Synthesis of 2,6-Diphenylbarbaralane by Oxidation of Dipotassium 2,6-Diphenylbicyclo[3.3.1]nonadienediide with 1,2-Dibromoethane. – Preparative Reversed-Phase Liquid Chromatography of Hydrocarbons[1]

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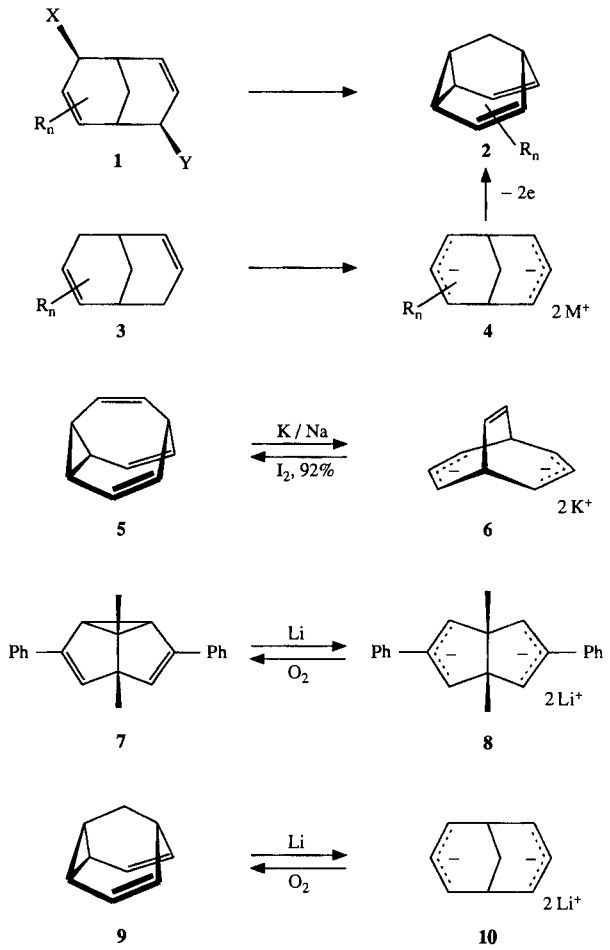
The diphenylbicyclo[3.3.1]nonadiene **11** is deprotonated by butylpotassium to afford the black-red crystalline dipotassium diphenylbicyclo[3.3.1]nonadienediide **12**. At low temperatures, **12** is oxidized in tetrahydrofuran solution by 1,2-dibromoethane yielding the diphenylbarbaralane **13** which is isolated in 57% yield on a 20-mmol scale after cyclic liquid chromatography on C18 reversed-phase silica gel with methanol. The packing procedure for suitable columns is also detailed.

The most versatile route to barbaralanes **2** has been pioneered by Fus, working in the group of Vogel[2], more than two decades ago. The final step of this synthesis involves cyclization of a substituted bicyclo[3.3.1]nona-2,6-diene **1** by a base-induced dehydrobromination. Subsequently, cyclization has been achieved by debromination with the zinc-copper couple[3,4]. As in the bicyclo[3.3.0]octadiene series[5], both cyclization reactions appear to follow a W- or semi-W-type mechanism like many 1,3-elimination reactions[6]. Therefore, only those precursors are potentially useful that possess the leaving groups in the *exo* configuration. Due to the preference for *exo* attack at the bicyclo[3.3.1]nonane skeleton, this requirement is met in the functionalization of bicyclo[3.3.1]nonadienes unless encumbering substituents are present. With an increasing number of substituents, however, the synthesis of suitable precursors **1** of highly substituted barbaralanes **2** becomes more and more difficult[7]. Therefore, a complementary methodology is desirable for such barbaralanes **2**. To this end, we have combined Goldstein's reversible charge control[8], which, for example, involves interconversion of bullvalene (**5**) and the bicyclic dianion **6** by electron transfer, with an efficient generation of the required 8π-electron dianions **4** by deprotonation of readily available bicyclic dienes **3**. We have developed this methodology using the known 2,6-diphenylbarbaralane **12**[9,10] as the target compound. Furthermore, we have adopted reversed-phase liquid chromatography to the preparative separation and purification of hydrocarbons which is also detailed here.



The interconversion of the diphenylsemibullvalene **7** and the dilithium bicyclo[3.3.0]octadienediide **8** by electron transfer has been reported by Müllen[11] and Schnieders[12]. Subsequently, the same procedure has been applied to the parent barbaralane (**9**) and dilithium bicyclo[3.3.1]nonadienediide (**10**) which is reoxidized by molecular oxygen to afford **9** as the main product. Attempts to reoxidize the corresponding diphenyl compound **12** (lithium instead of potassium) by molecular oxygen or iodine do not result in the formation of the recyclized barbaralane **13**. Instead, polymerization occurs[10]. Apparently, these theoretically interesting reactions have been carried out only in NMR sample-tube experiments for which experimental details are lacking. Nevertheless, they merit attention as a novel cyclization of a bicyclo[3.3.1]nonadiene derivative to a barbara-

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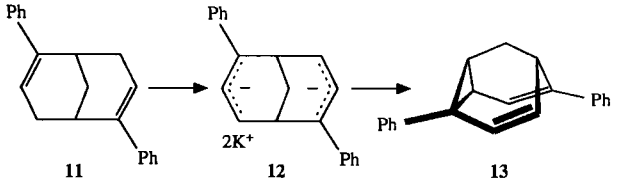
lane which does not require the previous introduction of leaving groups.

Because the diphenyldiene **11** is readily available and both, dipotassium bicyclononadienediide **12** and barbaralane **13** are well-known species, we have set out to realize the novel sequence **11** → **12** → **13** as a test of the projected barbaralane synthesis, notwithstanding previous failures to induce the step **12** (Li instead of K) → **13**[10]. When a solution of the diphenyldiene **11** in pentane is stirred with an excess of the Lochmann-Schlosser base[13,14], potassium *tert*-butoxide/butyllithium, the mixture turns very dark red, and the dipotassium salt **12** precipitates as a microcrystalline black-red powder which can be purified by dissolving in tetrahydrofuran and reprecipitating with pentane. The proton and carbon-13 spectra in [D_8]tetrahydrofuran are identical with those of the dipotassium salt **12** obtained by reduction of **13** with a potassium mirror[10].

When the deep red solution, prepared from crude **12** in tetrahydrofuran at −70 °C, is added dropwise to an excess of 1,2-dibromoethane in tetrahydrofuran, kept at the same temperature, the colour disappears immediately. A pale yellow solution is formed which contains only the barbaralane **13** besides traces of the diphenyldiene **11** as monitored by HPLC. Workup affords the barbaralane **13** as pale yellow crystals after chromatography on C18 reversed-phase silica gel with methanol. Inverse addition of the solutions gives also rise to the formation of **13**, which is accompanied by several unidentified byproducts, however. Similar results are obtained when the reaction is carried out below −80 °C or above −50 °C, or when hexachloroethane[15] or 1,2-dibromotetrachloroethane are used as the oxidant instead of 1,2-dibromoethane. Hexahaloethanes but not 1,2-dibromoethane have been employed previously in halogenation reactions of carbanions[15,16].

On the basis of the present results, it is difficult to distinguish between various mechanisms, e.g., the bromination of **12** followed by loss of bromide and cyclization on the one, and cyclization by electron transfer on the other hand. In view of similar cyclization reactions mentioned above[8,10–12], the latter mechanism seems more reasonable. We attribute the superiority of 1,2-dibromoethane over hexahaloethanes to a better fit between the HOMO and LUMO involved in the reaction or between the redox potentials of **12** and 1,2-dibromoethane.



Although the crude barbaralane **13** contains only a few percent of the diphenyldiene **11**, formed probably by the action of traces of moisture on the bicyclononadienediide **12**, a chromatographic method has been developed which allows the separation of **11** and **13** on a preparative scale. Because both compounds exhibit similar, very small retention times on silica gel chromatography with hydrocarbon solvents as eluents, we have resorted to reserved-phase chromatography which is well-established in the *analytical* separation of hydrocarbons[17]. The solvent mixtures methanol/water or acetonitrile/methanol/water, which separate **11** and **13** in the HPLC on C18-modified silica gel, are not suitable for the *preparative* separation because they do not dissolve **11** and **13** sufficiently to allow injection of a concentrated solution on the column. Injections of concentrated solutions, for example in tetrahydrofuran, result in crystallization and clogging of the column when methanol/water or acetonitrile/methanol/water mixtures are employed as eluents. Therefore, pure methanol has eventually been used though separation is less efficient, thus requiring several recycling steps (Figure 1). The small amounts of **11** in the crude barbaralane **13** can be readily separated by means of this technique, and barbaralane **13** has been obtained in 57% yield on a 20-mmol scale.

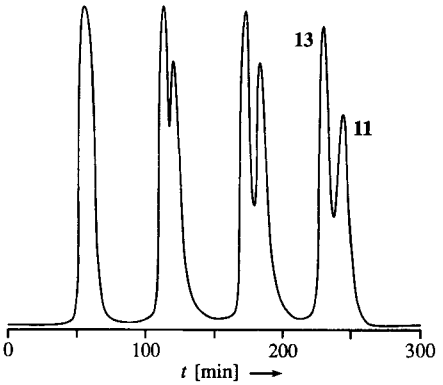


Figure 1. Separation of diphenylbicyclo[3.3.1]nonadiene **11** (0.5 g) and diphenylbarbaralane **13** (1.0 g) by cyclic medium-pressure liquid chromatography with methanol on a 70 × 6 cm column packed with C18 reversed-phase silica gel; ordinate: absorbance at 268 nm

The application of the novel cyclization methodology to the synthesis of 2,4,6,8-tetraphenylbarbaralane is the subject of a separate report[7].

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Experimental

Melting points: Sealed capillary tubes, apparatus from Büchi, Flawil, Switzerland. – High-performance liquid chromatography (HPLC): Bruker-Franzen LC 21-C equipped with a ChromScan and a Knauer UV detector 87.00 (λ = 268 nm), 250 × 4.6 mm stainless steel column packed with silica gel Europrep 60 C18, 10 μm (Knauer), 2 ml/min acetonitrile/methanol/water (35:53:12), retention time t_R [min]: 6.2 (**13**), 7.6 (**11**). – Flash chromatography: 40 × 4 cm glass column packed with silica gel 32–63 μm (ICN Biomedicals), pentane/ether (70:30), 1.8 bar, Knauer UV detector 87.00 (λ = 268 nm). – Preparative medium-pressure liquid chromatography (MPLC)[18–20]: Pump FC1 equipped with pump head K 110 and 0.2-l pulse damper, LEWA, Leonberg, 40 × 4 and 70 × 6 cm glass columns packed with silica gel Europrep 60–30 C18, 20–45 μm (Knauer), Knauer UV detector 87.00 with a 10-mm

super-preparative cell ($\lambda = 268$ nm). Digital registration and data processing with the program ChromStar of Bruker-Franzen.

Packing of a 70 × 6 cm Glass Column with C18 Reversed-Phase Silica Gel: The procedure given in ref.[18] for the packing of a 40 × 4 cm glass column with silica gel was modified. C18 reversed-phase silica gel Europrep 60–30 C18, 20–45 μm (Knauer) (1.8 kg) was suspended in degassed methanol/water (95:5; 4 l). After 0.5 h, the supernatant liquid was decanted by suction with a water aspirator. Degassed methanol/water (95:5; 1.5 l) was added again followed by shaking of the flask for 10 min until the suspension became homogeneous. After 0.5 h, the supernatant liquid was removed as before. This procedure was repeated eight times. A 70 × 6 and a 150 × 9 cm glass column, both thick-walled, were carefully rinsed with acetone, water, and again acetone followed by a solution of trimethylsilyl chloride (5 ml) in toluene (50 ml) which was eventually removed by means of acetone and water. The 150 × 9 cm glass column was attached on top of the 70 × 6 cm glass column by means of a PTFE adapter of 5 mm inner diameter. The lower column and $\frac{1}{4}$ of the upper column were filled with degassed methanol/water (95:5). The suspension of silica gel, prepared as described above, was introduced below the surface of the liquid by means of a 5-mm PTFE tubing. After most of the silica gel had settled through the PTFE adapter into the lower column (15–20 h), the upper column was replaced by a PTFE stopper connected to the solvent delivery system. Methanol/water (95:5) was pumped through the column at an initial pressure of 3 bar. When the surface of the silica gel reached the lower end of the narrow glass tube containing the PTFE stopper, pumping was interrupted and the narrow tube was refilled with the suspension of silica gel. Within several hours, the pressure was increased until a final pressure of 17 bar was reached (flow 63 ml/min) which was kept for additional 2 h. The number of plates N and the symmetry index SI were determined[21] with both acetone ($N = 9300$, $SI = 1.19$) and diethyl phthalate ($N = 5700$, $SI = 1.11$), and methanol/water (95:5) was used as eluent (63 ml/min at 17 bar).

A 40 × 4 cm glass column was packed in the same way. A 70 × 6 cm glass column was used as the upper column. The use of methanol/water (95:5; 62 ml/min at 19 bar) as eluent gave $N = 2100$, $SI = 1.35$ for acetone, and $N = 2000$, $SI = 1.27$ for diethyl phthalate.

Ether, pentane and tetrahydrofuran were distilled under argon from sodium/potassium alloy. Silica gel used for flash chromatography, water, and sodium sulfate were degassed and saturated with argon. 1,2-Dibromoethane was distilled from sodium hydride. Potassium *tert*-butoxide was sublimed twice at 10^{-2} Torr. All operations were carried out under argon. 2,6-Diphenylbicyclo[3.3.1]-nona-2,6-diene (**11**) was prepared according to ref.[9].

2,6-Diphenyltricyclo[3.3.1.0^{2,8}]nona-3,6-diene (**13**): A 250-ml two-necked flask equipped with a sintered glass funnel[22] was charged with **11** (5.45 g, 20.0 mmol) and potassium *tert*-butoxide (6.72 g, 60.0 mmol). A 1.56 M solution of butyllithium in hexane (48 ml, 72 mmol) was slowly added with stirring. The deep red suspension was stirred for 12 h. The microcrystalline black-red precipitate was filtered, washed with pentane (4 × 80 ml), dried for 10 min in a stream of argon, and cooled to −70°C. Tetrahydrofuran (200 ml) was added dropwise, because the dissolution was strongly exothermic, and the deep red mixture was stirred at −70°C for 1 h. This was added dropwise within 1 h (through a narrow PTFE tubing) to a vigorously stirred solution of 1,2-dibromoethane (5.2 ml, 60 mmol) in tetrahydrofuran (250 ml) kept at −70°C. Each drop was immediately decolourized. The resulting yellow solution was allowed to attain 20–25°C in 2 h. Ether (0.5 l) and water (0.3 l) were added, and the organic layer was extracted with water (2 × 0.3 l). Drying of the organic layer with sodium sulfate and distillation of the solvent in vacuo resulted in a yellow solid which, after flash chromatography, afforded a pale yellow solid. Two equal portions of this solid were dissolved in tetrahydrofuran (10 ml) and separated by reversed-phase MPLC into 3 fractions (40 × 4 cm glass column, 45 ml/min methanol at 16 bar). The third fractions were discarded. The combined first fractions and the combined second fractions were chromatographed separately on a 70 × 6 cm reversed-phase column with methanol as eluent (4 cycles with 40 ml/min at 20 bar) resulting in 1.20 g and 1.90 g, respectively, of lemon-coloured crystals (57%, m.p. 98–100°C, ref.[9] 108–110°C) which were pure according to HPLC and NMR.

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