

Electrochemical Reduction of 4-Methyl-4-(trichloromethyl)cyclohexa-2,5-dien-1-one

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Abstract—The properties of 4-methyl-4-(trichloromethyl)cyclohexa-2,5-dien-1-one which contains the trichloromethyl substituent at a quaternary carbon atom have been studied by cyclic voltammetry, rotating disk electrode voltammetry, and preparative electrolysis. Reductive dehalogenation involves initial two-electron reductive elimination of one of the geminal chlorine atoms followed by consecutive addition of proton, simultaneous elimination of the two residual halogen atoms to form carbene, and rearrangement of cyclohexadienone into the corresponding 4-methylcyclohepta-2,4,6-trien-1-one.

Keywords: cyclohexadienones, cathodic dehalogenation, 4-methylcyclohepta-2,4,6-trien-1-one (tropone)

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One of the transformation routes of the trichloromethyl substituent in organic compounds involves its reduction in the presence of radical initiators, which not infrequently leads to unusual results. Allyl trichloroacetate in the presence of $\text{Fe}(\text{CO})_5$ and methyl ester of *N*-benzoyl-L-proline undergoes cyclization to give a dihalo-substituted γ -lacton, whereas treatment with Bu_3SnH –AIBN results in reductive monodehalogenation of the trichloromethyl group [1]. Treatment of *N*-allyl-2,2,2-trichloroacetamide with Bu_3SnH –AIBN gives rise to *N*-allyl-2,2-dichloroacetamide and cyclization products, specifically pyrrolidones with geminal chlorine substituents in the ring, which are substituted by hydrogens in the presence of excess reagent [2]. Treatment of *N*-substituted trichloroacetamides with Ni –AcOH leads to cleavage of one C–Cl bond, and the resulting radicals undergo further chemical transformations to form unsaturated hydroindolones; the reaction in the presence of $\text{Cu}(\text{OAc})_2$ yields dichlorohydroindolones which can further transform into functionalized indoles [3]. The latter are necessary starting materials for the synthesis of 3-demethoxyerythridinone, an alkaloid isolated from *Erythrina lithosperma* and showing curare-like activity [4]. The reactions of 3-[2-(trichloromethylcarbonyl)phenyl]sydnone with RLi ($\text{R} = \text{Me}, \text{Bu}, \text{Ph}$), too, involve cleavage of only one C–Cl bond to form 3-[2-(dichloromethylcarbonyl)phenyl]sydnone [5].

Frank et al. [6] proposed an original method to epimerize D-fructose to a rare monosaccharide D-tartrate with simultaneous substitution, which consists in tethering two fructose hydroxyls by a trichloromethylethylidene bridge with subsequent complete reduction of C–Cl bonds under the action of Bu_3SnH –AIBN. This synthetic approach was later developed by Hager et al. [7, 8], who proposed procedures for introducing substituents in any position of monosaccharide molecules. Trichloroacetylation of a poorly reactive C^4 -OH group in D-glucuronic acid followed reduction with Bu_3SnH –AIBN to form *N*-acetyl derivative was applied in the synthesis of chondroitin sulfates [9–11] which are present in connective tissues of animals and show anti-inflammatory, analgesic, and tissue regenerative activity [12]. In view of the aforesaid, we considered it actual to model $\text{RCCl}_3 \rightarrow \text{RCCl}_2$ transformations.

Proceeding with the research on electrochemical dehalogenation [13–16], we have studied reductive dehalogenation of 4-methyl-4-(trichloromethyl)cyclohexa-2,5-dien-1-one which contains the trichloromethyl substituent at a quaternary carbon atom by cyclic voltammetry (CV), rotating disk electrode voltammetry (RDEV), and preparative electrolysis.

Previously we showed that cathodic reactions of side-chain or ring halogenated substituents in cyclohexadienones occur by different mechanisms depending on

the number and position of the halogen atoms in the dienone molecule. Reductive dehalogenation of two halogens in the 5-dibromomethyl substituent in 2-bromo-5-(dibromomethyl)-4-(dichloromethyl)-4-methylcyclohexa-2,5-diene-1-one occurs stepwise and involves addition of two electrons, protonation of the resulting carbanion, and elimination of one halogen (in total $+2e^-$, $+H^+$, $-Hlg^-$) at each step, like previously described for polychloromethanes (CH_2Cl_2 , $CHCl_3$, CCl_4) and polychloroacetonitriles ($NCCHCl_2$, $NCCHCl_3$) [16]. The same sequence is observed on cathodic debromination of 2-bromo- and 2,6-dibromo-4,4-dimethylcyclohexa-2,5-dien-1-ones, where bromines are α to the cyclohexadienone carbonyl group [14]. Thus, the redox reactions occur as consecutive reductive dehalogenation, and the reaction products retain the cyclohexadienone structural fragment.

However, the electrochemical reduction of cyclohexa-2,5-dien-1-ones **VI** and **VII**, in which the mono- or dihalomethyl fragment at the quaternary carbon atom C^4 is not conjugated with the ring π system, does not destroy the cyclohexadienone ring. The first, two-electron stage of the reductive dehalogenation of cyclohexa-2,5-dien-1-ones with the monohalomethyl substituent forms carbanion which undergoes anionic cyclopropyl-allyl rearrangement followed by proton addition to give 3,4-dimethylphenol (**VIII**) [14]. In the case of the dichloromethyl (or dibromomethyl substituent, neopentyl *gem*-dihalides undergo one-stage two-electron reductive elimination not involving protons ($+2e^-$, $-2Hlg^-$), and the carbene intermediate attacks the neighboring double bond in the ring, resulting in ring extension and formation of tropone **III** [15].

Reduction potentials of compounds **I–III**, measured by CV [Ag|AgCl|sat KCl] on a glassy carbon electrode in DMF in the presence of 0.1 M Bu_4NClO_4 ^a

Comp. no.	E_{pc} , V
I	–1.30 (1.13) ^b , –1.43 (1.13) ^b , 1.51 (–1.45, –0.36), –2.36
VI [17]	–1.44 (1.16) ^b , 1.52 (–1.46, –0.36), –2.37
III [17]	–1.52 (1.46), –0.45, –0.33, –2.37

^a (E_{pc}) Cathodic peak potentials (200 mV/s), the values in parentheses are the reverse peak potentials. ^b Reoxidation of Cl^- .

In the present work, we studied electrochemically-induced transformations of 4-methyl-4-(trichloromethyl)cyclohexa-2,5-dien-1-one (**I**) by means of CV and RDEV on glassy carbon and platinum electrodes. The resulting data are shown in the table, and the CV curves are presented in Figs. 1 and 2. The suggested mechanism of the electrochemical reduction is depicted in the scheme.

Compound **I** was not oxidized on a glassy carbon electrode in the operating potential range, which allowed us to trace reductive elimination of Cl^- by its reoxidation peaks appearing after corresponding cathodic peaks in the anodic region, when the direction of the potential sweep was reversed. The cathodic branch of the CV curve of compound **I** contained four peaks, the first two peaks relating to two-electron stages. In the reverse scan, Cl^- reoxidation (E_p 1.13 V) was observed after the potential of the first peak. This result implies that Cl^- eliminates already at the first stage. As shown in Scheme 1, there are several routes

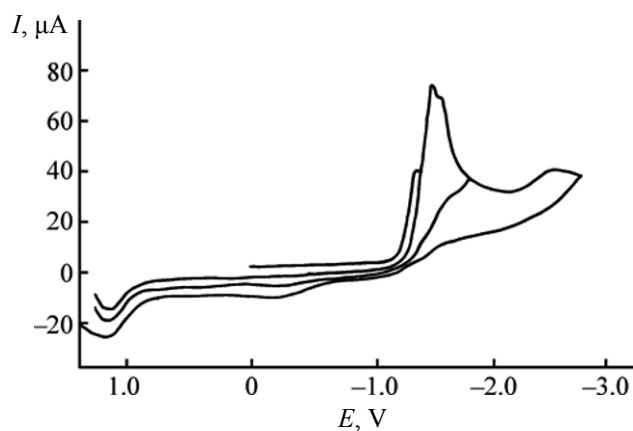


Fig. 1. Cyclic voltammograms of 4-methyl-4-(trichloromethyl)-2,5-dien-1-one (**I**), $c \ 2 \times 10^{-3}$ M. Glassy carbon electrode, DMF, 0.1 M Bu_4NClO_4 .

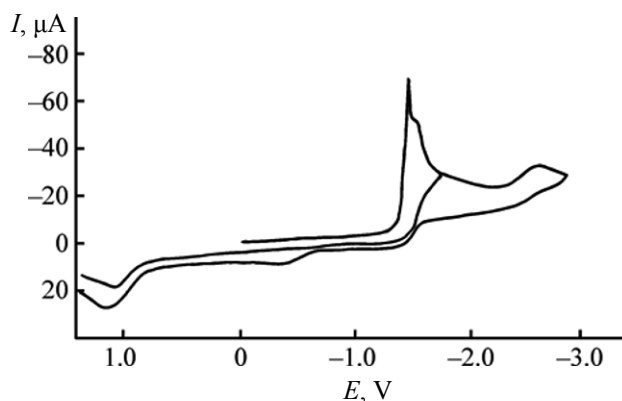
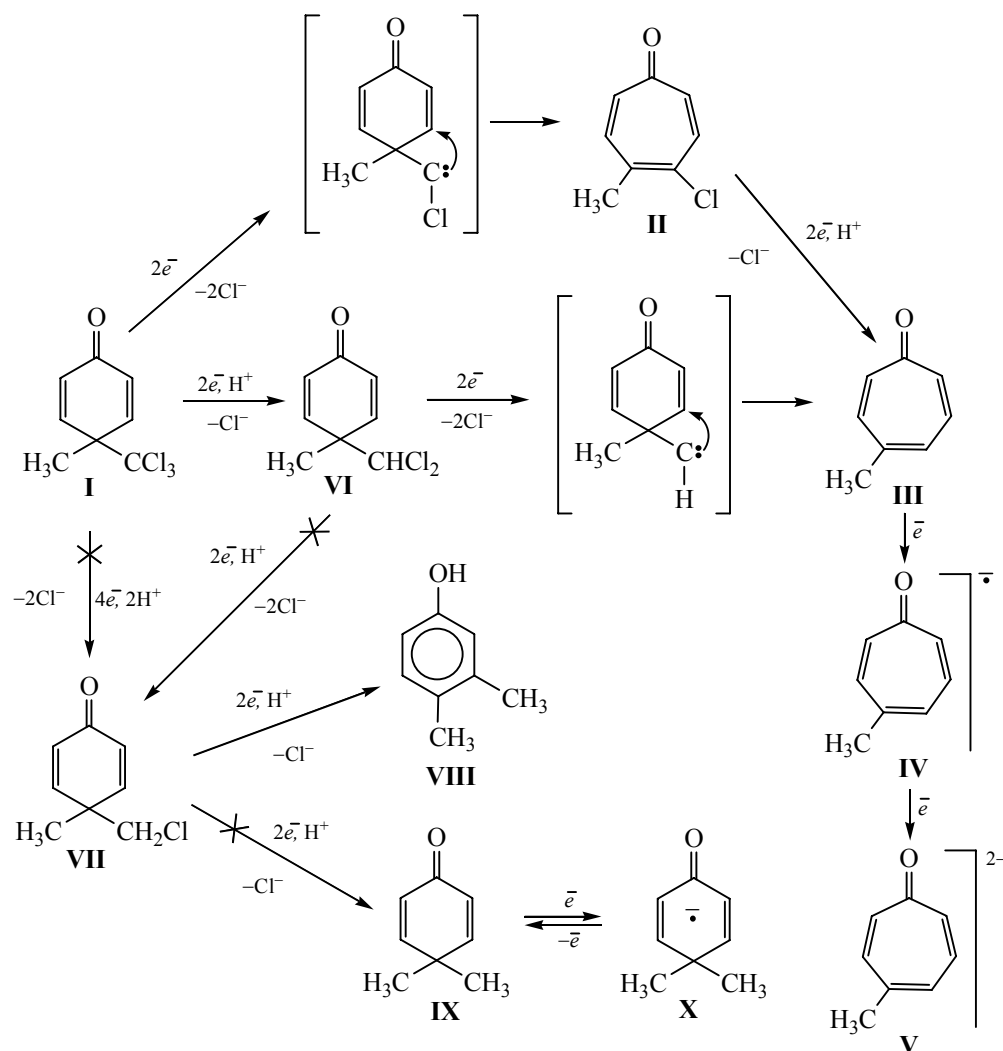


Fig. 2. Cyclic voltammograms of 4-(dichloromethyl)-4-methylcyclohexa-2,5-dien-1-one (**VI**), $c \ 2 \times 10^{-3}$ M. Glassy carbon electrode, DMF, 0.1 M Bu_4NClO_4 .

Scheme 1.



of electrochemical reductive dehalogenation plausible a priori for compound **I**. Simultaneous elimination of two halide ions and proton addition (in total $+4e^-$, -2Hlg^- , $+2\text{H}^+$) at the first stage should result in intermediate formation of monochloro derivative **VII** which, as shown previously [14], is reduced in a single two-electron stage to give 3,4-dimethylphenol (**VIII**), and the latter undergoes no further transformations. This mechanism suggests the cathodic branch of the CV curve of compound **I** to show only two peaks (**I** \rightarrow **VI** \rightarrow **VII**), which is not the case. The reduction route **I** \rightarrow **VII** \rightarrow **IX** \rightarrow **X** should be excluded from consideration, because the cathodic branch of the CV curve contains no reversible reduction peak of the 4,4-dimethylcyclohexa-2,5-dien-1-one (**IX**) intermediate at $E_{\text{pc}} -1.92$ V [13].

The proposed four-stage mechanism of reductive dehalogenation can involve two reaction sequences: **I** \rightarrow **II** \rightarrow **III** \rightarrow **IV** \rightarrow **V** and **I** \rightarrow **VI** \rightarrow **III** \rightarrow **IV** \rightarrow **V**. The CV curves provide insufficient evidence to decide between these two schemes, because the number of transferred electron at the first two stages is the same, and the third and fourth stages are identical. Moreover, as known, chemical reduction of the CCl_3 group can take both routes. The reaction of cyclohexadienone **I** which contains no substituents in positions 2 and 6 reacts with tetrakis(triphenylphosphine) complexes of zero-valent metals (Pd and Pt) involves elimination of two chlorine atoms followed by rearrangement to give 4-chloro-5-methyltropone (**II**) [17]. Analogous halogen-substituted tropone is formed on treatment of 2,6-di-*tert*-butyl-4-methyl-4-

(trichloromethyl)cyclohexa-2,5-dien-1-one with Bu_3SnH /AIBN [18]. However, under the action of tris(dibutylamino)phosphine in ethanol dienone **I** quantitatively converts into 4-(dichloromethyl)-4-methylcyclohexa-2,5-dien-1-one (**VI**) [19], whereas the photo-induced reaction of 4-methyl-4-(tribromomethyl)cyclohexa-2,5-dien-1-one with 1,3-dimethyl-2-phenylimidazole forms a mixture of 4-bromo-5-methyltropone and a monobrominated dienone [20].

To unambiguously decide between the two possible routes of electrochemical reduction, we isolated the reductive dehalogenation product formed at the first stage by preparative electrolysis. The preparative electrolysis of compound **I** was performed on a glassy carbon electrode at the potential of the first reduction peak ($E_{\text{pc}} -1.35$ V) for 3 h (until the current began to fall) and followed by gas chromatography–mass spectrometry (GC–MS). The principal product of the electrochemical transformation (30 wt % of the reaction mixture) was dichloro-substituted dienone **VI**. The rest 70% of the reaction mixture comprised of starting dienone **I** with a minor admixture of poorly soluble tarry substances (probably, polymerization products of reduction intermediates). Consequently, the first, two-electron stage at $E_{\text{pc}} -1.30$ V involves reductive elimination of one chloride ion and gives rise to dichloro derivative **V**.

Thus, the electrochemical reduction of 4-methyl-4-(trichloromethyl)cyclohexa-2,5-dien-1-one occurs as reductive dehalogenation in which chloride ions are eliminated by two different consecutive routes. Initially, addition of two electrons and Cl^- elimination take place; subsequent protonation of the resulting carbanion forms a product with preserved cyclohexadione fragment **VI**. The latter further undergoes one-stage two-electron reductive elimination of both chloride ions without participation of protons and with intermediate formation of a carbenoid reaction center which attacks the cyclohexadienone fragment of the molecule to form 4-methyltropone (**III**).

EXPERIMENTAL

The ^1H and ^{13}C NMR spectra were measured on a Bruker Avance-400 spectrometer in CDCl_3 at 23°C using internal TMS. The IR spectra were obtained on a UR-20 spectrophotometer in mineral oil and the UV spectra, on a Specord M-40 spectrophotometer in EtOH. The mass spectra were taken on a Finnigan MAT TSQ 7000 GC-MS system with the following parameters: SPB 5 capillary column ($30\text{ m} \times 0.25\text{ mm}$),

carrier gas helium (1 mL/min), temperature program 70°C (2 min)– $20^\circ\text{C}/\text{min}$ – 300°C (5 min), electron impact ionization (70 eV).

Electrochemistry was performed on an IPC-Pro M potentiostat. The working electrode was a glassy carbon electrode (d 2 mm), background electrolyte: 0.1 M Bu_4NClO_4 in DMF, reference electrode: Ag/AgCl/sat KCl, auxiliary electrode: Pt plate. The surface of working electrodes was polished with alumina powder with the particle size $< 10\text{ }\mu\text{m}$ (SIGMA-ALDRICH). The potential sweep rates were 200 and 20 mV/s for CV and RDEV, respectively. The number of transferred electrons in redox processes was determined by comparing the limiting peak current in RDEV experiments with the one-electron oxidation current of ferrocene taken in the same concentration. All measurements were performed under dry argon, the samples were dissolved in a predegassed solvent. Pure grade DMF was purified by stirring it over freshly calcined K_2CO_3 for 4 days followed by vacuum distillation first over P_2O_5 and then over anhydrous CuSO_4 .

Preparative electrolysis was performed in DMF in a three-electrode cell with the cathodic (V 10 mL) and anodic compartments separated with a glass membrane. The working electrode was a disc glassy carbon electrode (pressed in Teflon) with a surface area of 0.25 cm^2 , auxiliary electrode: Pt plate, reference electrode: Ag/AgCl/sat KCl. The working electrode was polished with alumina powder with the particle size $< 10\text{ }\mu\text{m}$ (SIGMA-ALDRICH) and treated with ethanol, distilled water, and DMF. The working solution ($5 \times 10^{-3}\text{ M}$) was doped with 0.1 M Bu_4NClO_4 as indifferent electrolyte. Electrolysis was performed in the potentiostatic mode under dry argon at room temperature. The electrode potential was set with a P 5827M potentiostat, based on preliminary polarization and CV data obtained on the same device. The electrolysis time was determined by the moment when the current began to fall (~ 3 h).

After electrolysis the mixture was diluted with 7.5 mL of water, and the electrolysis products were extracted with 15 mL of ether. The ethereal extract was successively washed with 5 and 2.5 mL of water. The ether was evaporated, and the residue was dried in a vacuum desiccator over P_2O_5 and paraffin. The mixture was subjected to TLC on Silufol UV-254 plates (eluent benzene–ether, 3 : 2) to isolate 2 compounds: 4-(dichloromethyl)-4-methylcyclohexa-2,5-dien-1-one (**VI**)

(R_f 0.63) and 4-methyl-4-(trichloromethyl) cyclohexa-2,5-dien-1-one (**I**) (R_f 0.78). Compounds **I** and **VI** were extracted from the corresponding bands with ether which was then evaporated.

The quantitative and qualitative analysis of the reaction mixtures was performed using GC–MS. Dienones **I** and **VI** were identified with the use of authentic samples, their retention times in the total ion chromatograms of the reaction mixtures were 8.2 and 7.6 min, respectively.

Compounds used in the work were synthesized by published procedures. The physicochemical and spectral characteristics of the products were supportive of their structures and coincident with published data.

4-Methyl-4-(trichloromethyl)-2,5-dien-1-one (I) was synthesized as described by Zincke and Suchl [21]. mp 101–102°C (hexane). IR spectrum, ν , cm^{-1} : 1610, 1635, 1670. ^1H NMR spectrum, δ , ppm: 1.69 s (3H, C^4Me), 6.44 d (2H, H^2 , H^6 , 3J 10.0 Hz), 7.18 d (2H, H^3 , H^5 , 3J 10.0 Hz). ^{13}C – $\{\text{H}^1\}$ NMR spectrum, δ_{C} , ppm: 23.06 (4-Me), 55.89 (C^4), 103.34 (CCl_3), 131.00 ($\text{C}^{2,6}$), 147.38 ($\text{C}^{3,5}$), 184.26 ($\text{C}=\text{O}$). UV spectrum: λ_{max} 231 nm ($\log \varepsilon$ 4.24). Mass spectrum, m/z (I_{rel} , %): 224 (7) $[M]^+$, 189 (28) $[M - \text{Cl}]^+$, 107 (100) $[M - \text{CCl}_3]^+$, 79 (19) $[M - \text{CCl}_3 - \text{CO}]^+$, 77 (28) $[M - \text{CCl}_3 - \text{CO} - 2\text{H}]^+$, 161 (11) $[M - \text{Cl} - \text{CO}]^+$, 125 (11) $[M - \text{Cl} - \text{CO} - \text{HCl}]^+$, 99 (5) $[M - \text{Cl} - \text{CO} - 2\text{HCl}]^+$.

4-(Dichloromethyl)-4-methylcyclohexa-2,5-dien-1-one (VI) was synthesized as described in [22]. The UV, IR, and ^1H and ^{13}C – $\{\text{H}^1\}$ NMR spectra coincide with those described in [15]. Mass spectrum, m/z (I_{rel} , %): 190 (14) $[M]^+$, 107 (100) $[M - \text{CHCl}_2]^+$, 79 (27) $[M - \text{CHCl}_2 - \text{CO}]^+$, 77 (45) $[M - \text{CHCl}_2 - \text{CO} - 2\text{H}]^+$, 155 (59) $[M - \text{Cl}]^+$, 127 (18) $[M - \text{Cl} - \text{CO}]^+$, 91 (32) $[M - \text{Cl} - \text{CO} - \text{HCl}]^+$.

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