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The Preparation and Lithiation of 3,3-Diphenyl-1,1,2-tribromocyclopropane

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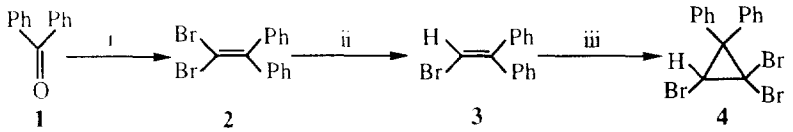
Abstract: 3,3-Diphenyl-1,1,2-tribromocyclopropane **4** was synthesized from benzophenone in three steps in an overall yield of 11.4%. Treatment of **4** with butyllithium in THF at low temperatures, generated 1-lithio- and 1,2-dilithiocyclopropenes which were characterized by their quenching products, **6**, **8**, **11**, and **12**.

3,3-Disubstituted and 3-monosubstituted polyhalogenocyclopropanes have been widely investigated,[1,2] mainly as precursors to vinyl carbenes[3] and highly strained vinyllithium compounds.[4,5] Recently, we[5] found that, upon lithiation, 3,3-dimethyltribromocyclopropane formed only monolithiocyclopropenes (at least three aggregates) in solution based on ^{13}C labeling, quenching, and low temperature CMR experiments. Dulayymi and Baird[6] reported that 1,1,2,2-tetrabromocyclopropane underwent ring opening to generate a vinyl carbene intermediate which could be trapped by alkenes to form vinyl- cyclopropane compounds. We now report the synthesis and lithiation of 3,3-diphenyl-1,1,2-tribromocyclopropane, in which the phenyl groups may interact with Li in the lithiated products.

Scheme 1 outlines the synthesis of 3,3-diphenyl-1,1,2-tribromocyclopropane.[7] We started the synthesis with commercially available benzophenone **1**. We first tried to convert **1** to **2** using



1 **2** **3** **4**

Scheme 1. The synthesis of **4**. Reagents and conditions: (**i**) 3.8 equiv. CBr_4, 8.3 equiv. PPh_3, C_6H_6, sealed bottle, 140°C, 50 h, 77%; (**ii**) 2.5 equiv. nBu_3SnH, pentane, Ar, 25°C, 24 h, 78%; (**iii**) excess $CHBr_3$, 50% aq. NaOH, cetrimide (catalyst), 5-10°C, then 25°C, 48 h, 19%.

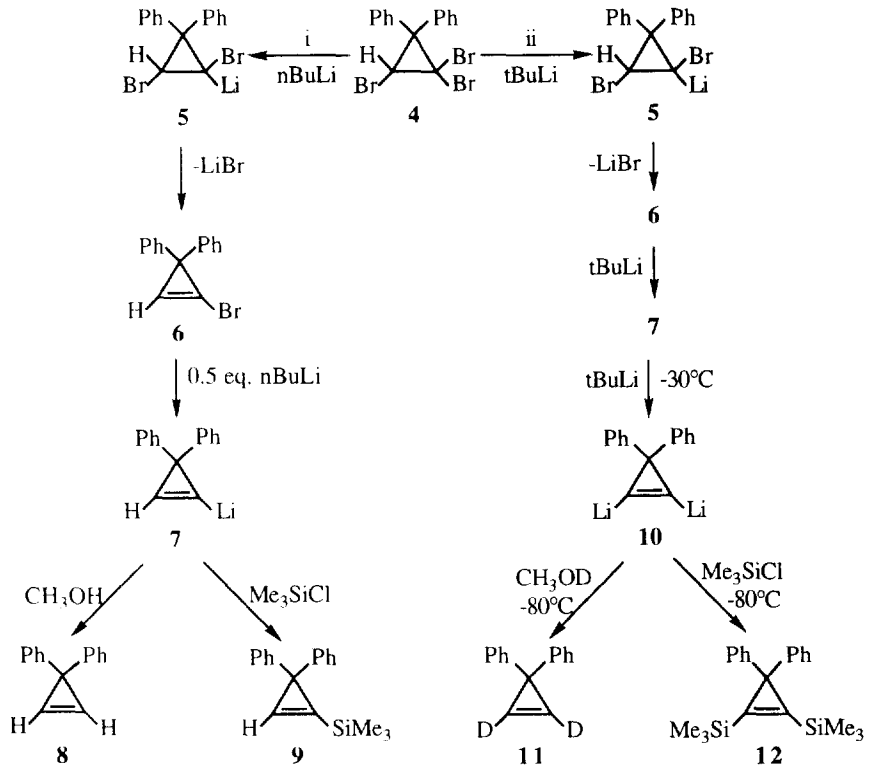
the general Wittig dihalomethylenation reaction conditions,[8] *i.e.*, dibromomethylenetriphenylphosphorane generated *in situ* from tetrabromomethane and triphenylphosphine in refluxing benzene. However, only a very low yield (about 15%) of difficult to purify **2** was obtained, probably due to steric hindrance by the phenyl groups. We improved the reaction by increasing the reaction temperature

in a sealed tube. In order to find the best reaction conditions, we mixed triphenylphosphine, benzophenone and benzene in a sealed thick-wall reaction bottle with magnetic stirring, then gently raised the oil bath temperature, and monitored the reaction progress by GC. The reaction was performed best at 140°C for 50 h, whereby the product was easy to separate and purify by either chromatography or recrystallization from methanol (77% yield). Next, one of the olefinic bromine atoms was replaced by hydrogen via tri-n-butyltin hydride (TBTH) reduction, either neat or in solution.[9, 10] For the reduction of **2** to **3**, our best conditions involved the addition of 2.5 equivalents of TBTH in several portions at room temperature using pentane as solvent, over 24 h. This demonstrates that **3** is relatively stable to reduction. After separation by chromatography and recrystallization from ethanol, we obtained pure **3** in 78% yield. Then we carried out the dibromocarbene cyclopropanation of **3** with bromoform using cetrimide as catalyst in aqueous base for 48 h to afford **4** in 19% yield.

The lithiation of **4**, summarized in Scheme 2, was performed in THF at low temperatures with butyllithium compounds, and was characterized by quenching and isolation of the products.[11] Thus 1.5 equiv. of nBuLi was dissolved in THF, then the solution cooled to below -100°C under argon, and a solution of **4** in THF added dropwise over 5 min. with magnetic stirring. After the solution was stirred for another 5 min., the reaction was quenched by addition of excess methanol. After separation by chromatography, **6** (about 70%) and **8** (about 50%) were obtained and characterized by H NMR, ^{13}C NMR and MS. This implies that **4** reacted with 1 equiv. of nBuLi to form **5**, which then eliminated LiBr to produce **6**, half of which reacted with the remaining nBuLi to form **7**, which was quenched by methanol to generate **8**. When MeOH was replaced by chlorotrimethylsilane as the quenching reagent, monosilane **9** was formed,[11] again supporting the intermediacy of monolithiocyclopropene **7**. In order to generate the 1,2-dilithiated **10**, we lithiated **4** with 3 equiv. of tBuLi, and raised the bath temperature to -30°C to let the third equiv. of tBuLi exchange with the C2 hydrogen in **7** to form **10**. After quenching, respectively, with excess MeOD and chlorotrimethylsilane at -80°C, **11** (35%) and **12** (30%) were obtained after separation by chromatography, which confirmed that 1,2-dilithiocyclopropene **10** was formed in solution. Thus phenyl groups, as well as methoxymethyl groups,[5] are able to assist in the formation of 1,2-dilithiocyclopropenes, whereas methyl groups cannot.

We defer any discussion of the structure of **7** and **10**, since we expect that they both exist in more than one aggregated state;[5, 12] NMR studies of suitably labelled versions of **7** and **10** will address this issue, and will be reported in due course.

Acknowledgments: We thank Professor Paul Vouros for providing CI-MS data for the title compound, and Mr. Fucheng Zhang for technical assistance.



Scheme 2. The lithiation of **4**. (**i**) 1.5 equiv. nBuLi, THF; (**ii**) 3 equiv. tBuLi, THF. The steps in both (**i**) and (**ii**) were performed at -100°C unless otherwise specified.

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7. Spectral/analytical data for new compounds: **2**: H-NMR ($CDCl_3$): δ7.27-7.35 (10 H, m, arom); m/e 338, 256, 178; mp. 82-82.5°C; **3**: H-NMR ($CDCl_3$): δ7.20-7.45 (10 H, m, arom), 6.79 (1 H, s); m/e 260, 258, 178; mp. 48-48.5°C; **4**: H-NMR ($CDCl_3$): δ7.20-7.60 (10 H, m, arom), 4.45 (1 H, s); ^{13}C-NMR ($CDCl_3$): δ141.9, 138.3, 130.2, 128.8, 128.4, 128.2, 127.6, 127.5, 47.1, 41.8, 38.9; CI-MS: m/e 432.86, 350.93, 271.00, 191.09; **Anal.**: Calcd. for $C_{15}H_{11}Br_3$: C, 41.81%; H, 2.57%; Br, 55.62%. Found: C, 41.71%; H, 2.59%; Br, 55.71%; mp. 120-120.5°C

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11. Data for new quench products: **6**: H NMR ($CDCl_3$): δ7.5-7.1 (10 H, m, arom.), 6.61 (1 H, s); ^{13}C-NMR ($CDCl_3$): δ131.0, 128.6, 127.7, 127.6, 126.2, 124.9, 124.1, 120.3, 38.2; **8**: H-NMR ($CDCl_3$): δ7.5-7.2 (10 H, m, arom.), 5.25 (2H, s); m/e 192, 165, 115; **11**: H-NMR ($CDCl_3$): δ7.45-7.25 (10 H, m, arom.); D-NMR (acetone): δ5.29 (2D, s); m/e 194, 167, 117; **12**: H-NMR ($CDCl_3$): δ7.35-7.15 (10 H, m, arom.), 1.22 (18 H, s); m/e 336, 248, 73; **9** was identified only by GC-MS, m/e 264, 189, 73.

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