(conditions similar to racemic synthesis throughout) produced an 80:20[18] mixture of (+)-**1**-(−)-**1**[19] (mp 140–142 °C).

The availability of ibogamine in 17% overall yield in four steps from diene **2** without yield optimization as well as in chiral form demonstrates the efficiency of this approach to this exciting class of compounds. The generality and further application of the newly described cyclization reaction is under further investigation.

Acknowledgment. We express our thanks to the National Science Foundation and the National Institutes of Health for their generous support of our programs. We also thank Dr. Neville Finch of Ciba-Geigy Corp. for an authentic sample of ibogamine.

References and Notes

(1) P. Potier, N. Langlois, Y. Langlois, and F. Gueritte, *J. Chem. Soc., Chem. Commun.*, 670 (1975); G. Büchi and R. E. Manning, *J. Am. Chem. Soc.*, **88**, 2532 (1966); J. Harley-Mason and A. U. Rahman, *Chem. Commun.*, 1048 (1967); N. Neuss, M. Gormann, N. J. Cone, and L. L. Huckstep, *Tetrahedron Lett.*, 783 (1968); J. P. Kutney, J. Beck, F. Blysma, and W. J. Cretney, *J. Am. Chem. Soc.*, **90**, 4504 (1968).
(2) K. F. Wiesner, Ed., *MTP Int. Rev. Sci.: Org. Chem., Ser. One*, **9**, 85 (1973).
(3) (a) G. Büchi, D. L. Coffen, K. Kocsis, P. E. Sonnet, and F. E. Ziegler, *J. Am. Chem. Soc.*, **87**, 2073 (1967); **88**, 3099 (1966). (b) W. Nagata, S. Hirai, T. Okumura, and K. Kawata, *ibid.*, **90**, 1650 (1968). (c) S. I. Sallay, *ibid.*, **89**, 6762 (1967). (d) P. Rosenmund, W. H. Haase, J. Bauer, and R. Frische, *Chem. Ber.*, **108**, 1871 (1975). (e) M. Ikezaki, T. Wakamatsu, and Y. Ban, *Chem. Commun.*, 88 (1969). (f) S. Hirai, K. Kawata, and W. Kagata, *ibid.*, 1016 (1968).
(4) B. M. Trost and J. P. Genêt, *J. Am. Chem. Soc.*, **98**, 8516 (1976).
(5) From enol acetylation of *trans*-hexenal: R. Denhenghi and C. R. Engel, *J. Am. Chem. Soc.*, **82**, 3201 (1960). Use of the *E,E–E,Z* mixture produces product derived from reaction of only the *E,E* isomer.
(6) Geometry was determined by ^{1}H NMR (270 MHz): >C*H*–CHO, δ 2.73 (ddd, J = 13.0, 3.6, 2.2 Hz), coupling to C*H*–OAc is J = 2.2 Hz indicating cis stereochemistry of formyl and acetoxy groups.
(7) D. R. Coulson, *Inorg. Syn.*, **13**, 121 (1972).
(8) M. S. Kharasch, R. C. Seyer, and F. R. Mayo, *J. Am. Chem. Soc.*, **60**, 882 (1938).
(9) Reaction based on Heck arylation: R. F. Heck, *J. Am. Chem. Soc.*, **90**, 5526 (1965); *Org. Syn.*, **51**, 17 (1971). See also Y. Fujiwura, R. Asano, I. Moritani, and S. Teranishi, *J. Org. Chem.*, **41**, 1681 (1976).
(10) Liquid chromatography was performed on a medium-pressure (60–80 psi) apparatus consisting of a 15 × 250 mm column packed with Woelm silica gel (0.032–0.063 mm).
(11) ^{13}C NMR was obtained in $CD_3C(=O)CD_3$ using a 1.7-mm tube, sample size ~5 mg (0.018 mol). Tentative assignments were based on a model constructed from indole ^{13}C resonance of epiibogamine and isoquinuclidine ^{13}C resonances of ibogaine obtained from E. Wenkert, D. W. Cochran, H. E. Gottlieb, E. W. Hagaman, R. B. Filho, F. J. Matos, and M. Madruga, *Helv. Chim. Acta*, **59**, 2437 (1976). 1; C(2), quaternary carbon not observed; C(3), 55.1; C(5), 50.7; C(6), 21.4; C(7), 101.1; C(8), quaternary carbon not observed; C(9), 118.2; C(10), 119.0; C(11), 120.9; C(12), 110.9; C(13), quaternary carbon not observed; C(14), 27.5; C(15), 33.0; C(16), 41.7; C(17), 35.0; C(18), 12.1; C(19), 28.6; C(20), 42.7; C(21), 58.3 ppm.
(12) Sample obtained from Dr. Neville Finch of Ciba-Geigy Corp.
(13) Reduction of σ-palladium complex with $NaBD_4$ proceeds with retention of configuration: J. K. Stille and R. A. Morgan, *J. Am. Chem. Soc.*, **88**, 5134 (1968).
(14) Mass spectral analysis (12 eV) of 1 formed using $NaBD_4$ indicated the following mixture: 18.6% nondeuterated, 72% monodeuterated, and 9.3% dideuterated. ^{1}H NMR (270 MHz) showed that (1) ~90% of the resonance at 1.63 ppm had disappeared, (2) ~90% of the resonance at 2.06 ppm (nondeuterated, dddd, J = 13.5, 11.5, 3.0, 3.0 Hz) had collapsed to a double multiplet (J = 11.5 Hz), (3) 90% of the resonance centered at 2.92 ppm (nondeuterated ddd, J = 11.5, 4.0, 2.0 Hz) had collapsed to a double doublet (J = 11.5, 2.0 Hz). Deuterium substitution had removed the large geminal coupling to the endo H (2.06 ppm) and the small (4 Hz) coupling to the methine α to the indole.
(15) The diene was prepared from tricyclo[4.2.1.0^{2,5}]non-7-en-3-one by ethylation, carbonyl reduction, acylation with *S,O*-methylmandeloyl chloride (from 97% optically pure acid[21]) and pyrolysis as described in B. M. Trost, J. Ippen, and W. C. Vladuchick, *J. Am. Chem. Soc.*, **99**, 8116 (1977); M. E. Jung, *J. Chem. Soc., Chem. Commun.*, 956 (1974).
(16) ^{1}H NMR (270 MHz) $CDCl_3$): δ 9.56 and 9.07 (2s, 0.8 and 0.2 H, respectively), 7.21 (m, 5 H), 5.83 and 5.67 (2m, 0.4 and 1.6 H), 5.55 and 5.50 (2m, 0.8 and 0.2 H), 4.59 and 4.58 (2s, 0.2 and 0.8 H), 3.30 and 3.29 (2s, 0.6 and 2.4 H), 2.58 and 2.36 (2ddd, 0.8 and 0.2 H, J = 13, 3.3, 2.8 Hz), 1.92 (m, 2 H), 1.22 (m, 3 H), 0.84 and 0.74 (2t, 0.6 and 2.4 H, J = 7.5 Hz). Exactly identical behavior of the ^{1}H NMR (270 MHz) resonances of the two products of the Diels-Alder reaction in decoupling experiments rules out their being stereo- or regioisomers.
(17) J. A. Dale and H. S. Moser, *J. Am. Chem. Soc.*, **90**, 3732 (1968).
(18) Correction of observed rotation (+31.4°) for starting mandelic acid *O*-methyl ether (97% optically pure) and there being an 80:20 mixture of epimers would give a calculated rotation for (+)-**1** of +55° (lit.[20] +52.7° (c 0.9, EtOH)).
(19) Although the vast majority of ibogamine (**1**) that has been isolated from natural sources has the (−)-16(*R*),20(*S*) configuration opposite to that of the ibogamine synthesized here, racemic ibogamine has been isolated from *Tabernaemontana retusa* (LAM.) PICHON. 2. M. J. Hoizey, L. Oliver, M. DeBray, M. Quirin, J. Lemen, and K. So, *Ann. Pharm. Fr.*, **28**, 127 (1970). In addition (−)-ibogamine could be prepared by our route by simply substituting the *R* isomer of mandelic acid *O*-methyl ether in the synthesis.
(20) (+)-Ibogamine has been prepared by K. Blaha, Z. Koblicova, and J. Trojanek, *Collect. Czech. Chem. Commun.*, **39**, 2258 (1974), who report mp 159–162 °C. For rotation, see note 18.
(21) T. Raznikiewicz, *Acta Chem. Scand.*, **16**, 1097 (1962).
(22) NIH Postdoctoral Fellow, 1977–1978, awarded by the National Cancer Institute, Fellowship No. 5 F 32 CA 05954-02.

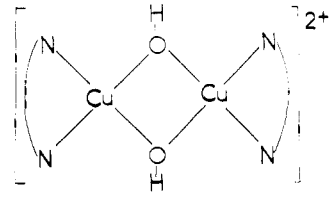
Barry M. Trost,* Stephen A. Godleski,[22] Jean P. Genêt
Department of Chemistry
University of Wisconsin—Madison
Madison, Wisconsin 53706
Received February 6, 1978

Interaction between Orthogonal Magnetic Orbitals in a Copper(II)–Oxovanadium(II) Heterobinuclear Complex

Sir:

In the last few years, several orbital models have been proposed to describe the mechanism of the exchange interaction in binuclear paramagnetic complexes.[1-7] In most of these models, the exchange interaction parameter J, which appears in the Heisenberg-Dirac-Van Vleck phenomenological Hamiltonian $-J\hat{S}_A\cdot\hat{S}_B$ whatever its sign may be, is interpreted as resulting from an antiferromagnetic component J_{AF} and a ferromagnetic component J_F. Several recent attempts to determine semiquantitiatively J_{AF} attest that the mechanism of the antiferromagnetic coupling is now rather well understood.[2,8,9] In contrast, it does not yet appear possible to predict the magnitude of the exchange interaction parameter in binuclear complexes when the metallic centers are ferromagnetically coupled. The main difficulty apparently arises because, as soon as the magnetic orbitals centered on the transition ions are no longer rigorously orthogonal, the J_{AF} component becomes important and very quickly dominates J_F. We recall that a magnetic orbital is defined as a singly occupied orbital, centered on a transition ion and partially delocalized toward the ligands surrounding this ion. Such a magnetic orbital may be considered as a molecular orbital of the monomeric part of the binuclear complex constituted by a transition ion surrounded by its terminal and bridging ligands.

So far, to our knowledge, no binuclear complex in which all the magnetic orbitals are rigorously orthogonal has been synthesized. To make this situation clear, let us consider the hydroxo-bridged copper(II) dimers of the type studied by Hatfield, Hogdson, and coauthors.[10,11] In these complexes the



copper(II) ions are located in C_{2v} sites, and the magnetic orbitals built from each of the metallic $d_{x^2-y^2}$ orbitals pointing along the Cu–N and Cu–O bonds have b_1 symmetry. The overlap integral $\langle b_1|b_1\rangle$ between these magnetic orbitals is in principle different from zero, except for a particular value of the bridging angle ∠ CuOCu which cannot be known exactly a priori.

Strict orthogonality of the magnetic orbitals for reasons of symmetry can occur in heterobinuclear complexes. We have synthesized one of the first such complexes, of the formula $CuVO(fsa)_2en\cdot CH_3OH$ where $(fsa)_2en^{4-}$ denotes the bichelating ligand derived from the Schiff base bis(2′-hydroxy-3′-

0002-7863/78/1500-3931$01.00/0

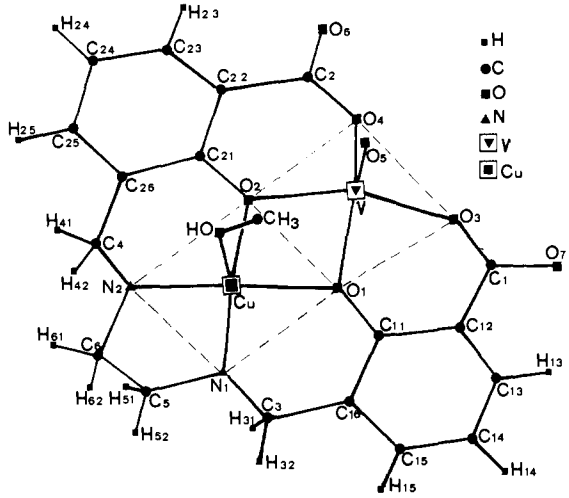
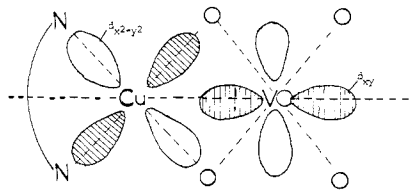


Figure 1. Perspective view of $CuVO(fsa)_2en{\cdot}CH_3OH$.

carboxybenzilidene)-1,2-diaminoethane. The synthesis was carried out as follows. A solution of lithium salt of the mononuclear complex $CuH_2(fsa)_2en{\cdot}{}^1/_2H_2O$[12] was prepared by stirring together 10^{-3} mol of this complex with 2.10^{-3} mol of $LiOH{-}H_2O$ in 80 mL of methanol. To this solution, was slowly added a solution of 10^{-3} mol of $VOSO_4{\cdot}5H_2O$ in 40 mL of methanol. About 0.6 10^{-3} mol of $CuH_2(fsa)_2en{\cdot}{}^1/_2H_2O$ reprecipitated. The mixture was then filtered and the resulting blue solution kept in a closed flask. Small, well-formed, blue single crystals appeared in 1 or 2 days. Anal. Calcd for $C_{19}H_{16}N_2O_7CuV$: C, 44.33; H, 3.13; N, 5.44. Found: C, 44.39; H, 3.23; N, 5.488.

The compound crystallizes in the monoclinic system, space group $P2_1/n$. The lattice constants are $a = 11.636$ (3) Å, $b = 13.612$ (3) Å, $c = 12.423$ (3) Å, and $\beta = 100.79$ (2)°. The unit cell of volume 1933 Å^3 contains four molecules ($\rho_{calcd} = 1.752$ g/cm^3, $\rho_{measd} = 1.78 \pm 0.05$ g/cm^3). The complete structure is not yet fully refined, but the main structural parameters are known sufficiently well to specify the molecular arrangement in Figure 1. Both copper(II) and vanadium(IV) ions are fivefold coordinated in the form of square pyramids, with apices occupied by an oxygen of the methanol and an oxygen of the vanadyl group, respectively. These pyramids share an O_1–O_2 edge, their square planes making a dihedral angle of 170°. The main feature of this structure is that, at the accuracy of the experimental results, the atoms O_5, V, Cu, and O(H) are in a mirror plane for both CuN_2O_3 and VO_5 square pyramids. Consequently, the site symmetries of the metallic ions and the whole molecular symmetry are very close to C_s. The single-ion ground states for both copper(II) and vanadium(IV) are spin doublets. The magnetic orbital around the copper(II), constructed from the $d_{x^2-y^2}$ metallic orbital, transforms as the a'', irreducible representations of the C_s point group. The magnetic orbital around vanadium(IV), constructed from the d_{xy} magnetic orbital, transforms as a'. The situation is schematized as shown.



The overlap integral $\langle a''|a'\rangle$ between the magnetic orbitals is identically zero, whatever the value of the bridging angle ∠CuOV may be. In this case the experimentally observed exchange interaction parameter J reduces to its ferromagnetic component and can be written[13]

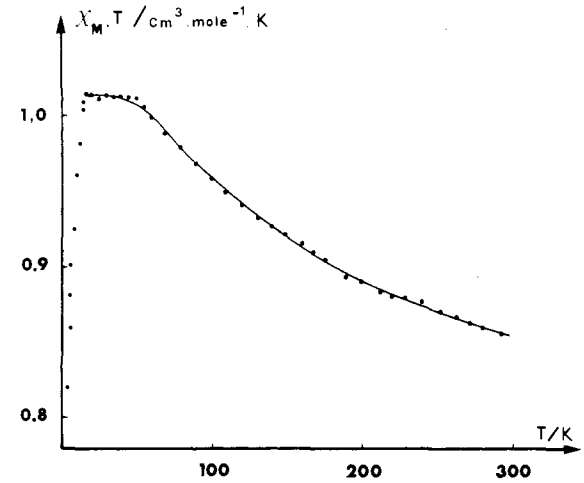


Figure 2. Experimental and theoretical temperature dependences of the product $\chi_M T$ for $CuVO(fsa)_2en{\cdot}CH_3OH$. The experimental points are noted ● and the theoretical curve for $g = 2.017$ and $J = 118$ cm^{-1} is in continuous line (see text).

$$J = \frac{1}{2}\langle a''(1)a'(2)|r_{12}^{-1}|a''(2)a'(1)\rangle$$

J can be determined from the temperature dependence of the molar magnetic susceptibility χ_M. The magnetic behavior of the copper(II)–oxovanadium(II) complex is given in Figure 2, which shows the variation of the product $\chi_M T$ vs. T over the temperature range $3 < T/K < 300$. The exchange interaction between the two single-ion spin doublets leads to two molecular levels characterized by spins $S = 0$ and $S = 1$, separated by $-J$. The increase of $\chi_M T$ upon cooling from room temperature to ~50 K confirms that the coupling is ferromagnetic. Below 50 K, the $S = 0$ level is totally depopulated, so that $\chi_M T$ is constant. Finally, below 18 K, the dominant phenomenon is one of intermolecular antiferromagnetic coupling between the $S = 1$ molecular spins. The fact that $\chi_M T$ is constant between 50 and 18 K shows that above the latter temperature the intermolecular coupling is negligible. In the temperature range 300–18 K, the experimental data closely follow the equation

$$\chi_M T = \frac{2N\beta^2}{k} g^2\left[3 + \exp\left(-\frac{J}{kT}\right)\right]^{-1}$$

with $g = 2.017$ and $J = 118$ cm^{-1}.[14]

In conclusion, the synthesis and the study of the magnetic properties of new heterobinuclear complexes in which the magnetic orbitals centered on different transition ions are strictly orthogonal should enable us to determine the main factors governing the magnitude of the ferromagnetic coupling. Such work is in progress in our group.

References and Notes

(1) I. G. Dance, *Inorg. Chim. Acta*, **9**, 77 (1974), and references therein.
(2) P. J. Hay, J. C. Thibeault, and R. Hoffmann, *J. Am. Chem. Soc.*, **97**, 4884 (1975), and references therein.
(3) O. Kahn and B. Briat, *J. Chem. Soc., Faraday Trans. 2*, **72**, 268 (1976); **72**, 1441 (1976); *Colloq. Int. CNRS*, **No. 255**, 251 (1976).
(4) J. J. Girerd, M. F. Charlot, and O. Kahn, *Mol. Phys.*, **34**, 1063 (1977).
(5) M. V. Eremin and Yu V. Rakitin, *Phys. Status Solidi B*, **80**, 579 (1977); **82**, 221 (1977).
(6) G. R. Tsaparlis and S. F.A. Kettle, *Theoret. Chim. Acta*, **45**, 95 (1977).
(7) L. Jansen and R. Block, *Angew. Chem., Int. Ed. Engl.*, **16**, 294 (1977).
(8) R. D. Harcourt and G. E. Martin, *J. Chem. Soc., Faraday Trans. 2*, **73**, 1 (1977).
(9) O. Kahn, B. Briat, and J. Galy, *J. Chem. Soc., Dalton Trans.*, 1453 (1977).
(10) W. E. Hatfield, *ACS Symp. Ser.*, **No. 5**, 108 (1974).
(11) V. H. Crawford, H. W. Richardson, J. R. Wasson, D. J. Hodgson, and W. E. Hatfield, *Inorg. Chem.*, **15**, 2107 (1976).
(12) M. Tanaka, M. Kitaoka, H. Okawa, and S. Kida, *Bull. Soc. Chim. Jpn.*, **49**, 2469 (1976).

(13) P. Tola, O. Kahn, C. Chauvel, and H. Coudanne, *Nouv. J. Chim.*, 1, 467 (1977).
(14) The measured susceptibilities are corrected for the temperature-independent susceptibility including the diamagnetism and the TIP. This correction is estimated at -320.10^{-6} cm^3 mol^{-1}.

O. Kahn,* P. Tola
Laboratoire de Spectrochimie des Eléments de Transition
Universite de Paris Sud, 91405 Orsay, France

J. Galy
Laboratoire de Chimie de Coordination
BP. 4142, 31030 Toulouse, France

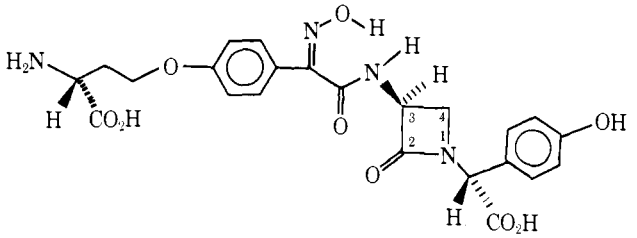
H. Coudanne
Laboratoire de Chimie des Matériaux Organiques
Universite de Paris Sud, 91405 Orsay, France
Received December 27, 1977

Total Synthesis of Nocardicin A. Synthesis of 3-ANA and Nocardicin A

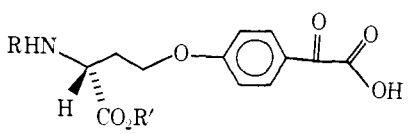
Sir:

In a concurrent communication[1] we have discussed the synthetic strategy involved in our synthesis of the side-chain fragment **2a** of nocardicin A (**1**). In this communication we wish to report the total synthesis of the nucleus **3** and of nocardicin A (**1**).

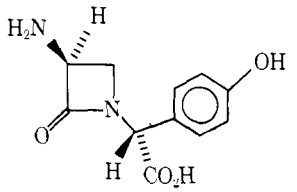
One restriction that we placed on the synthetic design which we elaborated for 3-ANA was that it use readily available



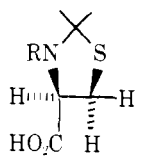
nocardicin A (**1**)



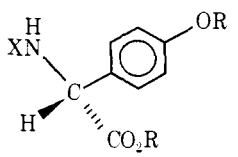
2a, R = R′ = H
b, R = ^{t}Boc: R′ = $CHPh_2$



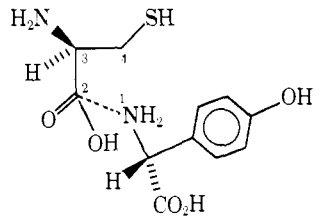
3



4a, R = H
b, R = PhC(=O)—



5, R = H; X = ^{t}Boc
6, R = $PhCH_2$; X = ^{t}Boc
7, R = $PhCH_2$; X = H·HCl
8, R = $PhCH_2$; X = H



L-cysteine D-*p*-hydroxyphenylglycine

Figure 1.

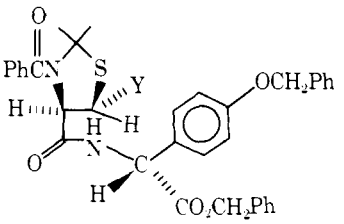
chiral starting materials. We chose L-cysteine and D-*p*-hydroxyphenylglycine. The construction of the crucial β-lactam ring requires the bond-forming reactions shown in Figure 1.

The bond formation between the α-amino group of D-*p*-hydroxyphenylglycine and the carboxyl of L-cysteine was a relatively trivial amide group synthesis. However, the second bond formation, that of the amino group to C-4 while retaining the chirality at C-3, represented a more challenging task. Our solution was to incorporate C-3 and C-4 in five-membered ring thus controlling stereochemistry by the geometry of the ring juncture.[4] The successful synthesis of 3-ANA (**3**) evolved in the following manner.

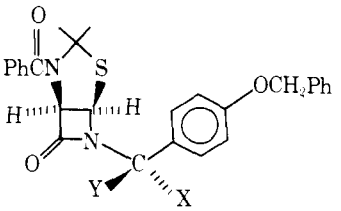
Condensation of L-cysteine with acetone (**4a**) (reflux, 3 days) followed by acylation with benzoyl chloride using propylene oxide as an acid scavenger (25 °C, 1 h) gave excellent yields of the thiazolidine **4b**: mp 170–175 °C; $[\alpha]_D$ (TFE) −165°; NMR ($CDCl_3$) δ 1.83 (3 H, s), 1.92 (3 H, s), 3.13 (2 H, m), 4.60 (1 H, m), 7.23 (5 H, s).

The amino group of D-*p*-hydroxyphenylglycine was protected as the *tert*-butoxycarbonyl derivative **5** and then **5** was treated with 2 equiv of KO-*t*-Bu in DMF followed by 2 equiv of benzyl bromide (25 °C, 16 h) to give the dibenzyl derivative **6**. Treatment of **6** in methylene chloride with dry gaseous hydrogen chloride gave the crystalline salt **7** in 85% yield from *p*-hydroxyphenylglycine: mp 194–198 °C; $[\alpha]_D$ (MeOH) −40.1°; NMR (Me_2SO-d_6) δ 5.22 (2 H, s), 5.30 (2 H, s), 7.13 (2 H, d, J = 9 Hz), 7.33 (5 H, s), 7.43 (2 H, d, J = 9 Hz), 7.48 (5 H, s).

Coupling of the free amine **8** (liberated from **7** using sodium bicarbonate) with **4b** was accomplished using DCC in methylene chloride to give the dipeptide **9** in 90% yield: mp 125–128 °C; $[\alpha]_D$ (Me_2SO) −100.4°; NMR ($CDCl_3$) δ 1.93 (3 H, s), 2.08 (3 H, s), 3.20 (2 H, br d), 4.70 (1 H, tr), 5.05 (2 H, s), 5.17



9, Y = H
10, Y = OCC_6H_5
11, Y = Cl



12, X = CO_2CH_2Ph; Y = H
13, X = H; Y = CO_2CH_2Ph

0002-7863/78/1500-3933$01.00/0