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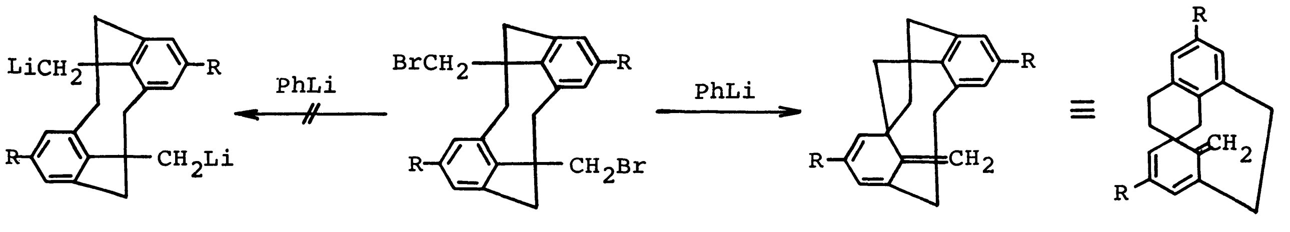
A NOVEL REACTION OF 8,16-BIS(BROMOMETHYL)[2.2]METACYCLOPHANES WITH PHENYL LITHIUM AND PREPARATION OF 8,16-UNSYMMETRICALLY DISUBSTITUTED [2.2]METACYCLOPHANES[1]

Masashi TASHIRO* and Takehiko YAMATO
Research Institute of Industrial Science, Kyushu University 86,
Hakozaki, Higashi-ku, Fukuoka 812

The reaction of 8,16-bis(bromomethyl)[2.2]metacyclophanes (2) with phenyl lithium in ethyl ether afforded the unexpected spiro compounds 3. It was also found that 8,16-unsymmetrically disubstituted [2.2]metacyclophanes 9 such as 8-methyl-16-halomethyl- and 8-methyl-16-methoxy derivatives were easily prepared from 3.

Recently, we have reported that[2] 8,16-bis(bromomethyl)[2.2]metacyclophanes (2) could be easily prepared by treatment of the corresponding 8,16-dimethyl derivatives with NBS.

We attempted to form 8,16-bis(lithiomethyl)[2.2]metacyclophanes from 2 with phenyl lithium. However, unexpected compound 3 was obtained in this reaction (Scheme 1). We wish to report the novel result in the present paper.



1 2 3

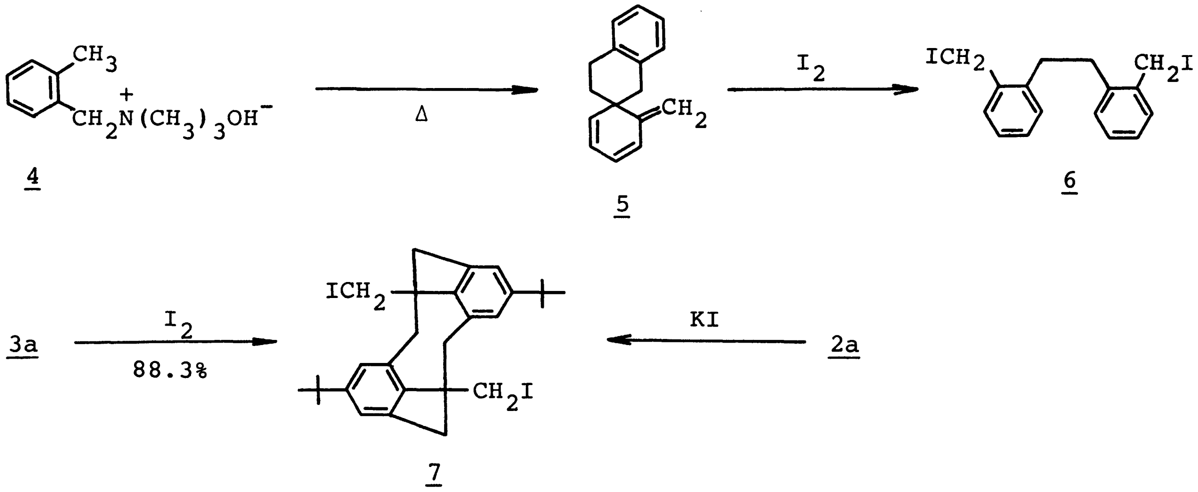
a: R=t-Bu (92.5%)

b: R=H (90%)

Scheme 1

When 2a-2b were treated with phenyl lithium in an ether solution, the unexpected products 3a-3b[3] were obtained, respectively. Typical procedure is shown below: To a solution of phenyl lithium (prepared from 25 mmol of bromobenzene and 50 mmol of lithium) in 30 ml of ether was added 1 mmol of 2a under refluxing conditions. After the reaction mixture was refluxed for additional 12 h, it was quenched with 10% ammonium chloride solution and extracted with dichloromethane. The extract was dried over sodium sulfate and evaporated in vacuo to leave the residue which was recrystallized from hexane to give 320 mg (92.5%) of 3a.

Errede has reported that[4] thermolysis of o-methylbenzyltrimethyl ammonium hydroxide (4) afforded spiro-(5,5)-2,3-benzo-6-methyleneundeca-7,9-diene (5) which was converted to the diiodide 6 with iodine. Similar treatment of 3a with iodine gave the bis(iodomethyl)metacyclophane 7 which[5] was previously obtained by halogen exchange reaction of 2a.

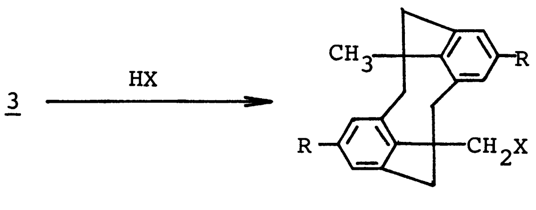


Scheme 2

It was also found that the reactions of 3a-3b with hydrogen halides, methanol in the presence of sulfuric acid, and acetic acid afforded the 8,16-unsymmetrically disubstituted [2.2]metacyclophanes (8a-8h),[7] respectively (Scheme 3).[6] The structures of 8a-8h were easily confirmed by their spectral data.

The structures of 3a and 3b were assumed by their spectral data and the comparison of their spectral data with those of 5 reported by Errede.[4] The chemical conversion of 3 described above strongly supports the sturucture proposed for 3.

Although mechanism of the formation of 3 from 2 is obscure, we propose the tentative mechanism as shown in Scheme 4.



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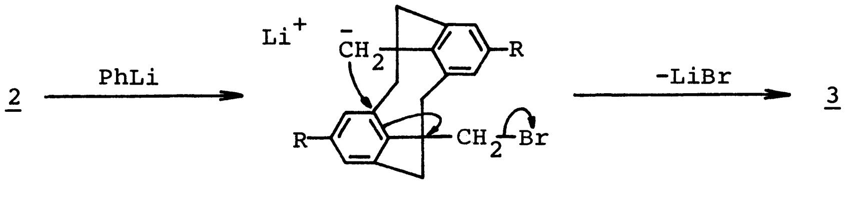
	Yield(%)	mp (°C)
a: R=t-Bu, X=Cl	66	271-273(d)
b: R=H, X=Cl	70	202-205(d)
c: R=t-Bu, X=Br	43	272-275(d)
d: R=H, X=Br	32	215-217(d)
e: R=t-Bu, $X=OCH_3$	79	183-184
f: R=H, $X=OCH_3$	90	146-149
g: R=t-Bu, $X=O\underset{\overset{\|}{O}}{C}CH_3$	68	178-180
h: R=H, $X=O\underset{\overset{\|}{O}}{C}\text{-}CH_3$	55	98-101

Scheme 3

The carbanion of an intermediate 9 might attack intramolecularly on the opposite aromatic ring to push out bromide ion from 9.



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Scheme 4

References

1. Metacyclophanes and Related Compounds. 3. Part 2. M. Tashiro and T. Yamato, to be published.
2. M. Tashiro and T. Yamato, J. Org. Chem., 46, 1543 (1981).
3. 3a: colorless prisms (hexane), mp 252-254°C, ^{1}H-NMR ($CDCl_3$) δ 1.07 (9H, s), 1.25 (9H, s), 1.82-3.15 (10H, m), 3.86 (1H, d, J = 1 Hz), 3.93 (1H, s), 5.73 (1H, d, J = 1 Hz), 5.92 (1H, s), 6.84 (1H, d, J = 1 Hz), 6.90 (1H, d, J = 1 Hz). Mass m/e 346 (M^+). UV (cyclohexane)λ_{max}(ε): 289 (2475), 268 (3094), 225 (11965).

   3b: colorless prisms (hexane), mp 101-102°C, ^{1}H-NMR ($CDCl_3$) δ 1.86-3.27 (10H, m), 3.96 (1H, d, J = 1 Hz), 4.05 (1H, s), 5.78-6.12 (3H, m), 6.80-7.10 (3H,

m). Mass m/e 234 (M^+). UV (cyclohexane)λ_{max}(ε): 290 (2996), 272 (2856), 225 (8291).

4. L. A. Errede, J. Am. Chem. Soc., 83, 949 (1961).
5. M. Tashiro and T. Yamato, J. Org. Chem., in press (1981).
6. After a mixture of 150 mg of 3a, 116.9 mg of iodine in 25 ml of carbon tetrachloride was stirred for 20 h at room temperature, it was evaporated in vacuo to leave the residue, to which was added a small amount of hexane to give 230 mg (88.3%) of 7.
7. 8a: colorless prisms (hexane), ^{1}H-NMR ($CDCl_3$) δ 0.58 (3H, s), 1.28 (9H, s), 1.32 (9H, s), 2.75-3.03 (8H, m), 3.07 (2H, s), 7.06 (2H, s), 7.15 (2H, s). Mass m/e 382, 384 (M^+).

   8b: colorless prisms (hexane), ^{1}H-NMR ($CDCl_3$) δ 0.57 (3H, s), 2.04-3.12 (8H, m), 3.05 (2H, s), 6.84-7.22 (6H, m). Mass m/e 270, 272 (M^+).

   8c: colorless prisms (hexane), ^{1}H-NMR ($CDCl_3$) δ 0.58 (3H, s), 1.28 (9H, s), 1.31 (9H, s), 2.76-3.02 (8H, m), 3.07 (2H, s), 7.06 (2H, s), 7.12 (2H, s). Mass m/e 426, 428 (M^+).

   8d: colorless prisms (hexane), ^{1}H-NMR ($CDCl_3$) δ 0.59 (3H, s), 2.68-3.14 (8H, m), 3.00 (2H, s), 6.84-7.22 (6H, m). Mass m/e 314, 316 (M^+).

   8e: colorless prisms (methanol), ^{1}H-NMR ($CDCl_3$) δ 0.58 (3H, s), 1.27 (9H, s), 1.33 (9H, s), 2.70 (2H, s), 2.87 (3H, s), 2.60-3.06 (8H, m), 7.04 (2H, s), 7.14 (2H, s). Mass m/e 378 (M^+).

   8f: colorless prisms (methanol), ^{1}H-NMR ($CDCl_3$) δ 0.57 (3H, s), 2.70 (2H, s), 2.77 (3H, s), 2.60-3.08 (8H, m), 6.82-7.19 (6H, m). Mass m/e 266 (M^+).

   8g: colorless prisms (methanol), ^{1}H-NMR ($CDCl_3$) δ 0.59 (3H, s), 1.28 (9H, s), 1.76 (3H, s), 2.72-3.06 (8H, m), 3.43 (2H, s), 7.08 (2H, s), 7.16 (2H, s). Mass m/e 406 (M^+).

   8h: colorless prisms (methanol), ^{1}H-NMR ($CDCl_3$) δ 0.58 (3H, s), 1.74 (3H, s), 2.68-3.06 (8H, m), 3.41 (2H, s), 6.88-7.22 (6H, m). Mass m/e 294 (M^+).

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