effected, albeit slowly. After destruction of the latter using 1:1 (v/v) tetrahydrofuran/4 M aqueous hydrochloric acid (vide ante), 595 mg (84%) of a mixture was obtained and shown by VPC analysis (6 ft × 0.125 in. Carbowax 20M column; oven temperature 138 °C; retention times: ketone, 2.0 min; alcohol, 2.4 min) to consist of 2-methylcyclohexanol and the corresponding ketone in an 85:15 ratio. The alcohol and ketone were further identified by coinjection with known samples of each compound. Subsequent NMR analysis (CHOH signals) indicated that the alcohol product was a 1:1 mixture of cis:trans stereoisomers.

Registry No. Benzaldehyde, 100-52-7; *p*-tolualdehyde, 104-87-0; *o*-chlorobenzaldehyde, 89-98-5; *m*-nitrobenzaldehyde, 99-61-6; cinnamaldehyde, 104-55-2; decanal, 112-31-2; (*E*)-citral, 141-27-5; (*Z*)-citral, 106-26-3; 4-phenyl-2-butanone, 2550-26-7; acetophenone, 98-86-2; cycloheptanone, 502-42-1; 2-methylcyclohexanone, 583-60-8; phenylcarbinol, 100-51-6; *p*-tolylcarbinol, 589-18-4; *o*-chlorophenylcarbinol, 17849-38-6; *m*-nitrophenylcarbinol, 619-25-0; cinnamyl alcohol, 104-54-1; 1-decanol, 112-30-1; (*E*)-3,7-dimethyl-2,6-octadien-1-ol, 106-24-1; (*Z*)-3,7-dimethyl-2,6-octadien-1-ol, 106-25-2; citronellol, 106-22-9; *cis*-2-methylcyclohexanol, 7443-70-1; *trans*-2-methylcyclohexanol, 7443-52-9; pyridine, 110-86-1; borane, 13283-31-3.

Synthesis and Diels–Alder Reactions of Anthra[2,3-*b*]thiophene

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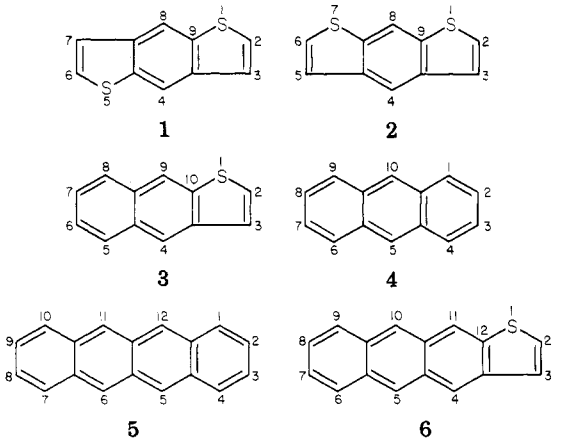
In 1970 Wynberg and co-workers reported studies directed toward the synthesis of heterotriptycenes.[1a-c] Following the findings of Dewar[2] and Brown[3] that a correlation exists between paralocalization energies and Diels–Alder reactivities, they calculated the paralocalization energies for different positions of addition in the linearly fused aromatic and heteroaromatic compounds **1–6**. The most reactive positions in **1–5** were those of the



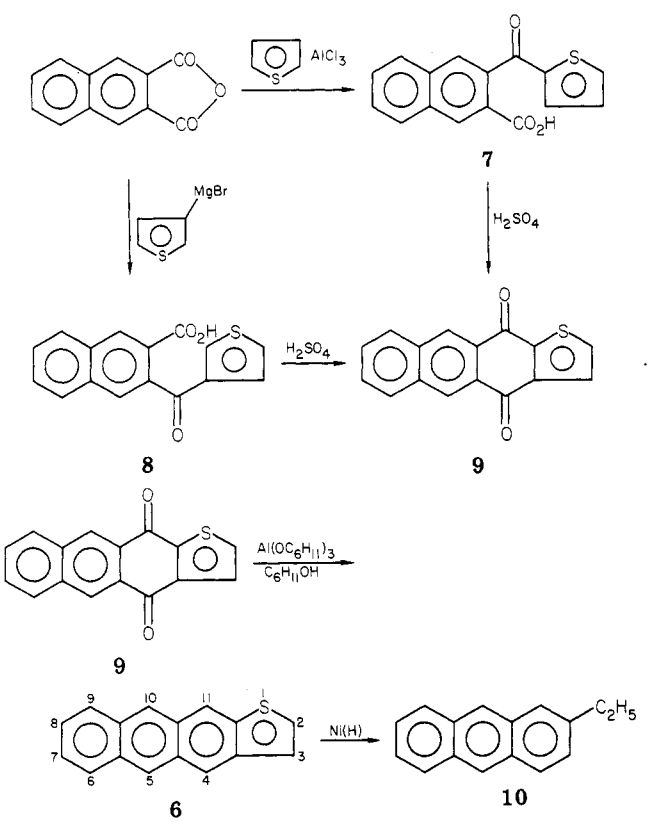
central ring in conformance to the known Diels–Alder reactions of **3**,[1a,4a] **4**, and **5**.[4b] For **6**, the lowest delocalization energy and highest predicted reactivity was at the 5,10-positions.

The present work describes a synthesis of anthra[2,3-*b*]thiophene (**6**) and a study of its reaction with three dienophiles.

The first reference to the synthesis of anthra[2,3-*b*]-thiophene was by Faller[5] who reported that Elbs reaction of 5-*o*-toluoylbenzo[*b*]thiophene afforded a mixture of products from which he isolated a high-melting yellow solid to which he assigned the structure **6**. Recently the synthesis of anthra[2,3-*b*]thiophene was reported by Castle and co-workers[6] who synthesized it in a five-step sequence by an unambiguous route.

The alternative synthesis described below (Scheme I) involves the same starting materials and accomplishes its goal in three steps.

Scheme I



Interaction of naphthalene-2,3-dicarboxylic anhydride with thiophene and succinic anhydride[7] produced **7** (88%). Interaction of the anhydride with 3-thienylmagnesium bromide[8] afforded the isomeric keto acid **8** (50%). Cyclization of either **7** or **8** by means of concentrated H_2SO_4 (steam bath) afforded the quinone **9** in 70% yield in each case. The quinone was reduced to anthra[2,3-*b*]thiophene (**6**) by means of aluminum cyclohexyl oxide in 59% yield.[9] The authenticity of the product was verified by desulfurization with Raney nickel to give 2-ethylanthracene (**10**),

(1) (a) H. Wynberg, J. de Wit, and H. J. M. Sinnige, *J. Org. Chem.*, **35**, 711 (1970); (b) J. de Wit and H. Wynberg, *Tetrahedron*, **29**, 1379 (1973); (c) J. de Wit, Ph.D. Thesis, University of Groningen, 1972, p 8.
(2) M. J. S. Dewar, *J. Am. Chem. Soc.*, **74**, 3357 (1952).
(3) R. D. Brown, *J. Chem. Soc.*, 691 (1950).
(4) (a) W. Carruthers, *J. Chem. Soc.*, 4477 (1963); (b) J. S. Meek, F. M. Dewey, and M. W. Hanna, *J. Org. Chem.*, **32**, 69 (1967).
(5) P. Faller, *C. R. Acad. Sci., Ser C.*, **267**, 543 (1968); *Chem. Abstr.*, **70**, 57562j (1969).
(6) Y. Tominaga, M. L. Lee, and R. N. Castle, *J. Heterocycl. Chem.*, **18**, 967 (1981).
(7) W. A. Lindley and D. W. H. MacDowell, *J. Org. Chem.*, **47**, 705 (1982).
(8) S. Gronowitz and K. Pettersson, *J. Heterocycl. Chem.*, **13**, 1099 (1976).
(9) J. Vodehnal and V. Stephen, *Collect. Czech. Chem. Commun.*, **36**, 3980 (1971); N. G. Gaylord and V. Stephen, *ibid.*, **39**, 1700 (1974); F. U. Ahmed, T. Rangarajan, and E. J. Eisenbraun, *Org. Prep. Proced. Int.*, **7**, 267 (1975).

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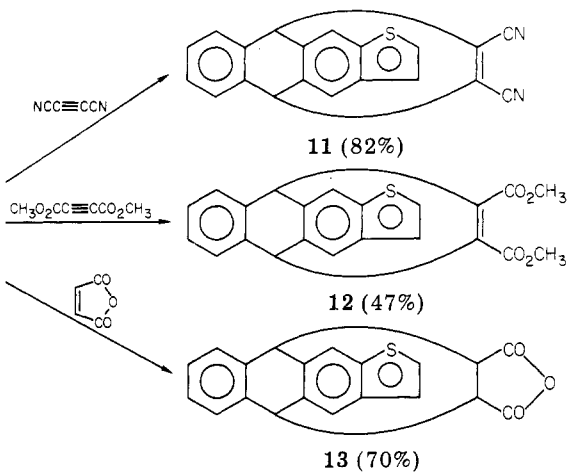
Scheme II



which was identified by comparison with an authentic sample.

Diels–Alder Reactions of Anthra[2,3-*b*]thiophene

In order to test the theoretical prediction of Wynberg, anthra[2,3-*b*]thiophene was reacted with dicyanoacetylene, dimethyl acetylenedicarboxylate, and maleic anhydride. Adducts were produced in each case (Scheme II).

In order to verify the positions of addition predicted by Wynberg,[1c] an X-ray crystallographic analysis was carried out on the adduct **11**. Recrystallization of **11** afforded suitable crystals for an X-ray structure determination. This particular adduct crystallizes in a monoclinic space group $C2/c$ (C_{2h},[6] no. 15) with refined lattice parameters of a = 24.790 (6), b = 9.753 (2), c = 15.580 (5) Å, β = 98.36 (2)°, V = 3727 (2) Å^3, and Z = 8 molecules/unit cell. Intensity data were collected out to a Bragg angle of 40° with an automated Picker diffractometer, using procedures described elsewhere.[10] The initial coordinates for nearly all of the non-hydrogen atoms in the anthra[2,3-*b*]thiophene backbone were determined by using direct methods. Subsequent Fourier synthesis revealed the positions of the remaining non-hydrogen atoms and indicated the presence of *two* structural disorders, one associated with the thiophene ring and the other with one of the methoxycarbonyl substituents of the dienophile. Despite the fact that these disorders prohibited a precise refinement of those portions of the molecular structure, the structure was sufficiently resolved to confirm that dimethyl acetylenedicarboxylate adds at the 5,10-positions of the anthra[2,3-*b*]thiophene molecule. A perspective view of the molecular configuration with the atom-labeling scheme is depicted in Figure 1. The details of the structural analysis are provided in the supplementary material.

The experimental findings show the correctness of the predictions of Wynberg regarding the Diels–Alder addition of dienophiles to anthra[2,3-*b*]thiophene.

Experimental Section[11]

3-(2-Thenoyl)-2-naphthoic acid (7) was prepared as reported in previous work.[7]

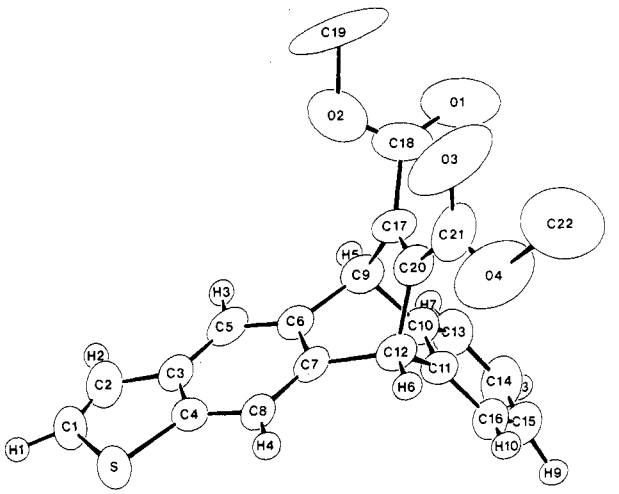


Figure 1. X-ray crystal structure of **11**.

3-(3-Thenoyl)-2-naphthoic Acid (8). A solution of 3-thienylmagnesium bromide was prepared from 3-bromothiophene (10.0 g, 61.3 mmol) and magnesium (14.9 g, 0.611 mol) by using the entrainment technique of Gronowitz and Pettersson.[8] The Grignard reagent was heated to reflux for 1 h and was added over a 1-h period to a warm, stirred suspension of naphthalene-2,3-dicarboxylic anhydride (10.93 g, 55.2 mmol) in benzene (200 mL) and HMPT (60 mL) with concomitant removal of ether via distillation. Following overnight reflux of the ether-free mixture, workup gave 7.9 g (51%) of the keto acid **4**. Recrystallization from ethyl acetate gave needles: mp 224–225 °C; IR (Nujol) 1660 cm^{-1}; NMR (Me_2SO-d_6) δ 8.65 (s, 1 H, naphthalene C_1-H), 7.4–8.4 (m, 8 H, remaining aromatic hydrogens).

Anal. Calcd for $C_{16}H_{10}O_3S$: C, 68.07; H, 3.57; S, 11.35. Found: C, 68.09; H, 3.68; S, 11.17.

4,11-Dihydroanthra[2,3-*b*]thiophene-4,11-dione (9). A solution of 3.38 g (12.0 mmol) of 3-(2-thenoyl)-2-naphthoic acid (**7**) in 30 mL of concentrated H_2SO_4 was heated on a steam bath for 3 h and was then poured on ice (300 g). Crystallization of the green solid from propionic acid gave the dione **5** as yellow needles (2.2 g (70%); mp 255 °C). An analytical sample (ethanol) melted at 258 °C: IR (KBr) 1670 cm^{-1}; mass spectrum (70 eV), m/e 264 (calcd m/e 264.3).

Anal. Calcd for $C_{16}H_8O_2S$: C, 72.71; H, 3.05; S, 12.13. Found: C, 72.59; H, 2.95; S, 12.10.

The dione **9** was also prepared from **8** in the same manner in 69% yield.

Anthra[2,3-*b*]thiophene (6). A flask containing 500 mg (18.5 mmol) of aluminum turnings, 12.5 mg of mercuric chloride, 0.2 mL of carbon tetrachloride, and 10 mL of distilled cyclohexanol was warmed to initiate the exothermic reaction. Once the ensuing vigorous reaction had subsided, the reaction mixture was heated at reflux until all the metal had reacted (3–4 h). To the gray mixture of aluminum cyclohexyl oxide was added 0.30 g (1.1 mmol) of 4,11-dihydroanthra[2,3-*b*]thiophene-4,11-dione (**9**), and the reaction mixture was heated at reflux overnight. Decomposition with ice and HCl gave a solid, which was filtered and recrystallized from toluene to give 0.16 g (59%) of anthra[2,3-*b*]thiophene as a yellow solid, mp (sealed tube) 340–341 °C. An analytical sample was prepared by sublimation at 180 °C (0.04 mm): mp 342 °C; IR (KBr) 890, 735, 725, and 660 cm^{-1} (aromatic CH); an NMR spectrum was not obtained due to insolubility of compound; mass spectrum (70 eV), m/e 234 (calcd m/e 234.3); UV max (dioxane) 276 mm (log ϵ 4.48).

Anal. Calcd for $C_{16}H_{10}S$: C, 82.01; H, 4.30; S, 13.68. Found: C, 81.92; H, 4.45; S, 13.42.

Desulfurization of Anthra[2,3-*b*]thiophene (6). Freshly prepared Raney nickel[12] was added to a suspension of 0.20 g (0.85 mmol) of anthra[2,3-*b*]thiophene in 40 mL of toluene. The resulting yellow suspension was heated to reflux with a concomitant

(10) J. L. Petersen and L. Griffith, *Inorg. Chem.*, **19**, 1852 (1980).

(11) All temperatures are uncorrected. Elemental analyses were performed by Galbraith Laboratories, Knoxville, TN. Nuclear magnetic resonance spectra were recorded on a Varian EM360 (60 MHz) with tetramethylsilane as an internal standard. Infrared spectra were recorded on a Bausch and Lomb 2000 spectrophotometer. Mass spectra were measured on a Nuclide 12-90-G single-focusing mass spectrometer or a Finnegan 4021 quadrupole mass spectrometer.

(12) L. Fieser and M. Fieser, "Reagents for Organic Synthesis", Wiley, New York, 1967, Vol. 1, p 729.

loss of the yellow color and filtered while hot to remove the catalyst. Evaporation of the toluene left an oil, which solidified upon cooling. The solid was recrystallized from ethanol to give 50 mg (28%) of 2-ethylanthracene, mp 148–150 °C (lit.[13] mp 148–150 °C). A mixed melting point with authentic 2-ethylanthracene was not depressed.

Diels–Alder Reactions of Anthra[2,3-*b*]thiophene. 5,10-Dihydro-12,13-dicyano-5,10-ethenoanthra[2,3-*b*]thiophene (11). Among several attempts to prepare dicyanoacetylene by published methods, the one reported by Byrd and co-workers[14] was the most efficient. A solution of anthra[2,3-*b*]thiophene (0.40 g, 1.71 mmol) and dicyanoacetylene (0.39 g, 5.12 mmol) in toluene (35 mL) was heated under reflux for 2 h. Evaporation of the solvent following decolorization with Norit gave a yellow-white solid, which was recrystallized from benzene–toluene as white crystals: mp 234–235 °C; 0.43 g (82%); IR (Nujol) 2220 cm^{-1}; NMR (acetone-d_6) δ 7.2–8.2 (m, 8 H, aromatic CH), 6.0 (s, 2 H, $C_{4,10}$-H).

Anal. Calcd for $C_{20}H_{10}N_2S$: C, 77.40; H, 3.25; N, 9.03; S, 10.33. Found: C, 77.38; H, 3.38; N, 9.09; S, 10.34.

5,10-Dihydro-12,13-bis(methoxycarbonyl)-5,10-ethenoanthra[2,3-*b*]thiophene (12). A solution of 0.40 g (1.71 mmol) of anthra[2,3-*b*]thiophene and 0.73 g (5.1 mmol, 3 equiv) of dimethyl acetylenedicarboxylate in 30 mL of xylene was heated at reflux for 40 h, treated with decolorizing carbon, heated at reflux for 10 min, and then filtered while hot. Evaporation of the solvent left a reddish oil, which was crystallized from aqueous methanol. The resulting solid was sublimed at 150 °C (0.005 mm) and was recrystallized from benzene/hexane to give 0.30 g (47%) of **12** in nearly colorless clusters: mp 194–195 °C; IR (Nujol) 1735 and 1745 (ester C=O), 1225 and 1275 cm^{-1} (ester CO); NMR ($CDCl_3$, 80 MHz) δ 7.80 (s, 1 H, aromatic CH), 7.74 (s, 1 H, aromatic CH), 6.93–7.41 (m, 6 H, aromatic CH), 5.49 (s, 2 H, $C_{5,10}$-H), 3.76 (s, 6 H, CO_2CH_3); UV max (95% C_2H_5OH) 233 nm (log ϵ 4.62).

Anal. Calcd for $C_{22}H_{16}O_4S$: C, 70.20; H, 4.28; S, 8.52. Found: C, 70.30; H, 4.28; S, 8.70.

5,10-Dihydro-5,10-ethanoanthra[2,3-*b*]thiophene-12,13-dicarboxylic Anhydride (13). A mixture of 0.084 g (0.85 mmol) of recrystallized maleic anhydride and 0.20 g (0.85 mmol) of anthra[2,3-*b*]thiophene in 10 mL of dry xylene was heated at reflux for 48 h. The solution was cooled slightly, treated with decolorizing carbon, heated at reflux for 5 min, filtered, and allowed to cool. The resulting white solid was filtered and recrystallized from benzene/hexane to afford 0.21 g (75%) of **13** as a white solid, mp 282 °C. An analytical sample was prepared by a second recrystallization from benzene/hexane: mp 282 °C; IR (Nujol) 1870 and 1860 cm^{-1} (anhydride C=O); NMR ($CDCl_3$, 80 MHz) δ 7.71–7.81 (m, 2 H, aromatic CH), 7.09–7.44 (m, 6 H, aromatic CH), 4.85 (s, 2 H, $C_{5,11}$-H), 3.53 (s, 2 H, $C_{12,13}$-H); mass spectrum (70 eV), *m/e* 332 (calcd *m/e* 332.38); UV max (95% C_2H_5OH) 237 nm (log ϵ 4.95), 266 (log ϵ 4.36), 271 (log ϵ 4.37).

Anal. Calcd for $C_{20}H_{12}O_3S$: C, 72.27; H, 3.64; S, 9.65. Found: C, 72.50; H, 3.75; S, 9.49.

Acknowledgment. Computer time for the X-ray diffraction data analysis was provided by the West Virginia Network for Education Telecomputing.

Registry No. **6**, 22108-55-0; **7**, 80090-33-1; **8**, 87434-26-2; **9**, 87434-27-3; **10**, 52251-71-5; **11**, 87434-28-4; **12**, 87434-29-5; **13**, 87434-30-8; NCC≡CCN, 1071-98-3; $CH_3O_2CC{\equiv}CCO_2CH_3$, 762-42-5; 3-bromothiophene, 872-31-1; naphthalene-2,3-dicarboxylic anhydride, 716-39-2; maleic anhydride, 108-31-6.

Supplementary Material Available: Description of structural analysis and tables of crystal data, positional and temperature factors, interatomic distances, and bond angles for nonhydrogen atoms, and observed and calculated structure factors (17 pages). Ordering information is given on any current masthead page.

(13) L. H. Klemm, A. J. Kohlik, and K. B. Desai, *J. Org. Chem.*, **28**, 625 (1963).

(14) N. R. Byrd, F. D. Kleist, and A. Rembaum, *J. Macromol. Sci. A*, **1**, 627 (1967).

Conversion of β-Hydroxyglutarohydroxamates to Carbapenem Precursors

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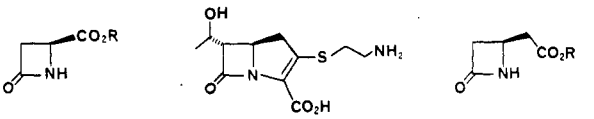
Received April 21, 1983

Isolation of the potent antibiotic thienamycin (1) and several similar antibiotics has stimulated an enormous effort aimed at the syntheses of these carbapenems.[1,2] Two very attractive intermediates for the synthesis of carbapenems are illustrated by structures **2** and **3**. We and others have previously described versatile approaches to the synthesis of chiral representatives of **2**.[3,4] The synthesis and utility of **3** has also been elegantly demonstrated by several groups.[4-10] Early in the development of our hydroxamate mediated approach to β-lactam synthesis, we recognized its potential for the preparation of chiral derivatives **3**.



2 1 3

A primary requirement for the initiation of the hydroxamate-mediated β-lactam synthesis is the availability of a suitably substituted β-hydroxy carboxylic acid.[11] Thus, the anticipated precursor to **3** was a monoester of β-hydroxyglutaric acid **5** (Scheme I). This precursor was especially attractive since the desired optical isomer [(R)-**5**] is readily available by chymotrypsin hydrolysis of the diester **4** (R=CH_3).[12]

In order to explore the feasibility of the synthesis proposed in Scheme I, we first tested the route with racemic materials. Thus, the racemic mono esters **5a,5b** were prepared from acetonedicarboxylic acid by straightforward processes. Coupling of these monoesters with O-substituted hydroxylamines in aqueous THF with a water-soluble carbodiimide gave the racemic O-substituted β-hydroxyglutaromonohydroxamic acids **6** in 50–80% yields. Treatment of **6a,6b** with the usual combination of diethyl azodicarboxylate and triphenylphosphine (DEAD/TPP)[11] under varying conditions gave multicomponent mixtures. After extractive workup and extensive chromatography, spectroscopic analyses indicated that mixtures of starting materials **6**, olefin (elimination products like **9**), desired β-lactam **7**, and the expected $Ph_3P{=}O$ and $EtO_2CNHNHCO_2Et$ were all obtained. In one of the cleaner cases, reaction of **6c** with DEAD/TPP for 10 min at room tempoerature gave a 78% yield of the olefins **9** and only a 22% yield of β-lactam **7c**. Several other cyclizations of hydroxamates **6** were tried with use of TPP/CCl_4/Et_3N,[11] TPP·Br_2, TPP·Cl_2, and TPP·(OTf). Prior conversion of **6** to the mesylate **8** (X = OMs) and subsequent treatment with base was also attempted. In all cases, mixtures were obtained with olefinic products usually being the major product. Details of these studies are provided in a dissertation.[13]

Substitution of trialkyl phosphites for triphenylphosphine during the use of the Mitsunobu reaction for the formation of β-lactams has been reported.[14] Thus, we attempted the cyclization of benzyl O-pivaloyl-β-

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