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Convenient Synthesis of 5-Benzyl-2,3,5-trichloro-4,4-dimethoxycyclopent-2-en-1-one and Some Its Reactions

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Abstract—5-Benzyl-2,3,5-trichloro-4,4-dimethoxycyclopent-2-en-1-one was synthesized by reaction of 1,2,3,4-tetrachloro-5,5-dimethoxycyclopentadiene with benzyl alcohol in methylene chloride in the presence of powdered sodium hydroxide and benzyltrimethylammonium chloride as phase-transfer catalyst. Deprotection of the title compound gave 2-benzyl-2,4,5-trichlorocyclopent-4-ene-1,3-dione which was subjected to unusual intramolecular carbocyclization initiated by molecular iodine.

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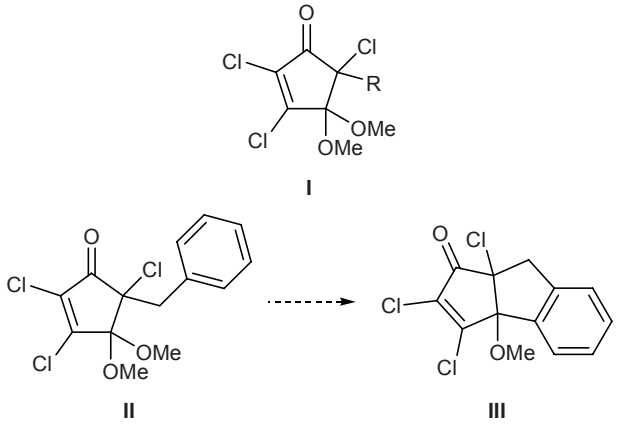
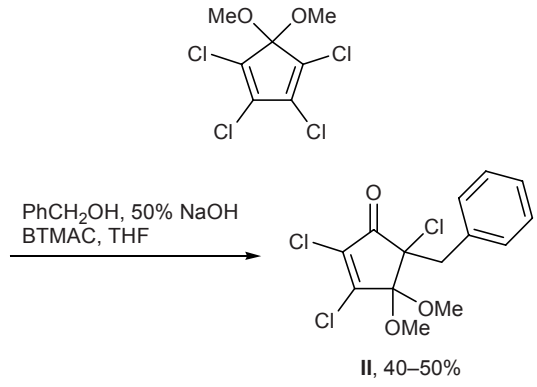
We recently [1] described convenient procedures for the transformations of hexachlorocyclopentadiene into practically important trichlorocyclopentenones **I** containing various substituents on C^5. In continuation of our studies on the synthetic potential of intramolecular carbocyclizations of trichlorocyclopentenones [2, 3], in the present work we focused on 5-benzyl derivative **II**. We anticipated that the presence in its molecule of two oxygen-containing centers and benzyl substituent will ensure generation and subsequent closure of oxycarbenium intermediates with formation of linearly fused tricyclic systems such as compound **III** (Scheme 1).

Scheme 1.



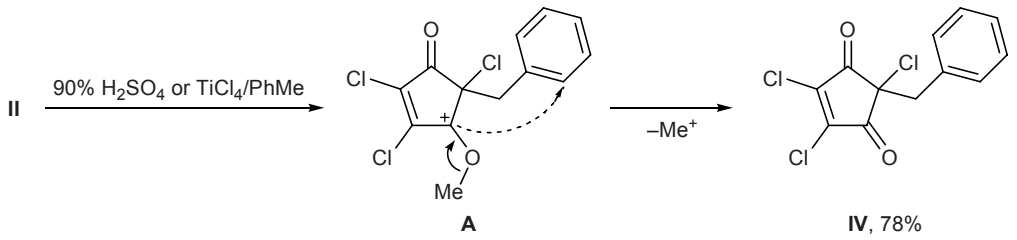
The procedure proposed previously [4] turned out to be inconvenient from the preparative viewpoint for the synthesis of a required amount of compound **II**. It involved the use of anhydrous dimethyl sulfoxide and preparation of sodium phenylmethanolate. We have found that benzyl derivative **II** can be successfully synthesized in a simpler way, under standard conditions of phase-transfer catalysis using KOH or NaOH, benzyl alcohol, and phase-transfer catalyst (Scheme 2). The yields of compound **II** thus obtained were comparable with those reported in [4], but the use of tetrahydrofuran or methylene chloride as solvent instead of difficultly removable DMSO considerably simplified the isolation procedure.

Scheme 2.

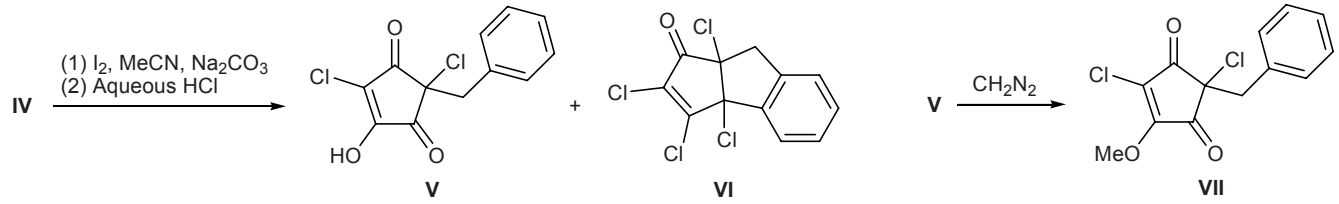


Having developed a convenient procedure for the preparation of ketone **II** we proceeded with studying possible ways of its carbocyclization. To generate carbenium ion at the acetal moiety of **II** we tried con-

Scheme 3.



Scheme 4.

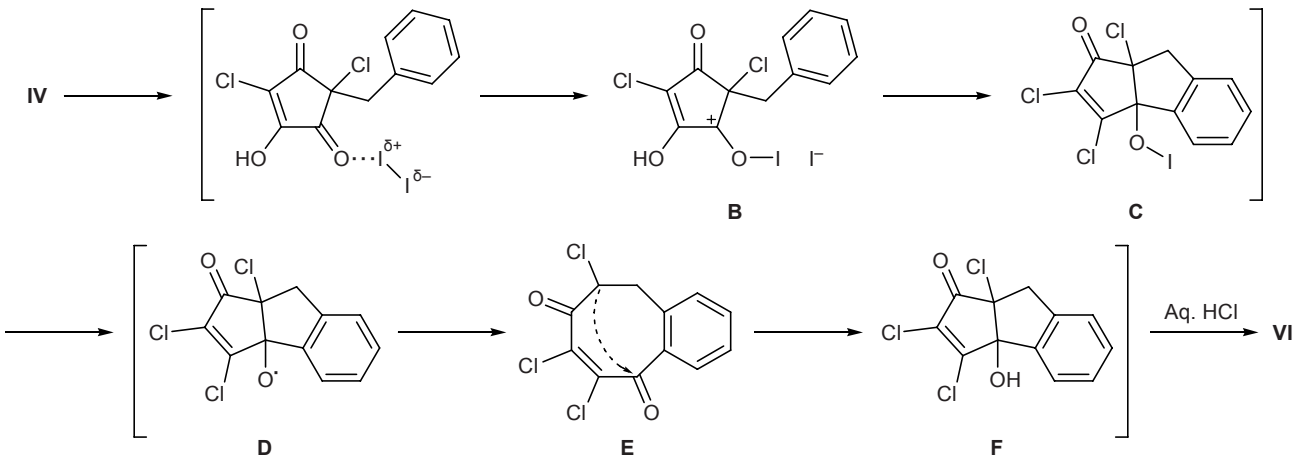


centrated sulfuric acid and titanium(IV) chloride. However, in no case the expected primary carbocation **A** was transformed into tricyclic compound **III**. Instead, loss of methyl cation led to the formation of cyclopentenedione derivative **IV** (Scheme 3). We succeeded in effecting the desired intramolecular cyclization with compound **IV**. For this purpose, it was treated with molecular iodine in acetonitrile. The reaction was slow, and it afforded 67% of enol **V** (67%) together with a minor amount of tricyclic compound **VI**. The structure of enol **V** was confirmed via methylation with diazomethane, which gave methoxy diketone **VII** in almost quantitative yield (Scheme 4).

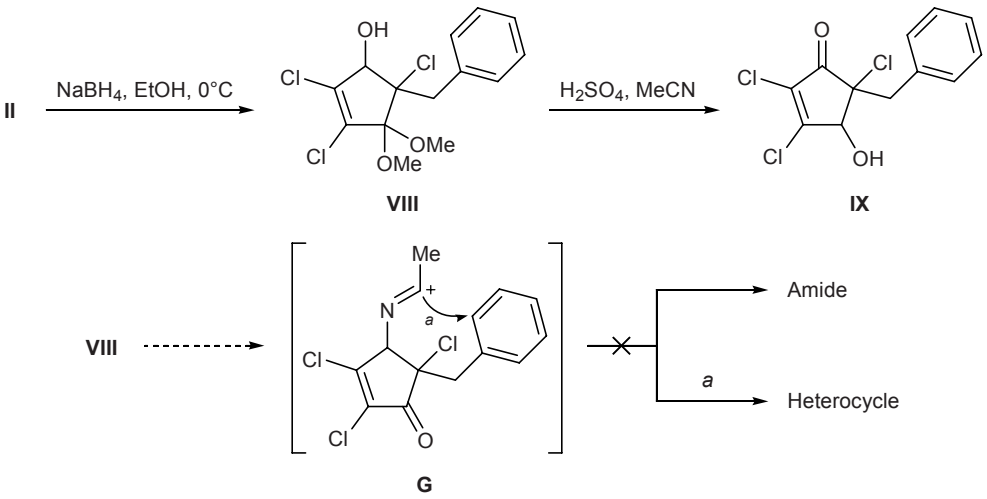
The mechanisms of formation of compounds **V** and **VI** are not clear. Hydroxy ketone **V** could be formed as a result of alkaline hydrolysis of **IV** at the C^3–Cl bond due to the presence of traces of moisture in the reaction mixture, though this version is strongly doubtful. As concerns the formation of tricyclic product **VI**, we have found no published analogies of intramolecular cyclization like **IV**→**VI**. We believe that the following mechanism is possible. The reaction of compound **IV** with I_2 gives rise to iodoxycarbenium ion **B** which is more stable than carbocation **A** (no elimination of I^+ occurs). Cation **B** undergoes intramolecular cyclization to produce tertiary hypoiodite **C**, and homolytic dissociation of the O–I bond gives alkoxy radical **D**. Fragmentation of the latter (presumably through intermediate **E**), followed by retro-aldolization–cyclization, yields tertiary alcohol **F** which is converted into tertiary chloride **VI** upon treatment of the reaction mixture with hydrochloric acid (Scheme 5).

While searching for other versions of intramolecular cyclization, ketone **II** was reduced to secondary alcohol **VIII** with sodium tetrahydridoborate, and alcohol **VIII** was brought into the Ritter reaction [5] with a view to generate iminocarbenium ion **G**. We believed that the latter is capable of being converted into the

Scheme 5.



Scheme 6.



corresponding amide or undergoing heterocyclization (Scheme 6). However, no expected transformation products of cation **G** were detected. The only product of the Ritter reaction was hydroxy ketone **IX**. Presumably, secondary carbocation **G** is not generated from alcohol **VIII** under these conditions.

EXPERIMENTAL

The IR spectra were recorded on UR-20 and Specord M-80 spectrometers from samples prepared as thin films or dispersed in mineral oil. The ^{1}H and ^{13}C NMR spectra were measured on a Bruker AM-300 instrument at 300 and 75.47 MHz, respectively, using $CDCl_3$ as solvent and TMS as internal reference. The mass spectra (electron impact, 70 eV) were obtained on a Thermo Finnigan MAT 95XP spectrometer (ion source temperature 200°C, sample injection temperature 5–270°C, temperature ramp 22 deg/min). Thin-layer chromatography was performed using Silufol and Sorbfil plates; spots were detected by calcination or spraying with an alkaline solution of potassium permanganate.

2-Benzyl-2,4,5-trichlorocyclopent-4-ene-1,3-dione (IV). *a*. Compound **II**, 0.2 g (0.66 mmol), was added to 5 ml of concentrated sulfuric acid cooled to 0°C, and the mixture was stirred for 2 h at 0°C and for 3–4 h at room temperature and extracted with chloroform (4×5 ml). The extracts were combined, washed with a solution of sodium chloride and a 5% solution of sodium hydrogen carbonate, dried over $MgSO_4$, and evaporated. The residue was recrystallized from ethyl acetate–petroleum ether (1:10). Yield 0.14 g (78%), colorless crystals, sublimes above 100°C. IR spectrum, ν, cm^{-1}: 511, 678, 835, 1201, 1270, 1234, 1568, 1724, 1741. ^{1}H NMR spectrum, δ, ppm: 3.54 s (2H, CH_2), 6.97 m (2H) and 7.22 m (3H, C_6H_5). ^{13}C NMR spectrum, δ_C, ppm: 41.81 (CH_2); 62.94 (C^2); 128.45, 129.08, 129.86, 131.63 (C_{arom}); 150.96 (C^5, C^4); 186.74 (C^1, C^3).

b. Compound **II**, 0.14 g (0.42 mmol), was dissolved in 10 ml of toluene, 0.28 g (1.45 mmol) of $TiCl_4$ was added, and the mixture was heated under reflux until the initial compound disappeared (~4–5 h, TLC). The mixture was then poured into ice water, the organic layer was separated, and the aqueous phase was extracted with chloroform (3×10 ml). The extracts were combined with the organic phase, washed with a solution of $NaHCO_3$ and a saturated solution of NaCl, dried over $MgSO_4$, and evaporated, and the residue was purified by recrystallization. Yield 0.06 mg (~50%).

Reaction of compound IV with iodine. Compound **IV**, 0.38 g (1.31 mmol), was dissolved in 10 ml of acetonitrile, 1.4 g (13.1 mmol) of anhydrous Na_2CO_3 and 1.66 g (6.53 mmol) of I_2 were added, and the mixture was stirred for ~2 h (until the initial compound disappeared according to the TLC data). The solvent was evaporated, the residue was treated with hydrochloric acid to pH 7 and extracted with chloroform (3×5 ml), and the extracts were combined, washed in succession with a solution of $Na_2S_2O_3$ (5 ml) and a saturated solution of NaCl (2×5 ml), dried over $MgSO_4$, and evaporated. The residue was subjected to column chromatography on silica gel using ethyl acetate–petroleum ether (1:20) as eluent to isolate 0.06 g (~15%) of compound **VI**. The aqueous phase was acidified to pH 3 with 30% hydrochloric acid and extracted with chloroform (4×5 ml), the extract was dried over $MgSO_4$, and evaporated, and the

residue was recrystallized from ethyl acetate–petroleum ether (1:10). Yield of compound **V** 0.24 g (~67%).

2-Benzyl-2,5-dichloro-4-hydroxycyclopent-4-ene-1,3-dione (V). Pale pink crystals, mp 157–160°C (from diethyl ether). IR spectrum, ν, cm^{-1}: 509, 601, 706, 748, 850, 1034, 1152, 1261, 1315, 1359, 1458, 1622, 1641, 1701, 1761, 3061, 3088, 3446. ^{1}H NMR spectrum (acetone-d_6), δ, ppm: 3.44 d.d (2H, CH_2, J = 13.1, 8.3 Hz), 6.99 br.s (2H) and 7.23 m (3H, C_6H_5). ^{13}C NMR spectrum (acetone-d_6), δ_C, ppm: 40.83 (CH_2); 63.49 (C^2); 126.15 (C^5); 127.67, 128.30, 129.66, 132.47 (C_{arom}); 164.21 (C^4); 186.28, 189.07 (C^1, C^3).

2,3,3a,8a-Tetrachloro-8,8a-dihydrocyclopenta-[*a*]inden-1-one (VI). Colorless crystals, mp 105–106.5°C (from diethyl ether). IR spectrum, ν, cm^{-1}: 673, 702, 887, 1132, 1192, 1238, 1377, 1463, 1587, 1753. ^{1}H NMR spectrum, δ, ppm: 3.64 d (1H, J = 17.98 Hz) and 3.85 d (1H, CH_2, J = 17.97 Hz); 7.22–7.42 m (2H), 7.42 m (1H), and 7.73 m (1H, C_6H_4). ^{13}C NMR spectrum, δ_C, ppm: 42.98 (CH_2); 74.75 (C^{8a}); 80.78 (C^{3a}); 125.21, 125.64, 128.73, 131.33, 136.96, 138.49 (C_{arom}); 131.52 (C^2); 161.02 (C^3); 188.49 (C=O). Mass spectrum, *m*/*z*: 306, 308, 310 $[M]^+$, 271, 273, 275 $[M - Cl]^+$, 236, 238 $[M - 2Cl]^+$, 243 $[M - Cl - CO]^+$, 173 $[M - CO - 3Cl]^+$.

2-Benzyl-2,5-dichloro-4-methoxycyclopent-4-ene-1,3-dione (VII) was obtained by treatment of 0.1 g (0.36 mmol) of compound **V** with diazomethane. Yield 0.1 g (>95%), yellow oily substance. ^{1}H NMR spectrum, δ, ppm: 3.49 d.d (2H, CH_2, J = 16.1, 13.0 Hz), 4.26 s (3H, OCH_3), 7.03 m (2H) and 7.24 m (3H, C_6H_5). ^{13}C NMR spectrum, δ_C, ppm: 41.59 (CH_2); 60.68 (OCH_3); 63.97 (C^2); 127.40 (C^5); 128.18, 128.85, 129.98, 132.40 (C_{arom}); 163.19 (C^4); 186.71, 189.09 (C^1, C^3).

5-Benzyl-2,3,5-trichloro-4,4-dimethoxycyclopent-2-en-1-ol (VIII). A suspension of 0.02 g (0.59 mmol) of $NaBH_4$ in 5 ml of methanol was cooled to 0°C, a solution of 0.1 g (0.59 mmol) of compound **II** in 3 ml of ethanol was added, and the mixture was stirred until the initial compound disappeared (TLC). The mixture was treated with 2 ml of water, the organic solvent was evaporated, and the residue was extracted with chloroform (4×5 ml). The extracts were combined, washed with a saturated solution of NaCl, dried over $MgSO_4$, and evaporated. Yield 0.06 g (60%), oily substance. ^{1}H NMR spectrum, δ, ppm: 2.20 d (1H, OH, J = 10.50 Hz), 3.32 d (1H, J = 14.50 Hz) and 3.43 d (1H, CH_2, J = 14.90 Hz), 3.48 s (3H) and 3.57 s (3H, OCH_3), 4.40 d (1H, OCH, J = 10.41 Hz), 7.31 m (5H, C_6H_5). ^{13}C NMR spectrum, δ_C, ppm: 42.49 (CH_2); 51.25, 51.96 (OMe); 77.25 (C^1); 81.85 (C^5); 104.93 (C^4); 127.03, 127.61, 130.98, 135.17 (C_{arom}); 136.12 (C^2, C^3).

5-Benzyl-2,3,5-trichloro-4-hydroxycyclopent-2-en-1-one (IX). A solution of 0.14 g (0.42 mmol) of compound **VIII** in 1 ml of acetonitrile was cooled to 0°C, 0.3 g (2.92 mmol) of concentrated sulfuric acid was added dropwise, and the mixture was heated to 35°C, stirred for 3 h at that temperature, cooled, and treated with 3 ml of ice water. Solid sodium carbonate, 0.2 g, was then added in portions, and the mixture was stirred for 5–10 min and extracted with diethyl ether (3×5 ml). The extracts were combined, dried over $MgSO_4$, and evaporated, and the residue was subjected to flash chromatography on silica gel using ethyl acetate–petroleum ether (1:1) as eluent. Yield 0.08 g (~70%), pale yellow oily substance. ^{1}H NMR spectrum, δ, ppm: 2.71 d (2H, OH, J = 10.60 Hz), 3.36 d (1H, J = 14.0 Hz) and 3.64 d (1H, CH_2, J = 14.0 Hz), 4.79 d (1H, OCH, J = 10.60 Hz), 7.21 m (2H) and 7.32 m (3H, C_6H_5). ^{13}C NMR spectrum, δ_C, ppm: 41.42 (CH_2); 72.67 (C^4); 73.99 (C^5); 128.01, 129.02, 130.58, 133.33 (C_{arom}); 131.92 (C^2); 161.66 (C^3); 189.01 (C^1).

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