temperature overnight. The excess trifluoroacetic anhydride and the solvent were removed under reduced pressure. The residue was dissolved in CH_2Cl_2 and the solution was washed with saturated aqueous $NaHCO_3$ solution, dried, and concentrated to give **17** (1.33 g, 92%) as a colorless oil: ^1H NMR (100 MHz) δ 4.05 (dd, J = 8.3, 14.9 Hz, 1 H), 4.33 (dd, J = 4.0, 14.9 Hz, 1 H), 6.16 (dd, J = 4.0, 8.3 Hz, 1 H), 6.38 (s, 1 H), 7.28-7.40 (m, 10 H); IR ($CHCl_3$) 1780, 1635 cm^{-1}; MS, m/z 393 (M^+).

Transformation of 17 into 9. A solution of **17** (2.15 g, 5.47 mmol), potassium hydroxide (611 mg, 10.9 mmol), and water (1.32 mL) in methanol (215 mL) was stirred at room temperature for 3 h. The solution was concentrated under reduced pressure and the residue was diluted with water, extracted with CH_2Cl_2, and dried. The solvent was removed under reduced pressure and the residue was chromatographed on silica gel, eluting with chloroform-ether (1:1), to give *N*-(2-hydroxy-2-phenylethyl)-5-phenylisothiazol-3-one (**18**) (984 mg, 60.6%) as colorless crystals, mp 171-171.5 °C (recrystallized from ethyl acetate): ^1H NMR (90 MHz) δ 3.86 (dd, J = 7.8, 14.6 Hz, 1 H), 4.16 (dd, J = 3.3, 14.6 Hz, 1 H), 4.54 (br s, 1 H), 5.01-5.14 (m, 1 H), 6.40 (s, 1 H), 7.23-7.54 (m, 10 H); IR (KBr) 3240, 1625 cm^{-1}; MS, m/z 297 (M^+).

Anal. Calcd for $C_{17}H_{15}NO_2S$: C, 68.66; H, 5.08; N, 4.71; S, 10.78. Found: C, 68.42; H, 5.08; N, 4.69: S, 10.91.

The product **18** (2.26 g, 7.63 mmol) thus obtained was stirred in 87 mL of CH_2Cl_2 with 1.58 mL of triethylamine and 0.64 mL of methanesulfonyl chloride for 1 h at 0 °C and then 20 min at room temperature. The reaction mixture was extracted with CH_2Cl_2 and the extracts were washed with water and dried. The solvent was removed and the residue was chromatographed on silica gel, eluting with chloroform-ether (1:1), to give *N*-[2-[(methylsulfonyl)oxy]-2-phenylethyl]-3-oxo-5-phenylisothiazole (**19**) (3 g, 100%) as an oil: ^1H NMR (60 MHz) δ 2.73 (s, 3 H), 4.05-4.23 (m, 2 H), 5.83 (dd, J = 5.0, 8.0 Hz, 1 H), 6.38 (s, 1 H), 7.33 (narrow m, 10 H).

The product **19** (974 mg, 2.60 mmol) was mixed with sodium iodide (1.0 g, 6.62 mmol) and dry acetone (26.5 mL), and stirred at 4 °C for 67 h. Following evaporation of the acetone and dilution of the remaining residue with chloroform, the insoluble solid was filtered and washed with chloroform. The combined chloroform layer was concentrated under reduced pressure and the residue was dissolved in 21.1 mL of THF at 0 °C. To the solution was added DBU (1.53 g, 10.20 mmol) in 21 mL of THF. The mixture was stirred for 2 h at room temperature and extracted with CH_2Cl_2, and the extracts were washed with 2 N HCl and saturated aqueous $NaHCO_3$ solution and dried. The solvent was removed and the residue was chromatographed on silica gel, eluting with chloroform-ether (1:1), to afford (*E*)-*N*-styryl-5-phenylisothiazol-3-one (**9**) (419 mg, 58%) as yellow crystals, mp 154-154.5 °C. The melting point and all spectral data are in full agreement with those of **9** described previously.

Single-Crystal X-ray Diffraction Analysis of (*E*)-*N*-Styryl-5-phenyl-3-oxoisothiazole (9). The crystal data for **9** are as follows: triclinic; space group $P\bar{1}$; a = 7.847 (1), b = 14.242 (3), and c = 6.331 (1) Å, α = 90.23 (1)°, β = 100.35 (1)°, γ = 102.23 (1)°, V = 679.4 (2) Å^3, Z = 2. The empirical formula is $C_{17}H_{13}NOS$, molecular weight is 279.35, and calculated density is 1.37 g cm^{-3}. The three-dimensional X-ray data were collected by using a crystal with dimensions 0.3 × 0.3 × 0.4 mm by the use of graphite-monochromated Mo Kα radiation (λ = 0.71069 Å) on a Syntex R3 automatic diffractometer up to a maximum 2θ of 55.0°. Of 3114 total unique reflections, 2710 were considered observed at the level of ($|F_o| > 3\sigma|F_o|$). Data were corrected for Lorentz and polarization effect in the usual way but not for absorption as the linear absorption coefficient is small enough [(Mo Kα) = 2.3 cm^{-1}]. The structure was solved by the direct method (MULTAN78) and refined anisotropically by full-matrix least-squares. All the hydrogen atoms, located on a difference Fourier map, were included in the final part of the refinement with the isotropic temperature factors. The final unweighted residual index (R) was 0.040 for non-zero reflections, and the weighted R_w was 0.039, the weighting scheme of which is $w = [a|F_o|^2 + b|F_o| + c]$ with a = 0.0012, b = -0.0191, c = 0.1677. There is no feature greater than 0.21 e A^{-3} on the final difference Fourier map. All the calculations were done on a HITAC M-200H computer of the Hiroshima University by using the structure analysis program system UNICS.[12]

Registry No. **1**, 60839-95-4; **2** (isomer 1), 110567-82-3; **2** (isomer 2), 110567-83-4; **3** (isomer 1), 110567-84-5; **3** (isomer 2), 110567-85-6; **4**, 110567-87-8; **5**, 110567-86-7; **5** (*S*-monooxide), 110567-99-2; **6**, 110567-88-9; **7**, 110567-89-0; **8**, 110567-90-3; **9**, 110567-91-4; **10**, 110567-92-5; **11**, 110567-93-6; **12**, 110567-94-7; **13**, 110567-95-8; **14**, 5216-04-6; **17**, 110567-96-9; **18**, 110567-97-0; **19**, 110567-98-1.

Supplementary Material Available: Tables of fractional coordinates, anisotropic thermal parameters, interatomic distances, and interatomic angles for **9** (4 pages). Ordering information is given on any current masthead page.

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Synthesis of Naturally Occurring Bithiophenes: A Photochemical Approach

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Received April 10, 1987

A photochemical approach to the synthesis of six naturally occurring bithiophenes is described. The irradiation of 5-iodo-2-thiophenecarbaldehyde (**3**) in the presence of 2-bromothiophene (**4**) or 2-methylthiophene (**15**) furnishes 5-bromo- (**5**) and 5-methyl-2,2′-bithiophene-5′-carbaldehyde (**16**) in 99 and 69% yields respectively. Compounds **5** and **16** are used in the synthesis of 5-(1-propynyl)-2,2′-bithiophene-5′-methanol (**7**), 5′-propynyl-2,2′-bithiophene-5-carbaldehyde (**8**), 5-ethynyl-5′-(1-propynyl)-2,2′-bithiophene (**9**), 5-ethenyl-5′-(1-propynyl)-2,2′-bithiophene (**11**), 5′-[(isovaleryloxy)methyl]-5-[4-(isovaleryloxy)but-1-ynyl]-2,2′-bithiophene (**14**), and 5-methyl-5′-[1-(buta-1,3-dienyl)]-2,2′-bithiophene (**17**) through known reactions. In particular, the most important synthetic methodology used is an alkynylation procedure accomplished in the presence of Pd(0) in phase-transfer conditions.

Introduction

Recently, we reported that the irradiation of 3- and 5-halogenothiophenecarbaldehydes or 3- and 5-halogenothiopheneketones **1** in benzene solution furnished good yields of the corresponding phenyl derivatives **2**.[1]

We also reported that the irradiation could be performed in thiophene solution to give the corresponding bithienyl

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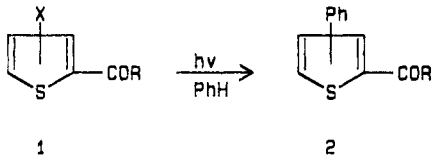


1 2

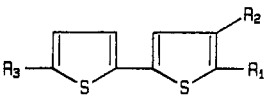
derivatives.

In this paper we report our results on the extension of this photochemical methodology to the synthesis of natural bithiophenes.

Bithiophene Natural Compounds. Bithiophenes and terthiophenes were isolated in numerous members of the *Compositae*[2] (Chart I). These compounds, and in particular α-terthienyl, have been extensively studied for their biological properties. In fact, they show a nematocidal activity[3] that is enhanced in the presence of sunlight (UV-A);[4] similarly, in the presence of UV-A, they show antibiotic,[5] ovicidal,[6] algicidal,[7] larvicidal,[8] and antifeedant[9] properties. Furthermore, they inhibit germination[10] of some plants and are phototoxic to some aquatic organisms.[11] They can produce hemolysis[12] and phototoxic dermatitis;[13] however, they are not able to induce chromosome damage.[14]

The presence of UV-A to have biological activity can be explained by considering that these types of compounds are photosensitizers of singlet oxygen and that singlet oxygen quenchers inhibit the enzymatic inactivation by α-terthienyl.[15]

Chart I



R_1 = 2-Thienyl, R_2 = R_3 = H

R_1 = -C≡C-CH_2, R_2=R_3=H

R_1 = -C≡C-CH_2CH_2OAc, R_2 = H, R_3 = -CH_2OAc

R_1 = -CH_2CH_2OAc, R_2 = H, R_3 = -C≡CCH_3

R_1 = -C≡C-CH(OH)CH_2Cl, R_2 = H, R_3 = -CH_3

R_1 = -CHCH-$CHCH_2$, R_2 = H, R_3 = -CH_3

R_1 = -C≡C-CH_2CH_2OCOi-Bu, R_2 = H, R_3 = -CH_2OCOi-Bu

R_1 = -CH_2OH, R_2 = H, R_3 = -C≡C—$CHCH_2$

R_1 = —C≡CH, R_2 = H, R_3 = —C≡CCH_3

R_1 = -$CHCH_2$, R_2 = H, R_3 = —C≡CCH_3

R_1 = -CHO, R_2 = H, R_3 = —C≡CCH_3

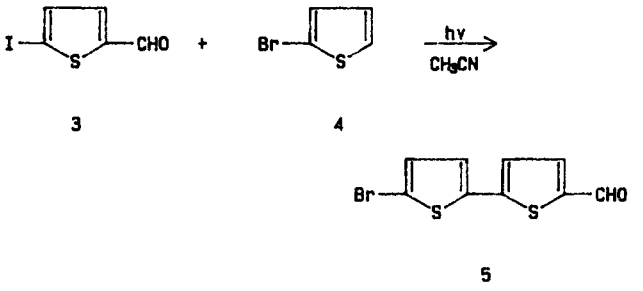
R_1 = -CH_2OH, R_2 = H, R_3 = —C≡CCH_3

R_1 = -CO_2CH_3, R_2 = H, R_3 = —C≡CCH_3

R_1 = 2-Thienyl, R_2 = -OCH_3, R_3 = H

R_1 = -CHO, R_2 = H, R_3 = 2-Thienyl

Scheme I



3 4 5

Because of their biological properties, these compounds are potentially useful against infestant insects, and the development of a general synthetic method is a significant target. Previously described syntheses of naturally occurring bithiophenes[16] are related to the preparation of monosubstituted bithiophenes; in fact, the introduction of a second functional group seems to be very difficult. For example, the Vilsmeyer–Haack reaction occurs in very low yields or not at all. Only recently, a Pd-catalyzed ethoxycarbonylation of bromobithienyls followed by iodination[17] allowed a bifunctionalized bithiophene to be obtained in reasonable yields.

Results and Discussion

A key step in our synthetic approach is the preparation of a bithienyl common precursor that can be converted into the target compounds by simple reactions. We thought that 5-bromo-2,2′-bithiophene-5′-carbaldehyde (**5**) could be considered a suitable synthon for our purpose.

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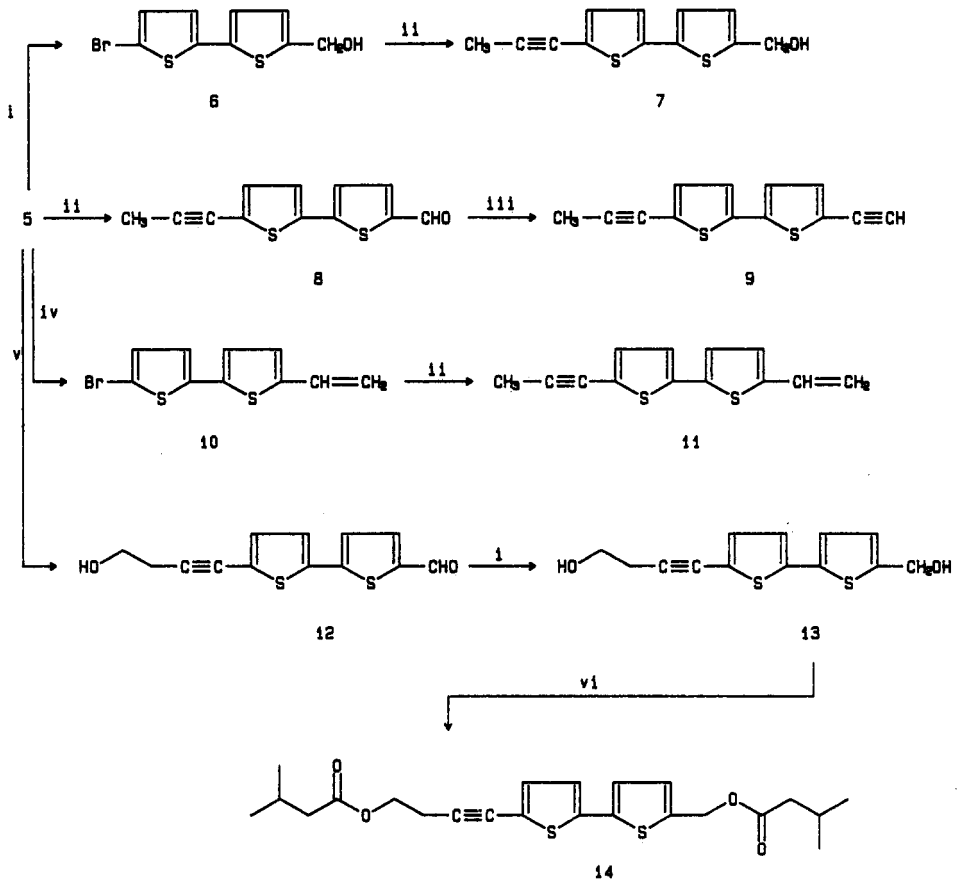
Scheme II[a]



[a] Reagents and conditions: (i) $NaBH_4$, MeOH; (ii) propyne, CuI, $Pd[P(Ph)_3]_4$, C_6H_6, TEBAC, 2.5 N NaOH; (iii) (a) Zn, CBr_4, PPh_3, (b) BuLi, H_2O; (iv) $(Ph)_3PCH_3Br$, NaH, DMSO; (v) $HOCH_2CH_2CCH$, CuI, $Pd[P(Ph)_3]_4$, C_6H_6, TEBAC, 2.5 N NaOH; (vi) $(CH_3)_2CHCH_2COCl$, py.

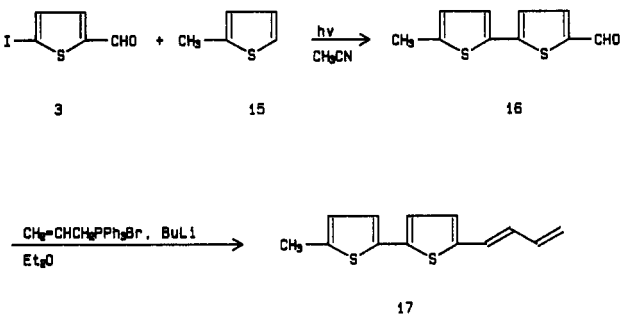
On the basis of our previous experience, **5** can be obtained through a photochemical reaction between 5-iodo-2-thiophenecarbaldehyde (**3**) and 2-bromothiophene (**4**). Compound **3** was easily prepared from 2-thiophenecarbaldehyde by reduction of the carbonyl group with $NaBH_4$. The alcohol was treated with iodine and HgO to give (5-iodo-2-thienyl)methanol, which was then oxidized by PCC to **3**.

As described previously,[18] the photochemical coupling can be carried out in acetonitrile; on the basis of the proposed mechanism, this solvent favors the formation of an exciplex intermediate. To avoid the homolytic cleavage of 2-bromothiophene,[19] the reaction was performed in presence of a Pyrex filter. Under these conditions, **5** was obtained in 99% yield (Scheme I).

Compound **5** was reduced to the corresponding alcohol **6** with $NaBH_4$. The subsequent reaction with propyne in presence of Pd(0), under phase-transfer conditions,[20] furnished **7**, a natural bithiophene isolated from *Arctium lappa*[2n] (Scheme II).

Compound **8** isolated from *A. lappa*,[2i,j] was also prepared directly by reaction of **5** with propyne (Scheme II). Furthermore, **8** can be used as a synthetic intermediate in the preparation of **9**, isolated from *Tagetes erecta*.[2l,m] In this case, **9** was obtained by treating **8** with zinc, triphenylphosphine, and carbon tetrabromide; the resulting dibromoolefin gave **9** by reaction with BuLi and then with water[21] (Scheme II).

Scheme III



Furthermore, **5** gave the olefin **10** through a Wittig reaction with $^-CH_2P^+Ph_3$ prepared from the corresponding phosphonium and with the dimethylsulfinyl carbanion. The known reaction with propyne furnished **11**, isolated from *T. erecta*[2n] (Scheme II).

Finally, **5** can be used in the synthesis of **14**, a compound isolated from *Eclipta erecta*.[2h] In this case, **5** was treated with 3-butyn-1-ol in the presence of Pd(0), CuI, and phase-transfer conditions to give **12**; then **12** can be reduced to the alcohol **13**. Esterification gave the natural product (Scheme II).

It is noteworthy that the reaction with propyne in the presence of Pd(0) can be performed on an alcohol (**6**), an

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aldehyde (5), and an olefin (10) without any loss of efficiency.

5-Iodo-2-thiophenecarbaldehyde (3) can be utilized as starting material in the synthesis of other bithiophenes. By irradiation of 3 in the presence of 2-methylthiophene 15, we were able to obtain 5-methyl-2,2'-bithiophene-5'-carbaldehyde (16), which can be used in the preparation of the natural bithiophene 17, isolated from *Bidens radiata*.[2g] Compound 16 was transformed directly to 17 through a Wittig reaction with allyltriphenylphosphorane (Scheme III).

As described above, our photochemical approach to bithiophenes 5 and 16 seems to be a versatile methodology; in fact, the very high yields of the conversions 3 → 5 and 3 → 16 allow us to obtain compounds either never described before or previously reported in low yields.[22]

This methodology seems to be very useful considering that we have not observed side reactions; for example, the photoisomerization of bithiophenes is a known process,[23] but in this case, we observe a great stability of 5 and 16 in the reaction conditions. This behavior, probably, is due to the presence of the carbonyl group, which inhibits the conversion to a cyclopropene intermediate. In fact, this conversion occurs in the first excited singlet state, while our compounds, considering that we have not observed any fluorescence spectrum, probably show a nearly quantitative intersystem crossing to a lowest excited triplet state.

Furthermore 5 is not able to react with the halogenothiophene to give the corresponding terthiophenes, showing that this photochemical reaction is a selective method for the preparation of the bithienyl skeleton.

In conclusion, this methodology, coupled with the palladium-mediated alkynylation developed by Rossi and co-workers allows us to prepare most of the naturally occurring bithiophenes.

Experimental Section

Melting points were obtained with a Kofler block and with a Mettler FP81 MBC cell equipped with a Mettler FP80 central processor. ^{1}H NMR spectra were recorded with Varian EM-360, Varian XL300, and Bruker WP-80 SY spectrometers, using CCl_4 or $CDCl_3$ as solvent with Me_4Si as internal standard. IR spectra were obtained on a Perkin-Elmer 457 spectrometer. Mass spectra were obtained with a Kratos instrument at 70 eV by using direct insertion at a source temperature of 150 °C. Commercial Merck silica gel was used for column chromatography. Merck precoated silica gel plates were used in TLC.

5-Iodo-2-thiophenecarbaldehyde (3). 2-Thiophenecarbaldehyde (10 g, 0.089 mol) was dissolved in MeOH (150 mL), and the resultant mixture was treated with $NaBH_4$ (35 g, 0.9 mol) at 0 °C. After 0.5 h, the mixture was poured into diluted H_2SO_4 and extracted many times with Et_2O. The neutral extracts were dried (Na_2SO_4). Removal of the solvent yielded a crude product that was dissolved in benzene (60 mL) and treated very slowly with alternate portions of iodine (24 g, 0.094 mol) and yellow mercuric oxide (20 g, 0.092 mol). The mixtures was stirred for 1 h and then filtered. Removal of the solvent yielded a crude product that was dissolved in anhydrous CH_2Cl_2 (200 mL) and treated with PCC (30 g 0.139 mol). The mixture was stirred overnight. The usual workup[24] furnished a crude product that was chromatographed on SiO_2. Elution with benzene gave pure 3: 14 g, 65%, mp 47–49 °C (lit.[25] mp 49 °C); ^{1}H NMR (CCl_4) δ 9.60 (s, 1 H), 7.25 (s, 2 H); IR (CCl_4) ν_{max} 2820, 2735, 2718, 1680, 1512, 1410, 1388, 1377, 1318, 1219, 1200, 1051, 952, 663 cm^{-1}; mass spectrum, m/z 238, 237.

5-Bromo-2,2'-bithiophene-5'-carbaldehyde (5). 5-Iodo-2-thiophenecarbaldehyde (3; 1 g, 4.2 mmol) was dissolved in acetonitrile (300 mL) in the presence of 2-bromothiophene[26] (4; 3 mL). The solution was outgassed with nitrogen for 1 h. The mixture was then irradiated in an immersion apparatus with a 500-W high-pressure mercury arc (Helios-Italquartz) surrounded by a Pyrex water jacket. After 3 h, the mixture was dissolved in chloroform and washed successively with 0.1 M $Na_2S_2O_3$ and then with brine. The organic phase was dried (Na_2SO_4), and the removal of the solvent under reduced pressure yielded a crude product that was chromatographed on SiO_2. Elution with $CHCl_3$–*n*-hexane (3:2) gave pure 5: 1.1 g, 99%; mp unmeasurable, decomposed without melting; ^{1}H NMR ($CDCl_3$) δ 9.70 (s, 1 H), 7.47 (d, 1 H, J = 4 Hz), 7.20 (d, 1 H, J = 4 Hz), 7.07 (d, 1 H, J = 5 Hz), 6.94 (d, 1 H, J = 5 Hz); IR ($CHCl_3$) ν_{max} 1670, 1453, 1050, 975 cm^{-1}; mass spectrum, m/z 274, 273, 272, 271. Anal. Calcd for $C_9H_5BrOS_2$: C, 39.5; H, 1.84. Found: C, 39.8; H, 1.80.

5-Bromo-2,2'-bithiophene-5'-methanol (6). 5 (1.2 g, 4.4 mmol), dissolved in MeOH (25 mL) and *p*-dioxane (25 mL), was treated with $NaBH_4$ (3.3 g, 87 mmol) at 0 °C. The mixture was stirred for 1 h; then the mixture was poured in diluted H_2SO_4 and extracted many times with Et_2O. The neutral extracts were dried (Na_2SO_4). Removal of the solvent yielded pure 6: 1.1 g, 91%; ^{1}H NMR ($CDCl_3$) δ 6.82 (m, 4 H), 4.68 (s, 2 H), 2.48 (s, 1 H); IR ($CHCl_3$) ν_{max} 3508, 3420, 2935, 2880, 1380, 1154, 1008, 974 cm^{-1}; mass spectrum, m/z 276, 274. Anal. Calcd for $C_9H_7BrOS_2$: C, 39.3; H, 2.56. Found: C, 39.6; H, 2.58.

5-(1-Propynyl)-2,2'-bithiophene-5'-methanol (7). The solution of 6 (1 g, 3.6 mmol) in benzene (12 mL) was outgassed with nitrogen. Benzyltriethylammonium chloride (60 mg, 0.26 mmol), CuI (80 mg, 0.42 mmol), and $Pd[P(Ph)_3]_4$ (300 mg, 0.26 mmol), were added. At 5 °C, the mixture was saturated with propyne. Deaerated 2.5 N NaOH (12 mL) was added, and the mixture was stirred under a propyne atmosphere for 3 h. Saturated NH_4Cl was added, and the mixture was stirred for 0.5 h. Then the mixture was extracted with $CHCl_3$. The neutral extracts were dried (Na_2SO_4). Removal of the solvent yielded a crude product that was chromatographed on SiO_2. Elution with $CHCl_3$–*n*-hexane (6:1) gave pure 7: 0.8 g, 95%; mp 87–88 °C (lit.[2n] mp 88–89 °C); ^{1}H NMR ($CDCl_3$) δ 7.0 (m, 3 H), 6.87 (d, 1 H, J = 4 Hz), 4.78 (s, 2 H), 2.37 (s, 1 H), 2.12 (s, 3 H); IR (film) ν_{max} 3350, 2240, 1450, 1379, 1220, 1192, 1165, 1020, 910, 873, 803, 760 cm^{-1}; mass spectrum, m/z 234. Anal. Calcd for $C_{12}H_{10}OS_2$: C, 61.51; H, 4.3. Found: C, 61.1; H, 4.0.

5'-Propynyl-2,2'-bithiophene-5-carbaldehyde (8). 5 (2 g, 7.3 mmol), in benzene (18 mL), was treated with TEBAC (136 mg, 0.6 mmol), CuI (180 mg, 0.95 mmol), $Pd[P(Ph)_3]_4$ (700 mg, 0.6 mmol), propyne, and 2.5 N NaOH (28 mL) as described for 7. The usual work up yielded a crude product that was chromatographed on SiO_2. Elution with benzene furnished pure 8: 1.4 g, 83%; mp 93–95 °C (lit.[2n] mp 93–94.5 °C); ^{1}H NMR ($CDCl_3$) δ 9.75 (s, 1 H), 7.71 (d, 1 H, J = 4 Hz), 7.2 (m, 2 H), 7.03 (d, 1 H, J = 4 Hz), 2.12 (s, 3 H); IR ($CHCl_3$) ν_{max} 2220, 1670 cm^{-1}; mass spectrum, m/z 232. Anal. Calcd for $C_{12}H_8OS_2$: C, 62.04; H, 3.47. Found: C, 61.94; H, 3.6.

5-Ethynyl-5'-(1-propynyl)-2,2'-bithiophene (9). Zn (664 mg, 10.2 mmol), PPh_3 (2.68 g, 10.2 mmol), and CBr_4 (3.4 g, 10.2 mmol) were suspended at room temperature in anhydrous CH_2Cl_2 (30 mL). The mixture was stirred for 48 h. Then 8 (1.2 g, 5.2 mmol) was added, and the mixture was stirred for 2 h. Pentane was added and the mixture filtered. The filtrate was evaporated, and the crude product was dissolved in anhydrous THF (20 mL). Under nitrogen, at −78 °C, 1.3 N BuLi (6 mL) was added. The mixture was stirred for 1 h at −78 °C and for 1 h at 25 °C. Then water was added, and the mixture was extracted with Et_2O, washed with brine, and dried (Na_2SO_4). The removal of the solvent yielded a crude product that was chromatographed on SiO_2; the elution with *n*-hexane gave pure 9: 860 mg; oil; ^{1}H NMR ($CDCl_3$) δ 7.03 (d, 1 H, J = 3 Hz), 6.93 (d, 1 H, J = 3 Hz), 6.86 (s, 2 H), 3.32 (s, 1 H), 2.03 (s, 3 H); IR (film) ν_{max} 3310, 3080, 3020, 2962, 2923, 2860, 2237, 2108, 1440, 1380, 1218, 800, 760 cm^{-1}; mass spectrum, m/z 228. Anal. Calcd for $C_{13}H_8S_2$: C, 68.39; H, 3.53. Found: C, 67.94; H, 3.14.

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5-Bromo-5′-ethenyl-2,2′-bithiophene (10). Sodium hydride (250 mg, 5.2 mmol) was washed with *n*-pentane to remove the oil. The flask was flushed with nitrogen, and DMSO (10 mL) was added. The mixture was heated at 75–80 °C until the evolution of hydrogen ceased. At 0 °C, methyltriphenylphosphonium bromide (1.9 g, 5.3 mmol) in DMSO (10 mL) was added. After 10 min, **5** (1.5 g, 5.5 mmol), dissolved in DMSO (10 mL), was added. The mixture was stirred at room temperature for 1 h. Then the mixture was poured in acidic water and extracted with $CHCl_3$. The organic layer was washed with brine and dried (Na_2SO_4). The removal of the solvent yielded a crude product that was chromatographed on SiO_2. The elution with *n*-hexane gave pure **10**: 1.2 g, 80%; ^1H NMR ($CDCl_3$) δ 7.3–6.0 (m, 5 H), 5.43 (dd, 1 H, J_1 = 18 Hz, J_2 = 1.5 Hz), 5.03 (dd, 1 H, J_1 = 10 Hz, J_2 = 1.5 Hz); IR (film) ν_{max} 1620, 1512, 1465, 1430, 1409, 1221, 1208, 1198, 975, 898, 787, 690 cm^{-1}; mass spectrum, *m/z* 272, 270. Anal. Calcd for $C_{10}H_7BrS_2$: C, 44.29; H, 2.6. Found: C, 44.4; H, 2.9.

5-Ethenyl-5′-(1-propynyl)-2,2′-bithiophene (11). **10** (1 g, 3.7 mmol), dissolved in benzene (9 mL), was treated with TEBAC (68 mg, 0.3 mmol), CuI (90 mg, 0.47 mmol), $Pd[P(Ph)_3]_4$ (345 mg, 0.3 mmol), propyne, and 2.5 N NaOH (14 mL), as described for **6**. The usual workup yielded a crude product that was chromatographed on SiO_2. Elution with *n*-hexane gave pure **11**: 0.72 g, 85%; ^1H NMR (C_2D_6CO) δ 7.3–6.0 (m, 5 H), 5.38 (dd, 1 H, J_1 = 16 Hz, J_2 = 1.5 Hz), 4.96 (dd, 1 H, J_1 = 10 Hz, J_2 = 1.5 Hz), 1.98 (s, 3 H); IR (film) ν_{max} 2240, 1622, 1468, 1450, 1431, 1380, 1230, 1210, 1200, 980, 900, 795, 775, 698 cm^{-1}; mass spectrum, *m/z* 230. Anal. Calcd for $C_{12}H_{10}S_2$: C, 67.79; H, 4.4. Found: C, 67.9; H, 4.7.

5-[1-(4-Hydroxybut-1-ynyl)]-2,2′-bithiophene-5′-carbaldehyde (12). **5** (1.1 g, 4 mmol), dissolved in benzene (14 mL), was treated with TEBAC (70 mg, 0.31 mmol), CuI (92 mg, 0.48 mmol), $Pd[P(Ph)_3]_4$ (348 mg, 0.3 mmol), 3-butyn-1-ol (6 mL), and 2.5 N NaOH (14 mL) as described for **7**. The usual workup furnished a crude product that was chromatographed on SiO_2. Elution with benzene–Et_2O (2:1) gave pure **12**: 0.8 g, 76%; ^1H NMR ($CDCl_3$) δ 9.83 (s, 1 H), 7.64 (d, 1 H, J = 4 Hz), 7.24 (d, 1 H, J = 4 Hz), 7.15 (d, 1 H, J = 4 Hz), 7.05 (d, 1 H, J = 4 Hz), 3.82 (t, 2 H, J = 7 Hz), 2.73 (d, 2 H, J = 7 Hz), 2.33 (s, 1 H); IR ($CHCl_3$) ν_{max} 3600, 3420, 2230, 1670, 1460, 1440, 1385, 1100 cm^{-1}; mass spectrum, *m/z* 262. Anal. Calcd for $C_{13}H_{10}O_2S_2$: C, 52.52; H, 3.84. Found: C, 52.4; H, 3.9.

5-[1-(4-Hydroxybut-1-ynyl)]-2,2′-bithiophene-5′-methanol (13). **12** (800 mg, 3 mmol) was treated with $NaBH_4$ as described for **6**. The usual workup furnished pure **13**: 780 mg, 97%; oil; ^1H NMR ($CDCl_3$) δ 7.0 (m, 4 H), 6.85 (d, 1 H, J = 4 Hz), 4.85 (s, 2 H), 3.84 (t, 2 H, J = 7 Hz), 2.70 (t, 2 H, J = 7 Hz), 2.35 (s, 1 H); IR ($CHCl_3$) ν_{max} 3600, 3420, 2230, 1450, 1385 cm^{-1}; mass spectrum, *m/z* 264. Anal. Calcd for $C_{13}H_{12}O_2S_2$: C, 59.06; H, 4.58. Found: C, 59.2; H, 4.3.

5′-[(Isovaleryloxy)methyl]-5-[4-(isovaleryloxy)but-3-ynyl]-2,2′-bithiophene (14). **13** (780 mg, 3 mmol), dissolved in dry pyridine (5 mL), was treated with isovaleryl chloride at 0 °C. After 0.5 h the mixture was poured in diluted HCl–ice and extracted with Et_2O. The neutral extracts were dried (Na_2SO_4). Removal of the solvent yielded a crude product that was chromatographed on SiO_2. Elution with *n*-hexane gave pure **13**: 900 mg, 71%; oil; ^1H NMR ($CDCl_3$) δ 7.0 (m, 4 H), 5.23 (s, 2 H), 4.18 (t, 4 H, J = 7 Hz), 2.52 (t, 4 H, J = 7 Hz), 2.21 (d, 4 H, J = 7 Hz), 2.12 (m, 2 H), 0.98 (d, 12 H, J = 6 Hz); IR ($CHCl_3$) ν_{max} 2220, 1740, 1190, 1170 cm^{-1}; mass spectrum, *m/z* 432.

5-Methyl-2,2′-bithiophene-5′-carbaldehyde (16). **3** (1 g, 4.2 mmol) was dissolved in acetonitrile (300 mL) in the presence of 2-methylthiophene (3 mL). The solution was outgassed with nitrogen for 1 h. The mixture was then irradiated in an immersion apparatus with a 500-W high-pressure mercury arc (Helios-Italquartz) surrounded by a Pyrex water jacket. After 3 h, the mixture was dissolved in chloroform and washed successively with 0.1 M $Na_2S_2O_3$ and then with brine. The organic phase was dried (Na_2SO_4), and the removal of the solvent yielded a crude product that was chromatographed on SiO_2. Elution with $CHCl_3$–*n*-hexane (3:2) gave pure **16** 0.6 g, 69%; mp 98–99 °C (lit.[27] mp 98–99 °C); ^1H NMR (CCl_4) δ 9.60 (s, 1 H), 7.57 (d, 1 H, J = 4 Hz), 7.0 (m, 3 H), 2.10 (s, 3 H); IR (film) ν_{max} 1660, 1520, 1475, 1445, 1420, 1415, 1240, 1220, 1065, 1050 cm^{-1}; mass spectrum, *m/z* 208, 207. Anal. Calcd for $C_{10}H_8OS_2$: C, 57.66; H, 3.87. Found: C, 57.3; H, 4.0.

5-Methyl-5′-[1-(buta-1,3-dienyl)]-2,2′-bithiophene (17). Allyltriphenylphosphonium bromide (2.34 g, 6.1 mmol) was suspended in anhydrous Et_2O (40 mL), and 1.2 N BuLi (5 mL) was added. The mixture was stirred for 2 h at room temperature. **16** (1.2 g, 5.8 mmol), dissolved in anhydrous THF (10 mL), was added. The mixture was stirred for 2 h and then filtered. The organic phase was diluted with $CHCl_3$, washed with diluted HCl and water, and dried (Na_2SO_4). Removal of the solvent yielded a crude product that was chroamtographed on SiO_2. Elution with *n*-hexane gave pure **17**: 0.82 g, 61%; mp unmeasurable; ^1H NMR (CCl_4) δ 7.0–6.0 (m, 5 H), 5.1 (m, 4 H), 2.38 (s, 3 H); IR (CCl_4) ν_{max} 1625, 1000, 940, 900 cm^{-1}; mass spectrum, *m/z* 232.

Registry No. **3**, 5370-19-4; **4**, 1003-09-4; **5**, 110046-60-1; **6**, 110046-61-2; **7**, 102054-38-6; **8**, 102054-37-5; **9**, 17257-07-7; **10**, 110046-62-3; **11**, 17257-06-6; **12**, 110046-63-4; **13**, 110046-64-5; **14**, 96853-77-9; **15**, 554-14-3; **16**, 32358-94-4; **17**, 93087-75-3; CH_2=$CHCH_2PPh_3Br$, 1560-54-9; $MePPh_3Br$, 1779-49-3; 2-thiophenecarboxaldehyde, 98-03-3; 2-thiophenemethanol, 636-72-6; 5-iodo-2-thiophenemethanol, 13781-27-6; propyne, 74-99-7; 3-butyn-1-ol, 927-74-2; isovaleryl chloride, 108-12-3; 5-(1-propyn-1-yl)-5′-(2,2-dibromoethenyl)-2,2′-bithiophene, 110046-65-6.

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Intramolecular Cyclization Products from Alkanolamines and Epichlorohydrin

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Received December 11, 1986

Tertiary (2-hydroxyethyl)dialkylamines reacted with epichlorohydrin to form mixtures containing equal amounts of 2-(hydroxymethyl)-4,4-dialkylmorpholinium chlorides and perhydro-6-hydroxy-4,4-dialkyl-1,4-oxazepinium chlorides. Secondary (2-hydroxyethyl)alkylamines gave a 9:1 ratio of the corresponding bases in agreement with the prediction of Baldwin's rules.

Reactions of amines with epichlorohydrin (**2**) are widely used in the manufacture of polyelectrolytes, modification of starch and fibers, and in epoxy resins. A detailed investigation of the reactions of tertiary alkanolamines with epichlorohydrin was undertaken because the NMR spectral properties of the product obtained from triethanolamine (TEA, **1c**) and epichlorohydrin did not agree with an authentic sample of the previously assigned structure,[1]

0022-3263/87/1952-5247$01.50/0