imately a 60:40 mixture of the desired 1-(cyclopenten-3-yl)ethanol and the coupling product 3-(cyclopenten-3-yl)cyclopentene. About 3 g of the product mixture was chromatographed on a 2 × 15 cm activity grade 3 alumina column using pentane and ether. The alcohol-containing fraction was dried and distilled; bp 81–82 °C (32 mm). GLC analysis on a 46-m Carbowax 20M glass capillary column showed the material was a 65:35 mixture of diastereomers: NMR (CCl_4) δ 1.1 (d, J = 6 Hz, 3 H, CH_3), 1.3–2.9 (m, 5 H), 3.2 (s, 1 H, OH), 3.5 (quintet, J = 6 Hz, 1 H, CHOH), 5.4–5.8 (m, 2 H, vinylic).

Anal. Calcd. for $C_7H_{12}O$: C, 75.00; H, 10.71 Found: C, 74.78; H, 10.69.

Samples of the 1-(cyclopenten-3-yl)ethanol diastereomers were collected from a 20% Carbowax 20M column. NMR analysis showed that they have identical absorptions except in the vinylic region. For the major product, NMR δ (CCl_4) 5.5 and 5.7 (a pair of symmetrical multiplets); for the minor product, NMR δ (CCl_4) 5.7 ppm (a singlet). The major product was identical with the material obtained from hydrolysis of the *anti*-6-methyl-2-bicyclo[3.1.0]hexyl 3,5-dinitrobenzoates. Thus, it was assigned as being the (*RR*)(*SS*) isomer and the minor product was assigned as being the (*RS*)(*SR*) isomer.

Hydrolysis Products from the *anti*-9-Methyl-2-bicyclo[6.1.0]nonyl 3,5-Dinitrobenzoates. The hydrolysis products in 80% aqueous acetone at 80 °C were obtained by following a similar procedure to that described above for the 2-bicyclo[3.1.0]hexyl system, and the product compositions were determined by using a combination of 47-m Carbowax 20M glass capillary column GLC and ^1H NMR techniques. A control experiment with the anti-endo alcohol, the most reactive of the various product alcohols, showed that it was stable under the reaction conditions.

Of the three minor hydrolysis products obtained from the anti-endo 3,5-dinitrobenzoate, the one that was formed in about 3% yield has an identical GLC retention time as one of the diastereomeric 1-(cycloocten-3-yl)ethanols prepared independently as described below. The other two, present in about equal amounts, have similar GLC retention times as those of the other C_{10} alcohols encountered in this study. However, they could not be isolated in sufficient quantities for identification.[11]

The sole minor product (2% yield) from hydrolysis of the anti-exo 3,5-dinitrobenzoate had the same GLC retention time as the major product (95% yield) obtained from perchloric acid in acetic acid catalyzed rearrangement of the anti-exo alcohol followed by lithium aluminum hydride in ether reduction of the acetates formed. On the basis of its spectra and from mechanistic expectations, this has been tentatively identified as *trans*-8-hydroxy-*cis*-9-methyl-*trans*-bicyclo[5.2.0]nonane: NMR (CCl_4) δ 1.1 (d, J = 7 Hz, 3 H, CH_3), 1.1–2.1 (m, 13 H), 1.7 (s, 1 H, OH), 3.1 (t, J = 7 Hz, 1 H, CHOH). A precise molecular weight was determined by mass spectrometry. Calcd for $C_{10}H_{18}O$: 154.1358. Found: 154.1375.

1-(Cycloocten-3-yl)ethanol. Following an analogous procedure to that described above for preparing 1-(cyclopenten-3-yl)ethanol but starting with 3-chlorocycloocteene,[12] a 60:40 mixture of two diastereomeric 1-(cycloocten-3-yl)ethanols together with some 3-(cycloocten-3-yl)cycloocteene coupling product was obtained. The major isomer had the same GLC retention time as that of one of the minor hydrolysis products of *anti*-9-methyl-*endo*-2-bicyclo[6.1.0]nonyl 3,5-dinitrobenzoate. A sample of the 1-(cycloocten-3-yl)ethanol mixture was collected by GLC and a precise molecular weight determined by mass spectrometry. Calcd for $C_{10}H_{18}O$: 154.1358. Found: 154.1354. For the major product, NMR (CCl_4) δ 1.1 (d, J = 6 Hz, 3 H, CH_3), 1.0–2.6 (m, 11 H), 1.6 (s, 1 H, OH), 3.5 (quintet, J = 6 Hz, 1 H, CHOH), 5.0–5.7 (m, 2 H, vinylic); for the minor product, NMR (CCl_4) 1.1 (d, J = 6 Hz, 3 H, CH_3), 1.0–2.6 (m, 11 H), 1.5 (s, 1 H, OH), 3.6 (quintet, J = 6 Hz, 1 H, CHOH), 5.2–5.9 ppm (m, 2 H, vinylic).

Acknowledgment. We acknowledge support for this work by a Faculty Research Grant from the Committee on Research of the University of California, Davis.

Registry No. (±)-**5**, 85249-33-8; (±)-**5** 3,5-DNB, 85203-30-1; (±)-**6**, 85249-34-9; (±)-**6** 3,5-DNB, 85249-35-0; (±)-**7**, 85203-31-2; (±)-**7** 3,5-DNB, 85203-32-3; (±)-**8**, 85203-33-4; (±)-**8** 3,5-DNB, 85203-34-5; (±)-**12**, 85203-35-6; (±)-*anti*-6-methyl-2-bicyclo[3.1.0]hexanone, 85249-36-1; bicyclo[6.1.0]nonan-2-one, 29800-55-3; (±)-cycloocten-3-ol, 62249-35-8; 1,1-diiodoethane, 594-02-5; (±)-*syn*-9-methyl-2-bicyclo[6.1.0]nonanone, 85249-37-2; (±)-*anti*-9-methyl-2-bicyclo[6.1.0]nonanone, 85249-38-3; (±)-*syn*-9-methyl-*endo*-2-bicyclo[6.1.0]nonanol, 85249-39-4; (±)-*syn*-6-methyl-*endo*-2-bicyclo[3.1.0]hexanol, 85203-36-7; (±)-cyclopenten-3-ol, 62894-08-0; (±)-*syn*-6-methyl-*exo*-2-bicyclo[3.1.0]-hexanol, 85203-37-8; (±)-3-chlorocyclopentene, 62894-09-1; acetaldehyde, 75-07-0; 3-(cyclopenten-3-yl)cyclopentene, 2690-18-8; (±)-(*R**,*S**)-1-(cyclopenten-3-yl)ethanol, 85203-38-9; (±)-*trans*-8-hydroxy-*cis*-9-methyl-*trans*-bicyclo[5.2.0]nonane, 85203-39-0; (±)-(*R**,*R**)-1-(cycloocten-3-yl)ethanol, 85203-40-3; (±)-(*R**,*S**)-1-(cycloocten-3-yl)ethanol, 85203-41-4; (±)-3-chlorocycloocteene, 85249-40-7; (±)-*syn*-9-methyl-*exo*-2-bicyclo[6.1.0]nonanol, 85249-41-8.

(11) For information concerning further rearrangements of 2-bicyclo[6.1.0]nonyl cations, see: Olah, G. A.; Prakash, G. R. S.; Rawdah, T. N. *J. Org. Chem.* **1980**, *45*, 965.

(12) Henninger, P. W.; Dukker, L. J.; Hasinga, E. *Recl. Trav. Chim. Pays-Bas* **1966**, *85*, 1171.

Synthesis of the Carbapenam System from Glutamic Acid and Acetoacetic Acid Derivatives[1]

Mario D. Bachi,* Ron Breiman, and Haim Meshulam

Department of Organic Chemistry, The Weizmann Institute of Science, Rehovot, Israel

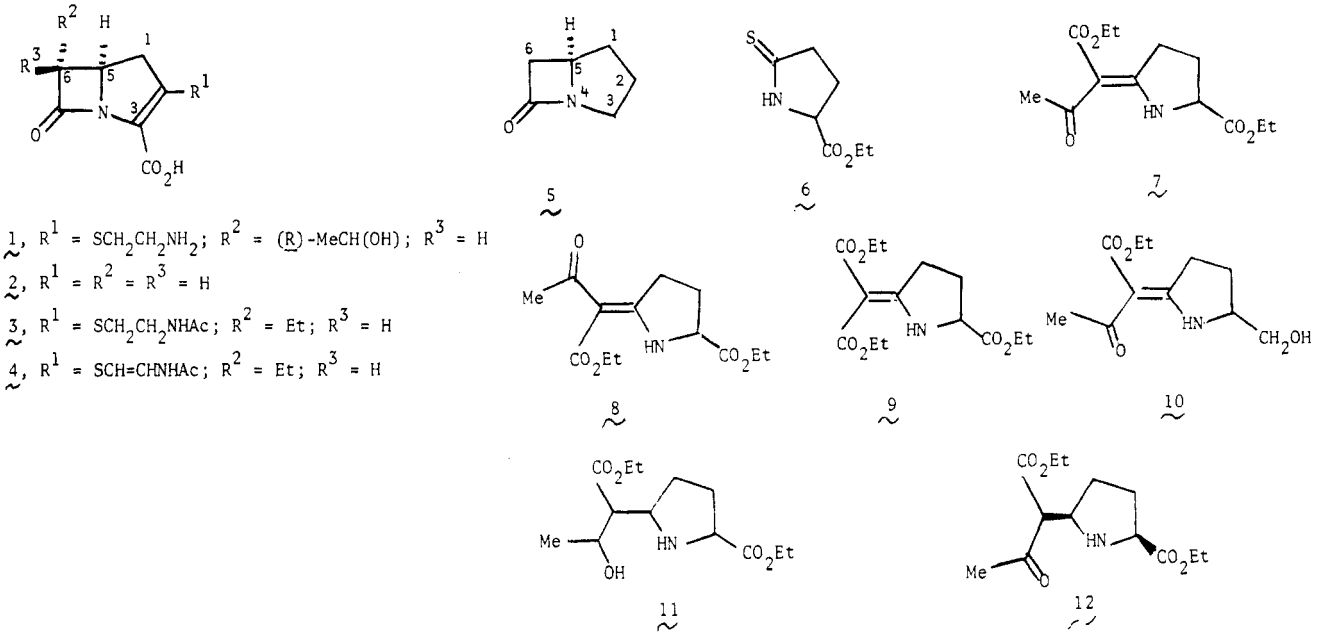
Received July 6, 1982

A synthesis of carbapenam-3-carboxylates is described. Ethyl pyroglutamate was converted into the corresponding thioamide **6** which was subjected to an alkylative sulfide contraction with ethyl 2-bromoacetoacetate. The resulting enamino keto ester **7** was hydrogenated to give, after appropriate manipulations with protecting groups, the two diastereoisomeric 2-[2-(*p*-nitrobenzyloxycarbonyl)-5-pyrrolidinyl]butanoic acids **22a** and **22b**. Dehydration with 1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride afforded the *p*-nitrobenzyl (±)-6β-ethylcarbapenam-3-carboxylate **25a** and its 6α epimer **25b**.

The discovery of the highly potent and broad-spectrum antibiotic thienamycin **1**[2] (Chart I) was followed by the isolation of other antibiotics deriving from the carbapenem-3-carboxylic acid **2** and bearing alkyl or hydroxyalkyl

0022-3263/83/1948-1439$01.50/0

Chart I



groups in either the 6α or 6β positions.[3] Noteworthy in the context of the present investigation are the 6-ethyl derivatives **3** and **4**[4] and their 6-epimers.[5] At the outset of this work, compounds deriving from the more saturated carbapenam system **5**, which formally links the molecular backbone of the penicillin with that of the thienamycin antibiotics, were considered as unstable elusive compounds which tend to polymerize.[6] Recently, however, a few syntheses of carbapenams including derivatives bearing a carboxylic salt or ester group at position 3 have been described.[7] We now report a simple synthesis of *p*-nitrobenzyl 6β-ethylcarbapenam-3β-carboxylate (**25a**)[8] and its 6α-epimer **25b**[8] by a route based on the use of glutamic acid and acetoacetic acid derivatives as starting materials. Glutamic acid was reported as a biogenetic precursor of the carbapenem antibiotics.[2a,3]

The construction of the target's molecular backbone from these starting materials requires the bonding of C-5 of glutamic acid with C-2 of acetoacetic acid. For this purpose ethyl (±)-pyroglutamate was converted into the thiolactam **6** which was treated with ethyl 2-bromoacetoacetate to give the alkylidenepyrrolidine **7**. Best results in this condensation, which involves sulfide contraction via alkylative coupling,[9] were obtained when the reaction was performed in one pot with $NaHCO_3$ as a base. Use of stronger bases as K_2CO_3, Et_3N, NaH, or EtONa resulted in a decrease of yield from 61% to 10% or less. The exocyclic double bond in the condensation product was assigned the *E* geometry as depicted in formula **7** rather than the alternative *Z* geometry shown in **8** on the grounds of its IR and NMR spectral data which indicate the existence of intramolecular hydrogen bonding between the pyrrolidine NH and the ketonic C=O groups.[10] Thus, the signal for the NH proton in the NMR spectrum of the keto diester **7** appears at a lower field than the corresponding signal in the spectrum of the similar triester **9**. The IR absorption band for the α,β-unsaturated ester carbonyl in **7** appears at a frequency comparable to that of the α,β-unsaturated ester in **9**, which is not intramolecularly hydrogen bonded. Compound **9** was prepared from the thiolactam **6** and diethyl 2-bromomalonate analogously to the described preparation of **7**.

The tetrasubstituted double bond in compound **7**, which constitutes part of cross-conjugated vinylogous amide and vinylogous urethan systems, was found to be rather resistant to reduction. Thus, treatment of **7** with sodium borohydride in boiling aqueous tetrahydrofuran resulted in the exclusive reduction of the nonconjugated ester grouping to give the hydroxy derivative **10**. The double bond in **7** also resisted catalytic hydrogenation over PtO_2 in acetic acid but was hydrogenated with the same catalyst in a solution of 20% trifluoroacetic acid in acetic acid. These strong acidic conditions precluded the employment

(1) Most of the investigations described in this paper constitute part of the thesis submitted by R.B. to the Feinberg Graduate School, The Weizmann Institute of Science, in partial fulfillment of the requirements for the Ph.D. degree.

(2) (a) Albers-Schonberg, G.; Arison, B. H.; Kaczka, E. A.; Kahan, F. M.; Kahan, J. S.; Lago, B.; Maisse, W. M.; Rhodes, R. E.; Smith, J. L. 16th Interscience Conference on Antimicrobial Agents and Chemotherapy, Chicago, IL, 1976, Abstract No. 299. (b) Albers-Schonberg, G.; Arison, B. H.; Hensens, O. D.; Hirshfield, J.; Hoogsteen, K.; Kaczka, E. A.; Rhodes, R. E.; Kahan, J. S.; Kahan, F. M.; Ratcliffe, R. W.; Walton, E.; Ruswinkle, L. J.; Morin, R. B.; Christensen, B. G. *J. Am. Chem. Soc.* **1978**, *100*, 6491.

(3) Cooper, R. D. G. In "Topics in Antibiotic Chemistry"; Sammes, P. G., Ed.; Ellis Horwood Ltd.: Chicheser, 1980; Vol 3, p 39.

(4) (a) Yamamoto, K.; Yoshioka, T.; Kato, Y.; Shibamoto, N.; Okamura, K.; Shimauchi, Y.; Ishikura, T. *J. Antibiot.* **1980**, *33*, 796. (b) Kametani, T.; Honda, T.; Nakayama, A.; Sasakai, Y.; Mochizuki, T.; Fukomoto, K. *J. Chem. Soc., Perkin Trans. 1* **1981**, 2228. (c) Shibamoto, N.; Koki, A.; Nishino, M.; Nakamura, K.; Kiyoshima, K.; Okamura, K.; Okabe, M.; Okamoto, R.; Fukagawa, Y.; Shimauchi, Y.; Ishikura, T. *J. Antibiot.* **1980**, *33*, 1128.

(5) Corbett, D. F.; Eglinton, A. J. *J. Chem. Soc., Chem. Commun.* **1980**, 1083.

(6) Wong, P. K.; Madhavarao, M.; Marten, D. F.; Rosenblum, M. *J. Am. Chem. Soc.* **1977**, *99*, 2823. Busson, R.; Vanderhaeghe, H. *J. Org. Chem.* **1978**, *43*, 4438. Low, G.; Ridley, D. D. *J. Chem. Soc., Perkin Trans.* 1 **1973**, 2024. Moll, F.; Thoma, H. *Z. Naturforsch, B: Anorg. Chem., Org. Chem.* **1969**, *24B*, 942.

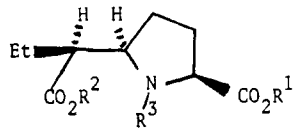
(7) (a) Schmitt, S. M.; Johnston, D. B. R.; Christensen, B. G. *J. Org. Chem.* **1980**, *45*, 1135. (b) Bateson, J. H.; Baxter, J. G.; Roberts, P. M.; Smale, T. C.; Southgate, R. *J. Chem. Soc., Perkin Trans. 1* **1981**, 3242. (c) Shibuya, M.; Kuretani, M.; Kuboto, S. *Tetrahedron Lett.* **1981**, *22*, 4453. (d) Linkies, A.; Pietsch, H.; Reuschling, D. *Ibid.* **1980**, *21*, 3869. (e) Bateson, J. H.; Roberts, P. M.; Smale, T. C.; Southgate, R. I. *J. Chem. Soc., Chem. Commun.* **1980**, 185.

(8) All compounds prepared are racemic; one enantiomer is depicted for convenience.

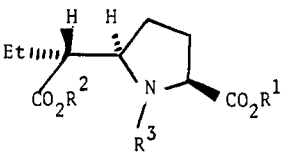
(9) Roth, M.; Dubs, P.; Götschi, E.; Eschenmoser, A. *Helv. Chim. Acta* **1971**, *54*, 710.

(10) Huisgen, R.; Herbig, K.; Siegel, A.; Huber, H. *Chem. Ber.* **1966**, *99*, 2526.

of acid-sensitive protecting groups for the carboxylates which might have been more convenient than the ethyl groups in later steps of the synthesis. The hydrogenation product consisted of two epimers of the hydroxyethyl derivatives **11** (50%) and two epimers of the ethyl derivatives **13** (39%) which a posteriori were assigned the structures **13a** and **13b** by correlation to their corresponding transformation products **25a** an **25b**.[8] This reduction probably involves an initial 1,4-hydrogenation of the cross-conjugated system from the opposite side the 2-ethoxycarbonyl group to give stereospecifically the saturated β-keto ester **12**, which is further reduced to the carbinols **11** or hydrogenolyzed to the ethyl derivatives **13**. A similar dual reduction of the ketonic carbonyl group has been previously observed in β-keto esters.[11] The failure of the carbinol **11** to undergo further hydrogenolysis to **13** when exposed to the same reaction conditions for a longer period of time indicates that it is not an intermediate in the formation of **13**.



a



b

13, $R^1 = R^2 = Et$; $R^3 = H$

14, $R^1 = R^2 = K$; $R^3 = H$

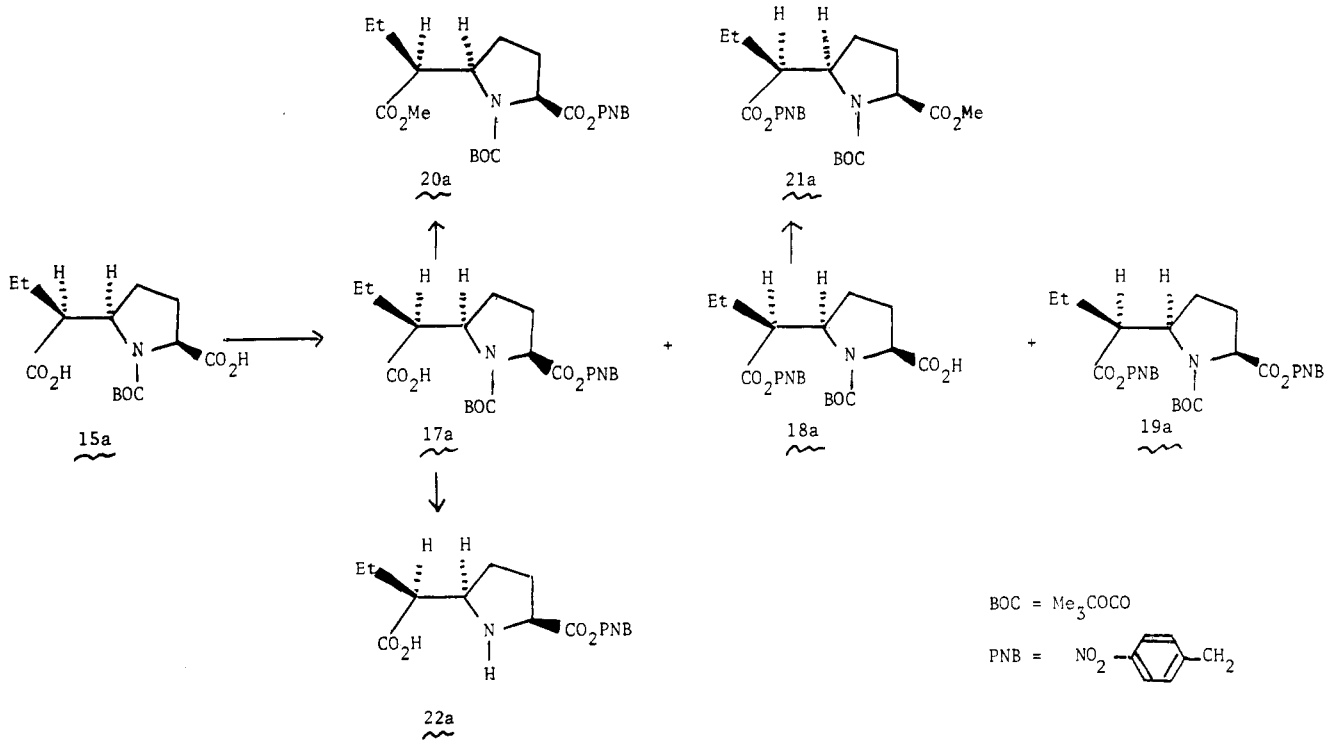
15, $R^1 = R^2 = H$; $R^3 = Me_3COCO$

16, $R^1 = R^2 = Me$; $R^3 = Me_3COCO$

Saponification of the diethyl esters **13** with potassium hydroxide followed by treatment of the resulting salts **14** with di-*tert*-butyl dicarbonate afforded a mixture of the two N-protected epimeric amino dicarboxylic acids **15a** and **15b** (86%). Treatment of this mixture with diazomethane afforded the dimethyl esters **16**. Pure **15a** was obtained by partial separation of the epimeric mixture of **15**. Selective esterification of **15a** with *p*-nitrobenzyl chloride, dicyclohexylamine, and potassium iodide in dimethylformamide afforded the desired *p*-nitrobenzyl ester **17a** (29%) along with its isomer **18a** (15%) and the diester **19a** (23%) (Scheme I). The last two compounds could be recycled, after hydrogenolysis[12] of the *p*-nitrobenzyl group, together with recovered starting material **15a**. The structure assignment of **17a** and **18a** and of their methyl esters **20a** and **21a** was based on the fragmentation patterns of their high-resolution mass spectra which show the corresponding characteristic fragments **23** and/or **24** (see Chart II and Experimental Section).

Deprotection of the amino group in the pyrrolidine **17a** (HCl in EtOAc) afforded the key compound **22a** which possesses the properly protected molecular backbone. Its conversion into a penam system requires the apparently simple operation of removing the elements of water from a β-amino carboxylic acid to form the β-lactam ring. However, attempts to cyclize the amino acid **22a** by conventional methods through the activation of the carboxylic group as its corresponding chloride or *p*-nitrophenyl ester or by using dicyclohexylcarbodiimide (DCC) were rather disappointing. When DCC was used, the IR spectrum of the crude reaction product indicated the presence of a β-lactamic compound which decomposed during attempted purification. To avoid any detrimental intermolecular reactions of the formed β-lactam or of its reactive precursor, we have elaborated a procedure by which the annelation to the bicyclic β-lactam and its primary purification, were performed in a dilute solution. 1-[3-(Dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride, which is soluble in both CH_2Cl_2 and in water, was used as the dehydrating agent. This reagent and the β-amino amino acid **22a** were dissolved in CH_2Cl_2 (concentration

Scheme I



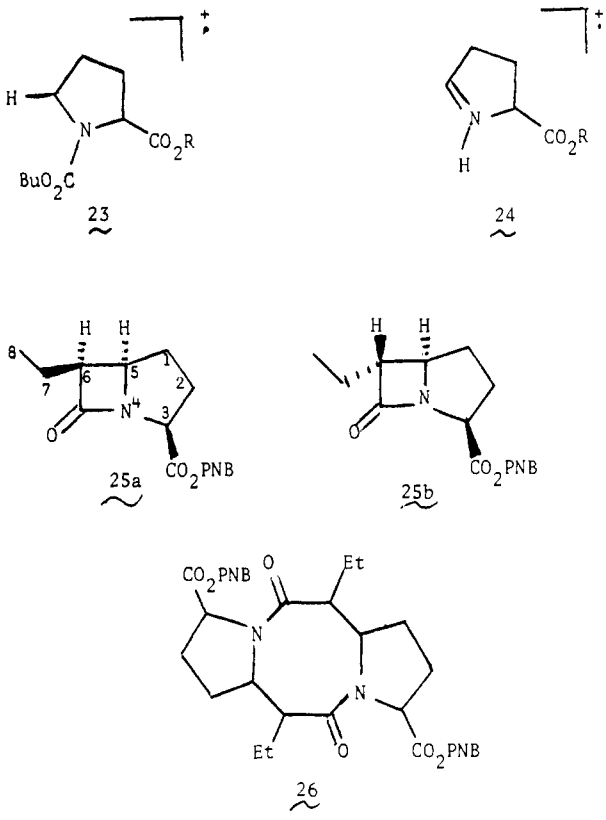
BOC = Me_3COCO

PNB = NO_2–C$_6$H$_4$–CH_2

(11) Rylander, P. In "Catalytic Hydrogenation in Organic Synthesis"; Academic Press: New York, 1979; p 86.

(12) Schawarz, H.; Arakawa, K. *J. Am. Chem. Soc.* **1959**, *81*, 5691.

Chart II



ca. 10^{-3} M), and after 22 h any excess of the carbodiimide and of any derivatives thereof, as well as any other water soluble compound, was removed from the dilute organic solution by washing with cold (0 °C) water. Flash chromatography of the crude product afforded *p*-nitrobenzyl 6β-ethylcarbapenam-3β-carboxylate (**25a**, 41%) and the dimer **26** (10%). When a mixture of the acids **15a** and **15b** was subjected to the sequence of reactions as described above for the case of pure **15a**, a mixture of the carbapenam **25a** and its 6α-epimer **25b** was obtained. Attempts to deblock the esters **25** by catalytic hydrogenolysis over palladium (5% on charcoal), either in dioxane, or in an ethyl acetate-aqueous $NaHCO_3$ mixture,[13] resulted in destruction of the β-lactam ring.

The assignment of the relative configuration to the three chiral centers in the carbapenams **25a**[8] and **25b**[8] resulted from the analysis of their 270-MHz H^1 NMR spectra which included pertinent decoupling by double irradiation. The coupling constants $J_{5,6}$ = 5 Hz, typical for *cis*-β-lactams, and $J_{5,6}$ = 2 Hz, typical for *trans*-β-lactams, are observed respectively in the spectra of **25a** and **25b**. The chemical shift for the C-3 protons in these compounds appear at δ 3.92 and 3.93, respectively, namely, within the range characteristic for the analogous proton in penams,[14] oxapenams,[15] and carbapenams,[7a,b] having C-3 carboxylates in a trans relationship with the C-5 proton. In compound **25a**, which possess a C-6α proton, a long-range coupling constant ($J_{3,6}$ = 1 Hz) was observed; no similar coupling was detected in the spectrum of **25b**, where this proton occupies a β-position. It is noteworthy that in the carbapenams **25a** and **25b** the steric nonbonding intramolecular compression is higher than in their corresponding C-3 epimers. The formation of the thermodynamically less stable isomers is a consequence of the kinetically controlled hydrogenation of the double bond in the intermediate **7**.

Experimental Section

IR spectra were recorded with a Perkin-Elmer 237 spectrophotometer. H^1 NMR data were determined on an 80-MHz Varian FT-80A, a 90HMHz Bruker FT-HFX-10, or a 270-MHz Bruker WH-270 instrument. Low- and high-resolution mass spectra were recorded on a Varian MAT-731 (double focusing) spectrometer. Melting points were measured by using a Büchi apparatus and are uncorrected.

Ethyl 5-Thioxopyrrolidine-2-carboxylate (6). A solution of ethyl pyroglutamate (54.95 g, 0.35 mol) in chloroform (200 mL) was added during 15 min to a stirred suspension of P_2S_5 (77.70 g, 0.35 mol) in carbon disulfide (150 mL). The reaction mixture was stirred for 22 h at 55–60 °C and then cooled and evaporated. The residue was stirred in a water–chloroform mixture until all the P_2S_5 decomposed. The organic phase was washed with water, dried ($MgSO_4$), and evaporated. Chromatography on silica gel (hexane–acetone, 4:1) followed by recrystallization (ether) afforded the thiolactam **6**: 42.38 g (70%); mp 72–73 °C; IR ($CHCl_3$) 3400, 1735, 1485 cm^{-1}; NMR (90 MHz, $CDCl_3$) δ 1.31 (t, J = 7 Hz, OCH_2CH_3), 2.26–2.55 (m, $CHCH_2CH_2$), 2.80–3.06 (m, CH_2CH_2CS), 4.25 (q, J = 7 Hz, OCH_2CH_3), 4.51 [dd, J = 7.5, 7 Hz, $NCH(CO_2)CH_2$], 8.15 (br, NH); high-resolution mass spectrum, calcd for $C_7H_{11}NO_2S$ m/e 173.0511, found m/e 173.0532; m/e 173 (M^+), 100 ($M^+ - CO_2Et$). Anal. Calcd for $C_7H_{11}NO_2S$: C, 48.55; H, 6.40; N, 8.09; S, 18.48. Found: C, 48.38; H, 6.58; N, 8.00; S, 18.20.

Ethyl 2-[2-(Ethoxycarbonyl)-5-pyrrolidinylidene]-3-oxobutyrate (7). Ethyl 2-bromo-3-oxobutyrate (41.80 g, 0.2 mol) and $NaHCO_3$ (33.60 g, 0.4 mol) were added to a solution of the thiolactam **6** (17.30 g, 0.1 mol) in dry CH_2Cl_2 (1400 mL). The suspension was heated under reflux for 36 h, cooled, filtered through Celite, and evaporated. Silica gel chromatography (toluene–ethyl acetate) followed by recrystallization (hexane) afforded the title compound **7**: 16.41 g (61%); mp 64–65 °C; IR ($CHCl_3$) 1740, 1690. 1600, 1540 cm^{-1}; NMR (80 MHz, $CDCl_3$) δ 1.29 (t, J = 7 Hz, OCH_2CH_3), 1.31 (t, J = 7 Hz, OCH_2CH_3), 2.07–2.40 (m, $CHCH_2CH_2$), 2.42 (s, CH_3CO), 3.11–3.31 (m, CH_2CH_2C), 4.22 (q, J = 7 Hz, 2 OCH_2CH_3), 4.50 (dd, J = 7.5, 7 Hz, $NCH(CO_2)CH_2$), 11.78 (br, NH, exchangeable with D_2O); high-resolution mass spectrum, calcd for $C_{13}H_{19}NO_5$ m/e 269.1263, found m/e 269.1246; m/e 269 (M^+), 224 (M^+ – OEt), 196 ($M^+ - CO_2Et$), 150 ($M^+ - CO_2Et - C_2H_6O$), 122 ($M^+ - CO_2Et - C_2H_6O - CO$). Anal. Calcd for $C_{13}H_{19}NO_5$: C, 57.98; H, 7.11; N, 5.20. Found: C, 58.16; H, 7.21; N, 5.26.

Diethyl 2-[2-(Ethoxycarbonyl)-5-pyrrolidinylidene]-malonate (9). Diethyl 2-bromomalonate (239 mg, 1 mmol) and $NaHCO_3$ (168 mg, 2 mmol) were added to a solution of the thiolactam **6** (86 mg, 0.5 mmol) in CH_2Cl_2 (3 mL). The suspension was heated under reflux for 24 h, cooled, filtered through Celite, and evaporated. The residue was chromatographed on a silica gel plate (ether) to give the title compound **9**: 63 mg (42%); IR ($CHCl_3$) 1740, 1695 (br), 1650, 1570; NMR (80 MHz, $CDCl_3$) δ 1.28 (t, J = 7 Hz, OCH_2CH_3), 1.30 (t, J = 7 Hz, OCH_2CH_3), 1.31 (t, J = 7 Hz, OCH_2CH_3), 2.10–2.50 (m, $CHCH_2CH_2$), 3.06–3.36 (m, C=C CH_2CH_2), 4.18 (q, J = 7 Hz, OCH_2CH_3), 4.21 (q, J = 7 Hz, 2 OCH_2CH_3), 4.43 (dd, J = 7.5, 7 Hz, $NCH(CO_2)CH_2$, 9.64 (br, NH); high-resolution mass spectrum, calcd for $C_{14}H_{21}NO_6$ m/e 299.1369, found m/e 299.1392; m/e 299 (M^+), 254 (M^+ – OEt), 226 ($M^+ - CO_2Et$), 180 ($M^+ - CO_2Et - C_2H_6O$), 152 ($M^+ - CO_2Et - C_2H_6O - CO$).

Ethyl 2-[2-(Hydroxymethyl)-5-pyrrolidinylidene]-3-oxobutyrate (10). To a suspension of the keto ester **7** (54 mg, 0.2 mmol) in a mixture of THF (4 mL) and water (1 mL) was added $NaBH_4$ (76 mg, 2 mmol). The reaction mixture was boiled under reflux for 90 min, and the THF was removed under reduced pressure. The aqueous solution was extracted with chloroform, and the extract was dried, evaporated, and chromatographed (silica gel) to give the carbinol **10**: 36 mg (80%); IR ($CHCl_3$) 1680, 1600, 1540 cm^{-1}; NMR (90 MHz, $CDCl_3$) δ 1.31 (t, J = 7 Hz, OCH_2CH_3), 1.50–2.30 (m, $CHCH_2CH_2$), 2.38 (s, $COCH_3$), 3.10–3.30 (m, C=

(13) Ernest, I.; Gosteli, J.; Greengrass, C. W.; Holick, W.; Jackman, D. E.; Pfaendler, H. R.; Woodward, R. B. *J. Am. Chem. Soc.* **1978**, *100*, 8214.
(14) Busson, R.; Vanderhaeghe, H. *J. Org. Chem.* **1976**, *41*, 2561.
(15) Alenxander, R. G.; Southgate, R. *J. Chem. Soc., Chem. Commun.* **1977**, 405.

CCH_2CH_2), 3.40–3.80 (m, $CHCH_2OH$), 11.70 (br, NH); high-resolution mass spectrum, calcd for $C_{11}H_{17}NO_4$ m/e 227.1157, found m/e 227.1167; m/e 227 (M^+), 212 ($M^+ - CH_3$), 196 ($M^+ - CH_2OH$), 182 ($M^+ - C_2H_5O$), 150 ($M^+ - CH_2OH - C_2H_6O$), 122 ($M^+ - CH_2OH - C_2H_6O - CO$).

Hydrogenation of 7. Platinum oxide (645 mg) was added to a solution of compound **7** (4.30 g, 16 mmol) in a mixture of acetic acid (84 mL) and trifluoroacetic acid (16 mL). The reaction mixture was shaken at room temperature under hydrogen at 4 atm, after 12 h a second portion of platinum oxide (65 mg) was added, and the hydrogenation was continued under the same conditions for an additional 12 h. Filtration through Celite followed by evaporation afforded a residue which was dissolved in cold chloroform (100 mL) and washed with cold dilute aqueous ammonia and with water (5 × 20 mL). Evaporation of the chloroform afforded a residue which was chromatographed on silica gel (hexan–ether) to give the following. (a) The diesters **13**:[16] 1.60 g (39%); IR ($CHCl_3$), 1725 cm^{-1}; NMR (80 MHz, $CDCl_3$) δ 0.92 (t, J = 7 Hz, CH_2CH_3), 1.26 (t, J = 7 Hz, 2 OCH_2CH_3), 1.40–2.60 (m, $CH_3CH_2CH(CO_2)$ and $CH(N)(CO_2)CH_2CH_2CH$), 2.42 (br, NH, exchangeable with D_2O), 3.24 (m, $CHCH(N)CH_2$), 3.75 (dd, J = 9, 6.5 Hz, $NCH(CO_2)CH_2$), 4.13 (q, J = 7 Hz, OCH_2CH_3), 4.16 (q, J = 7 Hz, OCH_2CH_3); high-resolution mass spectrum, calcd for $C_{13}H_{23}NO_4$ m/e 257.1626, found m/e 257.1616; m/e 257 (M^+), 184 ($M^+ - CO_2Et$), 142 ($M^+ - CH_3CH_2CHCO_2Et$), 138 ($M^+ - CO_2Et - C_2H_6O$), 110 ($M^+ - CO_2Et - C_2H_6O$ –CO). Anal. Calcd for $C_{13}H_{23}NO_4$: C, 60.68; H, 9.01; N, 5.45. Found: C, 60.40; H, 8.92; N, 5.49. (b) The less polar isomer of the hydroxy diester **11**: 1.80 g (25%); IR ($CHCl_3$) 1720 cm^{-1}; NMR (80 MHz, $CDCl_3$) δ 1.26 (t, J = 7 Hz, OCH_2CH_3), 1.28 (t, J = 7 Hz, OCH_2CH_3), 1.28 (d, J = 6.5 Hz, $OCHCH_3$), 1.50–2.40 (m, $CHCH_2CH_2CH$), 2.50 (dd, J = 6.5, 2.5 Hz, $CHCH(CO_2)CH$), 3.62 (br, NH and OH, exchangeable with D_2O), 3.50–4.00 (m, $CH_3CH(OH)CH$ and $CHCH(N)CH_2$), 4.16 (q, J = 7 Hz, OCH_2CH_3), 4.18 (q, J = 7 Hz, OCH_2CH_3), 4.18 (dd, J = 7, 6 Hz, $NCHCO_2CH_2$); high-resolution mass spectrum, calcd for $C_{13}H_{21}NO_4$ m/e 255.1470, found m/e 255.1494; m/e 255 ($M^+ - H_2O$), 200 ($M^+ - CO_2Et$), 182 ($M^+ - CO_2Et - H_2O$), 154 ($M^+ - CO_2Et - C_2H_6O$), 142 ($M^+ - CH_3CH(OH)CH(CO_2Et)$, 136 ($M^+ - CO_2Et - C_2H_6O - H_2O$). (c) The more polar isomer of the hydroxy diester **11**: 1.10 g (25%); IR 1720 cm^{-1}; NMR (80 MHz, $CDCl_3$) δ 1.26 (t, J = 7 Hz, OCH_2CH_3), 1.28 (d, J = 6.5 Hz, $OCHCH_3$), 1.30 (t, J = 7 Hz, OCH_2CH_3), 1.50–2.30 (m, $CHCH_2CH_2CH$), 2.46 (dd, J = 8, 3.5 Hz, $CHCH(CO_2)CH$), 2.90 (br, NH and OH, exchangeable with D_2O), 3.50–4.20 (m, $CH_3CH(OH)CH$, $CHCH(N)CH_2$, and $NCH(CO_2)CH_2$), 4.14 (q, J = 7 Hz, OCH_2CH_3), 4.18 (q, J = 7 Hz, OCH_2CH_3); mass spectrum, m/e 273 (M^+), 255 ($M^+ - H_2O$), 200 ($M^+ - CO_2Et$), 182 ($M^+ - CO_2Et - H_2O$), 154 ($M^+ - CO_2Et - C_2H_6O$), 142 ($M^+ - CH_3CH(OH)CHCO_2Et$), 136 ($M^+ - CO_2Et - C_2H_6O - H_2O$). Anal. Calcd for $C_{13}H_{23}NO_5$: C, 57.12; H, 8.48. Found: C, 57.05; H, 8.60.

2-[1-(*tert*-Butoxycarbonyl)-2-carboxy-5-pyrrolidinyl]butanoic Acids 15. To a solution of the diesters **13** (257 mg, 1 mmol) in ethanol (5 mL) was added a solution of potassium hydroxide (168 mg, 3 mmol) in water (5 mL). After the mixture was stirred for 12 h at room temperature, the solvent was evaporated. The residue, which consisted of the potassium salts **14**, was dissolved in a mixture of *tert*-butyl alcohol (2 mL) and water (1 mL), di-*tert*-butyl dicarbonate (240 mg, 1.1 mmol) was added, and the reaction mixture was stirred for 18 h, diluted with water, and extracted with *n*-pentane. The aqueous phase was acidified with $KHSO_4$ to pH 2 and then extracted with ethyl acetate. Evaporation of the solvent afforded the diacids **15**: 258 mg (86%, mixture of the isomers **15a,b**); NMR (90 MHz, $CDCl_3$) δ 0.97 (t, J = 7 Hz, CH_2CH_3), 1.15–2.20 (m, 3 CH_2), 1.48 (s, *t*-Bu), 3.0–3.4 (m, $CH_2CH(CO_2)CH$), 4.0–4.4 (m, $NCH(CO_2)CH_2$, and $CH_2CH(N)CH$), 10.19 (br, 2 CO_2H); R_f 0.45, 0.11 (silica gel plate, 98:1:1 Et_2O/MeOH/HOAc).

A sample of the diacids **15** was treated with diazomethane in ether to give the dimethyl esters **16** (quantitative):[16] NMR (80 MHz; $CDCl_3$) δ 0.90 (t, J = 7 Hz, CH_2CH_3), 1.15–2.15 (m, 3 CH_2), 1.44 (s, *t*-Bu), 2.60 (m, $CH_2CH(CO_2)CH$), 3.69 (s, OMe), 3.72 (s, OMe), 3.25–4.35 (m, $NCH(CO_2)CH_2$ and $CH_2CH(N)CH$); high-resolution mass spectrum, calcd for $C_{16}H_{27}NO_6$ m/e 329.1838, found m/e 329.1789; m/e 329 (M^+), 273 ($M^+ - C_4H_8$), 270 ($M^+ - CO_2Me$), 256 ($M^+ - OBu$), 228 ($M^+ - BuOCO$, or $M^+ - CH_3CH_2CHCO_2Me$), 170 ($M^+ - CO_2Me - C_4H_8 - CO_2$), 138 ($M^+ - CO_2Me - BuOCO - CH_4O$), 128 ($M^+ - CH_3CH_2CHCO_2Me - C_4H_8 - CO_2$).

Chromatography of the mixture of the isomers **15a** and **15b** on a silica gel column (diethyl ether–methanol), afforded the diacid **15a** followed by a mixture of **15a** and **15b**. The following analytical data were obtained for **15a**: IR ($CHCl_3$), 1711, 1693 cm^{-1}; NMR (270 MHz, $CDCl_3$) δ 0.98 (t, J = 7 Hz, CH_2CH_3), 1.47 and 1.52 (2 s, *t*-Bu of two conformers), 1.57–1.77 (m, CH_2CH_3), 1.88–2.10 (m, $NCHCH_2CH_2$), 2.19–2.44 (m, $NCH(CO_2)CH_2CH_2$), 2.98–3.16 and 3.27–3.45 (2 m, $CH_2CH(CO_2)CH$ of two conformers), 3.92–4.11 (m, $NCH(CH)CH_2$), 4.32–4.60 (m, $NCH(CO_2)CH_2$), 10.61 (br, 2 CO_2H); high-resolution mass spectrum, calcd for $C_{13}H_{22}NO_4$ m/e 256.1549, found m/e 256.1559; m/e 256 ($M^+ - CO_2H$), 245 ($M^+ - C_4H_8$), 228 ($M^+ - BuO$), 214 ($M^+ - CH_3CH_2CHCO_2H$), 200 (M^+-BuOCO) 156 ($M^+ - BuOCO - CO_2$), 138 ($C_8H_{12}NO^+$), 110 ($C_8H_{12}NO^+ - CO$); the low-resolution mass spectrum shows a weak peak at m/e 301 (M^+).

***p*-Nitrobenzyl Esters of the Dicarboxylic Acid 15a.** A solution of the diacid **15a** (273 mg, 0.91 mmol), dicyclohexylamine (164 mg, 0.91 mmol), *p*-nitrobenzyl chloride (187 mg, 1.1] mmol), and potassium iodide (18 mg, 0.01 mmol) in dry DMF (20 mL) was heated under argon at 100 °C for 19 h. The reaction mixture was brought to room temperature and diluted with ethyl acetate (50 mL). The precipitated dicyclohexylammonium hydrochloride was filtered off, and the filtrate was washed with water, dried, and evaporated. The residue was chromatographed on silica gel (20 g) to give the following.

(a) The di-*p*-nitrobenzyl ester **19a**: 120 mg (23%); eluted with ether–hexane (1:1); mp 111–112 °C (from CH_2Cl_2–hexane); IR ($CHCl_3$) 1730, 1690 cm^{-1}; NMR (270 MHz, $CDCl_3$) δ 0.86 (t, J = 7 Hz, CH_2CH_3), 1.36 and 1.47 (2 s, *t*-Bu of two conformers), 1.60–1.82 (m, CH_2CH_3), 1.84–2.10 (m, $NCHCH_2CH_2$ and one proton of $NCH(CO_2)CH_2CH_2$), 2.10–2.36 (m, one proton of $NCH(CO_2)CH_2CH_2$), 2.71–3.02 (m, $CH_2CH(CO_2)CH$), 4.01–4.28 (m, $NCH(CH)CH_2$), 4.28–4.53 (m, $NCH(CO_2)CH_2$, 5.17 and 5.25 (AB q, J = 14 Hz, 2 CH_2Ar), 7.51 and 8.20 (AB q, J = 8.8 Hz, 2 $C_6H_4NO_2$); high-resolution mass spectrum, calcd for $C_{14}H_{24}N_3O_9$ m/e 498.1506, found m/e 498.1511; m/e 498 ($M^+ - BuO$), 470 ($M^+ - BuOCO$), 391 ($M^+ - CO_2PNB$), 291 ($M^+ - CO_2PNB - C_4H_8OCO$), 249 ($M^+ - CH_3CH_2CHCO_2PNB - C_4H_8OCO$); the low-resolution mass spectrum shows a molecular ion at m/e 571 (M^+).

(b) The *p*-nitrobenzyl ester **18a**: 55 mg (14%); eluted with ether–hexane (1:1); IR ($CHCl_3$) 1730–1690 cm^{-1} (broad band); NMR (270 MHz, $CDCl_3$) δ 0.90 (t, J = 7 Hz, CH_2CH_3), 1.47 (s, *t*-Bu), 1.56–1.83 (m, CH_2CH_3), 1.84–2.05 (m, $NCH(CH)CH_2$), 2.04–2.51 (m, $CH_2CH(CO_2)CH$ and $NCH(CO_2)CH_2CH_2$), 3.84–4.23 (m, $NCH(CH)CH_2$), 4.23–4.50 (m, $NCH(CO_2)CH_2$), 5.12 and 5.27 (AB q, J = 13.5 Hz, CH_2Ar), 7.52 and 8.21 (AB q, J = 8.8 Hz, $C_6H_4NO_2$); high-resolution mass spectrum, calcd for $C_{20}H_{27}N_2O_6$ m/e 391.1868, found m/e 391.1849; m/e 391 ($M^+ - CO_2H$), 335 ($M^+ - BuOCO$), 291 ($M^+ - BuOCO - CO_2$), 214 ($M^+ - CH_3CH_2CHCO_2PNB$), 156 ($M^+ - CO_2PNB - C_4H_8OCO$), 110 ($C_7H_{12}N^+$).

A sample of **18a** was treated with diazomethane in ether to give the methyl ester **21a** (quantitative): high-resolution mass spectrum, calcd for $C_{18}H_{21}N_2O_7$ m/e 377.1348, found m/e 377.1360; m/e 377 ($M^+ - OBu$), 349 ($M^+ - BuOCO$), 128 ($M^+ - CH_3CH_2CHCO_2PNB - C_4H_8OCO$); the low-resolution mass spectrum shows a molecular ion at m/e 450.

(c) The *p*-nitrobenzyl ester **17a**: 113 mg (29%); eluted with ether; mp 143–145 °C (CH_2Cl_2–hexane); NMR (270 MHz, $CDCl_3$) δ 0.91 (t, J = 7 Hz, CH_2CH_3), 1.42 (s, *t*-Bu), 1.60–1.83 (m, CH_2CH_3), 1.83–2.12 (m, $NCH(CH)CH_2CH_2$ and one proton of $NCH(CO_2)CH_2CH_2$), 2.12–2.42 (m, one proton of $NCH(CO_2)CH_2CH_2$), 2.48–2.85 (m, $CH_2CH(CO_2)CH$), 4.01–4.29 (m, $NCH(CH)CH_2$), 4.29–4.55 (m, $NCH(CO_2)CH_2$), 5.14 and 5.26 (AB q J = 13.5 Hz, CH_2Ar), 7.53 and 8.22 (AB q, J = 8.8 Hz, $C_6H_4NO_2$); high-resolution mass spectrum, calcd for $C_{17}H_{20}N_2O_8$ m/e 380.1219, found m/e 380.1253; m/e 380 ($M^+ - C_4H_8$), 363 ($M^+ - OBu$), 349 ($M^+ - CH_3CH_2CHCO_2H$), 335 ($M^+ - BuOCO$), 291

(16) Epimers **a** and **b** were not differentiated in the 80-MHz NMR spectrum. In the case of **13**, the existence of two epimers was deduced from their derivatives and in the case of **16** from their precursors.

(M^+ - BuOCO - CO_2), 256 (M^+ - CO_2PNB), 249 (M^+ - C_4H_8OCO - $CH_3CH_2CHCO_2H$), 156 (M^+ - C_4H_8OCO - CO_2PNB), 138 ($C_8H_{12}NO^+$); the low-resolution mass spectrum shows a low-intensity molecular ion at m/e 436.

A sample of **17a** was treated with diazomethane in ether to give the methyl ester **20a** (quantitative); high-resolution mass spectrum, calcd for $C_{17}H_{21}N_2O_6$ m/e 349.1399, found m/e 349.1405; m/e 349 (M^+ - BuOCO), 249 (M^+ - $CH_3CH_2CHCO_2CH_3$ - C_4H_8OCO), 170 (M^+ - CO_2PNB - C_4H_8OCO); the low-resolution mass spectrum shows a molecular ion at m/e 450.

***p*-Nitrobenzyl (±)-6-Ethylcarbapenam-3-carboxylates 25a and 25b.** 2-[1-(*tert*-butoxycarbonyl)-2-(*p*-nitrobenzyloxycarbonyl)-5-pyrrolidinyl]butanoic acid (**17a**; 140 mg, 0.32 mmol) was dissolved in 1 N HCl in EtOAc (4 mL) and stirred for 2.5 h at room temperature. The solvent was evaporated, and CCl_4 was added and evaporated again. The residue was washed with ether and dried to give the hydrochloride of 2-[2-(*p*-nitrobenzyloxycarbonyl)-5-pyrrolidinyl]butanoic acid (**22a**) as a solid (119 mg, quantitative). To a cold solution (0 °C) of the hydrochloride of **22a** (112 mg, 0.30 mmol) in dry CH_2Cl_2 (180 mL) were added pyridine (34 mg, 0.43 mmol) and 1-(3′-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (154 mg, 0.80 mmol). The reaction mixture was stirred at 0 °C under argon for 1 h and then for 22 h at room temperature, and it was then washed with ice-cold water (4 × 50 mL), dried ($MgSO_4$), and evaporated. Flash chromatography of the residue (silica gel, 0.04–0.063 mm; ether–hexane, 2:1) afforded the carbapenam **25a**: 39 mg (41%); IR (CH_2Cl_2) 1760, 1742, 1610, 1522 cm^{-1}; NMR (270 MHz, CD_2Cl_2) δ 0.95 (t, J = 7.4 Hz, 8-H_3), 1.40–1.72 (m, 7-H_2), 1.74–1.96 (m, 1-H_2), 2.30 (m, 2-H_2), 3.13 (dddd, J = 9, 8, 5, 1 Hz, 6-H), 3.78 (ddd, J = 9, 6, 5 Hz, 5-H), 3.92 (dt, J = 5, 1 Hz, 3-H), 5.21 and 5.28 (AB q, J = 13.4 Hz, CH_2Ar), 7.58 and 8.22 (aB q, J = 8.8 Hz, $C_6H_4NO_2$); high-resolution mass spectrum, calcd for $C_{16}H_{18}N_2O_5$ m/e 318.1215, found m/e 318.1211; m/e 318 (M^+), 301 (M^+ - OH), 290 (M^+ - CO), 249 (M^+ - $CH_3CH_2C{=}C{=}O$), 182 (M^+ - PNB, 138 (M^+ - CO_2PNB), 137 ($CH_3C_6H_4NO_2^+$), 136 (PNB^+). Further elution with ether gave the dimer **26**: 10 mg (10%); IR (CH_2Cl_2) 1730, 1660 cm^{-1}; high-resolution mass spectrum, calcd for $C_{32}H_{36}N_4O_{10}$ m/e 636.2431, found m/e 636.2436; m/e 636 (M^+), 607 (M^+ - Et), 456 (M^+ - CO_2PNB), 428 (M^+ - CO_2PNB -CO).

When a mixture of the two isomers **15a** and **15b** was subjected to the sequence of reactions described above for the conversion of **15a** into **25a**, a mixture of the *cis*-6-ethylcarbapenam **25a** and its trans isomer **25b** was obtained. This mixture exhibits the same IR and high-resolution mass spectra as pure **25a**. NMR of **25b**, obtained by substraction of the spectrum of **25a** from that of the mixture (270 MHz, CD_2Cl_2): δ 1.00 (t, J = 7 Hz, 8-H_3), 1.30–1.75 (m, 7-H_2), 1.75–2.20 (m, 1-H_2), 2.25–2.39 (m, 2-H_2), 2.86 (ddd, J = 8, 6, 2 Hz, 6-H), 3.46 (ddd, J = 8, 5, 2 Hz, 5-H), 3.93 (t, J = 5 Hz, 3-H), 5.22 and 5.30 (AB q, J = 13.5 Hz, CH_2Ar), 7.58 and 8.21 (AB q, J = 9 Hz, $C_6H_4NO_2$).

Registry No. (±)-**6**, 84911-17-1; (±)-**7**, 84927-07-1; (±)-**9**, 84911-19-3; (±)-**10**, 84911-20-6; **11**, 84911-22-8; (±)-**13a**, 84911-21-7; (±)-**13b**, 84984-88-3; (±)-**14a**, 84911-23-9; (±)-**14b**, 84984-89-4; (±)-**15a**, 84911-24-0; (±)-**15b**, 84984-90-7; (±)-**16a**, 84911-25-1; (±)-**16b**, 84984-91-8; (±)-**17a**, 84911-29-5; (±)-**18a**, 84911-27-3; (±)-**19a**, 84911-26-2; (±)-**20a**, 84911-30-8; (±)-**21a**, 84911-28-4; (±)-**22a**·HCl, 84911-31-9; (±)-**25a**, 84911-32-0; (±)-**25b**, 84984-92-9; **26**, 84911-33-1; ethyl (±)-pyroglutamate, 66183-71-9; ethyl (±)-2-bromo-3-oxobutyrate, 84911-18-2; diethyl 2-bromomalonate, 685-87-0.

Reaction of Sydnones with Oxygen†

Masayuki Nakajima and Jean-Pierre Anselme*

Department of Chemistry, University of Massachusetts at Boston, Harbor Campus, Boston, Massachusetts 02125

Received October 4, 1982

The reaction of 3-benzyl- and 3-(*p*-chlorobenzyl)-4-phenylsydnones (**1a** and **1b**) and of 3-benzylsydnone (**1c**) with oxygen at room temperature in the dark is described. Possible rationalizations for the formation of the products obtained are suggested.

In the context of our study of the decarboxylations of α-nitrosamino acids,[1] some anhydro-α-nitrosamino acids[2] (sydnones[3]) were prepared. Sydnones, unsubstituted at the 4-position, are known to undergo electrophilic aromatic substitution.[3] Thus the conversion of α-nitrosamino acids to sydnones, followed by introduction of a substituent at the 4-position of the sydnone ring and regeneration of the α-nitrosamino acid, would constitute a means of obtaining *N*-nitrosamines[4] from glycines, via the decarboxylation of *N*-nitrosoglycines.[1,5]

During the course of the recrystallization of 3-benzyl-4-phenylsydnone (**1a**), a benzene–ether solution of sydnone **1a** upon long standing deposited colorless crystals, identified as benzoic acid. This result was surprising in view of the fact that the chemistry of sydnones had been studied extensively and thus was believed to be understood rather well. Yet no precedent could be found in the literature with regard to the fact that sydnones may be sensitive to oxygen. Recently George and his co-workers[6] have reported the *photosensitized* oxidation of sydnones with *singlet* oxygen. Therefore it was decided to undertake the investigation of the reaction of sydnones with oxygen.

† Taken in part from the Ph.D. Thesis of M. Nakajima, University of Massachusetts, Sept 1982. This is the 10th article dealing with the chemistry of *N*-nitrosamines and related compounds. For the previous publication, see K. Kano, C. A. Kelly, and J.-P. Anselme, *Tetrahedron Lett.*, 1427 (1982).

(1) M. Nakajima and J.-P. Anselme, *Tetrahedron Lett.*, 4037 (1979).
(2) A. R. Katritzky, *Chem. Ind. (London)*, 521 (1955).
(3) (a) J. D. Earl and A. W. Mackney, *J. Chem. Soc.*, 899 (1935); (b) F. H. C. Stewart, *Chem. Rev.*, **64**, 129 (1964); (c) M. Ohta and H. Kato, "Nonbenzenoid Aromatics", J. P. Snyder, Ed., Academic Press, New York, 1969, Vol. 1, 117; (d) W. D. Ollis and C. A. Ramsden, "Advances in Heterocyclic Chemistry", A. R. Katritzky and A. J. Boulton, Eds., Academic Press, New York, 1976, Vol. 19, p 3.
(4) This would appear to be perhaps one true case of reverse *polarization* (also called umpolung) as the 4-position of the sydnone is the position that is flanked *both* by the nitrosamino and the carbonyl group of α-nitrosoamino acids.
(5) (a) M. Nakajima and J.-P. Anselme, unpublished results; (b) M. Nakamura, N. Baba, and Y. Wada, *J. Food Sci.*, **41**, 874 (1976); (c) K. R. Bharucha, C. K. Cross, and L. J. Rubin, *J. Agric. Food Chem.*, **27**, 63 (1973).
(6) V. Bhat, V. M. Dixit, R. G. Ungarker, A. M. Trozzolo, and M. V. George, *J. Org. Chem.*, **44**, 2957 (1979).

0022-3263/83/1948-1444$01.50/0