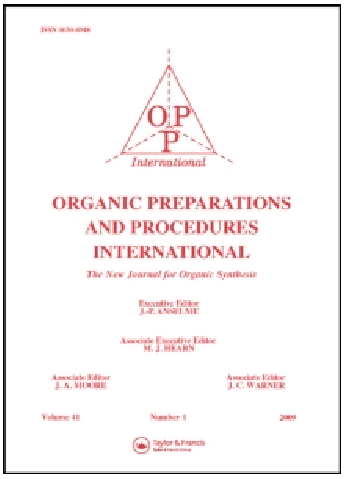

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SELECTIVE PREPARATION 29. PREPARATION OF 2,6-BIS(CHLOROMETHYL)- AND OF 2,6-BIS(MERCAPTOMETHYL)-4-SUBSTITUTED-TERT-BUTYLBENZENES†

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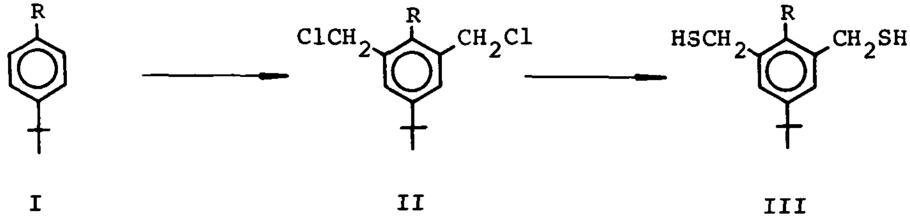
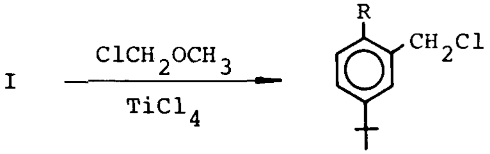
Mitchell and Boekelheide[1] reported that 2,6-bis(bromomethyl)- and 2,6-bis(mercaptomethyl)alkylbenzenes were good starting materials for the preparation of the corresponding [2,2]metacyclophanes. However, the preparative routes of both compounds are too long for the practical purposes. We now report a convenient preparation of 2,6-bis(chloromethyl)-(II) and 2,6-bis(mercaptomethyl)-4-substituted-*t*-butylbenzenes (III) from the corresponding 4-substituted-*t*-butylbenzenes (I) which were easily prepared from the corresponding substituted benzene (Ph-R).[2]



a: R = CH_3
b: R = CH_3CH_2
c: R = $CH_3CH_2CH_2$
d: R = OCH_3
e: R = F
f: R = Cl

It has been previously reported that[3] the chloromethylation of II with $ClCH_2OCH_3$ in the presence of $TiCl_4$ afforded the corresponding monochloromethyl derivatives (IV) but not II.

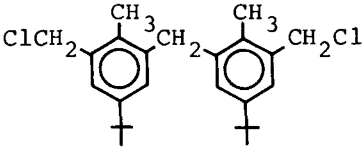


IV

TABLE Isolated Yields of II and III

	a	b	c	d	e	f
II	40	49	40	41	12	35
III	76	85	66	91	82	83

However, the chloromethylation[4] of I with $ClCH_2OCH_3$ in fuming H_2SO_4 gives the desired II (Table). In the case of Id, the chloromethylation was carried out with paraformaldehyde in the presence of HCl/H_3PO_4 to afford IId in 41% yield. In addition to the desired IIa, the chloromethylation of Ia yielded a small amount (5.2%) of 3,3'-bis(chloromethyl)2,2'-dimethyl-5,5'-di-t-butyldiphenylmethane (V).



V

When II was treated with thiourea in DMSO[5], the desired III were obtained in good yields.

From both types of compounds, some [2,2]metacyclophane derivatives were prepared in several steps. These results will be published in the near future.

EXPERIMENTAL

All melting points and boiling points are uncorrected. NMR spectra were determined at 60 MHz with a Hitachi R-20 NMR spectrometer with TMS as an internal reference. IR spectra were measured as KBr pellets or liquid film on NaCl plates on a Nippon Bunko IR-S spectrometer.

Chloromethylation of I. Typical Procedure.- To a mixture of 16.9 g (114 mmol) of Ia[4] and 75 ml of $ClCH_2OCH_3$ was added at refluxing temperature 30 ml of fuming H_2SO_4 (30 %) over period of 30 min. After the addition of fuming H_2SO_4, the reaction mixture was poured into a large amount of ice-water and extracted with dichloromethane. The extract CH_2Cl_2 solution was washed with water, dried over Na_2SO_4 and evaporated *in vacuo* to leave the residue which was extracted with hot hexane. The hot hexane extract was treated with activated carbon and cooled to room temperature to give 1.2 g (5.2 %) of V as colorless needles, mp. 165-166° (hexane); IR (KBr) 3040, 2960 cm^{-1}; NMR ($CDCl_3$): δ 1.20 (18H, s), 2.29 (6H, s), 3.96 (2H, s), 4.65 (4H, s), 6.83-7.20 (4H, m).

Anal. Calcd for $C_{25}H_{34}Cl_2$: C, 74.06; H, 8.45.
Found: C, 73.82; H, 8.52.

The filtrate was evaporated and distilled under reduced pressure to give 11.2 g (40.2 %) of IIa as colorless prisms bp. 137-140°/1 mm, mp. 75-76° (hexane).

Anal. Calcd for $C_{13}H_{18}Cl_2$: C, 63.70; H, 7.40.
Found: C, 63.79; H, 7.44.

IR (KBr): 3040, 2960, 1480, 1440, 1250, 740 cm^{-1}; NMR ($CDCl_3$):

δ 1.31 (9H, s), 2.44 (3H, s), 4.62 (4H, s), 7.31 (2H, s).

IIb: Colorless prisms, mp. 55-57° (hexane), bp. 140-144°/1 mm.
Anal. Calcd for $C_{14}H_{20}Cl_2$: C, 64.84; H, 7.78.
Found: C, 64.75; H, 7.85.

IR (KBr): 3040, 2960, 1480, 1445, 1255, 1200, 1050, 950, 880, 775, 680 cm^{-1}. NMR ($CDCl_3$): δ 1.24 (3H, t, J = 8 Hz), 1.29 (9H, s), 2.83 (2H, q, J = 8 Hz), 4.60 (4H, s), 7.25 (2H, s).

IIc: Colorless needles, mp. 85-87° (hexane), bp. 160-162°/1 mm.
Anal Calcd for $C_{15}H_{22}Cl_2$: C, 65.93; H, 8.12.
Found: C, 65.65; H, 8.12.

IR (KBr): 3040, 2960, 1480, 1450, 1260, 1200, 965, 890, 780, 725, 680 cm^{-1}. NMR ($CDCl_3$): δ 1.07 (3H, t, J = 7 Hz), 1.31 (9H, s), 1.43-1.74 (2H, m), 2.69-2.85 (2H, m), 4.60 (4H, s), 7.31 (2H, s).

IIe: Colorless prisms, mp. 72-74° (hexane), bp. 104-105°/1 mm.
Anal. Calcd for $C_{12}H_{15}Cl_2F$: C, 57.85; H, 6.07.
Found: C, 57.73; H, 6.39.

IR (KBr): 3040, 2960, 2550, 1480, 1360, 1250, 1200, 1100, 875, 815, 750 cm^{-1}. NMR ($CDCl_3$): δ 1.33 (9H, s), 4.60 (4H, s), 7.34 (2H, d, J = 7 Hz).

IIf: Colorless liquid, bp. 135-137°/1 mm.
Anal. Calcd for $C_{12}H_{15}Cl_3$: C, 54.26; H, 5.69.
Found: C, 54.09; H, 5.68.

IR (NaCl): 3040, 2960, 1440, 1360, 1260, 1230, 1140, 1040, 990, 890, 800, 750, 715, 680 cm^{-1}. NMR ($CDCl_3$): δ 1.32 (9H, s), 4.73 (4H, s), 7.51 (2H, s). In this case, 90 ml of fuming H_2SO_4

was used.

Preparation of IId.- After a mixture of 48.6 g (0.3 mol) of IId, 60 g (2 mole) of paraformaldehyde, 75 ml of acetic acid, 150 ml of H_3PO_4 (85 %) and 160 ml of conc. HCl (36 %) was heated at 85-90° under vigorous stirring for 12 hrs, the reaction mixture was extracted with benzene. The extract was neutralyzed with Na_2CO_3, washed with water, dried over Na_2SO_4 and evaporated in vacuo to leave the residue which was distilled to afford 32 g (41 %) of IIg as colorless needles (EtOH), mp. 76-77°, bp. 136-138°/3 mm.

Anal. Calcd for $C_{13}H_{18}Cl_2O_2$: C, 59.78; H, 6.95.

Found: C, 59.61; H, 6.93.

IR (KBr): 3040, 2960, 1480, 1440, 1270, 1215, 995, 890, 790, 700, 680 cm^{-1}. NMR (CCl_4); δ 1.28 (9H, s), 3.88 (3H, s), 4.60 (4H, s), 7.36 (2H, s).

The Preparation of III.Typical Procedure.- After a solution of 12.25 g (50 mmol) of IIa, 8.37 g (110 mmol) of thiourea in 75 ml of DMSO was stirred at room temperature under atmosphere of nitrogen for 14 hrs, the reaction mixture was poured into a solution of 25 g of NaOH in 250 ml of water, and then the solution was stirred for 1hr, acidified with 10 % HCl solution, and extracted with CH_2Cl_2. The CH_2Cl_2 solution was dried over Na_2SO_4 and evaporated in vacuo to give 9.1 g (75.8 %) of IIIa, as colorless prisms (hexane), mp. 90-91°.

Anal. Calcd for $C_{13}H_{20}S_2$: C, 64.94; H, 8.39.

Found: C, 65.20; H, 8.54.

IR (KBr): 3040, 2950, 2520, 1480, 1355, 1245, 1200, 970, 870, 735 cm^{-1}. NMR ($CDCl_3$): δ 1.28 (9H, s), 1.65 (2H, *t*, J = 8 Hz), 2.35 (3H, s), 3.72 (4H, d, J = 8 Hz), 7.12 (2H, s).

IIIb:Colorless liquid, bp. 143-145°/1 mm.

Anal. Calcd for $C_{14}H_{22}S_2$: C, 66.08; H, 8.72.
Found: C, 65.55; H, 8.72.

IR (NaCl): 3040, 2960, 2560, 1605, 1480, 1360, 1245, 1055, 880, 770 cm^{-1}. NMR ($CDCl_3$): δ 1.24 (3H, *t*, J = 8 Hz), 1.30 (9H, s), 1.72 (2H, *t*, J = 8 Hz), 2.78 (2H, q, J = 8 Hz), 3.75 (4H, d, J = 8 Hz), 7.10 (2H, s).

IIIc:Colorless liquid, bp. 146-148°/1 mm.

Anal. Calcd for $C_{15}H_{24}S_2$: C, 67.10; H, 9.01.
Found: C, 66.98; H, 9.04.

IR (NaCl): 3040, 2960, 2560, 1605, 1480, 1450, 1360, 1245, 980, 880, 730 cm^{-1}. NMR ($CDCl_3$): δ 1.06 (3H, *t*, J = 7 Hz), 1.28 (9H, s), 1.40-1.42 (2H, m), 1.72 (2H, *t*, J = 7 Hz), 2.69- 2.78 (2H, m), 3.74 (4H, d, J = 7 Hz), 7.16 (2H, s).

IIId:Colorless needles, mp. 81-82° (hexane).

Anal. Calcd for $C_{13}H_{20}S_2O_2$: C, 60.88; H, 7.86.
Found: C, 60.92; H, 7.88.

IR (KBr): 3040, 2950, 2550, 1480, 1250, 1205, 1100, 1000, 875, 810 cm^{-1}. NMR ($CDCl_3$): δ 1.30 (9H, s), 1.89 (2H, *t*, J = 8 Hz), 3.75 (4H, d, J = 8 Hz), 3.85 (3H, s), 7.20 (2H, s).

IVe: Colorless liquid, bp. 127-130°/1 mm.

Anal. Calcd for $C_{12}H_{17}S_2F$: C, 58.97; H, 7.01.
Found: C, 58.68; H, 6.98.

IR (NaCl): 3040, 2960, 2550, 1480, 1360, 1250, 1200, 1100, 875, 745 cm^{-1}. NMR ($CDCl_3$): δ 1.32 (9H, s), 1.90 (2H, *t*, J = 10 Hz), 3.76 (4H, d, J = 10 Hz), 7.26 (2H, d, J = 7 Hz).

IVf: Colorless liquid, bp. 145-147°/1 mm.

Anal. Calcd for $C_{12}H_{17}S_2Cl$: C, 55.25; H, 6.57.
Found: C, 55.03; H, 6.55.

IR (NaCl): 3040, 2960, 2530, 1959, 1450, 1360, 1250, 1140, 1040, 875, 800, 740 cm^{-1}. NMR ($CDCl_3$): δ 1.30 (9H, s), 1.97 (2H, *t*, J = 8 Hz), 3.85 (4H, d, J = 8 Hz), 7.32 (2H, s).

REFERENCES

† Part 28, M. Tashiro and Takehiko Yamato, Engineering Sciences Reports, Kyushu University, Vol. 1, No. 2, 13 (1980).

1. R. H. Mitchell and V. Boekelheide, J. Am. Chem. Soc., 96, 1547 (1973).
2. M. Tashiro and T. Yamato, J. Chem. Soc., Perkin I, 176 (1979).
3. M. Tashiro, T. Yamato and G. Fukata, J. Org. Chem., 43, 1413 (1978); see also H. B. Renfroe, J. A. Gurney and L. A. R. Hall, ibid., 37, 3045 (1972).
4. T. Otsubo, D. Stusche and V. Boekelheide, ibid., 43, 3446 (1978).
5. R. B. DuVernet, O. Wennerström; J. Lawson, T. Otsubo and V. Boekelheide, J. Am. Chem. Soc., 100, 2457 (1978).

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