Reaction of 4-methyl-4-tribromomethylcyclohexa-2,5-dien-1-one with zinc metal

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4-Methyl-4-tribromomethylcyclohexa-2,5-dien-1-one reacts with zinc dust in absolute DMF to give a mixture of 4-bromo-5-methylcyclohepta-2,4,6-trien-1-one, 4-methylcyclohepta-2,4,6-trien-1-one, and 4-dibromomethyl-4-methylcyclohexa-2,5-dien-1-one.

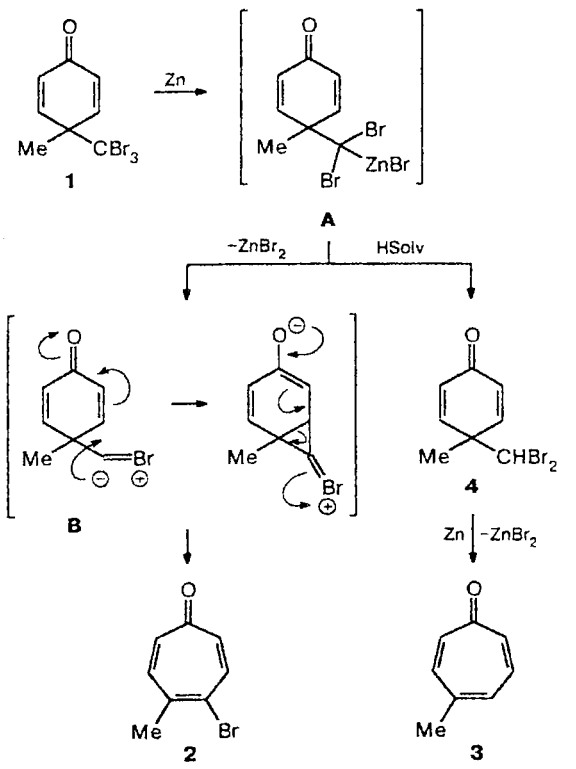
Key words: 4-methyl-4-tribromomethylcyclohexa-2,5-dien-1-one, reaction with zinc metal; 4-bromo-5-methyltropone, 4-methyltropone, mechanism of formation.

Reaction of 4-dibromomethylcyclohexa-2,5-dien-1-one with zinc gives methyltropones.[1,2] We have found that reaction of 4-methyl-4-tribromomethylcyclohexa-2,5-dien-1-one (**1**) with Zn in DMF, carried out under argon at room temperature, leads to three products: 4-bromo-5-methyltropone (**2**), 4-methyltropone (**3**), and 4-dibromomethyl-4-methylcyclohexa-2,5-dien-1-one (**4**). The possible pathways of the product formation are presented in Scheme 1.

At the first step of the reaction, insertion of a Zn atom into the C—Br bond of dienone **1** occurs, and unstable intermediate **A** is formed, which further reacts along two pathways. As a result of elimination of $ZnBr_2$ cyclodienone **A** is converted to bromocarbene intermediate **B**, which experiences an intramolecular nucleophilic addition to the activated double bond. The subsequent rearrangement gives stable bromomethyltropone **2**.

An alternative pathway for transformation of the intermediate **A** is solvolysis of the C—Zn bond giving dibromomethylcyclohexadienone **4**. In this case, DMF may be the proton source.[3] Further product **4** reacts with Zn to give 4-methyltropone **3** (see Scheme 1). We have previously reported such a transformation.[2] In our opinion, isolation of dibromomethylsubstituted dienone **4**, confirms unambiguously the initial formation of the intermediate **A**.

Scheme 1



Experimental

4-Methyl-4-tribromomethylcyclohexa-2,5-dien-1-one (1) was obtained by reaction of *p*-cresol with CBr_4 and $AlBr_3$ (yield 16%) using an earlier reported procedure.[4] The melting point and spectral characteristics of product **1** are consistent with the literature data.[5]

Reaction of compound 1 with Zn metal. Compound **1** (0.27 g, 0.75 mmol) and Zn dust (0.146 g, 2.25 mmol) in absolute DMF (1.0 mL) were stirred for 2 h at ~20 °C under argon, until the reaction was completed (TLC monitoring on Silufol UV-254 plates). The resulting mixture was quenched with water and extracted with ether. The products were separated using preparative TLC on silica gel (benzene—ether (3 : 2) as the eluent).

A fraction with R_f 0.64 contained **dienone 4**, yield 24 mg (8.6%), m.p. 65.5 °C (from hexane) (*cf.* Ref. 6). IR (Nujol), ν/cm^{-1}: 1670 (C=O). UV (EtOH), λ_{max}/nm (ε): 232 (13600), 390 (24). ^1H NMR ($CDCl_3$), δ: 1.46 (s, 3 H, Me); 5.63 (s, 1 H, $CHBr_2$); 6.35 (d, 2 H, H(2), H(6), $^3J_{H(2),H(3)}$ = 10 Hz); 6.90 (d, 2 H, H(3), H(5), $^3J_{H(3),H(2)}$ = 10 Hz).

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A fraction with R_f 0.25 contained **4-bromo-5-methyltropone** (2), yield 90 mg (45%), m.p. 80 °C (after recrystallization from benzene). IR (Nujol), ν/cm^{-1}: 1650 (C=O). UV (EtOH), λ_{max}/nm (ε): 237 (16980), 328 (7580). ^1H NMR ($CDCl_3$), δ: 2.47 (s, 3 H, Me); 6.68 (dd, H(2), $^3J_{H(2),H(3)}$ = 12.5 Hz, $^4J_{H(2),H(7)}$ = 3 Hz); 6.86 (dd, H(7), $^3J_{H(7),H(6)}$ = 12.5 Hz, $^4J_{H(7),H(2)}$ = 3 Hz); 7.05 (d, H(6), $^3J_{H(6),H(7)}$ = 12.5 Hz); 7.48 (d, H(3), $^3J_{H(3),H(2)}$ = 12.5 Hz). The compound obtained is similar to that earlier reported.[5]

A fraction with R_f 0.12 contained **4-methyltropone** (3) that was isolated as a yellow light oil; yield 24 mg (20%). ^1H NMR ($CDCl_3$), δ: 2.27 (H(4), $^4J_{H(4),H(5)}$ = 1.3 Hz, $^6J_{H(4),H(7)}$ = 0.7 Hz); 6.82 (H(5), $^3J_{H(5),H(6)}$ = 8.3 Hz, $^4J_{H(5),H(7)}$ = 1.2 Hz); 6.91 (H(7), $J_{H(7),H(6)}$ = 12.0 Hz); 6.95 (H(3), $^4J_{H(3),H(5)}$ = 1.7 Hz); 6.99 (H(2), $^3J_{H(2),H(3)}$ = 12.6 Hz, $^5J_{H(2),H(5)}$ = 0.5 Hz, $^4J_{H(2),H(7)}$ = 1.9 Hz); 7.01 (H(6), $J_{H(6),H(5)}$ = 8.3 Hz). MS, m/z: 120 [M^+]. The compound obtained is similar to that earlier reported.[1]

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Germylated steroids
1. Hydrogermylation of conjugated steroid enones

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Steroids germylated in position 16 were prepared for the first time by hydrogermylation of conjugated steroid enones. The addition of trichlorogermane to a conjugated Δ^{16}-double bond leads not only to an α-isomer, which is typical of steroids, but to a β-isomer as well. The isolated Δ^5-double bond is not involved in this reaction.

Key words: organogermanium compounds, germylated steroids.

Significant interest has been drawn in recent years to the biological effects of organogermanium compounds.[1] We might consider 1968, when the biological activity of 2-carboxyethylgermaniumsesquioxide was discovered,[2] as the beginning of the use of organogermanium compounds in medicine. Since that time, intense studies into the synthesis and biological action of organogermanium compounds have been carried out, and over a thousand papers and patents, including reviews and monographs, have been published. As a result, a lot of organogermanium compounds have been synthesized that possess antitumor and antiviral properties, serve as inductors of interferon and activators of macrophages, display the immuno-modulating effect, *etc.* At the same time, organogermanium compounds, unlike organosilicon and organotin compounds, are virtually nontoxic.

The compound that has been studied most thoroughly and used most widely is 2-carboxyethylgermaniumsesquioxide (trademark Ge-132), already mentioned above. This compound is synthesized by the hydrogermylation of acrylic acid with trichlorogermane followed by hydrolysis. This procedure was first suggested in Russia.[3]

There are no germanium-substituted natural compounds, steroids in particular, among the organogermanium compounds obtained to date. Although ste-

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