Notes

Metacyclophanes and Related Compounds. 5. Thermal Rearrangement of 10b,10c-Dialkyl-2,7-di-*tert*-butyl-*trans*-10b,10c-dihydropyrenes[1]

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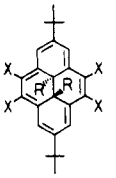
Boekelheide and his co-workers have reported[2-4] that the thermal decomposition of 10b,10c-dialkyl-*trans*-10b,10c-dihydropyrenes afforded the corresponding 5a,10b-dialkyl-10b,10c-dihydropyrenes.

Recently, we reported the preparation and halogenation of the title compounds 1. During the purification of compounds 1, we found that these compounds were unstable in boiling hexane with the exception of the dimethyl derivative as reported by Boekelheide et al.



1a, R = CH_3; X = H
b, R = CH_3CH_2; X = H
c, R = $CH_3CH_2CH_2$; X = H
d, R = $CH_3CH_2CH_2CH_2$; X = H
e, R = CH_3; X = Br
f, R = CH_3CH_2; X = Br
g, R = $CH_3CH_2CH_2$; X = Br
h, R = CH_3; R′ = CH_3CH_2; X = H
i, R = CH_3; R′ = $CH_3CH_2CH_2$; X = H
j, R = CH_3CH_2; R′ = $CH_3CH_2CH_2$; X = H

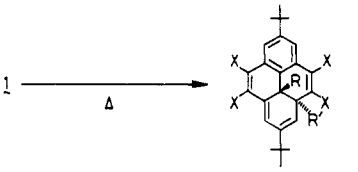
The present work presents more detailed studies of the thermal rearrangement of the title compounds 1, including the unsymmetrical 8,16-dialkyl derivatives.

Results and Discussion

The preparation of symmetrical 10b,10c-dialkyl-2,7-di-*tert*-butyl-*trans*-10b,10c-dihydropyrenes (1) has been described in a previous paper.[5] Unsymmetrical derivatives were prepared according to the reaction routes shown in Scheme I. The compounds 2 and 3 were also described previously.[6,7]

Thermal rearrangement of 1 was carried out under various conditions, and the results are summarized in Table I.

Table I. Thermal Rearrangement of 10b,10c-Dialkyl-2,7-di-*tert*-butyl-*trans*-10b,10c-dihydropyrenes (1)



8[e]

run	substrate (1)	method[a]	time	product (yield, %)[b]
1	a	A	5 min	8a (67)
2	a	B	62 h	8a (0)[c]
3	b	B	62 h	8b (75)
4	c	B	62 h	8c (67)
5	d	B	62 h	8d (60)
6	e	A	5 min	8e (55)
7	e	B	62 h	8e (0)[c]
8	f	B	62 h	8f (79)
9	g	B	62 h	8g (73)
10	h	B	62 h	8h (77)[c,d]
11	h	C	12 h	8h (65)
12	i	C	12 h	8i (60)
13	j	B	62 h	8j (50),[d] 8k (50)[d]

[a] A, 200–210 °C; B, cyclohexane reflux; C, toluene reflux. [b] The yields isolated are shown. [c] The starting material (1a,e,i) was recovered in 97%, 95%, and 33% yields, respectively. [d] The molar ratio of the products 8j and 8k was determined by ^1H NMR. [e] For compound 8: a, R = R′ = CH_3, X = H; b, R = R′ = CH_3CH_2, X = H; c, R = R′ = $CH_3CH_2CH_2$, X = H; d, R = R′ = $CH_3CH_2CH_2CH_2$, X = H; e, R = R′ = CH_3, X = Br; f, R = R′ = CH_3CH_2, X = Br; g, R = R′ = $CH_3CH_2CH_2$, X = Br; h, R = CH_3, R′ = CH_3CH_2, X = H; i, R = CH_3, R′ = $CH_3CH_2CH_2$, X = H; j, R = CH_3CH_2, R′ = $CH_3CH_2CH_2$, X = H; k, R = $CH_3CH_2CH_2$, R′ = CH_3CH_2, X = H.

In the case of **1a** and **1e**, the corresponding rearranged products **8a** and **8e** were, as expected from the results reported by Boekelheide and Hylton,[4] obtained only when these compounds were carried out at 200–210 °C in a sealed tube but not at lower temperatures in solution. However, the other compounds afforded the corresponding products smoothly at lower temperatures.

It should be noted that methyl groups in the unsymmetrical derivatives did not migrate, but other groups such as ethyl, *n*-propyl, and *n*-butyl migrated easily to give the corresponding rearranged products 8.

From the above results, the thermal migration of the alkyl groups[4] was widely recognized in the dialkyldihydropyrenes series, and it was also recognized that the methyl group can hardly be moved at low temperature.

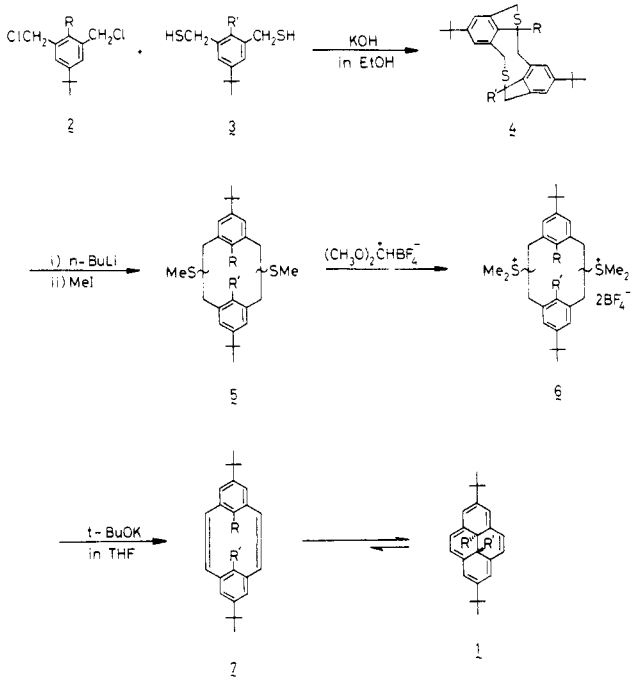
Experimental Section

All melting points are uncorrected. NMR spectra were determined at 100 MHz with a Nippon Denshi JEOL FT-100 NMR spectrometer with Me_4Si as an internal reference, and IR spectra were measured by using KBr pellets or liquid films on NaCl plates on a Nippon Bunko IR-A-102 spectrometer. Mass spectra were

(1) Part 4: Tashiro, M.; Yamato, T. *J. Am. Chem. Soc.*, in press.
(2) Boekelheide, V.; Miyasaka, T. *J. Am. Chem. Soc.* **1967**, *89*, 1709.
(3) Boekelheide, V.; Sturm, E. *J. Am. Chem. Soc.* **1969**, *91*, 902.
(4) Boekelheide, V.; Hylton, T. A. *J. Am. Chem. Soc.* **1970**, *92*, 3669.
(5) Tashiro, M.; Yamato, T. *Chem. Lett.* **1980**, 1127.
(6) Tashiro, M.; Yamato, T. *Org. Prep. Proced. Int.* **1981**, *18*, 1.
(7) Tashiro, M.; Yamato, T. *J. Org. Chem.* **1981**, *46*, 1545.

0022-3263/82/1947-2783$01.25/0

Scheme I



obtained on a Nippon Denshi JMS-01-SA-2 spectrometer at 75 eV by using a direct-inlet system.

Wittig Rearrangement of 4 to 5. Typical Procedure. To a stirred solution of 5.11 g (12 mmol) of **4h** in 60 mL of dry tetrahydrofuran under nitrogen was added 18 mL of a 15% hexane solution of *n*-butyllithium (42 mmol) with ice cooling. After the solution was stirred for 10 min at room temperature, 3.78 mL (60 mmol) of methyl iodide was added to the reaction mixture. The reaction mixture was worked up by addition of H_2O and CH_2Cl_2. After the dichloromethane extract had been washed with water, dried, and concentrated, the products were purified by chromatography on silica gel with hexane/benzene (1:1) to give **5h**: 5.44 g (99.3%); colorless crystals; mp 167–197 °C; IR (KBr) 3030, 2950, 2900, 1585, 1445, 1350, 1260, 1225, 1190, 985, 880, 830, 710 cm^{-1}; NMR ($CDCl_3$) δ 0.22–0.40 (3 H, CH_2CH_3), 0.60–0.64 (3 H, CH_3), 0.86–1.22 (2 H, CH_2CH_3) 1.28–1.36 (18 H, *t*-Bu), 2.14–2.20 (6 H, SCH_3), 2.45–2.80 (2 H, CH_2), 3.06–3.26 (2 H, CH_2), 3.95–4.20 (2 H, CH), 7.11–7.24 (2 H, Aromatic H), 7.69–7.84 (2 H, aromatic H).

Anal. Calcd for $C_{29}H_{42}S_2$: C, 76.59; H, 9.31. Found: C, 76.32; H, 9.32.

Compounds **5i** and **5j** were obtained from **4i** and **4j** by this method, respectively.

5i: 99.6%; colorless crystals; mp 175–205 °C; IR (KBr) 3040, 2960, 2930, 1590, 1450, 1360, 1265, 1235, 1200, 1175, 990, 880, 830, 735, 715 cm^{-1}; NMR ($CDCl_3$) δ 0.36–0.55 (3 H, $CH_2CH_2CH_3$), 0.58–0.63 (3 H, CH_3), 0.80–1.16 (4 H, $CH_2CH_2CH_3$), 1.26–1.36 (18 H, *t*-Bu), 2.14 (6 H, SMe), 2.44–2.78 (2 H, CH_2), 3.04–3.24 (2 H, CH_2), 3.94–4.20 (2 H, CH), 7.09–7.24 (2 H, aromatic H), 7.69–7.83 (2 H, aromatic H).

Anal. Calcd for $C_{30}H_{44}S_2$: C, 76.86; H, 9.46. Found: C, 76.33; H, 9.46.

5j: 99.1%; colorless crystals; mp 167–187 °C; IR (KBr) 3040, 2950, 2920, 1590, 1460, 1400, 1355, 1260, 1230, 1200, 1170, 1080, 980, 920, 880, 830, 730, 670 cm^{-1}; NMR ($CDCl_3$) δ 0.57–1.16 (12 H, CH_2CH_3 and $CH_2CH_2CH_3$), 1.31–1.36 (18 H, *t*-Bu), 2.16 (6 H, s, SMe), 2.50–2.74 (2 H, CH_2), 3.04–3.20 (2 H, CH_2), 4.04–4.20 (2 H, CH), 7.08 (2 H, aromatic H), 7.80 (2 H, aromatic H).

Anal. Calcd for $C_{31}H_{46}S_2$: C, 77.11; H, 9.60. Found: C, 76.74; H, 9.59.

Preparation of Sulfonium Salt 6. Typical Procedure. A solution of 2.74 g (6 mmol) of the mixture of isomers **5h** in 50 mL of dichloromethane was added with stirring to a suspension of 6.5 g (40 mmol) of dimethoxymethylium fluoroborate in 10 mL of dichloromethane held at −30 °C under an atmosphere of nitrogen. The mixture was allowed to warm to room temperature and was stirred for additional 4 h. Then, to the reaction mixture was added 40 mL of ethyl acetate, the mixture was stirred, and the solvent was decanted. fresh ethyl acetate (20 mL) was added to the oily residue, and it was stirred for 2 h more. The resulting crystalline precipitate was collected and dried, giving 3.80 g (96%) of **6h**: colorless crystals; mp >300 °C; IR (KBr) 3020, 2950, 1590, 1470, 1420, 1360, 1275, 1040, 810, 710 cm^{-1}; NMR (Me_2SO-d_6) δ 0.20–0.40 (3 H, CH_2CH_3), 0.64–0.80 (3 H, CH_3), 1.09–1.24 (2 H, CH_2CH_3), 1.32 (18 H, *t*-Bu), 2.92 (6 H, SMe_2^+), 3.10–3.56 (4 H, CH_2), 3.33 (6 H, SMe_2^+), 4.56–4.92 (1 H, $CHSMe_2^+$), 7.28–7.60 (4 H, aromatic (4 H, aromatic H). The other sulfonium salts **6i–j** were obtained from **5i–j** by this manner.

6i: 98.8%; colorless crystals; mp 287–291 °C dec; IR (KBr) 3020, 2950, 1590, 1470, 1420, 1360, 1270, 1040, 870, 810, 710 cm^{-1}; NMR (Me_2SO-d_6) δ 0.40–1.28 (10 H, CH_3 and $CH_2CH_2CH_3$), 1.32–1.34 (18 H, *t*-Bu), 2.92 (6 H, SMe_2^+), 3.08–3.60 (4 H, CH_2), 3.32 (6 H, SMe_2^+), 4.58–4.93 (2 H, $CHSMe_2^+$), 7.44–7.56 (4 H, aromatic H).

6j: 99.8%; colorless crystals; mp 286–299 °C; IR (KBr) 3020, 1590, 1470, 1360, 1270, 1060, 870, 815, 770, 730 cm^{-1}; NMR (Me_2SO-d_6) δ 0.20–1.30 (12 H), 2.92 (6 H, SMe_2^+), 3.08–3.60 (4 H, CH_2), 3.32 (6 H, SMe_2^+), 3.68–3.93 (2 H, $CHSMe_2^+$), 7.30–7.60 (4 H, aromatic H).

Hofmann Elimination of 6 To Give 1. Typical Procedure. To a solution of 1.42 g (12.7 mmol) of potassium *tert*-butoxide in 120 mL of tetrahydrofuran there was added with stirring 2.52 g (3.81 mmol) of **6h**. After the reaction mixture was stirred at room temperature under a nitrogen atmosphere for 4 h, benzene was added, and the mixture was made acidic by addition of dilute aqueous hydrochloric acid. The organic layer was separated, washed with water, dried, and concentrated. The residue was chromatographed over silica gel with petroleum ether for elution to give 1.2 g (88.2%) of **1h**: dark green prisms; mp 166–167 °C dec; IR (KBr) 3040, 2960, 1590, 1455, 1365, 1355, 1220, 945, 875, 780, 660 cm^{-1}; NMR ($CDCl_3$) δ −3.98 (3 H, s), −3.73 (2 H, q, J = 7.5 Hz), −1.75 (3 H, t, J = 7.5 Hz), 1.66 (9 H, s), 1.68 (9 H, s), 8.20–8.64 (8 H, m); mass spectrum, m/e 358 (M^+).

Anal. Calcd for $C_{27}H_{34}$: C, 90.44; H, 9.56. Found: C, 89.90; H, 9.58.

Compounds **1i** and **1j** were obtained by this method.

1i: 91.5%; deep green prisms; mp 157–158 °C; IR (KBr) 3040, 2950, 1590, 1455, 1375, 1350, 1340, 1220, 880, 785, 675 cm^{-1}; NMR ($CDCl_3$) δ −4.0 (3 H, S), −3.84 to −3.66 (2 H, m), −1.65 to −1.40 (2 H, m), −0.56 (3 H, t, J = 7.5 Hz), 1.66 (9 H, s), 1.68 (9 H, s), 8.34 (2 H, d, J = 8 Hz), 8.46 (2 H, d, J = 8 Hz), 8.45 (2 H, s), 8.55 (2 H, s); mass spectrum, m/e 372 (M^+).

Anal. Calcd for $C_{28}H_{36}$: C, 90.26; H, 9.74. Found: C, 90.23; H, 9.69.

1j: 88.4%; deep brown prisms; mp 145–146 °C; IR (KBr) 3020, 2940, 1580, 1440, 1360, 1350, 1220, 1100, 950, 870, 775, 700, 655 cm^{-1}; NMR ($CDCl_3$) δ −3.76 to −3.56 (4 H, m), −1.74 (3 H, t, J = 7.5 Hz), −1.68 to −1.32 (2 H, m), −0.56 (3 H, t, J = 7.5 Hz), 1.66 (9 H, s), 1.67 (9 H, s), 7.38 (4 H, s), 7.49 (2 H, s), 7.52 (2 H, s); mass spectrum, m/e 386 (M^+).

Anal. Calcd for $C_{29}H_{38}$: C, 90.09; H, 9.91. Found: C, 89.90; H, 9.86.

Thermal Rearrangement of 1a. 2,7-Di-*tert*-butyl-10b,10c-dimethyl-*trans*-10b,10c-dihydropyrene (**1a**; 100 mg, 0.29 mmol) was placed in the sealed tube and was heated to about 210–220 °C for 5 min. The color of the reaction mixture had changed from deep green to yellow. After the reaction mixture was cooled and extracted with dichloromethane, the solvent was removed in vacuo to leave a residue which was chromatographed over an active alumina with hexane for elution to give pale yellow crystals. Recrystallization from MeOH–H_2O gave 67.4 mg (67.4%) of **8a**: yellow prisms (MeOH–H_2O); IR (KBr) 3030, 2950, 1620, 1600, 1460, 1350, 1210, 870, 805, 730, 670 cm^{-1}; NMR ($CDCl_3$) δ 1.05 (3 H, s), 1.08 (9 H, s), 1.28 (9 H, s), 1.28 (3 H, s), 5.43 (1 H, d, J = 1.5 Hz), 5.83 (1 H, d, J = 1.5 Hz), 5.98 (1 H, d, J = 10 Hz), 6.16 (1 H, d, J = 10 Hz), 6.32 (1 H, d, J = 10 Hz), 6.35 (1 H, d, J = 10 Hz), 6.88 (2 H, s); mass spectrum, m/e 344 (M^+).

Anal. Calcd for $C_{26}H_{32}$: C, 90.64; H, 9.36. Found: C, 90.36; H, 9.59.

Thermal Rearrangement of 1b. A solution off 100 mg (0.269 mmol) of **1b** in 200 mL of cyclohexane was refluxed for 62 h. After the reaction mixture was cooled, the solvent was removed in vacuo to leave a residue which was chromatographed over a silica gel with hexanne for elution to give pale yellow solid. Recrystallization

from MeOH–H_2O gave 75 mg (75%) of **8b**: pale yellow needles (MeOH–H_2O); mp 152–153 °C; IR (KBr) 3010, 2950, 1615, 1590, 1450, 1360, 1200, 870, 850, 810, 720 cm^{-1}; NMR ($CDCl_3$) δ 0.68 (3 H, t, J = 8 Hz), 0.76 (3 H, t, J = 8 Hz), 1.12 (9 H, s), 1.32 (9 H, s), 1.60–2.20 (4 H, m), 5.44 (1 H, d, J = 1.5 Hz), 5.87 (1 H, d, J = 1.5 Hz), 6.01 (1 H, d, J = 10 Hz), 6.23 (2 H, s), 6.38 (1 H, d, J = 10 Hz), 6.85 (1 H, d, J = 2 Hz), 6.90 (1 H, d, J = 2 Hz); mass spectrum, m/e 372 (M^+).

Anal. Calcd for $C_{28}H_{36}$: C, 90.26; H, 9.74. Found: C, 89.98; H, 9.75.

The yields of products were summarized in Table I. The thermal rearrangements of **1c–i** were carried out under the same conditions, worked up, and treated as described above.

8c: pale yellow needles (MeOH–H_2O); mp 162–164 °C; IR (KBr) 3020, 2950, 1610, 1590, 1450, 1350, 1260, 1200, 870, 850, 730, 675 cm^{-1}; NMR ($CDCl_3$) δ 0.64 (3 H, t, J = 7 Hz), 0.71 (3 H, t, J = 7 Hz), 1.11 (9 H, s), 1.32 (9 H, s), 0.96–1.40 (4 H, m), 1.60–2.10 (4 H, m), 5.43 (1 H, d, J = 1.5 Hz), 5.86 (1 H, d, J = 1.5 Hz), 6.01 (1 H, d, J = 10 Hz), 6.23 (2 H, s), 6.35 (1 H, d, J = 10 Hz), 6.85 (1 H, d, J = 2 Hz), 6.89 (1 H, d, J = 2 Hz); mass spectrum, m/e 400 (M^+).

Anal. Calcd for $C_{30}H_{40}$: C, 89.94; H, 10.06. Found: C, 89.60; H, 10.15.

8d: pale yellow prisims (MeOH–H_2O); mp 75–78 °C; IR (KBr) 3020, 2950, 1610, 1590, 1455, 1360, 1250, 1200, 875, 730 cm^{-1}; NMR ($CDCl_3$) δ 0.70 (3 H, t, J = 7 Hz), 0.75 (3 H, t, J = 7 Hz), 0.84–2.10 (12 H, m), 1.09 (9 H, s), 1.31 (9 H, s), 5.44 (1 H, d, J = 1.5 Hz), 5.86 (1 H, d, J = 1.5 Hz), 6.01 (1 H, d, J = 10 Hz), 6.23 (2 H, s), 6.36 (1 H, d, J = 10 Hz), 6.84 (1 H, d, J = 2 Hz), 6.88 (1 H, d, J = 2 Hz); mass spectrum, m/e 428 (M^+).

Anal. Calcd for $C_{32}H_{44}$: C, 89.65; H, 10.35. Found: C, 89.49; H, 10.16.

8e: yellow prisms (MeOH–H_2O); mp 180–182 °C; IR (KBr) 3040, 2950, 1620, 1590, 1450, 1360, 1260, 1230, 1195, 960, 875, 865, 850, 810 cm^{-1}; NMR ($CDCl_3$) δ 1.10 (3 H, s), 1.16 (9 H, s), 1.37 (3 H, s), 1.37 (9 H, s), 6.20 (1 H, d, J = 1.5 Hz), 6.60 (1 H, d, J = 1.5 Hz), 7.64 (1 H, d, J = 2 Hz), 7.76 (1 H, d, J = 2 Hz).

Anal. Calcd for $C_{26}H_{28}Br_4$: C, 47.30; H, 4.28. Found: C, 47.13; H, 4.40.

8f: pale brown needles (MeOH–H_2O); mp 148–149 °C; IR (KBr) 3040, 2950, 1620, 1590, 1450, 1360, 1255, 1020, 960, 875, 820, 775 cm^{-1}; NMR ($CDCl_3$) δ 0.68 (3 H, t, J = 8 Hz), 0.84 (3 H, t, J = 8 Hz), 1.17 (9 H, s), 1.37 (9 H, s), 1.60–2.28 (4 H, m), 6.22 (1 H, d, J = 1.5 Hz), 6.61 (1 H, d, J = 1.5 Hz), 7.61 (1 H, d, J = 2 Hz), 7.71 (1 H, d, J = 2 Hz).

Anal. Calcd for $C_{28}H_{32}Br_4$: C, 48.65; H, 4.69. Found: C, 48.76; H, 4.63.

8g: yellow prisms (MeOH–H_2O); mp 154–157 °C; IR (KBr) 3040, 2950, 1620, 1590, 1450, 1360, 1230, 1200, 960, 875, 860, 820, 840 cm^{-1}; NMR ($CDCl_3$) δ 0.67 (3 H, t, J = 7 Hz), 0.70 (3 H, t, J = 7 Hz), 1.16 (9 H, s), 1.38 (9 H, s), 1.00–1.40 (4 H, m), 1.60–2.10 (4 H, m), 6.22 (1 H, d, J = 1.5 Hz), 6.60 (1 H, d, J = 1.5 Hz), 7.62 (1 H, d, J = 2 Hz), 7.73 (1 H, d, J = 2 Hz).

Anal. Calcd for $C_{30}H_{36}Br_4$: C, 50.31; H, 5.07. Found: C, 50.20; H, 5.15.

8h: pale yellow needles (MeOH–H_2O); mp 155–156 °C; IR (KBr) 3030, 2960, 1620, 1475, 1460, 1370, 1360, 1350, 1205, 875, 860, 820, 730, 670 cm^{-1}; NMR ($CDCl_3$) δ 0.75 (3 H, t, J = 8 Hz), 1.11 (9 H, s), 1.27 (3 H, s), 1.30 (9 H, s), 1.86 (2 H, q, J = 8 Hz), 5.50 (1 H, d, J = 1.5 Hz), 5.86 (1 H, d, J = 1.5 Hz), 6.02 (1 H, d, J = 10 Hz), 6.16 (1 H, d, J = 10 Hz), 6.32 (1 H, d, J = 10 Hz), 6.40 (1 H, d, J = 10 Hz), 6.89 (2 H, s); mass spectrum m/e 358 (M^+).

Anal. Calcd for $C_{27}H_{34}$: C, 90.44; H, 9.56. Found: C, 89.96; H, 9.62.

8i: pale yellow needles (MeOH–H_2O); mp 128–130 °C; IR (KBr) 3020, 2950, 1615, 1455, 1355, 1200, 875, 860, 820, 730, 665 cm^{-1}; NMR ($CDCl_3$) δ 0.71 (3 H, t, J= 7 Hz), 1.11 (9 H, s), 1.26 (3 H, s), 1.32 (9 H, s), 0.96–1.40 (2 H, m), 1.50–1.90 (2 H, m), 5.50 (1 H, d, J = 1.5 Hz), 5.87 (1 H, d, J = 1.5 Hz)8 6.02 (1 H, d, J = 10 Hz), 6.18 (1 H, d, J = 10 Hz), 6.33 (1 H, d, J = 10 Hz), 6.38 (1 H, d, J = 10 Hz), 6.90 (2 H, s); mass spectrum, m/e 372 (M^+).

Anal. Calcd for $C_{28}H_{36}$: C, 90.26; H, 9.74. Found: C, 90.02; H, 9.74.

In the case of **1j**, a mixture of **8j** and **8k** was obtained in 90% yield. However, the attempt at separation of **8j** and **8k** failed.

Registry No. **1a**, 76626-75-0; **1b**, 76626-76-1; **1c**, 76626-77-2; **1d**, 81555-09-1; **1e**, 76447-51-3; **1f**, 76466-35-8; **1g**, 76626-78-3; **1h**, 81555-10-4; **1i**, 81555-11-5; **1j**, 81555-12-6; **4h**, 81600-81-9; **4i**, 81600-82-0; **4j**, 81600-83-1; **5h**, 76447-00-2; **5i**, 76447-01-3; **5j**, 76447-03-5; **6h**, 81583-53-1; **6i**, 81583-55-3; **6j**, 81583-57-5; **8a**, 81555-13-7; **8b**, 81555-14-8; **8c**, 81555-15-9; **8d**, 81555-16-0; **8e**, 81555-17-1; **8f**, 81555-18-2; **8g**, 81555-19-3; **8h**, 81555-20-6; **8i**, 81555-21-7; **8j**, 81555-22-8; **8k**, 81555-23-9.

Desulfurization of Alkyl Phthalimido Disulfides

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In the course of our investigation[3] of the coenzyme, lipoic acid (**2b**, Scheme I), we required thiophthalimide **4** for the attachment of the dihydrolipoate moiety to a thiamine analogue. Simple *N*-(alkylthio)phthalimides (cf. **4**) are generally prepared by the reaction of sulfenyl halides with potassium phthalate or phthalimide/Et_3N.[4] The reaction of **1**[5] with SO_2Cl_2, Cl_2 or Br_2 in attempts to form the required sulfenyl halide, however, gave methyl lipoate (**2a**) as the only product.

The successful synthesis of thiophthalimide **4**[3b] (Scheme I) entails the initial conversion of acetyldihydrolipoate **1** into alkyl phthalimido disulfide **3**,[6] followed by the selective monodesulfurization **3** → **4**. As shown Table I (entries 1–5), the monodesulfurization of secondary and tertiary alkyl phthalimido disulfides is achieved by a range of phosphines. Use of the polymeric phosphine (entry 3) described by Relles and Schluenz in the desulfurization reactions facilitates the separation of the desired alkyl thiophthalimide from the phosphine sulfide byproduct. The reaction of alkyl phthalimido disulfides with 1 equiv of the more nucleophilic tris(diethylamino)phosphine is not selective. Isopropyl phthalimido disulfide (Table I, entry 6) reacts with 1 equiv of $(Et_2N)_3P$ to give a mixture of starting disulfide plus the products of mono- and didesulfurization. In two cases examined (Table I, entries 7 and 8), 2 equivs of $(Et_2N)_3P$ was found to cleanly remove both sulfur atoms from alkyl phthalimido disulfides. At least one limitation of the procedure is shown by the reaction of 2-(methoxycarbonyl)ethyl phthalimido disulfide with $(Et_2N)_3P$ (Table I, entry 9) which yields phthalimide and the phosphine sulfide as the only characterizable

(1) Alfred P. Sloan Fellow, 1980–1982.

(2) Natural Sciences and Engineering Research Council of Canada, Predoctoral Fellow, 1980–1981.

(3) (a) Rastetter, W. H.; Adams, J.; Frost, J. W.; Nummy, L. J.; Frommer, J. E.; Roberts, K. B. *J. Am. Chem. Soc.* **1979**, *101*, 2752. (b) Rastetter, W. H.; Adams, J. *J. Org. Chem.* **1981**, *46*, 1882.

(4) (a) Behforouz, M.; Kerwood, J. E. *J. Org. Chem.* **1969**, *34*, 51. (b) Harpp, D. N.; Back, T. G. *Ibid.* **1971**, *36*, 3828.

(5) Gunsalus, I. C.; Barton, L. S.; Gruber, W. *J. Am. Chem. Soc.* **1956**, *78*, 1736. See also ref 3b.

(6) The alkyl phthalimido disulfides reported herein were prepared according to: Harpp, D. N.; Ash, D. K. *Int. J. Sulfur Chem., Part A* **1971**, *1*, 57.

(7) (a) Relles, H. M.; Schluenz, R. W. In "Polymer Supported Reactions in Organic Synthesis"; Hodge, P., Sherrington, D. C., Eds.; Wiley: New York, 1980; p 475. (b) Relles, H. M.; Schluenz, R. W. *J. Am. Chem. Soc.* **1974**, *96*, 6769.

0022-3263/82/1947-2785$01.25/0