L-Aspartic anhydride hydrochloride[8] (6) was suspended in ethyl acetate saturated with carbonyl sulfide gas at −78 °C. Triethylamine (2 equiv) was added, and, after a 4.5-h reaction period, the mixture was quenched with excess aqueous hydrochloric acid at low temperature. A standard workup afforded a 51% yield of white, crystalline, optically pure 1. Although 6 is known to react with nucleophiles to give regioisomeric ring-opened products,[9] its reaction at the amino group with an electrophilic species, e.g., COS, is unprecedented.

In summary, we have found that 1 is a synthetically accessible, potentially valuable derivative of L-aspartic acid; the optimum conditions for its preparation in optically pure form have been determined. The use of 1 in a superior synthesis of aspartame will be reported in the near future.[10]

Experimental Section

Melting points were determined with a Thomas-Hoover capillary apparatus and are uncorrected. Infrared spectra were recorded with a Perkin-Elmer Model 21 spectrophotometer. NMR spectra were obtained with a Varian XL-100 or EM-360L spectrometer with Me_4Si as an internal standard. Optical rotations were determined by using a Perkin-Elmer 141 polarimeter. Microanalyses were performed by the Pfizer Analytical Department.

General Procedure for the Preparation of *N*-(Alkoxythiocarbonyl)-L-aspartic Acid Derivatives 4a,b. L-Aspartic acid (0.150 mol) was suspended in 15 mL of water 0 °C, and 50% aqueous sodium hydroxide solution (0.300 mol) was added dropwise. The appropriate xanthate ester (0.165 mol) in 15 mL of methanol was added in one portion. The mixture was heated at 45 °C for 2 h, cooled to room temperature, and washed with two 30-mL portions of CH_2Cl_2. The CH_2Cl_2 extracts were discarded, and the aqueous phase was acidified with 12 N HCl at 0 °C. The solution was saturated with solid sodium chloride and extracted with two 100-mL portions of ethyl acetate. The organic extracts were dried ($MgSO_4$) and evaporated to give white crystalline product.

***N*-(Methoxythiocarbonyl)-L-aspartic acid (4a)** was prepared from dimethyl xanthate[11] according to the above procedure: 87%; mp 127–128 °C dec; $[\alpha]^{25}_D$ + 70.5° (*c* 1, THF); ^1H NMR (Me_2SO-d_6) δ 2.73 (d, 2 H, *J* = 6 Hz), 3.63 (s, 3 H), 4.43 (dt, 1 H, *J* = 6 Hz, 8 Hz), 6.63 (d, 1 H, *J* = 8 Hz); IR (KBr) 1715, 1515 cm^{-1}.

An analytical sample was crystallized from ether/hexane. Anal. Calcd for $C_6H_9NO_5S$: C, 34.81; H, 4.35; N, 6.76; S, 15.46. Found: C, 34.80; H, 4.33; N, 6.75; S, 15.66.

***N*-(Ethoxythiocarbonyl)-L-aspartic acid (4b)** was similarly prepared from methyl ethyl xanthate:[11] 89%; mp 133 °C dec; $[\alpha]^{25}_D$ + 57.1° (*c* 1, THF); ^1H NMR (Me_2SO-d_6) δ 1.23 (t, 3 H, *J* = 7 Hz), 2.67 (d, 2 H, *J* = 6 Hz), 4.37 (q, 2 H, *J* = 7 Hz), 4.93 (dt, 1 H, *J* = 6 Hz, 8 Hz), 9.26 (d, 1 H, *J* = 8 Hz); IR (KBr) 1739, 1724, 1515 cm^{-1}.

An analytical sample was recrystallized from ether/hexane. Anal. Calcd for $C_7H_{11}NO_5S$: C, 38.00; H, 5.01; N, 6.33; S, 14.50. Found: C, 38.39; H, 4.99; N, 6.19; S, 14.24.

General Procedure for the Preparation of *N*-(Thiocarboxy)-L-aspartic Anhydride 1 from 4a,b. The *N*-(alkoxythiocarbonyl)-L-aspartic acid derivative (**4a** or **4b**, 1.00 mol) was dissolved in 1200 mL of ethyl acetate at 0 °C, and phosphorous tribromide (0.50 mol) was added in one portion. The cooling bath was removed and the temperature allowed to rise spontaneously to 35–40 °C. The solution was stirred for 10 min, after which time a granular white precipitate had formed. The reaction mixture was cooled to 0–5 °C, and the product was collected by filtration, washed with a small volume of ether, and dried. The material thus obtained was analytically pure.

***N*-(Methoxythiocarbonyl)-L-aspartic acid (4a)** was cyclized according to the above procedure to give a 95% yield of **1**: mp 200–205 °C dec; $[\alpha]^{25}_D$ −109° (*c* 1, THF); ^1H NMR (Me_2SO-d_6) δ 2.83 (d, 2 H, *J* = 5 Hz), 4.70 (t, 1 H, *J* = 5 Hz), 9.23 (br s, 2 H, exchangeable); IR (KBr) 3225, 1739, 1724, 1653, 1399 cm^{-1}. Anal. Calcd for $C_5H_5NO_4S$: C, 34.28; H, 2.88; N, 8.00; S, 18.31. Found: C, 34.36; H, 3.03; N, 7.84; S, 18.19.

Preparation of *N*-(Thiocarboxy)-L-aspartic Acid Anhydride 1 from L-Aspartic Anhydride Hydrochloride and COS. L-Aspartic anhydride hydrochloride[8] (6; 3.02 g, 20 mmol) was suspended in 150 mL of ethyl acetate at −78 °C; carbonyl sulfide gas[12] was then bubbled into the solution over a period of 10 min. Triethylamine (5.6 mL, 40 mmol) was added in one portion at −78 °C. Carbonyl sulfide addition was continued for 30 min, and then the reaction mixture was stirred for 4 h at −78 °C. The cold solution was quenched with 50 mL of 1 N HCl and allowed to warm to room temperature. The layers were separated, and the aqueous phase was extracted with 100 mL of ethyl acetate. The combined organic extracts were dried ($MgSO_4$) and evaporated. The white crystalline residue was digested in ether, collected by filtration, and dried. Compound **1** was obtained in 51% yield; this material was identical (melting point, $[\alpha]^{25}_D$, NMR) with samples of **1** prepared from **4a,b**.

Registry No. 1, 77217-04-0; 3, 56-84-8; 4a, 77217-03-9; 4b, 78255-92-2; 6, 34029-31-7; MeOC(S)SMe, 19708-81-7; EtOC(S)SMe, 623-54-1.

(8) L-Aspartic anhydride hydrochloride was prepared by the action of $POCl_3$ on L-aspartic acid: Ariyoshi, Y.; Yamatani, T.; Uchiyama, N.; Sato, N. *Bull. Chem. Soc. Jpn.* **1972**, *45*, 2208.

(9) Ariyoshi, Y.; Yamatani, T.; Uchiyama, N.; Adachi, Y.; Sato, N. *Bull. Chem. Soc. Jpn.* **1973**, *46*, 1893.

(10) Manuscript in preparation.

(11) The required xanthate esters were easily prepared in high yield by S-alkylation of sodium ethyl xanthate or potassium methyl xanthate with dimethyl sulfate in water.

(12) Carbonyl sulfide is commercially available from Matheson Co., Inc.

Synthesis of 3,2′:5′,3″-Terthiophene and Other Terthiophenes by the Thiophenecarboxaldehyde → Ethynylthiophene → Dithienylbutadiyne Route

Jean-Pierre Beny, Som N. Dhawan, Jacques Kagan,* and Satinder Sundlass

Department of Chemistry, University of Illinois, Chicago, Illinois 60680

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Out of 14 possible terthiophene isomers, only 4 have been described in the literature to date. The best known is α-terthienyl (2,2′:5′,2″-terthiophene, **5a**), first obtained as a byproduct in the synthesis of bithienyl[1] and later characterized in the flowers of the common Marigold (*Tagetes erecta*),[2] as well as in other plants belonging to the family Compositae,[3] which frequently also contain related thiophene components.[4] Natural and synthetic α-terthienyls have interesting nematocidal activity,[5] and recently the ultraviolet light mediated antibiotic activity of α-terthienyl[6] and its enhanced nematocidal activity in

(1) Steinkopf, W.; Leitsmann, R.; Hofmann, K. H. *Justus Liebigs Ann. Chem.* **1941**, *546*, 180.

(2) Zeichmeister, L.; Sandoval, A. *Arch. Biochem.* **1945**, *8*, 425.

(3) Gommers, F. J.; Voor in'tHolt, D. J. M. *Neth. J. Plant Pathol.* **1976**, *82*, 1.

(4) (a) Bohlmann, F.; Zdero, C. *Chem. Ber.* **1970**, *103*, 834. (b) Bohlmann, F.; Zdero, C. *Ibid.* **1976**, *109*, 901. (c) Krishnaswamy, N. R.; Seshadri, T. R.; Sharma, B. R. *Curr. Sci.* **1966**, *35*, 542. (d) Krishnaswamy, N. R.; Seshadri, T. R.; Sharma, B. R. *Tetrahedron Lett.* **1966**, 4227.

(5) (a) N. V. Philips' Gloeilampenfabrieken, British Patent 880 801, 1961; *Chem. Abstr.* **1962**, *56*, 106244. (b) Takano, T.; Iwata, T.; Atarashi, S.; Okado, S. *Yakugaku-Kenkyu* **1965**, *36*, 132; *Chem. Abstr.* **1966**, *64*, 7299*b*.

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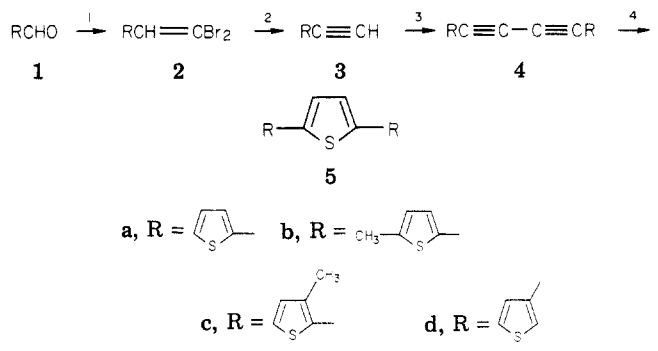
Scheme I[a]



[a] Reagents: (1) $P(C_6H_5)_3$, CBr_4, 0 °C. (2) a, *n*-BuLi, −78 °C; b, H_2O. (3) CuCl, air, 35 °C. (4) $Na_2S·9H_2O$, 65 °C.

the presence of ultraviolet light have been reported.[7] One reasonable mechanism accounting for these different types of biological activity may involve the generation of singlet oxygen,[8] although oxygen-independent photochemical binding to DNA has also been suggested.[9]

The other known terthiophenes are the 2,2′:4′,2″,[10] 2,3′:4′,2″,[11] and 3,3′:4′,3″[12] isomers. Their biological properties have apparently not been described in the literature.

Although many syntheses of α-terthienyl have been recorded,[1,13] we recently used a different approach in order to obtain a sample labeled with carbon-14 in good yield.[14] The synthesis started with the conversion of 2-thiophenecarboxaldehyde (**1a**) into 2-ethynylthiophene (**3a**) by the procedure of Corey and Fuchs,[15] which involves a Wittig reaction with carbon tetrabromide,[16] followed by treatment of the resulting **2a** with *n*-butyllithium. Oxidative coupling with cuprous chloride and air[17] converted **3a** into the dithienylbutadiyne **4a**, from which the desired product **5a** was obtained with an overall yield of 63% by treatment with sodium sulfide in refluxing methanol[18] (Scheme I).

The use of this convenient procedure was briefly investigated for the synthesis of methyl-substituted α-terthienyls. No difficulties were encountered during the conversion of 5-methyl-2-thiophenecarboxaldehyde (**1b**) into 5,5″-dimethyl-2,2′:5′,2″-terthiophene (**5b**). The overall yield of isolated product, pure from NMR, was 60%. However, while the isomeric 3-methyl-2-thiophenecarboxaldehyde (**1c**) did undergo both the Wittig reaction to **2c** in 97% yield and the subsequent dehydrobromination to **3c** in 48% yield, the synthesis of the corresponding terthiophene **5c** could not be achieved by this method because the butadiyne **4c**, readily obtained almost quantitatively by oxidative coupling of **3c**, was found to be completely unreactive during the sodium sulfide treatment.

The introduction of sulfur into **4c** was attempted via lithium triethylborohydride reduction of yellow sulfur (S_8) according to Gladysz et al.[19] However, this procedure not only did not produce any of the desired product from **4c** but was not even satisfactory for performing the conversion of diphenylbutadiyne into 2,5-diphenylthiophene, a facile reaction with sodium sulfide in methanol. The desired transformation of **4c** into **5c** was finally achieved almost quantitatively by substituting the higher boiling 2-methoxyethanol for methanol in the treatment with sodium sulfide.

The synthetic route outlined above was applied to the commercially available 3-thiophenecarboxaldehyde (**1d**). The Wittig reaction to **2d** took place in 93% yield, and the *n*-butyllithium treatment converted this product into 3-ethynylthiophene (**3d**) in 56% yield. Oxidative coupling produced in 73% yield 1,4-bis(3-thienyl)butadiyne (**4d**), which was finally converted quantitatively into the previously unknown 3,2′:5′,3″-terthiophene (**5d**).

All the butadiynes and terthiophenes obtained in this report were found to be photoantibiotic and phototoxic compounds, and these properties will be described elsewhere.

The technique used by Bakker et al.[8] for α-terthienyl demonstrated that the terthiophene **5d** was also an efficient singlet-oxygen sensitizer. The irradiation at 350 nm of a solution of adamantylideneadamantane (2.98×10^{-3} M in CH_2Cl_2) in the presence of **5d** (3.2×10^{-3} M) for 40 min produced 42.5% conversion into adamantanone, characterized directly by GLC without isolation of the dioxetane intermediate. This result may be calibrated by comparison with α-terthienyl, which led to 48.3% conversion of the olefin into adamantanone under exactly the same conditions, and with methylene blue, a typical singlet-oxygen sensitizer, which led to the conversion of just about half that much (24.3%).

Experimental Section

Melting points were determined with a Koffler apparatus. ^1H NMR spectra were recorded on Varian A-60 or T-60 spectrometers with Me_4Si as an internal standard and are described on the δ scale. Microanalyses were performed by Micro-Tech Laboratories, Skokie, IL.

2-(2,2-Dibromoethenyl)thiophene (2a). Triphenylphosphine (100 mmol, 26.2 g) and carbon tetrabromide (50 mmol, 16.6 g) were placed in a well-dried, 500-mL round-bottomed flask equipped with a magnetic stirrer and a gas inlet. Anhydrous dichloromethane (100 mL) was added under nitrogen, the mixture was stirred at 0 °C (ice bath) for 5 min, and 2-thiophenecarboxaldehyde (40 mmol, 4.48 g) was added. After stirring for 1 h at room temperature under nitrogen, the reaction mixture was extracted with pentane (4 vol) according to the original report.[15] Chromatography on silica gel 60–200 mesh (10 g/g;

(6) (a) Chan, G. F. Q.; Towers, G. H. N.; Mitchell, J. C. *Phytochemistry* **1975**, *14*, 2295. (b) Graham, K.; Graham, E. A.; Towers, G. H. N. *Can. J. Zool.* **1980**, *58*, 1955. (c) MacRae, W. D.; Irwin, D. A. J.; Bisalputra, T.; Towers, G. H. N. *Photobiochem. Photobiophys.* **1980**, *1*, 309. (d) MacRae, W. D.; Chan, G. F. Q.; Wat, C. K.; Towers, G. H. N.; Lam, J. *Experientia* **1980**, *36*, 1096.

(7) Gommers, F. J. *Meded. Landbouwhogesch. Wageningen* **1973**, *73*, 1.

(8) Bakker, J.; Gommers, F. J.; Nieuwenhuis, I.; Wynberg, H. *J. Biol. Chem.* **1979**, *254*, 1841.

(9) Kagan, J.; Gabriel, R.; Reed, S. A. *Photochem. Photobiol.* **1980**, *31*, 465.

(10) Wynberg, H.; Logathetis, A.; VerPloeg, D. *J. Am. Chem. Soc.* **1957**, *79*, 1972.

(11) Uhlenbroek, J. H.; Bijloo, J. D. *Recl. Trav. Chim. Pays-Bas* **1960**, *79*, 1181.

(12) Dodson, A. R. *Diss. Abstr.* **1962**, *22*, 4181; *Chem. Abstr.* **1962**, *57*, 11140*f*.

(13) (a) Zechmeister, L.; Sease, *J. Am. Chem. Soc.* **1947**, *69*, 273. (b) Tundo, A. *Boll. Sci. Fac. Chim. Ind. Bologna* **1960**, *18*, 102; *Chem. Abstr.* **1962**, *56*, 7250*i*. (c) Schulte, K. E.; Reisch, J.; Hörner, L. *Chem. Ber.* **1962**, *95*, 1943. (d) Harvey, J., Jr. U.S. Patent 3 086 854; *Chem. Abstr.* **1963**, *59*, 11430*d*. (e) Kooreman, H. J.; Wynberg, H. *Recl. Trav. Chim. Pays-Bas* **1967**, *86*, 37. (f) Schulte, K. E.; Heuke, G.; Ruecker, G.; Foerster, S. *Tetrahedron* **1968**, *24*, 1899. (g) Yamazaki, M.; Onodera, N.; Kurosu, Y.; Kawada, H. Japanese Patent 7 549 273, 1975; *Chem. Abstr.* **1975**, *83*, 206091*c*. (h) Asano, T.; Ito, S.; Saito, N.; Hatakedo, K. *Heterocycles* **1977**, *6*, 317. (i) Bestmann, H. J.; Schapee, W. *Tetrahedron Lett.* **1979**, 243.

(14) Beny, J. P.; Kagan, J. *J. Labelled Compd. Radiopharm.*, in press.

(15) Corey, E. J.; Fuchs, P. L. *Tetrahedron Lett.* **1972**, 4831.

(16) Ramirez, F.; Desai, N. B.; McKelvie, N. *J. Am. Chem. Soc.* **1962**, *84*, 1745.

(17) Fritzsche, U.; Hunig, S. *Tetrahedron Lett.* **1972**, 4831.

(18) Schulte, K. E.; Reisch, J.; Herrman, N.; Bohn, G. *Arch. Pharm. (Weinheim, Ger.)* **1963**, *296*, 456.

(19) Gladysz, J. A.; Wong, V. K.; Jick, B. S. *J. Chem. Soc., Chem. Commun.* **1978**, 838.

eluent: hexane–$CHCl_3$, 9:1) yielded 10.3 g (96%) of **2a**: mp 56–57 °C. Crystallization from hexane furnished white crystals: mp 57–58 °C; NMR ($CDCl_3$) δ 6.99 (dd, 1 H, J = 1.4 and 4.9 Hz), 7.17 (dd, 1 H, J = 1.4 and 3.7 Hz), 7.34 (dd, 1 H, J = 1.4 and 4.9 Hz), 7.60 (s, 1 H); mass spectrum, m/e 270, 268 (100%) and 266 (M^+), 189 and 187 (M – Br), 108 (M – 2 Br).

Anal. Calcd for $C_6H_4SBr_2$: C, 26.89; H, 1.50; S, 11.96; Br, 59.64. Found: C, 26.71; H, 1.48; S, 11.52; Br, 59.66.

2-(2,2-Dibromoethenyl)-5-methylthiophene (2b). The above procedure with 5-methyl-2-thiophenecarboxaldehyde (5.04 g, 40 mmol) yielded 9.2 g (100%) of **2b** after chromatography. An analytical sample was obtained after recrystallization from pentane as white crystals: mp 64–65 °C; NMR ($CDCl_3$) δ 2.45 (br s, 3 H), 6.68 (dq, 1 H, J = 1 and 3.5 Hz), 7.04 (d, 1 H, J = 3.5 Hz), 7.51 (s, 1 H); mass spectrum, m/e 284, 282 (100%) and 280 (M^+), 203 and 201 (M – Br), 122 (M – 2Br).

Anal. Calcd for $C_7H_6Br_2S$: C, 29.81; H, 2.15; S, 11.37; Br, 56.67. Found: C, 29.57; H, 2.08; S, 11.35; Br, 56.53.

2-(2,2-Dibromoethenyl)-3-methylthiophene (2c). The above procedure applied on 3-methyl-2-thiophenecarboxaldehyde (5.04 g, 40 mmol) yielded 11.0 g (97%) of chromatographed **2c**. An analytical sample was obtained after recrystallization from hexane as white crystals: mp 37–38.5 °C; NMR ($CDCl_3$) δ 2.20 (s, 3 H, CH_3), 6.81 (d, 1 H, J = 5.2 Hz), 7.28 (d, 1 H, J = 5.2 Hz), 7.59 (s, 1 H); mass spectrum, m/e 284, 282 (100%) and 280 (M^+), 203 and 201 (M – Br), 122 (M – 2Br).

Anal. Calcd for $C_7H_6Br_2S$: C, 29.81; H,2.15; Br, 56.67; S, 11.37. Found: C, 29.61; H, 2.12; Br, 56.52; S, 11.42.

3-(2,2-Dibromoethenyl)thiophene (2d). Following exactly the above procedure, we obtained 1.0 g (93%) of **2d** after chromatography from 0.448 g (40 mmol) of 3-thiophenecarboxaldehyde: mp 25 °C; NMR ($CDCl_3$) δ 7.3 (m, 2 H), 7.43 (s, 1 H), 7.63 (m, 1 H); mass spectrum, m/e 270, 268 (100%) and 266 (M^+), 189 and 187 (M – Br), 108 (M – 2Br).

2-Ethynylthiophene (3a). A solution of **2a** (30 mmol, 8.04 g) in 300 mL of dry ether was cooled to −78 °C under nitrogen, and n-butyllithium (66 mmol) was added dropwise. After stirring for 1 h at −78 °C, the mixture was allowed to warm up to room temperature, and was stirred for 1 h longer. The mixture was treated as usual[15,20] and finally distilled to produce 2.2 g (68%) of **3a**: bp 46 °C (15 torr) [lit.[21] bp 54–60 °C (20 torr)]; NMR ($CDCl_3$) δ 3.13 (s, 1 H), 6.93 (dd, 1 H, J = 4 and 5 Hz), 7.22 (m, 2 H).

2-Ethynyl-5-methylthiophene (3b). Following the above procedure with 8.46 g (30 mmol) of **2b**, we obtained 2.3 g (68%) of **3b**: by 103–105 °C (50 Torr); IR (CCl_4) 3300 (C≡CH), 2120 (C≡C) cm^{-1}; NMR ($CDCl_3$) δ 2.43 (br s, 3 H), 3.25 (s, 1 H), 6.60 (dq, 1 H, J = 1.2 and 3.5 Hz), 7.07 (d, 1 H, J = 3.5 Hz); mass spectrum, m/e 122 (M^+, 100%), 121 (M – H).

2-Ethynyl-3-methylthiophene (3c). Following the above procedure with 8.46 g (30 mmol) of **2c**, we obtained 1.8 g (48%) of **3c**: bp 110 °C (50 Torr); IR (CCl_4) 3300 (C≡CH), 2120 (C≡C) cm^{-1}; NMR ($CDCl_3$) δ 2.28 (s, 3 H), 3.40 (s, 1 H), 6.77 (d, 1 H, J = 5.2 Hz), 7.08 (d, 1 H); mass spectrum, m/e 122 (M^+, 100%), 121 (M – H).

3-Ethynylthiophene (3d). Following the above procedure, we obtained 1.8 g (56%) of **3d** from 8.04 g (30 mmol) of **2d**: bp 48–50 °C (15 Torr); IR (CCl_4) 3300 (C≡CH) and 2120 (C≡C) cm^{-1}; NMR ($CDCl_3$) δ 3.03 (br s, 1 H), 7.2 (m, 2 H), 7.53 (m, 1 H).

1,4-Bis(2-thienyl)butadiyne (4a). To a magnetically well-stirred suspension of cuprous chloride (2 mmol, 198 mg) in dimethoxyethane (10 mL) was added 0.56 mL of *N,N,N′,N′*-tetramethylethylenediamine (3 mmol). After 10 min at room temperature, **3a** was added (10 mmol, 1.08 g), and the mixture was kept at 30–35 °C for 1 h while air was bubbled through the solution. The mixture was then poured into water and extracted with ether as described.[17] The concentrated organic layer yielded 1.00 g of **4a**, which was recrystallized from EtOH as pale beige needles: 87% yield; mp 92–93 °C (lit.[22] mp 88–90 °C); UV (CH_3OH) λ_{max} 235 nm (ε 17 700), 287 (24 000), 354 (21 300); NMR ($CDCl_3$) δ 7.0 (dd, 2 H, J = 3.7 and 4.9 Hz), 7.2–7.4 (m, 4 H).

1,4-Bis(5-methyl-2-thienyl)butadiyne (4b). The coupling of 1.22 g (10 mmol) of **3b** following the above procedure gave 1.14 g (94%) of **4b**, mp 89–91 °C. An analytical sample was obtained by recrystallization from hexane as yellow needles: mp 90.5–91 °C; UV λ_{max} 239 (ε 14 200), 294 (22 500), 341 (21 000), 366 (15 900); NMR ($CDCl_3$) δ 2.45 (d, 6 H, J = 1 Hz), 6.58 (dq, 2 H, J = 1 and 3.5 Hz), 7.10 (d, 2 H, J = 3.5 Hz); mass spectrum, m/e 242 (M^+, 100%).

Anal. Calcd for $C_{14}H_{10}S_2$: C, 69.38; H, 4.16; S, 26.46. Found: C, 69.23; H, 4.13; S, 26.43.

1,4-Bis(3-methyl-2-thienyl)butadiyne (4c). The coupling of 1.22 g (10 mmol) of **3c** following the above procedure gave 1.18 g of **4c**, mp 76–80 °C. Recyrstallization from hexane furnished pale yellow needles (74%): mp 88–89 °C; UV (CH_3OH) λ_{max} 234 nm (ε 16 100), 275 (29 000), 335 (21 700), 358 (17 200); NMR ($CDCl_3$) δ 2.37 (s, 6 H), 6.83 (d, 2 H, J = 5.2 Hz), 7.20 (d, 2 H, J = 5.2 Hz); mass spectrum, m/e 242 (M^+, 100%).

Anal. Calcd for $C_{14}H_{10}S_2$: C, 69.38; H, 4.16; S, 26.46. Found: C, 69.15; H, 4.15; S, 26.20.

1,4-Bis(3-thienyl)butadiyne (4d). The coupling of **3d** (1.70 g, 15.7 mmol) of **3d** following the above procedure led to 1.23 g (73%) of **4d** after crystallization of the crude mixture from EtOH: mp 111.5–112.5 °C; UV (CH_3OH) λ_{max} 219 nm (ε 42 100), 251 (21 100), 261 (20 300), 304 (22 600), 325 (18 700); NMR ($CDCl_3$) δ 7.2 (m, 4 H), 7.47 (dd, 2 H, J = 1.5 and 2.5 Hz); mass spectrum, m/e 214 (M^+, 100%).

Anal. Calcd for $C_{12}H_6S_2$: C, 67.25; H, 2.82; S, 29.92. Found: C, 67.15; H, 2.90; S, 29.67.

2,2′:5′,2″-Terthiophene (5a). A mixture of **4a** (642 mg, 3 mmol), $Na_2S{\cdot}9H_2O$ (2.9 g, 12 mmol), and methanol (250 mL) was refluxed overnight. The solution was cooled and evaporated to dryness. The residue was washed with water, filtered, and recrystallized in 95% EtOH to give 625 mg of **5a** (84%). An analytical sample was obtained after another recrystallization from MeOH as yellow-orange plates: mp 93–94 °C (lit.[13c] mp 95 °C); UV (CH_3OH) λ_{max} 254 nm (ε 7100), 350 (21 300); NMR ($CDCl_3$) δ 6.95–7.25 (m); mass spectrum, m/e 248 (M^+, 100%).

Anal. Calcd for $C_{12}H_8S_3$: C, 58.03; H, 3.25; S, 38.73. Found: C, 57.86; H, 3.29; S, 38.44.

5,5″-Dimethyl-2,2′:5′,2″-terthiophene (5b). Following exactly the above procedure but using a 24-h reflux, we obtained 0.78 g of **5b** from 0.73 g (3 mmol) of **4b**: mp 98–100 °C. Crystallization from hexane furnished pure **5b** in 60% yield as orange needles: mp 100.5–101 °C (lit.[5a] mp 100–101 °C); UV (CH_3OH) λ_{max} 254 nm (ε 10 300), 360 (26 200); NMR ($CDCl_3$) δ 2.47 (d, J = 1 Hz, 6 H), 6.62 (m, 2 H), 6.9 (m, 4 H); mass spectrum, m/e 276 (M^+, 100%).

3,3″-Dimethyl-2,2′:5′,2″-terthiophene (5c). A solution of **4c** (484 mg, 2 mmol) and $Na_2S{\cdot}9H_2O$ (1.92 g, 8 mmol) in 50 mL of 2-methoxyethanol was refluxed overnight. Most of the solvent was removed under vacuum, 100 mL of water was added, and the mixture was extracted with three 50-mL portions of ether. The combined organic extracts were washed twice with water, dried over $MgSO_4$, and concentrated under vacuum to yield 525 mg (94.6%) of **5c**, pure from NMR and TLC. After two recrystallizations from hexanes, the mp was 55–56 °C; UV (CH_3OH) λ_{max} 218 nm (ε 12 000), 254 (10 000), 348 (20 300); NMR (Me_2SO-d_6) δ 2.37 (s, 6 H), 7.00 (d, J = 5 Hz, 2 H), 7.20 (s, 2 H), 7.47 (d, J = 5 Hz, 2 H); mass spectrum, m/e 276 (M^+, 100%).

Anal. Calcd for $C_{14}H_{12}S_3$: C, 60.87; H, 4.35; S, 34.78. Found: C, 60.78; H, 4.46; S, 34.73.

3,2′:5′,3″-Terthiophene (5d). Following the procedure described for **5a**, were obtained 1 g (100%) of **5d** from 856 mg (4 mmol) of **4d**. An analytical sample was obtained as pale yellow needles after crystallization from dimethoxyethane: mp 193 °C; UV (CH_3OH) λ_{max} 210 nm (ε 19 700), 324 (24 700); NMR (CCl_4) δ 7.0–7.4 (m, 6 H), 7.5 (m, 2 H); mass spectrum, m/e 248 (M^+, 100%).

Anal. Calcd for $C_{12}H_8S_3$: C, 58.03; H, 3.25; S, 38.73. Found: C, 57.80; H, 3.20; S, 38.72.

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(20) Patrick, T. B.; Honegger, J. L. *J. Org. Chem.* **1974**, *39*, 3791.
(21) Patrick, T. B.; Disher, J. M.; Probst, W. J. *J. Org. Chem.* **1972**, *37*, 4467.
(22) Vaitiekunas, A.; Nord, F. F. *J. Am. Chem. Soc.* **1954**, *76*, 2733.

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Registry No. **1a**, 98-03-3; **1b**, 13679-70-4; **1c**, 5834-16-2; **1d**, 498-62-4; **2a**, 77295-66-0; **2b**, 81294-08-8; **2c**, 77386-41-5; **2d**, 81294-09-9; **3a**, 4298-52-6; **3b**, 81294-10-2; **3c**, 81294-11-3; **3d**, 67237-53-0; **4a**, 16900-51-9; **4b**, 81294-12-4; **4c**, 81294-13-5; **4d**, 81294-14-6; **5a**, 1081-34-1; **5b**, 59949-61-0; **5c**, 81294-15-7; **5d**, 81294-16-8.

Relative Reactivities of Substituted Allenes toward Cycloaddition with Tetraphenylcyclopentadienone. Further Implications on the Viability of the Concerted ($_\pi2_s$ + $_\pi2_a$) Cycloaddition Process

Daniel J. Pasto* and Peter F. Heid

Department of Chemistry, University of Notre Dame, Notre Dame, Indiana 46556

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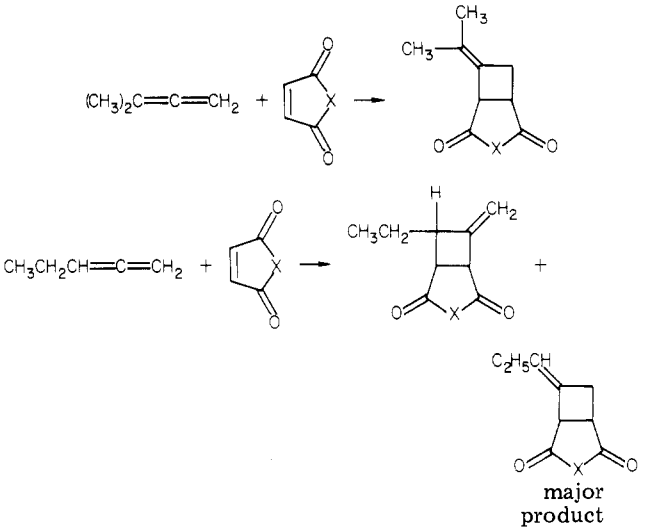
Recent studies in our laboratories have been directed toward gaining a better understanding of the mechanistic details of the cycloaddition and cyclodimerization reactions of allenes. As an alternative to the previously proposed nonconcerted, diradical-intermediate and concerted ($_\pi2_s$ + $_\pi2_a$) mechanisms, a concerted six-electron [$_\pi2_s$ + ($_\pi2_s$ + $_\pi2_s$)] process has been discussed.[1] A comparison of the two concerted processes using PMO theory suggested that the six-electron process should be favored over the four-electron process, and that in cycloaddition reactions with unsymmetrically substituted allenes differences in chemoselectivities should be observed.[1] For example, the cycloaddition of 1,1-dimethylallene via the ($_\pi2_s$ + $_\pi2_a$) process is predicted to be strongly favored across the more highly substituted double bond, while in the six-electron process cycloaddition across the less highly substituted double bond is favored.[1] In the case of monosubstituted allenes the same trends are predicted, although to a lesser degree. The predictions for the [$_\pi2_s$ + ($_\pi2_s$ + $_\pi2_s$)] process were in agreement with the chemoselectivities reported in the cycloaddition reactions of 1,1-dimethylallene and ethylallene with maleic anhydride[2] and those later obtained with *N*-phenylmaleimide (NPMI),[3] suggesting that the ($_\pi2_s$ + $_\pi2_a$) process was not operative in these cases.[1]

The results observed with maleic anhydride and NPMI suggested that it might not be possible to determine the chemoselectivity features of the ($_\pi2_s$ + $_\pi2_a$) concerted process of allenes with two-electron, electron-poor (LUMO controlled) reagents. Since according to PMO theory ($_\pi4_s$ + $_\pi2_s$) cycloaddition reactions of allenes with four-electron, electron-poor (also LUMO controlled) reagents should show the same trends in chemoselectivities and relative reactivities as in the ($_\pi2_s$ + $_\pi2_a$) process, a study of the cycloaddition reactions of allenes with such reagents was undertaken. Preliminary experiments were carried out with hexachlorocyclopentadiene and tetraphenylcyclopentadienone (TPCD). In the attempted reactions with hexachlorocyclopentadiene rearrangement reactions were encountered which could not be circumvented.[4] Preliminary results describing the chemoselectivities observed in the cycloaddition reactions of 1,1-dimethylallene and ethylallene with TPCD have been reported[5] and were consistent with the predictions based on PMO theory. The present note describes further extensions of these studies and focuses, in particular, on the results of relative reactivity studies for comparison with those results obtained in the cycloaddition reactions of allenes with NPMI[3] and 1,1-dichloro-2,2-difluoroethene.[6]



X = O, NC_6H_5

The overall reactions of the substituted allenes with TPCD are illustrated in Scheme I. The chemoselectivities observed in the cycloaddition reactions of isobutyl- and *tert*-butylallene are similar to those observed with ethylallene (see Table I). Attempts were also made to observe the cycloadditions with 1-ethyl-1-methylallene and 1-*tert*-butyl-1-methylallene. Under the reaction conditions, however, the former underwent prior rearrangement to form a mixture of conjugated dienes and no products of expected structure could be detected, while in the case of the latter no reaction was observed even over an extended period of time.

The relative reactivities of the substituted allenes toward cycloaddition with TPCD have been determined by competitive reaction techniques and are presented in Table II. (The relative reactivity of 1-*tert*-butyl-1-methylallene represents an upper limit and, in fact, may be very much lower.) For comparison purposes the relative reactivities observed in the cycloaddition reactions with NPMI[3] are also included in Table II. It should be noted that the relative reactivities of the monosubstituted allenes in the two cycloaddition reactions are quite similar; however, the relative reactivity of 1,1-dimethylallene is dramatically different in the two reactions. *Thus, both the chemoselectivity and relative reactivity data indicate that the cycloaddition reactions of allenes with NPMI do not occur via the ($_\pi2_s$ + $_\pi2_a$) process.*

The partial relative reactivities for cycloaddition across the C_1–C_2 and C_2–C_3 π systems (Table III) in the monoalkylallene series provide a basis for a detailed analysis of the factors affecting both the chemoselectivities and total relative reactivities. The partial relative reactivities for attack on the two π systems of ethyl- and isobutylallene are similar and decrease significantly on going to *tert*-butylallene. The reasons for the observed trends become apparent on consideration of the steric effects developed

(1) Pasto, D. J. *J. Am. Chem. Soc.* **1979**, *101*, 37.
(2) Alder, K.; Ackermann, O. *Chem. Ber.* **1957**, *90*, 1697.
(3) Pasto, D. J.; Heid, P. F.; Warren, S. E. *J. Am. Chem. Soc.* **1982**, *104*, in press.
(4) The treatment of 1,1-dimethylallene with freshly distilled hexachlorocyclopentadiene (from sodium carbonate) resulted in the rapid rearrangement of the allene to 3-methyl-1,3-butadiene, which then underwent cycloaddition predominantly across the least substituted double bond (9:1 ratio).
(5) Pasto, D. J. *Tetrahedron Lett.* **1980**, *21*, 4787.
(6) Pasto, D. J.; Warren, S. E. *J. Am. Chem. Soc.* **1982**, *104*, in press.

0022-3263/82/1947-2204$01.25/0