosynthesis of ethylene by plants has made it necessary to distinguish between the enantiotopic methylene groups of ACC. The limited amounts of compounds and our desire to analyze in a nondestructive and nonisotopic diluting technique suggested the use of nuclear magnetic resonance. Since the two methylene carbons of ACC are enantiotopic, they are isochronous and cannot be distinguished by NMR.[5] However, enantiotopic groups can be rendered diastereotopic and thus anisochronous by several techniques: (1) use of a chiral solvent, (2) use of a chiral lanthanide shift reagent, and (3) derivatization with a chiral reagent.[6] The last procedure has

(1) Boller, T.; Herner, R. C.; Kende, H. *Planta* **1979**, *145*, 293–303.
(2) Yu, Y.-B., Adams, D. O.; Yang, S. F. *Arch. Biochem. Biophys.* **1979**, *198*, 280–286.
(3) Khani-Oskouee, S.; Jones, J. P.; Woodard, R. W. *Biochem. Biophys. Res. Commun.* **1984**, *121*, 181–187.
(4) Ramalingam, K.; Kalvin, D.; Woodard, R. W. *J. Labelled Compds. Radiopharm.* **1984**, *21*, 833–841.
(5) Jennings, W. B. *Chem. Rev.* **1975**, *75*, 307–322.
(6) Mislow, K.; Raban, M. *Top. Stereochem.* **1967**, *1*, 1.

0022-3263/85/1950-4796$01.50/0

Table I. ^{1}H NMR Chemical Shift, δ (ppm, Downfield of Me_4Si) of Amino Acids and of the β-Carbon of Amino Acid A of Various Cyclodipeptides C(A-B) in Trifluoroacetic Acid-d_1 at 32 °C

compd	δ value	multiplicity
A^{i}BA	1.2378	singlet
ACC	1.5152	multiplet (AA'BB')
	1.6370	multiplet (AA'BB')
A^{i}BA[a]	1.1368	singlet
ACC[a]	1.108	
	1.380	
c[L-Ala-L-Ala	1.476	doublet
c[L-Ala-L-Phe]	0.770	doublet
c[D-Ala-L-Phe]	1.359	doublet
c[A^{i}BA-L-Ala]	1.282	singlet
	1.277	singlet
c[A^{i}BA-L-Phe]	0.4481	singlet
	1.1511	singlet
c[ACC-L-Phe]	1.451	multiplet
	0.891	multiplet
	0.739	multiplet
	0.366	multiplet
c[ACC-D-Phe][a]	1.0417	multiplet
	0.7514	multiplet
	0.4432	multiplet
	0.578	multiplet

[a] Me_2SO.

the best potential to allow selective control of which prochiral methylene is shifted.[7]

Kopple et al.[8] reported an upfield shift of 1–1.5 ppm of one of the enantiotopic protons of glycine when glycine was incorporated into a diketopiperazine ring (cyclic dipeptide) with either L- or D-phenylalanine.[9] The glycine proton cis[10] to the aromatic ring experiences a shielding effect and is shifted to a higher field apparently independent of the solvent.[8] Further ^{1}H NMR studies[11,12] of a number of cyclic dipeptides have demonstrated that the preferred conformation of the arylmethylene side chain is one in which the aromatic ring faces (or folds over) the diketopiperazine ring. In several cases[8] where the thermodynamic parameters were studied a folded conformation for the arylmethylene side chain was favored by an enthalpy change averaging −3 kcal/mol.

Based on these observations we have prepared cyclo[ACC-L-Phe] and the other diketopiperazine derivatives shown in Tables I and II and measured both their ^{1}H and ^{13}C NMR spectra in an attempt to develop a method to distinquish between the enantiomeric methylene groups of ACC.

Experimental Section

General Procedures. All melting points were obtained on a Mel-Temp apparatus and are uncorrected. Elemental analyses were conducted by M-H-W Laboratories, Phoenix, AZ, and all previously unreported compounds were within ±0.4% of the calculated values. All amino acids and their derivatives were purchased from U.S. Biochemical and used without further purification. Cyclo[L-Phe-L-Phe] was purchased from Bachem Fine Chemicals and cyclo[L-Ala-L-Ala] was purchased from Vega Biochemicals, and both were used without further purification. All organic and inorganic reagents were purchased from the usual chemical sources and were used without further purification. Organic solvents were dried by the standard methods.[13] TLC plates (silica) were purchased from Analtech. The plates were visualized by a Mineralight short wave UV lamp and/or by spraying with ninhydrin. Medium grade silica gel (Merck, 70–230 mesh) was used for column chromatography.

The 90.56 MHz ^{13}C NMR spectra were obtained with a Bruker WP-360 FT NMR spectrometer with a pulse width of 15 μs with 32 K data points for a spectral width of 25 000 Hz and with an exponential line-broadening of 2 Hz. The ^{13}C spectra were either

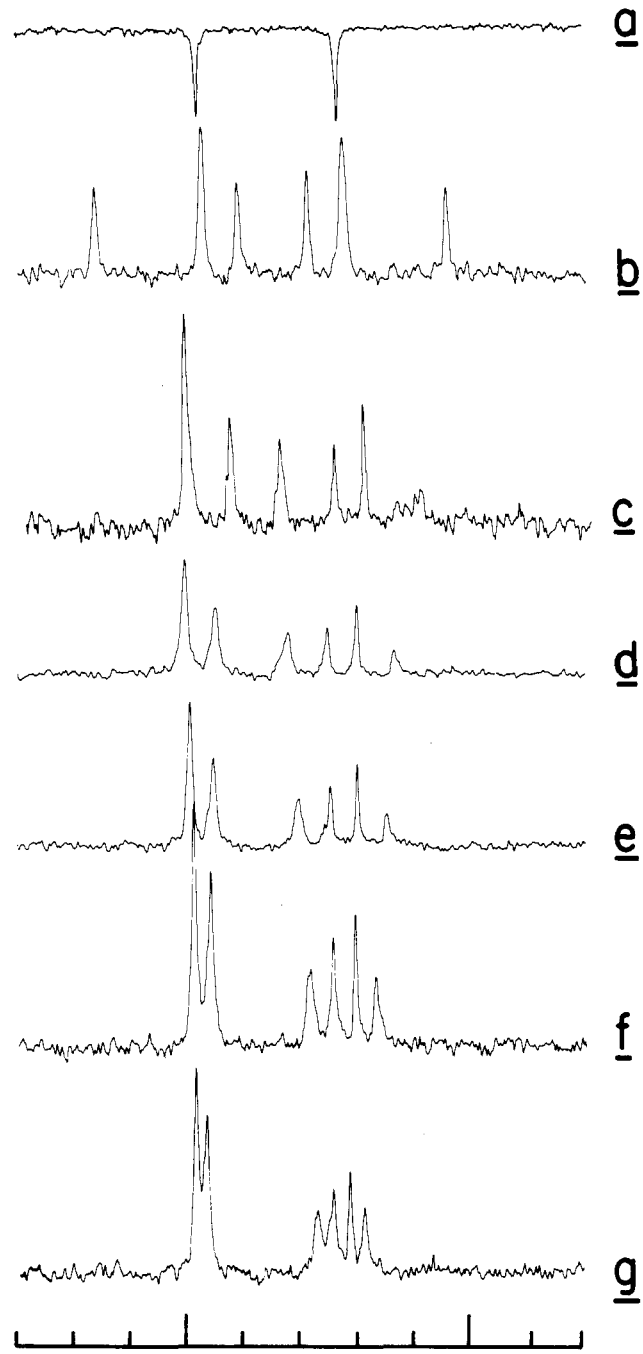

Figure 1. ^{13}C NMR of cyclo[ACC-L-Phe] (a) ^{1}H decoupled (b) ^{1}H coupled and selected ^{1}H irradiation at δ 0.36 at decoupling powers of (c) 12 L, (d) 8 L (e) 6 L, (f) 3 L, (g) 0 L.

(7) Even though lanthanide and chiral-lanthanide shift reagents generally shift known groups in known directions, the method is not as reliable as conversion to a diastereomer of known structure.
(8) Kopple, K. D.; Marr, D. H. *J. Am. Chem. Soc.* **1967**, *89*, 6193–6200.
(9) The configuration of the phenylalanine (D or L) is unimportant as long as it is optically pure and of known configuration.
(10) The terms cis and trans are used in the standard usage as in cyclohexane nomenclature. If L-phenylalanine(*S*) is used the pro-(*S*) proton of glycine is cis and if D-phenylalanine(*R*) is used the pro-*R* proton of glycine is cis.
(11) (a) Kricheldorf, H. R. *Org. Magn. Reson.* **1980**, *13*, 52–58. (b) Liberek, B.; Bednarek, M. *Pol. J. Chem.* **1978**, *52*, 1099–1101.
(12) Vicar, J.; Piriou, F.; Fromagest, P.; Blaha, K.; Fermandjian, S. *Coll. Czech. Chem. Commun.* **1980**, *45*, 482–490.
(13) Gordon, A. J.; Ford, R. A. "The Chemist's Companion"; John Wiley and Sons: New York 1972; pp 429–436.
(14) Konig, W.; Geiger, R. *Chem. Ber.* **1970**, *103*, 788.
(15) Nitecki, D. E.; Halpern. B.; Westley, J. W. *J. Org. Chem.* **1968**, *33*, 864–866.

Table II. ^{13}C NMR Chemical Shift δ (ppm, Downfield of Me_4Si) of Various Cyclodipeptides C(A-B) in Trifluoroacetic Acid-d_1 at Indicated Temperature

		δ of A residues			δ of B residues			
cyclodipeptides	°C	carbonyl	C-α	C-β	carbonyl	C-α	C-β	further carbons
c[L-Ala-L-Ala]	32	174.94	53.67	21.81				
c[L-Ala-L-Phe]	32	174.29	52.92	20.48	172.19	58.41	41.37	130.31, 131.08, 131.88, 134.96
c[D-Ala-L-Phe]	32	174.75	51.97	18.86	173.43	58.64	41.46	130.25, 131.02, 131.67, 134.75
c[L-Ala-L-Phe]	60	174.00	52.86	20.38	171.98	58.36	41.34	130.11, 130.92, 131.68, 134.99
c[D-Ala-L-Phe]	60	174.46	51.96	18.83	173.15	58.59	41.43	130.07, 130.88, 131.48, 134.82
c[A^{i}BA-L-Ala]	32	176.77	59.85	29.38, 28.42	174.55	53.64	21.22	
c[A^{i}BA-D-Phe]	32	176.79	59.69	29.24, 28.72	172.28	59.03	41.84	130.68, 131.49, 132.28, 135.45
c[ACC-D-Phe]	32	174.46	38.92	19.46, 17.02	174.06	59.06	38.98	130.24, 130.90, 131.82, 135.01
c[ACC-D-Phe]	60	174.24	38.91	19.28, 16.94	173.89	59.07	41.64	130.06, 130.79, 131.64, 135.07
c[ACC-L-Ala][a,b]	30	169.32	36.20	18.99, 14.03	168.30	50.54	14.03	
c[ACC-L-Ala][c,b]	30	170.13	36.68	19.31, 14.35	169.11	51.19	14.62	
c[ACC-D-Ala][c,b]	30	169.38	36.25	19.04, 14.08	168.35	50.60	14.08	
c[ACC-D-Phe][a]	32	168.03	35.79	15.34, 12.83	167.70	56.36	41.37	126.64, 128.00, 130.14, 136.06
c[ACC-D-Phe][c]	32	168.22	35.67	15.31, 12.62	167.84	56.39	40.77	
ACC	32	177.05	38.29	17.16				
ACC[a]	32	172.30	34.90	12.90				
A^{i}BA	32	178.53	61.96	25.04				

[a] Me_2SO. [b] See ref 21. [c] Me_2SO–CH_3OH.

broadband decoupled, off-resonance decoupled (to determine $^1J_{CH}$ values), or inverse-gated decoupled (to suppress NOE). The 360.13-MHz ^1H NMR spectra were obtained with a Bruker WP-360 FT NMR spectrometer with a pulse width of 2 μs with 32 K data points for a spectral width of 6260 Hz and with an exponential line broadening of 0 Hz. Routine ^1H NMR spectra were obtained with a Varian EM-360 60 MHz spectrometer with tetramethylsilane as the internal standard for nonaqueous solution and 2,2-dimethyl-2-silapentane-5-sulfonate (DSS) for aqueous solutions. Samples for NMR analysis were dried over P_2O_5 at 56 °C for 24 h under vacuum.

The diketopiperazines used in this study were prepared by the following general procedure.

Preparation of *t*-Boc-dipeptide Esters (14). The *t*-Boc-amino acid (1 mmol), 1-hydroxybenzotriazole (1 mmol) and dicyclohexylcarbodiimide (1 mmol) in 10 mL of dry methylene chloride at 0 °C were added to 10 mL of dry methylene chloride containing the amino acid methyl ester hydrochloride (1 mmol) which had been neutralized with triethylamine below 0 °C, and the mixture was stirred overnight at 5 °C. The reaction mixture was filtered, concentrated in vacuo, suspended in cold ethyl acetate, and filtered. The filtrate was washed with cold 1 N HCl (3 × 50 mL), cold 0.1 N NaOH (3 × 50 mL), water (1 × 50 mL), and brine (1 × 50 mL). The ethyl acetate was dried over Na_2SO_4, filtered, and concentrated in vacuo. The peptides were purified by column chromatography.

Preparation of 2,5-Diketopiperazines (15). The *t*-Boc-dipeptide methyl ester (1 mmol) was dissolved in formic acid (20 mL) and stirred at room temperature for 2 h under nitrogen. The formic acid was removed in vacuo at 30 °C, and the residual solvent was removed under high vacuum. The crude dipeptide ester formate was dissolved in dry *sec*-butyl alcohol (20 mL) and dry toluene (10 mL), and the solution was boiled for 2 h (the solvent level was maintained by addition of fresh *sec*-butyl alcohol). Generally, the diketopiperazines crystallized out of the hot mixtures; however, the solutions were concentrated in vacuo. The residues were taken up in hot methanol and reconcentrated twice. The products were purified by column chromatography and/or recrystallization.

Results

In order to determine if the shielding effect of a benzyl in the 6-position of a 2,5-diketopiperazine can also exert an upfield shift on the ^1H's and/or ^{13}C's of a methyl or methylene group in the 3-position of a diketopiperazine, cyclo[L-Ala-L-Phe], cyclo[D-Ala-L-Phe], and cyclo[L-Ala-L-Ala] were synthesized, and their ^1H and ^{13}C NMR were measured. As can be seen in Table I, the ^1H resonance of the methyl group of alanine in cyclo[L-Ala-L-Ala] differs very little (0.1 ppm) from that of the methyl group in cyclo[D-Ala-L-Phe]. However, when the benzyl group of phenylalanine and the methyl group of alanine are cis (cyclo[L-Ala-L-Phe] or cyclo[D-Ala-D-Phe]), there is an 0.6-ppm upfield shift in the proton resonances of the methyl group due to the shielding of the methyl group by the phenyl ring. The ^{13}C NMR data is more complicated, but the trend as shown in Table II indicates a downfield shift of the ^{13}C signal of the shielded methyl of alanine in cyclo[L-Ala-L-Phe] as compared to the ^{13}C signal of the methyl group of alanine in cyclo[D-Ala-L-Phe]. The ^{13}C resonances of the methyl group of alanine of both phenyl-containing derivatives are, however, shifted upfield of the ^{13}C resonance of the methyl groups of cyclo[L-Ala-L-Ala]. To further demonstrate the ability of the benzyl group of phenylalanine to shield cis and not trans methyls in the 6-position of diketopiperazines, cyclo[A^{i}BA-L-Ala] and cyclo[A^{i}BA-L-phe] were synthesized. Since the methyl groups of 2-aminoisobutyric acid (A^{i}BA) are enantiotopic, the ^1H and ^{13}C spectra of the corresponding diketopiperazine, cyclo[A^{i}BA-L-Phe], will provide a good test for the use of phenylalanine-containing diketopiperazines as an analytical tool for distinguishing between enantiotopic groups β to an α-amino acid center. The ^1H NMR data indicate an ~0.7-ppm upfield shift of one of the methyls of A^{i}BA when incorporated into a diketopiperazine with either D- or L-phenylalanine. It is interesting to note that the ^1H resonances of the enantiotopic methyl of A^{i}BA when incorporated into a diketopiperazine with L-alanine also become anisochronous (~0.0048 ppm) but in an unpredictable fashion. The ^{13}C resonances of the two methyl groups of A^{i}BA are 0.52 ppm different in cyclo[A^{i}BA-L-Phe] and 0.97 ppm different in cyclo[A^{i}BA-L-Ala].

In the ^1H NMR spectrum of cyclo[ACC-L-Phe] the two six-line multiplets (AA′BB′ spin system)[16] of ACC now are separated into four eight-line multiplets. The question that must be addressed is which two protons are attached to which methylene and which protons and carbon are cis to the benzyl group. Based on the ^1H NMR spectra of the *cis*- and *trans*-cyclo[Ala-Phe], we have assigned the ^1H signals at δ 1.4 and 0.36 to represent one of the protons on the methylene trans to the benzyl (unshielded) and one of the protons on the methylene cis to the benzyl (shielded), respectively. Which of the remaining two protons' signals (δ 0.74 or 0.89) is geminal to the signal at δ 1.4 was determined by decoupling experiments. Data

(16) Bovey, F. A. "Nuclear Magnetic Resonance Spectroscopy"; Academic Press: New York, 1969; p 119.

from the homonuclear decoupled ^1H NMR spectrum of the cyclopropane region gave somewhat limited information since all four protons are coupled to each other. The irradiation of the ^1H δ 0.36 caused a collapse of the ^1H δ 0.74 into an apparent six-line multiplet and an irradiation of the ^1H signal δ 0.74 caused a collapse of the ^1H δ 0.36 into a similar six-line multiplet. One would have expected either a triplet or doublet of doublets from these decoupling experiments. We, however, believe this suggests that the ^1H signals at δ 1.4 and 0.89 are due to attachment to the methylene carbon trans to the benzyl ring, and the geminal ^1H's δ 0.74 and 0.36 to be attached to the methylene cis to the benzyl ring since similar results were obtained in the homonuclear decoupling experiments at δ 0.74 and δ 0.36. To substantiate that the ^{13}C signal downfield (δ 19.46) is the methylene cis to the benzyl and that the protons which resonate at δ 0.74 and 0.36 are attached to said carbon and that the ^{13}C signal at δ 17.02 is trans to the benzyl group and coupled to the protons at δ 1.4 and 0.89, the selective proton-decoupled ^{13}C spectrum shown in Figure 1 was recorded. Figure 1 shows the ^{13}C spectrum with the ^1H at δ 0.36 selectively irradiated at various decoupling powers. The ^{13}C spectra with the ^1H at δ 0.74, 0.89, and 1.4, each irradiated at equivalent decoupling powers, gave results comparable to those shown in Figure 1. These selective ^1H-decoupled ^{13}C spectra provide further evidence that the ^1H's at δ 0.74 and 0.36 are attached to the ^{13}C at δ 19.46 which is the cyclopropane methylene carbon cis to the benzyl group in the diketopiperazine cyclo[ACC-L-Phe]. Recently the group of Hill et al.[17] has synthesized (*R*)- and (*S*)-[2,2-$^2H_2$]ACC by two independent routes and incorporated one of the enantiomers into a diketopiperazine with L-(*S*)-phenylalanine. The ^1H NMR spectrum of the diketopiperazine cyclo[D-(*R*)-ACC-L-Phe] gave two sharp doublets at δ 0.36 and 0.74 (J = 5.2 Hz). Subramanian et al.[18] have also synthesized (*R*)- and (*S*)-[2,2-$^2H_2$]ACC by a third method. The ^1H NMR spectra of the diketopiperazines derived from L-(*S*)-phenylalanine and each of their individual enantiomers gave results consistent with the assignments made in this paper and that of Hill.[17]

Conclusion

In order to determine the stereochemical mechanism of the enzyme 1-aminocyclopropane-1-carboxylic acid synthase one will have to analyze the position of the deuterium(s) in ACC obtained from the feeding of regio- or stereospecific deuterated *S*-adenosyl-L-methionine. We have shown in the present study that it is possible to distinquish between the enantiotopic methylene groups of ACC by derivatizing ACC with L-phenylalanine (or D-phenylalanine). The ^{13}C NMR signal of the L-methylene carbon of ACC will be shifted downfield[19,20] and the D-methylene carbon will be shifted upfield. The ^1H NMR signal of the hydrogen atoms attached to the L-methylene carbon of ACC will be shifted upfield.

Acknowledgment. This work was supported by U.S. Public Health Service Grant GM30097.

Registry No. c[L-Ala-L-Ala], 5845-61-4; c[L-Ala-L-Phe], 15180-22-0; c[D-Ala-L-Phe], 15136-19-3; c[A^{i}BA-L-Ala], 98735-75-2; c[A^{i}BA-D-Phe], 98735-76-3; c[ACC-D-Phe], 98735-77-4; c(ACC-L-Ala], 98735-78-5; c[ACC-D-Ala], 98735-79-6; c[A^{i}BA-L-Phe], 95235-24-8; c[ACC-L-Phe], 98735-80-9; 1-aminocyclopropane-1-carboxylic acid, 22059-21-8.

(17) Hill, R. K.; Prakash, S. R.; Wiesendanger, R.; Angst, W.; Martinoni, B.; Arigoni, D.; Liu, H.-W.; Walsh, C. T. *J. Am. Chem. Soc.* **1984**, *106*, 796–798.

(18) Subramanian, P.; Woodard, R. W. in "Proceeding of the Ninth American Peptide Symposium", Kopple, K. D., Deber, C. M., Hruby, V. J., Eds.; Pierce Chemical Co.: Rockford, IL, 1985.

(19) The opposite results would be obtained if one used D-phenylalanine, i.e., the D-methylene carbon of ACC would be shifted downfield, and the L-methylene carbon would be shifted upfield.

(20) Since deuterium has a nuclear spin of one in a proton-decoupled ^{13}C NMR spectrum, a carbon with deuterium attached directly to it would appear as a triplet, whose lines would be of equal intensity. In addition, the signal is usally centered 0.3–0.6-ppm upfield of the normal proton signal and the $J(^{13}C-^2H)$ values are one-sixth those of the equivalent $J(^{13}C-^1H)$.

(21) Jasensky, R. D., Ph.D. Thesis, The University of Wisconsin—Madison, Madison, WI, 1979.

Photochemical Behavior of Thioketenes in Solution: Reaction from S_2

Sharat Singh,[†] Hildegard Nimmesgern,[‡] Ernst Schaumann,*[‡] and Vaidhyanathan Ramamurthy*[†]

Department of Organic Chemistry, Indian Institute of Science, Bangalore-560 012, India, and Institut für Organische Chemie, Universitat Hamburg, Hamburg, West Germany

Received March 12, 1985

The higher excited-state reactions of sterically encumbered thioketenes **1a–d** in solution were investigated. Substituted thiiranes, thio esters, thioacetophenones, and 1,2-diones are formed on photoexcitation of thioketenes in hydroxylic and nonhydroxylic solvents. Thioketenes while unreactive upon excitation to S_1 produce thiiranylidene carbene and zwitterionic intermediates upon excitation to S_2. The reactive state is identified to be S_2 ($\pi\pi^*$). The excited thioketene resists carbon monosulfide elimination but undergoes rearrangement. The photobehavior of thioketenes, established in solution for the first time, differs significantly from that of ketenes, and it cannot be extrapolated from that of structurally analogous ketenes and allenes.

The photochemistry of ketenes is well documented,[1] while that of allenes and cumulenes has been of recent interest.[2] Thioketenes, which are structurally analogous to the above systems, have received only scant attention due to their poor stability. However, in the last decade

[†] Indian Institute of Science.
[‡] Universitat Hamburg.

(1) Russel, R. L.; Rowland, F. S. *J. Am. Chem. Soc.* **1970**, *92*, 7508. Kirmse, W.; Spaleck, W. *Angew. Chem., Int. Ed. Engl.* **1981**, *20*, 776. Kirmse, W. "Carbene Chemistry"; Academic Press: New York, 1971.

0022-3263/85/1950-4799$01.50/0