## Cope Rearrangements in the Benzo[b]thiophene Series<sup>†</sup>

Tushar P. Sura and Denis W. H. MacDowell\*

Department of Chemistry, West Virginia University, Morgantown, West Virginia 26506-6045

Received January 20, 1993

The inability to observe Cope rearrangement products at elevated temperatures for diethyl  $\alpha$ -allyl-2-naphthalenemalonate (1) and diethyl  $\alpha$ -allyl-9-phenanthrenemalonate (2) does not extend to the analogous systems resulting from replacement of the aromatic units by 2- and 3-benzo[b]thiophene nuclei. Thermal rearrangement of diethyl  $\alpha$ -allyl-3-benzo[b]thiophenemalonate (5) at 215–255 °C for 11 h produces the expected Cope rearrangement product diethyl 2-allyl-3-benzo[b]thiophenemalonate (10) (8%) accompanied by trans- and cis-ethyl 2,3-dihydro-1-(ethoxycarbonyl)-1H-benzo-[b]cyclopenta[d]thiophene-2-acetate (9a) (10%) and (9b) (5%), respectively. The structure elucidation of 10, 9a, and 9b was done by spectroscopy. The attempted structure verification of 10 by an independent route gave diethyl 2-(1-propenyl)-3-benzo[b]thiophenemalonate (12) which when heated at 230-240 °C for 18 h gave 1-carbethoxy-2-hydroxy-3-methyldibenzothiophene (16) as a major product. Similar results were observed with 2-substituted analogues of 5, both diethyl 3-allyl-2-benzo[b]thiophenemalonate (24) and ethyl 1,2-dihydro-3-(ethoxycarbonyl)-3H-benzo[b]cyclopenta-[d] thiophene-2-acetate (25) being formed. In this case the structure of 24 was verified by synthesis. An extension of this involved a study of thermal rearrangement of analogous compound ethyl  $\alpha$ -allyl- $\alpha$ -cyano-3-benzo[b]thiopheneacetate (30). Thermal rearrangement of 30 at 235–245 °C for 8 h gave the expected Cope rearrangement product ethyl  $\alpha$ -cyano-2-allyl-3-benzo[b]thiopheneacetate (32) (6%) along with an unexpected diastereomeric mixture of 1-cyano-1-(ethoxycarbonyl)-2-methyl-2,3-dihydro-1*H*-benzo[b]cyclopenta[d]thiophenes (33) (18%). Speculative mechanistic considerations are offered regarding the mode of transformation of 12 to 16 and 32 to 33.

The thermal intramolecular rearrangement of 1,5hexadiene systems, commonly known as the Cope rearrangement and now classified as [3.3] sigmatropic rearrangements<sup>1</sup> has been well documented and may be represented as follows.



Papers published<sup>2,3</sup> in 1956 reported situations when the  $R_1R_2$  portions of the hexadiene systems was part of an aromatic ring. Failure to observe any rearrangement was reported in the case of RR shown in eq 1.



 $R = H \text{ or } -OCH_3 \text{ and } X, Y = CN, CO_2C_2H_5, C_6H_5$ 

However when the aromatic portions of hexadiene system was naphthalene (1) or phenanthrene (2) as shown in eq 2, rearrangement was observed, but products of rearrangement were not as anticipated but were 3 and 4, respectively.

In 1986, when MacDowell and Pupura<sup>4</sup> replaced the benzene portion in eq 1 by 2- and 3-thienyl moieties, not



only the normal Cope rearrangement was observed, but it was also followed by cyclization to produce the abnormal products, in parallel to the phenanthrene or naphthalene series as shown in Scheme I.

A mechanistic explanation<sup>4</sup> was given for the cyclization of the normal Cope rearrangement product to the cyclized product. Attempted thermal rearrangement of diethyl  $\alpha$ -allyl-2,5-dimethyl-thiophenemalonate gave no indication of the occurrence of any rearrangement.

The present work extends the previous work by blocking one side of the thiophene ring with a benzene ring to produce the benzo[b]thiophene analogues of the naphthalene series formerly studied by Cope. The initial objective was to study the effect of heat on both the 2- and 3-substituted diethyl  $\alpha$ -allylbenzo[b]thiophenemalonates in order to see which course the reaction would follow, the normal Cope rearrangement or not. An extension of this involved a study of thermal rearrangement of the analogous cyanoacetates.

Synthesis of Diethyl  $\alpha$ -Allyl-3-benzol blthiophenemalonate (5). Diethyl  $\alpha$ -allyl-3-benzo[b]thiophenemalonate  $(5)^5$  was synthesized from ethyl 3-benzo[b]thiopheneacetate (6) in a three-step, one-pot reaction carried out without isolation of the intermediate 7 by the

<sup>&</sup>lt;sup>†</sup> Dedicated to Professor Gabor B. Fodor on the occasion of his 77th birthday.

 <sup>(1)</sup> Rhoads, S. J.; Raulins, N. R. Organic Reactions, John Wiley and Sons, Inc.: New York, 1975; Vol. 22, p 1.
 (2) Cope, A. C.; Field, L.; MacDowell, D. W. H.; Wright, M. E. J. Am.

Chem. Soc. 1956, 78, 2547

<sup>(3)</sup> Cope, A. C.; Meili, J. E.; MacDowell, D. W. H. J. Am. Chem. Soc. 1956, 78, 2551.

<sup>(4)</sup> MacDowell, D. W. H.; Purpura, J. M. J. Org. Chem. 1986, 51, 183. (5) Purpura, J. M. M. S. Thesis, West Virginia University, Morgantown, 1981

<sup>© 1993</sup> American Chemical Society



treatment of 6 with sodium ethoxide and diethyl carbonate followed by addition of allyl bromide.

An alternative approach (Scheme II) permitted the isolation of 7. The reaction of Houbiers and Muris<sup>6</sup> as used by MacDowell and Purpura<sup>4</sup> permitted the direct alkylation of 3-iodobenzo[b]thiophene (8)<sup>7</sup> to afford the malonate in 48% yield. Alkylation of 7 with allyl bromide gave the desired 5 in 47% yield along with some 6 presumably formed by a retro-Claisen condensation reaction.<sup>8</sup>

Thermal Rearrangement of Diethyl  $\alpha$ -Allyl-3-benzo[b]thiophenemalonate (5). Preliminary investigation<sup>5</sup> of the thermal rearrangement of 5 gave only (Scheme III) ethyl 2,3-dihydro-1-(ethoxycarbonyl)-1*H*-benzo[b]cyclopenta[d]thiophene-2-acetate (9), the "abnormal" Cope product, at 230-40 °C.

In order to see if the normal Cope rearrangement product 10 was initially produced in the thermal rearrangement, 5 was heated at 175–80 °C for 36 h (Scheme III). Isolation of crude material by column chromatography gave 31% of a product 10 along with 67% unreacted starting material. An <sup>1</sup>H NMR spectrum of the polar compound 10 showed not only the presence of vinyl hydrogens but also a singlet at  $\delta$  5.03; however, a doublet for the allylic hydrogen which was at  $\delta$  3.21 in 5 occurred at  $\delta$  3.68 in 10 (Table I). In a <sup>13</sup>C NMR spectrum of this compound 10, allylic and benzylic carbons of 5 shifted upfield from  $\delta$  39.97 to 33.01 and  $\delta$  60.15 to 50.62, respectively. A mass spectrum showed the molecular ion peak at 332. On the basis of the above evidence, the more polar compound was assigned the structure diethyl 2-allyl-3-benzo[b]thiophenemalonate (10) which is the regular Cope rearrangement product and is the benzo[b]thiophene analogue of the product which Cope expected but did not obtain in the study of the phenanthrene and naphthalene analogues.<sup>2,3</sup> When 5 was heated at 180-85 °C for a longer time period, 42 h, the <sup>1</sup>H NMR spectrum of the crude product indicated the product to starting material ratio of 55:48 based on the integration of the methylene protons of the allylic group. The chromatographic separation gave 10 in 44% yield, an improvement in the yield of the regular Cope product 10.

Diethyl  $\alpha$ -allyl-3-benzo[b]thiophenemalonate (5) was heated (Scheme III) at a higher temperature (215–25 °C) for 11 h to obtain cyclized products as before.

Column chromatography of the crude material 9 by the gradient elution method gave 8% of the normal Coperearranged product 10. Further careful elution of the column gave 10% (major, 9a) and 5% (minor, 9b) transand cis-ethyl 2,3-dihydro-1-(ethoxycarbonyl)-1H-benzo-[b]cyclopenta[d]thiophene-2-acetate, respectively. With the full physical and spectroscopic characterization of the adducts by <sup>1</sup>H NMR and <sup>1</sup>H-<sup>1</sup>H COSY, experimental data allowed proton assignments as depicted in the Table II.

The HETCOR experiment allowed the assignment of the carbon of cyclopentane ring (Table IV). The doublet for a proton at the C-1 position of the *cis* isomer **9b** ( $\delta$  3.87) was shifted downfield in the trans isomer 9a and was hidden under the methylene protons of the ester groups  $(\delta 4.03-4.23)$ . Irradiation of the proton, having a chemical shift of  $\delta$  3.35–3.61 at the 2-position in 9a, enhanced the peak at  $\delta$  4.20 in the ester groups region and affected the multiplet signals between  $\delta$  2.64 and  $\delta$  3.24 each of which collapsed into a doublet. Furthermore, saponification of a mixture 9 with ethanolic KOH gave a diacid 11 (50%)as the only product which was assigned trans geometry (J = 5.1 Hz) (Table II) based on the analogy with the results obtained by Cope and co-workers<sup>3</sup> for the rearrangement of the naphthalene analogue and its structure elucidation. The separation of diastereomers was achieved and the diesters were assigned unambiguously the geometry trans and cis based on the coupling constant (J = 7.8 Hz) for the vicinal trans protons on carbons C-1 and C-2 and their comparison with the diacid 11 (Table II).

When the normal Cope product 10 was heated for 8 h at 235–45 °C, a mixture of cyclized products (33%) trans-9a and cis-9b was obtained.

Attempted Synthesis of Diethyl 2-Allyl-3-benzo-[b]thiophenemalonate (10). Synthesis of Diethyl 2-(1-**Propenyl)-3-benzo[b]thiophenemalonate** (12). At this point the synthesis of 10 was attempted. The first halogenmetal exchange of 2,3-dibromobenzo[b]thiophene (13)<sup>9</sup> with 1 equiv of butyllithium at -10 to -15 °C selectively gave 3-bromo-2-benzo[b]thiophene (14) in lylation to give 2-allyl-3-bromobenzo[b]thiophene (14) in

<sup>(6)</sup> Houbiers, J. P.; Muris, P. G. Brit. Patent 2 009 158, 1978; Chem. Abstr. 1980, 92, 215266b.

<sup>(7)</sup> Gaertner, R. J. Am. Chem. Soc. 1952, 74, 4950.

<sup>(8)</sup> Cope, A. C.; Holmes, H. L.; House, H. O. Organic Reactions; John Wiley and Sons, Inc.: New York, 1957, Vol. IX, p 107.

<sup>(9)</sup> Ried, W.; Bender, H. Chem. Ber. 1955, 88, 34.
(10) Dickinson, R. P.; Iddon, B. J. Chem. Soc. (C) 1970, 2592.

Table I. <sup>1</sup>H NMR Data for the Various Diethyl Allylbenzo[b]thiophenemalonates

	5	10	17	24
ArH	7.76–7.83 (m, 3H), 7.28–7.32 (m, 2H)	7.72–7.79 (m, 2H), 7.23–7.36 (m, 2H)	7.69–7.79 (m, 2H), 7.41 (s, 1H), 7.23–7.31 (m, 2H)	7.65–7.82 (m, 2H), 7.26–7.35 (m, 2H)
CH-CH2	5.78 (ddt, 1H, $J =$ 17, 10, 7.1 Hz)	5.99 (ddt, 1H, $J = 16.9$ , 10.1, 6.2 Hz)	$5.73 (\mathrm{ddt}, 1\mathrm{H}, J = 17, 10, 7.1 \mathrm{Hz})$	5.91 (ddt, 1H, $J = 16.7$ , 10, 5.8 Hz)
CH-CH2	5.03 (dd, 1H, $J = 17$ Hz), 5.01 (dd, 1H, $J = 10$ Hz)	5.11-5.19 (m, 2H)	5.11 (dd, 1H, $J = 17$ Hz), 5.05 (dd, 1H, $J = 10$ Hz)	5.03 (dd, 1H, $J = 10, 1.6$ Hz), 5.01 (dd, 1H, $J = 16.7, 1.6$ Hz)
ArCHC		5.03 (s, 1H)		5.13 (s, 1H)
$CCH_2R$	3.19-3.22 (d, 2H, $J = 7.1$ Hz)	3.68 (dt, 2H, J = 6.23, 1.5 Hz)	3.17 (d, 2H, J = 7.1 Hz)	3.62 (ddd, 2H, J = 5.8, 1.6 Hz)
$CO_2CH_2$	4.12–4.33 (m, 4H)	4.11-4.29 (m, 4H)	4.16-4.29 (m, 4H)	4.17-4.29 (m, 4H)
CH₃	1.16 (t, 6H)	1.22 (t, 6H)	1.16 (t, 6H)	1.26 (t, 6H)

Table II. <sup>1</sup>H NMR Data of Thermally Rearranged Products of Diethyl  $\alpha$ -Allyl-3-benzo[b]thiophenemalonate (5)

	trans-9a	cis-9b	diacid 11
ArH	7.71-7.75 (d, 1H), 7.58-7.62 (d, 1H), 7.18-7.33 (m, 2H)	7.69–7.76 (m, 2H), 7.21–7.35 (m, 2H)	7.89–7.92 (d, 1H), 7.67–7.70 (d, 1H), 7.26–7.38 (m, 2H)
C1-H	4.23 (dd, 1H, $J = 7.8$ , 1.8 Hz)	3.87 (dt, 1H, J = 4.2, 1.8 Hz)	3.80 (d, 1H, J = 5.1 Hz)
C2-H	3.35-3.61 (m, 1H)	3.64-3.77 (m, 1H)	3.42-3.55 (m, 1H)
C3-H	3.16 (dd, 1H, J = 16.3, 7.8 Hz)	$3.47 (\mathrm{ddd},^a 1\mathrm{H}, J = 16.3, 8.2, 1.8 \mathrm{Hz})$	$3.33 (\mathrm{ddd},^{a}\mathrm{1H},J=14,8,1.8\mathrm{Hz})$
C3-H	2.99 (ddd, $^{a}$ 1H, $J = 16.3, 9.3, 1.8$ Hz)	2.73 (dd, 1H, J = 16.3, 4.5 Hz)	$2.72 (\mathrm{dd}, 1\mathrm{H}, J = 16, 5.1 \mathrm{Hz})$
$CH_2X$	2.88 (dd, 1H, $J = 16.3, 7.8$ Hz)	2.69 (dd, 1H, $J = 15.9, 7$ Hz)	2.57-2.63 (m, 2H)
$CH_2X$	2.72 (dd, 1H, J = 16.3, 7.8 Hz)	2.60 (dd, 1H, $J = 15.9, 7$ Hz)	-
CH <sub>2</sub> CH <sub>3</sub>	4.03-4.21 (m, 4H)	4.20 (q, 2H), 4.15 (q, 2H)	-
CH <sub>8</sub>	1.27 (t, 3H), 1.20 (t, 3H)	1.26 (t, 3H), 1.25 (t, 3H)	-
CO <sub>2</sub> H	-	-	12.47 (s, 2H)

<sup>a</sup> Long-range coupling  $J_{1-3}$ H.

Table III. <sup>1</sup>H NMR Data of Thermally Rearranged Products of Diethyl α-Allyl-2-benzo[b]thiophenemalonate (17)

	major 25b	minor 25a	diacid 29
ArH	7.75–7.78 (m, 1H), 7.54–7.58 (m, 1H), 7.24–7.36 (m, 2H)	7.73-7.79 (m, 1H), 7.52-7.63 (m, 1H), 7.21-7.39 (m, 2H)	7.89-7.92 (m, 1H), 7.63-7.67 (m, 1H), 7.27-7.48 (m, 2H)
C1-H	$3.33 (\mathrm{ddd},^a 1\mathrm{H}, J = 15.3, 8.4, 1.8 \mathrm{Hz})$	$3.15 (\mathrm{dd}, 1\mathrm{H}, J = 14.7, 7.8 \mathrm{Hz})$	3.22 (ddd, 1H, J = 15.2, 8.5, 1.8 Hz)
C1-H	2.64 (ddd, $^{a}$ 1H, $J = 15.3$ , 6.2, 1.8 Hz)	2.81 (ddd, <sup><i>a</i></sup> 1H, $J = 14.7$ , 8, 1.6 Hz)	2.60 (dd, 1H, $J = 15.2$ , 1.8 Hz)
C2-H	3.64 (m, 1H)	3.61 (m, 1H)	3.44 (m, 1H)
C3-H	3.94 (dt, 1H, J = 6.4, 1.8 Hz)	<b>b</b> .	4.00 (d, 1H, J = 6.8 Hz)
$CH_2X$	$2.80 (\mathrm{dd}, 1\mathrm{H}, J = 15.6, 6.4 \mathrm{Hz})$	2.83 (dd, 1H, $J = 16.3, 7.3$ Hz)	2.72 (dd, 1H, J = 16, 5.7 Hz)
$CH_2X$	2.65 (dd, 1H, J = 15.6, 8.1 Hz)	2.68 (dd, 1H, $J = 16.3$ , 8.2 Hz)	2.59 (dd, 1H, J = 16, 8.7 Hz)
CH <sub>2</sub> CH <sub>3</sub>	4.09-4.30 (m, 4H)	4.10–4.29 <sup>b</sup> (m, 5H), 4.15 (q, 2H)	-
CH₃	1.32 (t, 3H), 1.27 (t, 3H)	1.29 (t, 3H), 1.26 (t, 3H)	-
CO <sub>2</sub> H	-	-	12.57 (bs, 2H)

<sup>a</sup> Long-range coupling  $J_{1-3}$ H. <sup>b</sup> Hidden under.

Table IV.HETCOR Experimental Data for theAssignment of Carbon Peaks of Cyclopentane Ring

	trans-9a	cis-9b	diacid 11	major 25b	diacid 29
C1	48.79	52.43	51.74ª	53.47	52.71
C2	43.71	<b>43.79</b>	43.62	42.91	42.52
C3	35.89ª	35.50	34.95	33.18	32.65
$CH_2X$	35.25ª	40.09	51.60ª	38.81	38.99

<sup>a</sup> Assignments could be reversed.





80% yield (Scheme IV). A second halogen-metal interchange at -70 °C was followed by treatment with an ethereal solution of iodine also at -70 °C to give 2-allyl-3-iodobenzo[b]thiophene (15) in 66% yield. This was used immediately without characterization, following the procedure described for the synthesis of 7 from 8 (Scheme II). On the basis of spectroscopic data (<sup>1</sup>H and <sup>13</sup>C NMR spectra and MS) the pure product obtained by chromatography was characterized as diethyl 2-(1-propenyl)-3benzo[b]thiophenemalonate (12) wherein the terminal allylic double bond ( $\delta$  3.63 for CH<sub>2</sub>CH=CH<sub>2</sub>) had rearranged to a more substituted conjugated vinylic double bond ( $\delta$  1.90 for CH=CHCH<sub>3</sub>). A yield of 19% based on 15 was obtained. No 10 was isolated. It is believed that in this reaction the presence of the copper(I) bromide together with the moderately elevated temperature may have caused the rearrangement to the propenyl derivative. This is surprising since the alkylation proceeded normally in the case of the thiophene analogue of 15.<sup>4</sup>

Thermal Rearrangement of Diethyl 2-(1-Propenyl)-3-benzo[b]thiophenemalonate (12). A sample of 12 was heated at 230-40 °C for 18 h (Scheme V). Isolation of a product by chromatography gave a light yellow solid (38%) as a major product. An <sup>1</sup>H NMR spectrum of the yellow solid material contained an A<sub>3</sub>B<sub>2</sub> type splitting pattern typical of CH<sub>3</sub>CH<sub>2</sub>X in the ratio of 3:2 and a singlet at  $\delta$ 2.36 corresponding to 3H. Also no vinyl hydrogens were present and there were singlets in the aromatic region at  $\delta$  7.68 and at 10.19 equivalent to 1H. An IR spectrum showed peaks at 3300(s) typical of an OH group. A <sup>13</sup>C NMR spectrum indicated twelve aromatic carbons besides three carbons in the upfield region and an ester carbonyl at  $\delta$  170.39. The mass spectrum indicated the molecular ion peak 286. On the basis of the spectroscopic data and



by analogy,<sup>11</sup> this compound was assigned the structure of 1-carbethoxy-2-hydroxy-3-methyldibenzothiophene (16). The formation of 16 by the thermal cyclization of 12 may have proceeded through an enol-type intermediate A. In a possible mechanism for this thermal cyclization, the first step in the process involves the formation of an enol-type structure which underwent cyclization to form a sixmembered ring. Once formed, this ring undergoes aromatization by elimination of an ethanol molecule to form the hydroxy ester 16. In agreement with the mechanism as proposed in Scheme V, it was observed that the <sup>1</sup>H NMR spectrum of the crude cold thermal reaction product contained a peak suggesting the presence of ethanol.

Synthesis of Diethyl  $\alpha$ -Allyl-2-benzo[b]thiophenemalonate (17). A straightforward approach involved allylation of diethyl 2-benzo[b]thiophenemalonate (18) which was first synthesized by two different methods as outlined in Scheme VI. In the first method 18 was obtained (54% yield) by reaction of ethyl 2-benzo[b]thiopheneacetate (19) with excess of diethyl carbonate in presence of dry sodium ethoxide (path A). The starting material 19 was obtained directly by treating diethyl [2-(2-benzo[b]thienyl)-1-(dimethylamino)vinyl]phosphonate (20)<sup>12</sup> with saturated ethanolic HCl solution (93%).

The second route as outlined in Scheme VI (path B) served as a model reaction.<sup>14</sup> 2-Benzo[b]thienyllithium



was treated with diethyl oxomalonate (DEOM)<sup>13</sup> below -70 °C to give 22 in 13% yield. It was hoped that the yield would be increased if the 2-benzo[b]thienvllithium was replaced with the less-reactive organomagnesium compound. 2-Benzo[b]thienylmagnesium bromide was obtained by treating 2-benzo[b]thienyllithium with the freshly prepared magnesium bromide etherate. Treatment of 2-benzo[b]thienylmagnesium bromide with DEOM at -70 °C on workup gave diethyl  $\alpha$ -hydroxy-2-benzo[b]thiophenemalonate (22) in 25% yield. Completion of the synthesis depends on removal of the vestigial  $\alpha$ -hydroxy group of the intermediate 22. Acetylation of the hindered tertiary alcohol 22 was achieved (97%) with acetic anhydride and triethylamine in presence of the acylation catalyst 4-(dimethylamino)pyridine (DMAP) in methylene chloride. Reductive  $\alpha$ -deacetoxylation<sup>14</sup> of diethyl  $\alpha$ -acetoxy-2-benzo[b]thiophenemalonate (23) was carried out with naphthalenide radical anion, in effect as a titration. Acid workup, followed by chromatography to remove naphthalene, gave nearly pure 18 (53%) with an overall yield of 13% starting with benzo[b] thiophene (21) in three steps.

Direct allylation of 18 as for the synthesis of 17 (Scheme VII, path A) gave mostly an inseparable mixture. The lower boiling component was characterized as 19 by comparison (TLC, <sup>1</sup>H NMR) with an authentic sample synthesized for the preparation of 18. The higher boiling component (27%) was characterized as diethyl  $\alpha$ -allyl-2-benzo[b]thiophenemalonate (17) on the basis of IR, <sup>1</sup>H and <sup>13</sup>C NMR spectra, and MS. With the difficulty encountered in the above method a second route (path B) for the preparation of 17 was undertaken as outlined in Scheme VII. The ester enolate of 18 was prepared by adding a solution of sodium naphthalenide in HMPA to a stirred solution of 23, as before. Treatment with allyl bromide followed by the usual workup gave 17 in 45% yield starting with 23.

Thermal Rearrangement of Diethyl  $\alpha$ -Allyl-2-benzo[b]thiophenemalonate (17). Diethyl  $\alpha$ -allyl-2-benzo-[b]thiophenemalonate (17) was heated at 170-80 °C for 18 h. By column chromatography of the crude material, 26% of the starting material was recovered; however, the <sup>1</sup>H NMR spectrum of a more polar compound 24 was significantly different from the spectrum of 17 and very similar to that of 10 except that the signal for the  $\alpha$ -hydrogen of the malonate 24 was shifted downfield by 0.10 ppm. The doublet of the allyl hydrogen which resonates at  $\delta$  3.17 in 17 had shifted to  $\delta$  3.62 in 24. The singlet in the aromatic region at  $\delta$  7.41 with an integration value of one hydrogen for 17 disappeared at the same time

(11) Ashby, J.; Ayad, M.; Meth-Cohn, O. J. Chem. Soc., Perkin Trans. 1 1974, 1744.

<sup>(12)</sup> Degenhardt, C. R. Synth. Commun. 1982, 12, 415.

 <sup>(13)</sup> Pardo, S. N.; Salomon, R. G. J. Org. Chem. 1981, 46, 2598.
 (14) Ghosh, S.; Pardo, S. N.; Salomon, R. G. J. Org. Chem. 1982, 47,

<sup>(14)</sup> Ghosh, S.; Pardo, S. N.; Salomon, R. G. J. Org. Chem. 1 4692.



a singlet at  $\delta$  5.13 in the more polar product 24 was also found indicating that an  $\alpha$ -hydrogen on the malonate group was present (Table I). A <sup>13</sup>C NMR spectrum showed significant change also where peaks at  $\delta$  60.52 and  $\delta$  42.16 in 17 were shifted upfield to  $\delta$  52.01 and  $\delta$  30.73, respectively, for 24. This compound is believed to be the normal Cope-rearranged product diethyl 3-allyl-2-benzo-[b]thiophenemalonate (24) (Scheme VIII). The isolated yield of 24 was 45%.

Diethyl  $\alpha$ -allyl-2-benzo[b]thiophenemalonate (17) was then heated at 235-45 °C for 10 h. The <sup>1</sup>H NMR spectrum of the crude product showed it was a mixture of normal Cope-rearranged product 24 and the cyclized compound ethyl 1,2-dihydro-3-(ethoxycarbonyl)-3H-benzo[b]cyclopenta[d]thiophene-2-acetate (25) (Scheme VIII). The ratio of diastereomers of cyclized products 25a/25b was 41:59 based on the integration of the protons of the cyclopentane ring. The isolation of the crude material by column chromatography gave 14% of nearly pure 24. Further careful elution first gave a small amount of minor isomer 25a (12%) followed by a mixture of diastereomers 25a and 25b in 50:50 ratio (based on integration of the <sup>1</sup>H NMR spectrum) (5%) and followed by a major isomer 25b (24%). The stereochemistry of these two isomers was not established but each isomer had a different <sup>1</sup>H NMR spectrum wherein the doublet at  $\delta$  3.94 present in the major isomer 25b was shifted downfield in the minor isomer 25a and hidden under the methylene protons of the ester groups as shown in Table III.

Synthesis of Diethyl 3-Allyl-2-benzo[b]thiophenemalonate (24). The synthetic route shown in Scheme IX followed the method used for the synthesis of 18. The Grignard reagent from 3-allylbenzo[b]thiophene (26)<sup>21</sup> was transferred to a solution of diethyl oxomalonate cooled below -70 °C. Nearly pure diethyl  $\alpha$ -hydroxy-3-allyl-2benzo[b]thiophenemalonate (27) was obtained (37%) on usual workup followed by acetylation which gave diethyl  $\alpha$ -acetoxy-3-allyl-2-benzo[b]thiophenemalonate (28) in 40% yield. The crucial  $\alpha$ -deacetoxylation reaction with sodium naphthalenide in HMPA gave 24 as a major product (76%) with an overall yield of 11%.



Thermal Rearrangement of Diethyl 3-Allyl-2-benzo[b]thiophenemalonate (24). Diethyl 3-allyl-2-benzo-[b]thiophenemalonate (24) was (Scheme X) heated at 260– 70 °C for 12 h. A <sup>1</sup>H NMR spectrum of the crude material showed no vinyl protons but did show the presence of cyclized product. The separation of the crude material by column chromatography only gave a mixture of diastereomers of 25 (15%) which could not be further separated.

This mixture of diastereomers 25 was saponified with KOH in aqueous ethanol, which epimerized the secondary ester group at the C-3 position to yield the diacid 29 (69%) which was assigned the *trans* stereochemistry (Table III) by analogy with the results as obtained above and by the <sup>1</sup>H NMR spectrum (J = 6.8 Hz).

Synthesis of Ethyl  $\alpha$ -Allyl- $\alpha$ -cyano-3-benzo[b]thiopheneacetate (30). When diethyl malonate was substituted by ethyl cyanoacetate, in the method as described by Houbiers and Muris,<sup>6</sup> it gave nearly pure ethyl  $\alpha$ -cyano-3-benzo[b]thiopheneacetate (31) in 40% yield [72% yield based on recovered 3-iodobenzo[b]thiophene (8)] (Table V). Allylation of 31 was carried out in an aprotic solvent using NaH<sup>15</sup> to afford ethyl  $\alpha$ -allyl- $\alpha$ -cyano-3-benzo[b]thiopheneacetate (30) in 61% yield (Scheme XI).

Thermal Rearrangement of Ethyl  $\alpha$ -Allyl- $\alpha$ -cyano-3-benzo[b]thiopheneacetate (30). The thermal rearrangement of 30 was undertaken for two reasons: first, to study the effect of replacement of one of the ethoxycarbonyl groups of 5 by a cyano group to give 30; second, to throw some light on the proposed mechanism of cyclization of the normal Cope product where both the ester groups are participating in the proposed mechanism<sup>4</sup> and to ascertain whether or not the rearrangement of 30 will give a product analogous to the cyclopentabenzo[b]thiophene derivative 9.

When 30 was heated at 205-215 °C for 7 h (Scheme XII), the <sup>1</sup>H NMR spectrum of the crude product showed it to be a mixture of 32 and 30 in ratio of 80:20 based on the allylic protons of these compounds. The purification of the crude product by distillation gave 73% of 32 as a yellow viscous oil.

The <sup>1</sup>H NMR spectrum of the yellow viscous oil showed no peak at  $\delta$  7.58 but there was a singlet at  $\delta$  5.15 for the

<sup>(15)</sup> MacDowell, D. W. H.; Patrik, T. B.; Frame, B. K.; Ellison, D. L. J. Org. Chem. 1967, 32, 1226.

Table V. <sup>1</sup>H NMR Data for the Various Ethyl α-Cyano-benzo[b]thiopheneacetate Derivatives

	31	30	32
Ar-H	7.80–7.86 (m, 2H), 7.60 (s, 1H), 7.32–7.43 (m, 2H)	8.01-8.05 (m, 1H), 7.83-7.87 (m, 1H), 7.58 (s, 1H), 7.33-7.46 (m, 2H)	7.78–7.89 (m, 2H), 7.23–7.76 (m, 2H)
CH-CH2		5.88 (ddt, 1H, $J = 17, 10, 7$ Hz)	5.98 (ddt. 1H, J = 17.2, 9.7, 6.2 Hz)
CH-CH <sub>2</sub>		5.29 (dd, 1H, $J = 17$ , 1.4 Hz), 5.27 (dd, 1H, $J = 10$ , 1.4 Hz)	5.16–5.24 (m, 2H)
ArCHC	5.10 (s, 1H)		5.15 (s. 1H)
$CCH_2R$		3.12-3.30 (m, 2H)	3.70-3.73 (dt. 2H, $J = 6.2, 1.5$ Hz)
$CO_2CH_2$	4.13-4.24 (m, 2H)	4.23 (g, 2H)	4.11-4.31 (m, 2H)
CH <sub>8</sub>	1.20 (t, 3H)	1.20 (t, 3H)	1.20 (t, 3H)
	Scheme XII	phene (33) where bo	th cyano and ester groups are on the





methine hydrogen of the cyanoacetate group. The quartet at  $\delta$  4.23 for the methylene protons of the ethyl group had changed in a multiplet and the allylic protons were shifted downfield from  $\delta$  3.12–3.30 to  $\delta$  3.70–3.73 (Table V). A <sup>13</sup>C NMR spectrum of the yellow viscous oil also revealed that peaks at  $\delta$  117.54, 50.36, and 39.93 for the cyano carbon, tertiary carbon, and allylic carbon, respectively, of **30** had shifted upfield to  $\delta$  114.72, 35.93, and 32.65 in **32**. In **32** these peaks were assigned to the cyano carbon, methine carbon, and allylic carbon by comparison with corresponding peaks for ethyl  $\alpha$ -cyano-3-benzo[b]thiopheneacetate (**31**). With this spectroscopic evidence the product was assigned the structure **32**.

Following the isolation of the regular Cope-rearrangement product 32, thermal studies were conducted to ascertain if a cyclized product similar to 9 could also be obtained. Initially, 30 was heated under nitrogen at 235-45 °C for 8 h (Scheme XII). Elution of the crude product by column chromatography gave 6% of 32 and an unexpected unseparable mixture (16%) of what appeared to be diastereomers of 33; however, considerable decomposition had occurred. The <sup>1</sup>H NMR spectrum of the major product revealed that no allyl, vinyl, or methine hydrogen of cyanoacetate were present. Also a singlet in the aromatic region was absent and the methyl group of the ethyl ester moiety showed two nonequivalent triplets in the upfield region. Two more doublets in the ratio of 64:36 were found at  $\delta$  1.51 and 1.43, respectively. Irradiation of a proton at  $\delta$  3.56–3.79 transformed the two doublets into singlets at  $\delta$  1.5 and 1.43, respectively. This effect was also observed for signals between  $\delta 2.4-3.5$  which also collapsed to doublets from the doublet of doublets. When a proton at  $\delta$  3.38 was irradiated in a decoupling experiment, it showed the effect on a multiplet of the proton at  $\delta$  3.56–3.79 and on a doublets of doublet at  $\delta$  2.83 which then collapsed into a single doublet. It seems that the proton at  $\delta$  3.56–3.79 is coupled with the protons of the major isomer at  $\delta$  3.38, 2.83, and 1.51 and the minor isomer at  $\delta$  3.22, 2.99, and 1.43 in the unseparable mixture of diastereomers. A <sup>13</sup>C NMR spectrum also showed the two diastereomeric ester carbonyl carbons peaks at  $\delta$  167.43 and 166.11, respectively. A GC/MS spectrum also showed two peaks, both having a molecular ion peak at 285. On the basis of the above data, this thermal rearranged product was assigned the structure 1-cyano-1-(ethoxycarbonyl)-2methyl-2,3-dihydro-1H-benzo[b]cyclopenta[d]thiophene (33) where both cyano and ester groups are on the same carbon.

It was also found that heating the isolated 32 at 225–35 °C for 3 h afforded the cyclized product 33 in 5% yield, as a mixture of diastereomers in the ratio of 59:41, along with unchanged starting material. This result suggests that this rearrangement may have occurred *via* a heteroene reaction of the normal Cope product in which the first step probably involves the enolization of the ester group as in Scheme V. This then undergoes cyclization to produce 33 (Scheme XII).

In conclusion, the above studies show that allylated benzo[b]thiophenemalonates and an analogous cyanoacetate, unlike allylated naphthalenemalonate or phenanthrenemalonate and like allylthiophene analogues, undergo thermal rearrangement to give normal Cope products. Furthermore, the normal Cope rearrangement products thus obtained undergo cyclization to give cyclopenta derivatives as in the case of naphthalene and phenanthrene analogues.

## **Experimental Section**

All boiling and melting points are uncorrected and the latter were measured in a Mel-Temp apparatus. Infrared (IR) spectra were recorded on a Perkin-Elmer 1310 spectrophotometer. <sup>1</sup>H (270 MHz) and <sup>13</sup>C (67.9 MHz) NMR spectra were obtained on a JEOL GX-270 spectrometer using tetramethylsilane as an internal standard. 2D1HNMR spectra were obtained on a Varian Gemini-300 spectrometer. All NMR spectra were recorded in deuteriochloroform unless otherwise noted and are expressed in parts per million downfield from tetramethylsilane: couplings are in hertz. Mass spectra were obtained on a Finnigan 4500 GC/MS instrument at 70 eV and a Hewlett-Packard 5890 GC/ MS instrument. Thin-layer chromatography (TLC) was performed with Eastman Kodak silica gel 13181 plates. Developed plates were visualized by UV light or in an I<sub>2</sub> crystal chamber. Column chromatography was carried out on Merck silica gel 60 (70-230 mesh ASTM). Elemental analyses were performed by Galbraith Laboratories, Inc., Knoxville, TN.

Synthesis of Diethyl  $\alpha$ -Allyl-3-benzo[b]thiophenemalonate (5). (A) Synthesis of Diethyl 3-Benzo[b]thiophenemalonate (7). This procedure was modeled after the method of Houbiers and Muris.<sup>6</sup> A solution of 38.5 g (0.24 mol) of diethyl malonate in 200 mL of freshly distilled quinoline was stirred at 60-65 °C. To this solution was added portionwise 10.9 g (0.23 mol) of a 50% dispersion of sodium hydride in mineral oil under N<sub>2</sub>.

After the liberation of hydrogen gas had ceased, 35.7 g (0.14 mol) of 8<sup>7</sup> and 21.6 g (0.16 mol) of copper(I) bromide were added to the reaction mixture. The mixture was stirred overnight at 100–105 °C and was then poured into a mixture of ice, concentrated HCl, and water. The precipitated copper salts were removed by filtration and washed with methylene chloride. The methylene chloride layer was removed and the aqueous layer was extracted with methylene chloride. The methylene chloride layers were combined and were washed with water and saturated salt solution and dried (Na<sub>2</sub>SO<sub>4</sub>). Removal of the methylene chloride left a viscous brown residue which was distilled under reduced pressure to remove excess of unreacted diethyl malonate. Chromatography of the tar-like residue with a chloroform/ benzene mixture (2:3) as eluant allowed isolation of 11.2 g of 7

in a yield of 48% based on the recovered 15 g of recyclable starting material 8. The product was crystallized from ligroin (bp 63–75 °C) to give light yellow crystals; mp 49–50 °C; IR (KBr) 2990, 1740, 1720, 1265, 1040, 780 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  7.76–7.86 (m, 2H, ArH), 7.65 (s, 1H, ArH), 7.30–7.42 (m, 2H, ArH), 5.06 (s, 1H, CC)<sub>4</sub>CH<sub>2</sub>CH<sub>3</sub>), 1.25 (t, 6H, CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 1.25 (t, 6H, CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>); <sup>13</sup>C NMR  $\delta$  167.44, 139.97, 137.94, 126.70, 126.24, 124.50, 124.28, 122.84, 121.66, 62.00, 51.78, 14.01. Anal. Calcd for C<sub>15</sub>H<sub>16</sub>O<sub>4</sub>S: C, 61.63; H, 5.52; S, 10.97. Found: C, 61.99; H, 5.54; S, 11.21.

(B). Synthesis of Diethyl  $\alpha$ -Allyl-3-benzo[b]thiophenemalonate (5). To an ethanolic solution of sodium ethoxide prepared from 463 mg (20 mmol) of sodium metal was added dropwise a solution of 5.88 g (20 mmol) of diethyl 3-benzo[b]thiophenemalonate in 30 mL of absolute ethanol. The reaction mixture was heated to reflux for 1.5 h and was then cooled to room temperature. A solution of 2.44 g (20 mmol) of allyl bromide in 25 mL of absolute ethanol was added in one portion to the reaction mixture which was heated to reflux for 3 h and was then cooled to room temperature. Removal of sodium bromide and ethanol followed by washing and drying gave 5.25 g of a yellow viscous liquid residue. The <sup>1</sup>H NMR spectrum and TLC, using benzene/hexane (1:1) as a developing system, clearly showed the presence of a mixture of 6 and 5, when compared to authentic samples. This mixture proved to be inseparable by fractional distillation. To the mixture, was added hexane and the solution was kept in a refrigerator overnight when colorless crystals were obtained (3.1 g).

On evaporation of the hexane a liquid was obtained. It was found to be identical (IR, <sup>1</sup>H NMR, <sup>13</sup>C NMR) with an authentic sample<sup>5</sup> of 6 (2.15 g): IR (neat) 3060–3040, 2900, 1730, 1180, 1155, 760 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  7.69–7.80 (m, 2H, ArH), 7.25– 7.35 (m, 3H, ArH), 4.11 (q, 2H, CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 3.78 (s, 1H, ArCH<sub>2</sub>C), 1.18 (t, 3H, CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>); <sup>13</sup>C NMR  $\delta$  170.50, 140.15, 138.58, 128.37, 124.40, 124.31, 124.07, 122.74, 121.70, 60.90, 34.43, 14.11.

The colorless crystals were then identified as 5 (47%); mp 47-48 °C [lit.<sup>5</sup> bp 159-63 °C (0.2 mm)]; IR (KBr) 3120, 2980, 1730, 1240, 1043, 920, 765 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>) (Table I); <sup>13</sup>C NMR  $\delta$  169.56, 140.24, 137.33, 132.96, 131.10, 125.28, 124.03, 123.76, 123.24, 122.81, 118.63, 61.69, 60.15, 39.97, 13.94; MS m/e (rel inten) 332 (M<sup>+</sup>, 31), 291 (56), 240 (100), 217 (43), 185 (70). Anal. Calcd for C<sub>18</sub>H<sub>20</sub>O<sub>4</sub>S: C, 65.04; H, 6.06. Found: C, 64.96; H, 6.02.

Thermal Rearrangement of Diethyl  $\alpha$ -Allyl-3-benzo[b]thiophenemalonate (5). General Method: The following general procedure was used to prepare the samples which were subjected to thermal rearrangement. Samples were placed in thick-walled tubes, degassed, and then sealed under a nitrogen atmosphere at reduced pressure (calcd <1 mm). Once the tube was sealed, it was placed in a tube furnace and heated at the desired temperature. Sometimes sample tubes were also heated to the desired temperature in a silicon oil bath or mineral oil bath. After the heating period was completed, the tube was allowed to cool to room temperature and then was opened carefully.

Method A: A glass tube  $(20 \times 2 \text{ cm})$  containing 260 mg of 5 was heated at 175-180 °C for 36 h. The TLC of the crude product in hexane/toluene (3:2) system on a silica gel plate showed two spots, one due to starting material and the other due to the diethyl 2-allyl-3-benzo[b]thiophenemalonate (10). The crude product (250 mg) was loaded on a silica gel column and eluted with hexane/ toluene (3:7) mixture in 50-mL fractions. Elution, monitored by TLC, gave 175 mg of starting material and 80 mg of 10 (31%). The crude 10 was further purified by short-path distillation to obtain an analytical sample as a light yellow viscous oil: IR (neat) 3030-2990, 1730-20, 1300, 1140, 1035, 930, 760, 730 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCla) (Table I); <sup>13</sup>C NMR & 167.63, 142.20, 138.98, 138.25, 134.97, 124.06, 123.89, 123.00, 122.65, 122.06, 117.09, 61.84, 50.62, 33.01, 14.00; MS m/e (rel inten) 332 (M<sup>+</sup>, 20), 286 (8), 258 (12), 240 (5), 185 (100). Anal. Calcd for C<sub>18</sub>H<sub>20</sub>O<sub>4</sub>S: C, 65.04; H, 6.06, S, 9.65. Found: C, 65.04; H, 6.04, S, 9.78.

Method B: In a similar operation 5 (3.0 g) was heated at 180–185 °C for 42 h. The chromatographic separation of the crude product on a silica gel column using hexane/benzene (1:9) as an eluant gave 1.32 g (44%) 10 and 1.39 g of starting material. The yield of product was 82% based on the starting material consumed.

Method C: A glass tube (20 cm  $\times$  2 cm) containing 600 mg of 5 was heated at 215–225 °C for 11 h. The crude compound (598 mg) was chromatographed over silica gel. Elution with hexane/toluene (1:4), monitored both by TLC and the <sup>1</sup>H NMR spectrum of the fractions collected, gave 46 mg of 10. Further gradient elution with toluene/chloroform (6.5:1) gave 58 mg of yellow *trans*-9a (10%) and 30 mg of reddish-brown *cis*-9b (5%). In the overall yield of 40% isolated by column chromatography, the yield of normal Cope product was 8% and was found to be identical with the authentic sample obtained previously. IR and elemental analysis of the diastereomeric mixture 9 gave the following results: IR (neat) 3000–2800, 1740–10, 1430, 1370, 1180– 50, 1020, 755, 730 cm<sup>-1</sup>. Anal. Calcd for C<sub>18</sub>H<sub>20</sub>O<sub>4</sub>S: C, 65.04; H, 6.06; S, 9.65. Found: C, 64.94; H, 6.12; S, 9.71.

trans-9a: <sup>1</sup>H NMR (CDCl<sub>3</sub>) (Table II); <sup>13</sup>C NMR (CDCl<sub>3</sub>)  $\delta$  172.18, 171.76, 144.73, 144.33, 137.35, 134.35, 124.37, 123.53, 123.32, 121.33, 60.65, 60.51, 14.28, 14.22, and Table IV.

*cis*-**9b**: <sup>1</sup>H NMR (CDCl<sub>8</sub>) (Table II); <sup>13</sup>C NMR (CDCl<sub>9</sub>) & 172.74, 171.98, 144.87, 143.85, 135.90, 134.46, 124.36, 123.56, 123.36, 121.84, 61.16, 60.65, 14.31, 14.27, and Table IV.

Method D: Thermal Rearrangement of Diethyl 2-Allyl-3-benzo[b]-thiophenemalonate (10). The isolated 10 (690 mg) was sealed in a glass tube  $(20 \times 2 \text{ cm})$ . The tube was heated to 235-245 °C for 8 h. The <sup>1</sup>H NMR spectrum of the crude material showed a mixture of starting material and cyclized product which was then loaded on a silica gel column. Then the elution with hexane/benzene (60%), monitored by proton NMR spectrum and TLC, first gave 252 mg starting material. Then the gradient elution with benzene/chloroform (30-50%) gave 180 mg (26%) of *trans*-9a and 46 mg (7%) of *cis*-9b, respectively.

Saponification of Ethyl 2,3-Dihydro-1-(ethoxycarbonyl)-1*H*-benzo[*b*]cyclopenta[*d*]thiophene-2-acetate (9). A mixture of 1 mL of ethanol and 1 mL of 5% aqueous KOH was added to 144 mg of 9. The mixture was stirred at room temperature for 15 min and was then extracted with  $(3 \times 2 \text{ mL})$  ether to remove organic impurities. The aqueous layer was then acidified with concd HCl and the buff-colored precipitate thus obtained was crystallized from ethyl acetate-hexane to give 60 mg (50%) of 3-carboxy-1,2-dihydro-3*H*-benzo[*b*]cyclopenta[*d*]thiophene-2-acetic acid (11) as white crystals: mp 189–91 °C (dec); IR (KBr) 3500–2700, 1680, 1420–1390, 1210, 1185, 900, 740, 720 cm<sup>-1</sup>; <sup>1</sup>H NMR (DMSO-d<sub>6</sub>) (Table II); <sup>13</sup>C NMR (DMSO-d<sub>6</sub>)  $\delta$  173.91, 173.21, 143.97, 143.34, 136.47, 134.14, 124.41, 123.53, 121.53, 121.55, and Table IV. Anal. Calcd for C<sub>14</sub>H<sub>12</sub>O<sub>4</sub>S: C, 60.86; H, 4.38; S, 11.60. Found: C, 60.83; H, 4.43; S, 11.49.

Attempted Synthesis of Diethyl 2-Allyl-3-benzo[b]thiophenemalonate (10): Synthesis of Diethyl 2-(1-Propenyl)-3-benzo[b]thiophenemalonate (12). (A) Synthesis of 2,3-Dibromobenzo[b]thiophene (13). This compound was prepared in 93% yield by a modification of the procedure described by Ried and Bender.<sup>9</sup> A solution of 53.6 g (0.40 mol) of 21 in 200 mL of chloroform was magnetically stirred and to this mixture was added 128 g (41.3 mL, 0.80 mol) of bromine in 100 mL of chloroform dropwise at room temperature over 1.5 h. After stirring for 18 h, solid Na<sub>2</sub>CO<sub>3</sub> was added to neutralize the hydrobromic acid. The organic layer was washed with water and  $Na_2S_2O_3$  and then dried ( $Na_2SO_4$ ). On evaporation of the solvent 112 g brown solid was obtained which was crystallized from methanol to give a sticky yellow solid. Further purification of this solid by distillation under reduced pressure gave a light vellow colored solid which was then recrystallized from methanol to give 109 g (93%) of the desired product 13, mp 58-59 °C [lit.<sup>9</sup> mp 58 °C].

(B) Synthesis of 2-Allyl-3-bromoben zo[b]thiophene (14). To a solution of 3-bromo-2-benzo[b]thienyllithium<sup>10</sup> prepared from 13 (120 g, 0.41 mol) by halogen-metal exchange with 1.1 equiv BuLi at 0 °C was added with stirring a solution of allyl bromide (39 mL, 0.45 mol) in ether (40 mL) in one portion. After 10 h stirring at room temperature, the ice-cold water was added to the clear yellow mixture. The organic layer was separated and the aqueous layer was extracted with ether. The organic layer and ether extracts were combined and washed with saturated Na<sub>2</sub>CO<sub>3</sub> and saturated salt solution and dried (Na<sub>2</sub>SO<sub>4</sub>). Removal of the ether left a brownish-yellow liquid which was fractionated to give 83 g (80%) of 14 boiling at 111-13 °C (0.15 mm) as a greenish-yellow liquid. 14 was then redistilled in order to obtain an analytical sample; bp 105-6 °C (0.05 mm); IR (neat) 3060, 3000-2900, 1630, 1430, 1250, 750, 725, 620 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 7.66-7.72 (m, 2H, ArH), 7.23-7.38 (m, 2H, ArH), 5.94 (ddt, J = 16.8, 10 and 6.4 Hz, 1H, CH=CH<sub>2</sub>), 5.18 (dd, J = 16.8 and 1.2 Hz, 1H, CH=CH<sub>2</sub>), 5.14 (dd, J = 10 and 1.2 Hz, 1H, CH=CH<sub>2</sub>), 3.63 (d, 2H, CH<sub>2</sub>-CH=CH<sub>2</sub>); <sup>13</sup>C NMR δ 138.34, 138.01, 137.36, 134.04, 124.83, 124.80, 122.67, 122.22, 117.41, 106.14, 34.11. Anal. Calcd for C11H9BrS: C, 52.19; H, 3.58; S, 12.67. Found: C, 52.19; H, 3.72; S, 12.74.

(C) Synthesis of 2-Allyl-3-iodobenzo[b]thiophene (15). According to the method of Dickinson and Iddon,<sup>10</sup> a solution of 2-allyl-3-benzo[b]thienyllithium was prepared under N<sub>2</sub> by adding dropwise 91 mL (1.65 M solution in hexane) of butyllithium to a yellow-colored solution of 38.0 g (0.15 mol) of 14 in 250 mL of anhydrous ether at -70 °C. The resulting mixture was stirred at -70 °C for a further 45 min. The yellow solution of 2-allyl-3-benzo[b]thienyllithium was then added to 42.3 g (0.33 mol) of iodine in 500 mL of anhydrous ether also cooled to -70 °C. After the addition of the lithiated compound was complete, the violet color of the ethereal iodine solution disappeared. The reaction mixture was then allowed to warm up to room temperature at which point ice-cold water was added. The organic layer was separated, the aqueous layer was extracted with ether, and the ether and organic layers were combined. The combined organic phase was washed with saturated Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub>, water, and saturated salt solution and dried ( $Na_2SO_4$ ). Removal of the ether left a dark purple liquid which was fractionated to give 29.5 g (66%) of 15 as a vellow liquid, bp 121-7 °C (0.3 mm), which darkened on storing to a reddish-brown liquid. It was used immediately without characterization.

(D) Synthesis of Diethyl 2-(1-Propenyl)-3-benzo[b]thiophenemalonate (12). This procedure was an adaptation of the method Houbiers and Muris.<sup>16</sup> To a stirred solution of 9.22 g (0.058 mol) of diethyl malonate in 60 mL of freshly distilled quinoline under N2 was added 2.6 g of a 50% suspension of NaH in mineral oil (0.054 mol) portionwise at a temperature of 70-75 °C. After the liberation of hydrogen gas had ceased, 9.96 g (0.033 mol) of 15 and 6.48 g (0.036 mol) of copper(I) bromide were added. The temperature was raised to 115-120 °C and the reaction mixture was stirred for 6h under  $N_2$ . The usual workup, followed by chromatography on a silica gel column and eluted first with hexane/benzene (1:1), gave 3.76 g of the starting material. Further elution with 40% chloroform/benzene afforded a semisolid (2.09 g) which was recrystallized from hexane to give light yellow crystals, mp 90-91 °C: yield 19% based on the starting 15; IR (KBr) 3000–2800, 1710, 1240, 1190, 1020, 975, 750 cm<sup>-1</sup>;  ${}^{1}H$  NMR (CDCl<sub>3</sub>) § 7.65-7.76 (m, 2H, ArH), 7.20-7.31 (m, 2H, ArH), 6.72 (dq, J = 15.3 and 1.7 Hz, 1H, C=CHAr), 6.24 (dq, J = 15.3 and6.6 Hz, 1H, C=CHCH<sub>3</sub>), 5.09 (s, 1H, CCHAr), 4.19 (q, 4H, CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 1.90 (dd, J = 6.6 and 1.7 Hz, 3H, C=CHCH<sub>3</sub>), 1.19 (t, 6H, CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>); <sup>13</sup>C NMR δ 167.67, 141.59, 139.37, 137.52, 131.19, 124.52, 124.19, 122.82, 122.73, 121.97, 61.90, 50.66, 18.81, 14.02; MS m/e (rel inten) 332 (M<sup>+</sup>, 35), 259 (7), 185 (100). Anal. Calcd for C<sub>18</sub>H<sub>20</sub>O<sub>4</sub>S: C, 65.04; H, 6.06; S, 9.65. Found: C, 65.26; H, 5.90; S, 10.04.

Thermal Rearrangement of Diethyl 2-(1-Propenyl)-3benzo[b]thiophenemalonate (12). 12 (600 mg, 1.81 mmol) was heated  $(N_2)$  at 230-240 °C for 18 h. The crude product was obtained on cooling. Chromatography on a silica gel column using hexane/benzene (1:1) as a eluant gave 230 mg of 16 as a major product. An analytical sample of 16 was obtained by recrystallization from chloroform to afford a yellow crystals: mp 120-1 °C; IR (KBr) 3300, 3000-2900, 1690, 1440, 1285, 1170, 860, 740 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 10.19 (s, 1H, OH), 8.17-8.21 (m, 1H, ArH), 7.78-7.82 (m, 1H, ArH), 7.68 (s, 1H, ArH), 7.31-7.42 (m, 2H, ArH), 4.56 (q, 2H, CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 2.36 (s, 3H, CH<sub>3</sub>), 1.41 (t, 3H, COCH<sub>2</sub>CH<sub>3</sub>); <sup>13</sup>C NMR δ 170.39, 157.39, 140.62, 134.87, 131.40, 131.31, 128.51, 126.68, 126.01, 125.91, 123.17, 122.68, 109.08, 61.88, 16.49, 13.88; MS, m/e (rel inten) 286 (M<sup>+</sup>, 36), 257 (2), 240 (100), 212 (35), 184 (100), 171 (3), 152 (22). Anal. Calcd for C<sub>16</sub>H<sub>14</sub>O<sub>3</sub>S: C, 67.11; H, 4.93; S, 11.20. Found: C, 67.18; H, 4.99; S, 10.94.

Synthesis of Diethyl  $\alpha$ -Allyl-2-benzo[b]thiophenemalonate (17). (A) Synthesis of Diethyl 2-Benzo[b]thiophenemalonate (18). Method I: (a) Synthesis of Ethyl 2-Benzo-[b]thiopheneacetate (19). This procedure was modeled after J. Org. Chem., Vol. 58, No. 16, 1993 4367

solution of 20<sup>12</sup> (29.9 g, 0.088 mol) in absolute ethanol (150 mL) saturated with HCl gas was heated to reflux for 24 h and was then concentrated in vacuo. Usual workup gave 19 (18.1 g, 93%) as a pale vellow liquid: bp 125-6 °C (0.2 mm) [lit.<sup>17</sup> bp 150 °C (2 mm)]; IR (neat) 3060, 2900-2980, 1730, 1200, 1030, 750, 730 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>) & 7.62-7.74 (m, 2H, ArH), 7.19-7.29 (m. 2H, ArH), 7.10 (s, 1H, ArH), 4.15 (q, 2H, CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 3.80 (s, 2H, ArCH<sub>2</sub>C), 1.22 (t, 3H, CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>); <sup>13</sup>C NMR δ 169.83, 140.02. 139.68, 136.32, 124.19, 124.02, 123.42, 123.16, 122.05, 61.22, 36.34, 14.10.

(b) Synthesis of Diethyl 2-Benzo[b]thiophenemalonate (18). According to the method of Blicke and Leonard,<sup>19</sup> to dry sodium ethoxide prepared from sodium (1.99 g, 87 mmol) was added an excess of freshly distilled diethyl carbonate (66.3 g, 66 mL, 56 mmol) in one portion, and the resulting solution was rapidly stirred while 18.2 g (83 mmol) of 19 was added. The temperature of the mixture was maintained at 78-85 °C while the ethanol formed was continuously removed from the reaction mixture under reduced pressure. After 5h only diethyl carbonate was being removed from the reaction mixture which was allowed to cool to room temperature, worked up as usual to give a solid (21.2 g) which was purified by recrystallization from hexane to give 17 g (54%) of pale yellow needles: mp 70-72 °C; IR (KBr) 3000-2900, 1750, 1730, 1220, 1180, 1115, 1030, 750, 725 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 7.71-7.81 (m, 2H, ArH), 7.35 (s, 1H, ArH), 7.30-7.33 (m, 2H, ArH), 4.96 (s, 1H, ArCHC), 4.23–4.31 (pair of q, 4H,  $CO_2CH_2CH_3$ ), 1.29 (t, 6H,  $CO_2CH_2CH_3$ ); <sup>13</sup>C NMR  $\delta$  166.92, 140.37, 139.09, 134.52, 124.78, 124.54, 124.31, 123.66, 122.14, 62.31, 53.94, 14.03. Anal. Calcd for C<sub>15</sub>H<sub>16</sub>O<sub>4</sub>S: C, 61.63; H, 5.52; S, 10.97. Found: C, 61.55; H, 5.27; S, 11.30.

Method II: (a) Synthesis of Diethyl a-Hydroxy-2-benzo-[b]thiophenemalonate (22). Method A: Via 2-Benzo[b]thienyllithium. To a magnetically stirred solution of 21 (10.1 g, 0.075 mol) in ether (200 mL) at 0 °C was added dropwise a solution of 47 mL of butyllithium (1.6 M solution in hexane) diluted with ether (50 mL) under N2. After the complete addition, the reaction mixture was stirred for 0.5 h. The yellow-colored solution thus obtained was added to a stirred solution of DEOM (14.8 g, 0.085 mol) in THF (100 mL) below -70 °C. The bath temperature was then allowed to increase slowly to room temperature, and stirring was continued at room temperature for 2 h. The reaction mixture was poured into a crushed ice-HCl mixture and washed up by standard procedure to give a dark reddish-brown viscous. The chromatography of the crude mixture with a hexane/benzene (10%) mixture, loaded on a silica gel column, first gave the starting material 21 (3.65 g), followed by elution with a benzene/CHCl<sub>3</sub> (10%) mixture to give 3.0 g (13%) of a yellow oil (21% based on starting material recovered) of 22. Further purification by distillation gave a light yellow solid which was then crystallized from hexane: mp 41-43 °C [bp 183-5 °C (0.9 mm)]; IR (neat) 3600-3200, 3020-2900, 1750-10, 1450, 1250–10, 1135, 850, 740, 710 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  7.70–7.79 (m, 2H, ArH), 7.57 (s, 1H, ArH), 7.23–7.33 (m, 2H, ArH), 4.80 (bs, 1H, OH), 4.21-4.39 (m, 4H, CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 1.28 (t, 6H, -CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>); <sup>13</sup>C NMR δ 168.58, 140.00, 139.91, 139.25, 124.61, 124.26, 123.92, 123.68, 122.06, 78.66, 63.43, 13.89. Anal. Calcd for C<sub>15</sub>H<sub>16</sub>O<sub>5</sub>S: C, 58.43, H, 5.23, S, 10.40. Found: C, 58.05, H, 5.23, S, 10.60.

Method B: Via 2-Benzo[b]thienylmagnesium Bromide. To a suspension of MgBr<sub>2</sub> etherate prepared from Mg turnings (4.74 g) and freshly distilled ethylene dibromide (24.2 g, 0.13 mol) in ether-benzene was added 200 mL of ether. The resulting solution of MgBr<sub>2</sub> etherate was then transferred to a freshly prepared 2-benzo[b] thienyllithium (ca. 0.12 mol) solution, under positive N<sub>2</sub> pressure, maintaining the temperature between -10° to 0 °C during the addition and then allowing it to warm up to room temperature over a 30-min period.

The resulting grey solution of 2-benzo[b]thienylmagnesium bromide was transferred to a THF solution of DEOM (22.6 g, 0.13 mol) held rigorously at -70 °C. The cloudy bright yellow

the general method of Ogura. Ito, and Tsuchihashi.<sup>18</sup> A stirred

<sup>(17)</sup> Blicke, F. F.; Sheets, D. G. J. Am. Chem. Soc. 1948, 70, 3768.
(18) (a) Ogura, K.; Ito, Y.; Tsuchihashi, G. Bull. Chem. Soc. Jpn. 1979, 52, 2013. (b) Ogura, K.; Mitamura, S.; Kishi, K.; Tsuchihashi, G. Synthesis 1979, 880.

<sup>(16) (</sup>a) Dickinson, R. P.; Iddon, B.; Sommerville, R. G. Int. J. Sulfur Chem. 1973, 8, 233 and 236.

<sup>(19)</sup> Blicke, F. F.; Leonard, F. J. Am. Chem. Soc. 1946, 68, 1934.

reaction mixture was stirred for an additional hour at -70 °C and was then allowed to warm slowly overnight to room temperature. Decomposition and workup as in the previous preparation gave a viscous oil which was subjected to column chromatography over silica gel. Purification by chromatography as described in the previous preparation gave 10.2 g (25%) of 22, identified by the comparison of its IR and <sup>1</sup>H NMR spectra with those of the authentic sample obtained by the previous method.

(b) Synthesis of Diethyl α-Acetoxy-2-benzo[b]thiophenemalonate (23). The general procedure of acetylation of diethyl aryltartronates as described by Saloman, Pardo, and Ghosh<sup>14</sup> was used. A solution of 22 (10.3 g, 0.033 mol) in CH<sub>2</sub>Cl<sub>2</sub> (150 mL) was stirred magnetically under N<sub>2</sub>. To this solution were added 44.7 mL of acetic anhydride (0.47 mol), 22.3 mL of triethylamine (0.16 mol), and 2.23 g of 4-(dimethylamino)pyridine (0.018 mol), and the resulting mixture was stirred for 2 days at room temperature. The dark-brown reaction mixture was poured into ice-cold water. The acetic acid generated was then neutralized by adding solid NaHCO<sub>3</sub> until no more evolution of CO<sub>2</sub> was observed. The organic residue was extracted with ether. The combined organic phases were washed with ice-cold aqueous 10% HCl, water, and brine and dried (Na<sub>2</sub>SO<sub>4</sub>). Removal of the ether gave a dark-brown liquid which was purified by column chromatography on a silica gel column using hexane/ether (30%) as eluant to give 11.2 g (97%) of nearly pure 23 which was crystallized from benzene/hexane to give yellow crystals: mp 65-68 °C; IR (neat) 3000-2900, 1770-20, 1430, 1360, 1230, 1150, 1055, 745, 720 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>) & 7.72-7.81 (m, 2H, ArH), 7.60 (s, 1H, ArH), 7.30-7.34 (m, 2H, ArH), 4.26-4.34 (pair of q, 4H, CO<sub>2</sub>CH<sub>2</sub>-CH<sub>3</sub>), 2.27 (s, 3H, COCH<sub>3</sub>), 1.23 (t, 6H, CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>); <sup>13</sup>C NMR δ 169.17, 164.77, 140.05, 138.73, 136.84, 125.12, 124.52, 124.16, 122.05, 81.00, 63.02, 20.86, 13.85. Anal. Calcd for C17H18O6S: C, 58.27; H, 5.18; S, 9.15. Found: C, 58.10; H, 5.10; S, 9.29.

(c) Synthesis of Diethyl 2-Benzo[b]thiophenemalonate (18) by Reductive  $\alpha$ -Deacetoxylation. To a yellow stirred solution of 500 mg (1.43 mmol) of 23 and 20 mL of dry benzene under  $N_2$  was slowly added a solution of sodium naphthalenide in HMPA<sup>14</sup> until the dark green color persisted for 20-30 s. The resulting mixture was quenched by pouring it into ice-cold 10% HCl and the usual workup was followed. The solid crude product (contaminated with naphthalene) was chromatographed through a short column of silica gel; naphthalene was eluted first with hexane. The reduced product was eluted with toluene to afford 230 mg (53%) of a yellow solid, mp 70–72 °C, found to be identical (TLC, <sup>1</sup>H NMR) with the authentic sample of 18 obtained by previous method.

(B) Synthesis of Diethyl α-Allyl-2-benzo[b]thiophenemalonate (17). Method I: Following the method used for the analogous compound 5, alkylation of 18 (6.27 g, 0.023 mol) with an excess of allyl bromide (5.56 g, 0.046 mol) gave after usual workup 7.34 g (96%) of a yellow mobile liquid. TLC of the crude product using benzene as a developing system clearly showed the presence of two products very close in  $R_{\rm f}$  values and less polar than starting 18. The crude product was inseparable by column chromatography and upon fractionation under reduced pressure gave 2.33 g of 19, bp 127-144 °C (0.35 mm), having an <sup>1</sup>H NMR spectrum identical with that of the authentic sample as obtained before and 2.05 g (27%) of 17, bp 150-57 °C (0.35 mm): IR (neat) 3100-2900, 1730, 1460, 1430, 1230-20, 1150, 925, 860, 750, 730 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>) (Table I); <sup>18</sup>C NMR δ 168.98, 140.06, 139.94, 138.81, 132.07, 124.29, 124.06, 123.50, 123.48, 121.79, 119.19, 61.96, 60.52, 42.16, 13.90; MS m/e (rel inten) 332 (M<sup>+</sup> 42), 291 (88), 259 (36), 240 (71), 217 (61), 185 (100). Anal. Calcd for C<sub>18</sub>H<sub>20</sub>O<sub>4</sub>S: C, 65.04; H, 6.06. Found: C, 64.96; H, 6.07.

Method II: By Reductive Allylation. To a stirred solution of 23 (4.36 g, 0.012 mol) in dry benzene (400 mL) was added dropwise a solution of sodium naphthalenide in HMPA until the dark-green color of the reagent persisted for 20-30 s. Allyl bromide (1.5 mL, 0.017 mol) was then added dropwise to the reaction mixture with stirring which was then heated to reflux for 1.5 h. After cooling, the resulting suspension was filtered and the benzene was evaporated. Then the reaction mixture was quenched by pouring it into cold 10% HCl. The usual workup gave a viscous oil which was chromatographed over silica gel, and the naphthalene was eluted first with hexane/toluene (1:1). Further elution with toluene/chloroform (30%) gave 1.85 g of 17

as a yellow viscous liquid (45%), found to be identical (TLC, <sup>1</sup>H NMR) with the authentic sample obtained previously.

Thermal Rearrangement of Diethyl  $\alpha$ -Allyl-2-benzo[b]thiophenemalonate (17). Method A: A glass tube  $(20 \times 2 \text{ cm})$ containing 200 mg of 17 was heated to 170-180 °C for 18 h. TLC of the crude product using a toluene system showed the presence of a slightly more polar spot along with the starting material spot. When the column was eluted with hexane/toluene (60%)and monitored by TLC, 52 mg (26%) of starting material was recovered and its identity was confirmed by <sup>1</sup>H NMR spectroscopy. On further elution with neat toluene 90 mg (45%) of 24 was isolated. Yield was 61% on the basis of starting material recovered. An analytical sample was obtained by short-path distillation; IR (neat) 3100-2900, 1740, 1470, 1440, 1220, 1160. 1040, 770, 745 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>) (Table I); <sup>13</sup>C NMR δ 167.04. 139.84, 138.84, 134.78, 132.64, 130.10, 124.65, 123.95, 122.27, 122.20, 116.17, 62.21, 52.01, 30.73, 13.99. Anal. Calcd for C<sub>18</sub>H<sub>20</sub>O<sub>4</sub>S: C, 65.04; H, 6.08; S, 9.65. Found: C, 64.97; H, 5.96; S, 10.04.

Method B: In a similar operation 2.0 g of 17 was heated to 235-245 °C for 10 h. The crude dark product (1.99 g) in toluene was then loaded on a silica gel column. Elution first with petroleum ether/toluene (50%) gave 266 mg of a mixture of starting material and normal Cope product. Further elution with toluene gave 308 mg (14%) of nearly pure normal Cope product 24. Further careful elution with toluene/CHCl<sub>3</sub> (12%) gave 240 mg (12%) of nearly pure minor isomer 25a as a yellow viscous oil, followed by a mixture of cyclized diastereomers of 25 (100 mg) (5%) in a 50:50 ratio based on the integration curve of the <sup>1</sup>H NMR spectrum. Continued elution with toluene/CHCl<sub>3</sub> (40%) gave 480 mg (24%) of major isomer 25b as a yellow viscous oil. The total yield was 76%. Analysis of the diastereomeric mixture 25 gave the following results. Anal. Calcd for C18H20O4S: C, 65.04; H, 6.06. Found: C, 65.04; H, 5.95.

Major 25b: IR (neat) 3100-2800, 1750-30, 1440, 1380, 1200, 1035, 760, 740 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>8</sub>) (Table III); <sup>13</sup>C NMR (CDCl<sub>3</sub>) § 172.01, 171.83, 145.08, 140.14, 138.58, 134.67, 124.30, 123.91, 123.38, 121.79, 61.34, 60.34, 14.22, and Table IV

Minor 25a: IR (neat) 3100-2800, 1750-30, 1450, 1380, 1190, 1050, 760, 740 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>8</sub>) (Table III); <sup>18</sup>C NMR (CDCl<sub>3</sub>) § 172.25, 171.44, 144.88, 141.68, 139.29, 134.72, 124.32, 123.98, 123.46, 121.98, 61.00, 60.59, 50.83, 43.49, 36.17, 32.96, 14.24

Synthesis of Diethyl 3-Allyl-2-benzo[b]thiophenemalonate (24). (a) Synthesis of Diethyl  $\alpha$ -Hydroxy-3-allyl-2benzo[b]thiophenemalonate (27). To a stirred solution of 15.7 g (0.090 mol) of  $26^{21}$  in 300 mL of ether cooled to 0 °C under N<sub>2</sub> was added dropwise 84 mL of butyllithium (1.6 M solution in hexane) in ether (100 mL). After the addition was complete, the colored solution was stirred for a further 0.5 h. To the resulting 3-allyl-2-benzo[b]thienyllithium was added a freshly prepared solution of magnesium bromide etherate (ca. 0.090 mol) in ether (300 mL) at 0 °C. The grey suspension of 3-allyl-2-benzo[b]thienylmagnesium bromide warmed up to room temperature (0.5 h) and then cooled down to 0 °C was transferred to a solution of 23.5 g (20.6 mL, 0.14 mol) of diethyl oxomalonate (DEOM) in 500 mL of dry THF at -70 °C. The temperature was maintained at -70 °C for 1 h and then the mixture was warmed up to room temperature. A mixture of ice and 10% HCl was added and the reaction mixture was rapidly stirred. Ether was added and the solution was worked up as usual. The crude product was purified by column chromatography on silica gel using hexane/chloroform (30%) as eluant to give 11.7 g (37% and 57\% based on 10.3 g of starting material recovered) of nearly pure 27 which was further purified by distillation to give a viscous brown-red oil, bp 175–78 °C (4.5 mm); IR (neat) 3700-3100, 3100-2900, 1760-30, 1440, 1380, 1290–20, 1110, 1040, 780, 750 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>8</sub>)  $\delta$  7.69–7.78 (m, 2H, ArH), 7.26–7.35 (m, 2H, ArH), 5.92 (ddt, J =17, 10.4 and 5.7 Hz, 1H, CH=CH2), 4.99-5.08 (m, 2H, CH=CH2), 4.80 (s, 1H, -OH), 4.20-4.39 (m, 4H, CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 3.69 (ddd, J = 5.7 and 1.6 Hz, 2H, CH<sub>2</sub>-CH=CH<sub>2</sub>), 1.28 (t, 6H, CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>); <sup>13</sup>C NMR δ 169.08, 140.56, 138.54, 135.51, 135.22, 132.18, 124.62, 123.89, 122.83, 122.10, 116.02, 78.66, 63.47, 31.83, 13.86,

(20) Cherry, W. H.; Davies, W.; Ennis, B. C.; Porter, Q. N. Aust. J. Chem. 1967, 20, 313. (21) Anisimov, A. V.; Luzikov, Yu. N.; Nikolaeva, V. M.; Viktorova, E.

A. Zh. Org. Khim. 1979, 15 (1), 172; Chem. Abstr. 1979, 90, 203796v.

The hydroxy ester was not further purified but was used directly in the next step.

(b) Synthesis of Diethyl  $\alpha$ -Acetoxy-3-Allyl-2-benzo[b]thiophenemalonate (28). A mixture of 27 (2.65 g, 7.61 mmol), acetic anhydride (10.3 mL, 109 mmol), 4-(dimethylamino)pyridine (0.51 g, 4.1 mmol), and triethylamine (5.1 mL, 37 mmol) in CH<sub>2</sub>-Cl<sub>2</sub> (50 mL) was stirred for 2 days at room temperature under N<sub>2</sub> followed by workup as for 23 as described above to give a dark brown viscous liquid which was purified by chromatography on a silica gel column using toluene as eluant to give 1.2 g (40%) of 28 which was distilled under reduced pressure to give a yellow viscous liquid; bp 180-7 °C (0.25 mm); IR (neat) 3100-2800, 1770-20, 1360, 1250-10, 1175, 1050, 760, 730 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 7.65-7.80 (m, 2H, ArH), 7.30-7.34 (m, 2H, ArH), 5.93 (ddt, J = 17.2, 10.2, and 5.3 Hz, 1H, CH=CH<sub>2</sub>), 5.02 (dd, J = 10.3 and 1.6 Hz, 1H, CH=CH<sub>2</sub>), 4.88 (dd, J = 17.2 and 1.6, 1H, CH=CH<sub>2</sub>), 4.17-4.36 (m, 4H,  $CO_2CH_2CH_3$ ), 3.80 (d, J = 5.3 Hz, 2H,  $CH_2$ -CH=CH<sub>2</sub>), 2.21 (s, 3H, COCH<sub>3</sub>), 1.24 (t, 6H, CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>); <sup>13</sup>C NMR & 168.95, 165.01, 139.58, 139.17, 135.10, 133.15, 131.69, 125.11, 124.06, 122.81, 122.05, 116.01, 81.07, 63.01, 30.86, 20.68, 13.82. Anal. Calcd for C<sub>20</sub>H<sub>22</sub>O<sub>6</sub>S: C, 61.52; H, 5.68; S, 8.21. Found: C, 61.33; H, 5.69; S, 8.14.

(c) Synthesis of Diethyl 3-Allyl-2-benzo[b]thiophenemalonate (24). To a stirred solution of 28 (4.0 g, 0.01 mol) in dry benzene (300 mL) under N<sub>2</sub> was added dropwise a solution of sodium naphthalenide in HMPA, as described before, giving 2.6 g of a product (76%) which was further purified by shortpath distillation to give 24, as a yellow mobile liquid. The IR and <sup>1</sup>H NMR spectra of 24 were identical with the spectra described in method A under the thermal rearrangement of 17.

Thermal Rearrangement of Diethyl 3-Allyl-2-benzo[b]thiophenemalonate (24). A glass tube  $(20 \times 2 \text{ cm})$  containing 500 mg of 24 was heated to 260–270 °C for 12 h. A <sup>1</sup>NMR spectrum of the crude material revealed that no starting material was present but did show the presence of cyclized product 25. The elution with toluene/chloroform (70%) gave 74 mg (15%) of a mixture of unseparable diastereomers of 25 which could not be separated.

Saponification of Ethyl 1,2-Dihydro-3-(ethoxycarbonyl)-3*H*-benzo[*b*]cyclopenta[*d*]thiophene-2-acetate (25). As described before for analogous diester 9, saponification of 25 (131 mg) on workup followed by crystallization from ethanol/hexane gave 75 mg (69%) of 3-carboxy-1,2-dihydro-3*H*-benzo[*b*]cyclopenta[*d*]thiophene-2-acetic acid (29) as white crystals, mp 249– 52 °C dec; IR (KBr) 3550–2500, 1690, 1420, 1275, 1240–1220, 750, 720 cm<sup>-1</sup>; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) (Table III); <sup>13</sup>C NMR (DMSO*d*<sub>6</sub>)  $\delta$  173.28, 172.94, 144.03, 139.63, 139.11, 134.29, 124.34, 123.80, 123.37, 121.70, and Table IV. Anal. Calcd for C<sub>14</sub>H<sub>12</sub>O<sub>4</sub>S: C, 60.86; H, 4.38. Found: C, 60.90; H, 4.30.

Synthesis of Ethyl a-Allyl-a-cyano-3-benzo[b]thiopheneacetate (30). (A) Synthesis of Ethyl  $\alpha$ -Cyano-3-benzo-[b]thiopheneacetate (31). This procedure was an adaptation of the method of Houbiers and Muris.<sup>6</sup> To 150 mL of DMF was added with stirring 8.7 g (77 mmol) of ethyl  $\alpha$ -cyanoacetate and 8.66 g (77 mmol) of anhydrous potassium tert-butoxide. Then 13.4g (51.5 mmol) of 8 and 8.66g (51.5 mmol) of copper(I) bromide were added. The resulting mixture was stirred under N<sub>2</sub> at a temperature of 70 °C for 3 h and the tert-butyl alcohol formed during the reaction was removed by distillation. The workup as before followed by chromatography on a silica gel column using benzene as an eluant gave 5.1 g (40%) of 31, as a yellow oil (72%) based on recovered starting material). The product was further purified by distillation: bp 168-70 °C (0.8 mm); IR (neat) 3100, 3000-2900, 2260, 1745, 1460, 1430, 1250, 1025, 770, 735 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>) (Table V); <sup>13</sup>C NMR & 164.06, 140.33, 136.10, 127.17, 125.12, 124.80, 123.68, 123.06, 121.53, 115.1, 63.44, 38.22, 13.82. Anal. Calcd for C<sub>13</sub>H<sub>11</sub>NO<sub>2</sub>S: C, 63.65; H, 4.52; S, 13.07. Found: C, 63.59; H, 4.67; S, 13.03.

(B) Synthesis of Ethyl α-Allyl-α-cyano-3-benzo[b]thiopheneacetate (30). The preparation of ethyl  $\alpha$ -allyl- $\alpha$ -cyano-3-benzo[b]thiopheneacetate followed a literature procedure.<sup>15</sup> To a solution of 0.56 g (11.6 mmol) of a 50% dispersion of NaH in mineral oil in 50 mL of dry THF was added a solution 2.36 g (9.64 mmol) of 31 in 10 mL of dry THF dropwise over a 5-min period, and the mixture was stirred for 30 min. after which time hydrogen evolution had ceased. To the stirred mixture was then added dropwise a solution of 1.75 g (1.4 mL, 14.5 mmol) of freshly distilled allyl bromide in 10 mL of THF. The resulting mixture was stirred and heated to reflux for 3 h. Ice and water were added to the cooled mixture followed by the usual workup to give an oily residue which was purified by chromatography on a silica gel column with a hexane/benzene (1:1) system as an eluant and vielded 1.69 g (61%) of 30, as a yellow viscous oil. An analytical sample was obtained by short-path distillation as a yellow transparent viscous oil; bp 158 °C (0.25 mm); IR (neat) 3140-2920, 2250, 1740, 1225, 770, 735 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>) (Table V); <sup>13</sup>C NMR § 166.50, 140.81, 135.55, 130.34, 127.93, 125.78, 124.98, 124.74, 123.22, 122.32, 121.42, 117.54, 63.41, 50.36, 39.93, 13.91; MS m/e (rel inten) 285 (M<sup>+</sup>, 43), 244 (100), 216 (94), 212 (57), 185 (45). Anal. Calcd for C18H15NO2S: C, 67.34; H, 5.30; S, 11.24. Found: C, 67.68; H, 5.29; S, 11.41.

Thermal Rearrangement of Ethyl α-Allyl-α-cyano-3benzo[b]thiopheneacetate (30). Method A: A glass tube (10 × 2 cm) containing 16.5 g of 30 was heated to 205–215 °C for 7 h. The crude dark brown liquid was then fractionated to give 1.2 g (73%) of 32, as a yellow viscous oil: IR (neat) 3100–3060, 3000–2900, 2250, 1745, 1460, 1440, 1250, 1100, 1030, 765, 740 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>) (Table V); <sup>13</sup>C NMR δ 164.28, 143.23, 138.19, 137.45, 134.13, 124.83, 124.62, 122.46, 121.37, 119.04, 117.85, 114.72, 63.39, 35.93, 32.65, 13.98. Anal. Calcd for C<sub>16</sub>H<sub>16</sub>NO<sub>2</sub>S: C, 67.34; H, 5.30; S, 11.24. Found: C, 66.98; H, 5.32; S, 11.05.

Method B: In a similar method 30 (5.04 g) was heated to 235-245 °C for 8 h. The reddish-brown crude material thus obtained was chromatographed on a silica gel column using benzene/hexane (3:1) system as an eluant, giving 312 mg (6%) 32 and 760 mg (16%) of a mixture of diastereomers of 33, as a yellow viscous oil: IR (neat) 3100-2800, 2240, 1730, 1425, 1230, 1020, 760, 730 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 7.24-7.41 (m, 4H, ArH), 7.71-7.80 (m, 4H, ArH), 4.17-4.37 (m, 4H, CO<sub>2</sub>CH<sub>2</sub>CH<sub>8</sub>), 3.56- $3.79 (m, 2H, CH-CH_3), 3.34-3.43 (dd, J = 15.9, 7.5 Hz, 1H, C-CH_2-$ C), 3.18-3.27 (dd, J = 15.4, 7.7 Hz, 1H, C-CH<sub>2</sub>-C), 2.95-3.04 (dd, J = 15.4, 9.2 Hz, 1H, CCH<sub>2</sub>C), 2.79–2.87 (dd, J = 15.9, 6.6 Hz, 1H, CCH<sub>2</sub>C), 1.51 (d, J = 7.14 Hz, 3H, CHCH<sub>3</sub>), 1.43 (d, J = 6.96Hz, 3H, CHCH<sub>3</sub>), 1.33 (t, 3H, CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 1.26 (t, 3H, CO<sub>2</sub>- $CH_2CH_3$ ). Integration of <sup>1</sup>H NMR spectrum indicated a ratio of 64:36 between these two diastereomers: <sup>13</sup>C NMR δ 167.43, 166.11, 147.41, 147.09, 144.35, 143.96, 134.69, 133.44, 132.80, 132.56, 132.50, 125.06, 125.01, 124.34, 123.55, 121.02, 120.68, 118.16, 115.75, 63.34, 62.90, 55.21, 53.35, 51.96, 48.09, 36.68, 36.25, 17.84, 15.03, 14.17, 14.09; MS m/e (rel inten) 285 (M+, 31), 258 (0.4), 212 (100), 185 (30). Anal. Calcd for C<sub>16</sub>H<sub>15</sub>NO<sub>2</sub>S: C, 67.34; H, 5.30, S, 11.24. Found: C, 67.04; H, 5.47; S, 11.38.

Method C: Thermal Rearrangement of Ethyl  $\alpha$ -Cyano-2-allyl-3-benzo[b]thiopheneacetate (32). 32 (293 mg) was similarly heated to 225-235 °C for 3 h. The crude material upon elution with benzene/hexane (50:50) gave 38 mg of a mixture of 32 and 33 in the ratio of 65:35 and 15 mg of pure unreacted starting material. The yield of 33 was 5% and consists of a mixture of diastereomers in the ratio of 59:41.

Acknowledgment. We are grateful to J.M. Purpura for doing preliminary work. We wish to thank Dr. William Moore and Dr. Peter Gannett for their help and suggestions.