

Synthesis of Calix[4]arene–Crown-6 with Alkoxysilyl-Containing Substituents

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Abstract—An efficient procedure has been proposed for the synthesis of calix[4]arene–crown-6 conjugate having triethoxysilyl fragments in the *para* positions. The calixarene fragment adopts a 1,3-alternate conformation. Unlike known methods of synthesis of analogous structures, the proposed procedure ensures introduction of two ethoxysilyl groups into the oppositely located benzene rings in the macrocycle.

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The ability of calix[4]arene derivatives to selectively bind metal cations is used to solve a variety of problems. In particular, these compounds are used in extraction, chromatographic separation, and determination of alkali, alkaline-earth, and other metal cations. Sorbents modified with calixarene fragments attract considerable interest [1–8]. In order to synthesize a calixarene–crown ether conjugate capable of forming covalent bonds to produce a polymeric matrix, it was necessary to introduce into the macrocycle triethoxysilyl groups; hydrolysis of the latter, followed by polymerization of calixarene–crown ether via formation of siloxane bonds, could lead to a polymeric support which would be able to bind metal cations, specifically cesium and strontium ions [9, 10]. It is important that the triethoxysilyl groups and the polyether fragment be arranged at different sides of the aromatic skeleton to minimize steric hindrances to approach of metal cations to the calixarene fragment.

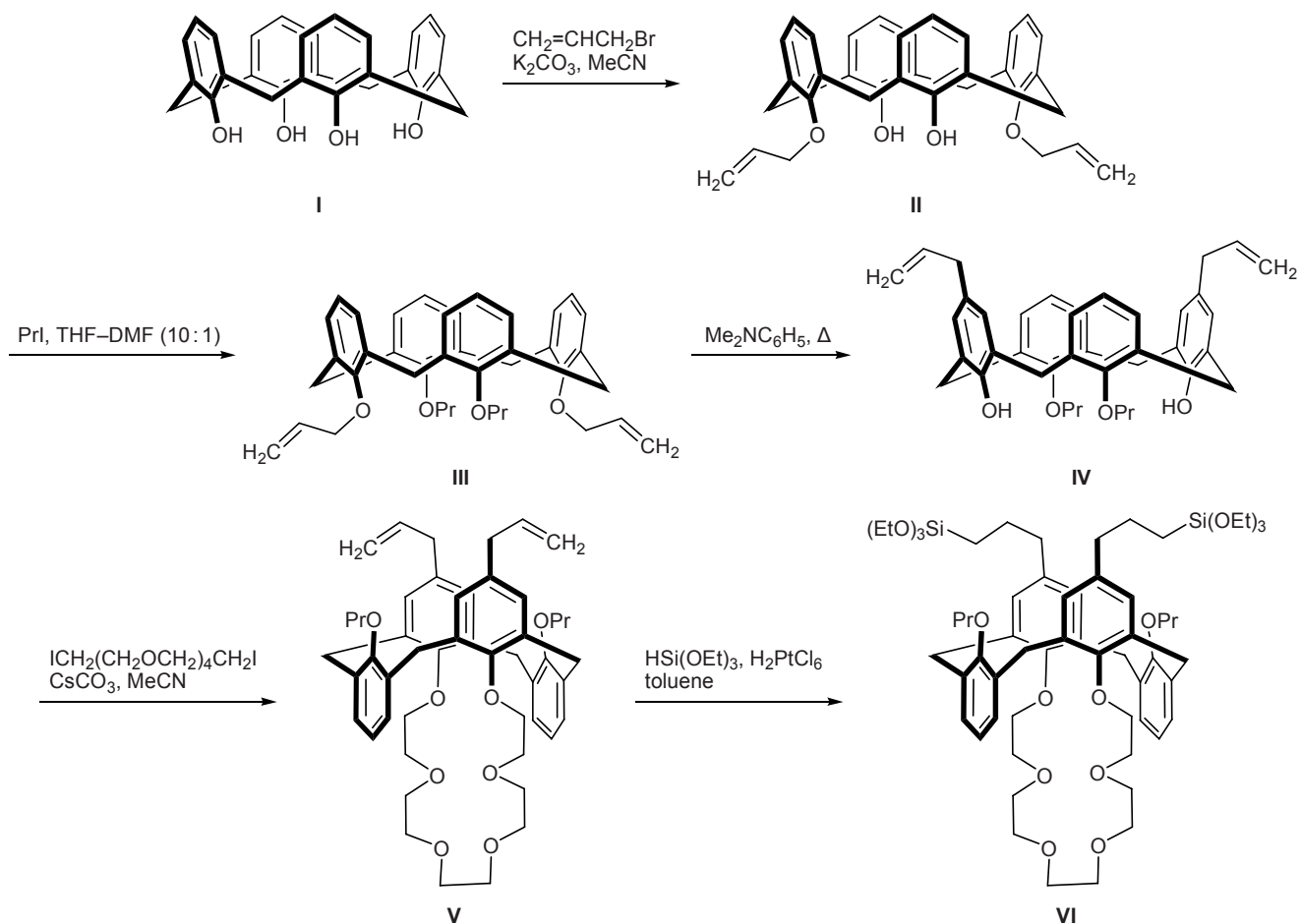
With the goal of building up effective complexing agents toward cesium (or strontium) cations, in the present work we tried to synthesize 5,17-bis[3-(triethoxysilyl)propyl]-26,28-dipropoxycalix[4]arene–crown-6 conjugate with 1,3-alternate conformation of the calixarene fragment. The synthesis of such compound implies modification of the upper rim with allyl fragments and the subsequent reaction of the latter with triethoxysilane to obtain the target calixarene derivative containing ethoxysilyl groups. Two procedures for the synthesis of alkoxysilyl calixarene derivatives were reported in [9–11]. One of these was used to obtain silica gel activated by calixcrown via hetero-

phase reaction of the corresponding macrocyclic compound containing two allyl fragments with the sorbent surface in anhydrous toluene [9]. The other procedure implied heating of initial allyl derivative with triethoxysilane in boiling anhydrous THF in the presence of Cp_6PtH_2 [11]; analogous reaction with compound **V** gave only the corresponding mono(triethoxysilylpropyl) mono(prop-2-enyl) derivative.

We performed some transformations of calix[4]arene **I** derivatives. Molecules **I–IV** adopt mainly *cone* conformation. This follows from the presence in their ^1H NMR spectra of two doublets from methylene protons in the calixarene ring. Calixcrown **V** was synthesized according to a modified procedure using 1,14-diiodo-3,6,9,12-tetraoxatetradecane as alkylating agent. We thus succeeded in raising the yield of the target product and considerably shortening the reaction time. However, insofar as iodide ion is simultaneously a readily departing group and a counterion which is fairly difficult to remove from the outer sphere of the calixarene–cesium complex formed during the process, purification of the final calixcrown is complicated. Therefore, we proposed an alternative procedure for the synthesis of calixcrowns whose molecules adopt a 1,3-*alternate* conformation. The procedure implies preparation of macrocycle in the 1,3-*alternate* conformation at an intermediate step of the transformation calix[4]arene \rightarrow 5,17-bis(prop-2-en-1-yl)-26,28-dipropoxycalix[4]arene–crown-6 (Scheme 1).

The reaction of 25,27-bis(prop-2-en-1-yloxy)-26,28-dihydroxycalix[4]arene with propyl iodide in the presence of cesium carbonate gave the corresponding

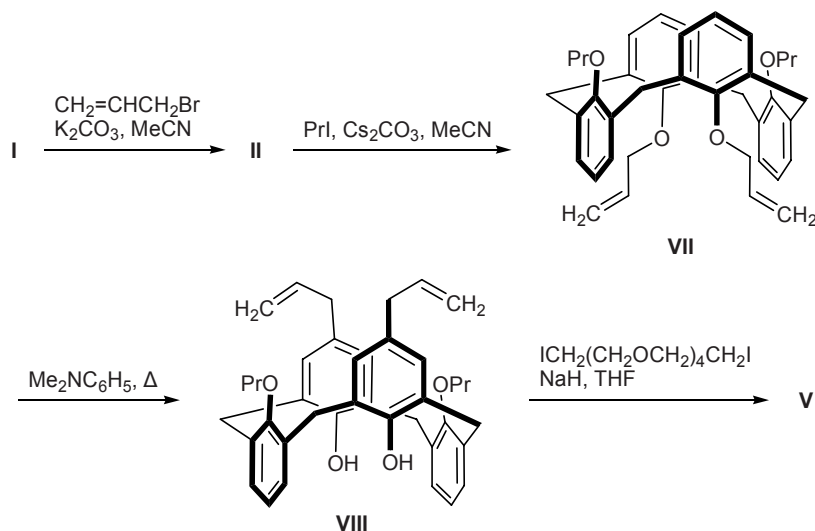
Scheme 1.



tetrasubstituted compound **VII** having two allyl and two propyl groups at the lower rim as 1,3-*alternate* conformer. In the alkylation of calixarene **VIII** with allyl groups in the *para* positions using sodium hy-

dride as a base, the macroring did not change its conformation due to strong binding of sodium ions to oxygen atoms in the anionic phenoxide moieties of the calixarene molecule. Therefore, modification of

Scheme 2.



5,17-bis(prop-2-en-1-yl)-25,27-dihydroxy-26,28-dipropoxycalix[4]arene (**VIII**) with 1,14-diiodo-3,6,9,12-tetraoxatetradecane was carried out in the presence of sodium hydride in tetrahydrofuran, which strongly facilitated the isolation and purification of the target product whose molecules retained 1,3-*alternate* conformation (Scheme 2). The properties of the product were identical to those of compound **V**.

The target 5,17-bis[3-(triethoxysilyl)propyl]-26,28-dipropoxycalix[4]arene-crown-6 was synthesized by reaction of **V** with triethoxysilane using anhydrous toluene as solvent. We thus succeeded in shortening the reaction time, raising the yield, and simplifying the purification procedure; replacement of the catalyst by H_2PtCl_6 did not affect the reaction rate and yield to an appreciable extent.

The ^{13}C NMR spectrum of calixarene **V** contained signals from carbon atoms in the allyl groups attached to the aromatic rings (δ_C 138.2, 116.5, and 41.1 ppm). No such signals were present in the spectrum of triethoxysilyl derivative **VI**, but those belonging to carbon atoms in the ethoxysilyl (δ_C 57.8, 58.1, 18.6, and 17.6 ppm) and propyl fragments (δ_C 39.6, 24.5, and 11.0 ppm) were observed. Comparison of the NMR spectra of compounds **V** and **VI** with published data indicated 1,3-*alternate* conformation of the calix[4]arene fragments in their molecules.

EXPERIMENTAL

The 1H and ^{13}C NMR spectra were recorded on a Varian VXR-300 spectrometer (300 MHz) from ~10% solutions in $CDCl_3$ using tetramethylsilane as internal reference. The fast atom bombardment mass spectra (Xe, 8 kV) were measured on a VG 70-70EQ instrument, and the electron-impact mass spectra (70 eV) were obtained on an MKh-1321 mass spectrometer.

25,26,27,28-Tetrahydroxycalix[4]arene (**I**) was synthesized according to the procedure described in [12]. Its properties coincided with published data.

25,27-Dihydroxy-26,28-bis(prop-2-en-1-yloxy)-calix[4]arene (II). A suspension of 5.0 g (11.8 mmol) of calix[4]arene **I**, 1.79 g (13.0 mmol) of potassium carbonate, and 2.92 g (24.1 mmol) of allyl bromide in 100 ml of anhydrous acetonitrile was heated under reflux for 15 h with stirring. The solvent was distilled off, the residue was dissolved in 100 ml of chloroform, and the solution was washed in succession with dilute hydrochloric acid (2×25 ml), a solution of sodium carbonate, and water. The organic phase was separated

and dried over $MgSO_4$, the solvent was removed, and the residue was recrystallized from methanol–chloroform. Yield 85%, mp 187–188°C. 1H NMR spectrum, δ , ppm: 3.37 d (4H, $ArCH_2Ar$, $J = 13.0$ Hz), 4.33 d (4H, $ArCH_2Ar$, $J = 13.0$ Hz), 4.55 m (4H, $CH_2CH=CH_2$), 5.9–5.2 m (4H, $CH=CH_2$), 7.1–6.0 m (14H, H_{arom} , $CH_2CH=CH_2$), 7.9 s (2H, OH).

25,27-Bis(prop-2-en-1-yloxy)-26,28-dipropoxycalix[4]arene (III) (cone conformer). A suspension of 1.4 g (46 mmol) of 80% sodium hydride in a mixture of 200 ml of anhydrous THF and 20 ml of anhydrous DMF was cooled to 0°C, 5.1 g (11 mmol) of compound **II** was added in portions, the mixture was stirred for 1 h at room temperature, a solution of 7.75 g (45.6 mmol) of propyl iodide in a mixture of 10 ml of anhydrous THF and 1 ml of anhydrous DMF was added, and the mixture was heated for 18 h under reflux with stirring. The mixture was cooled, 15 ml of methanol was added to neutralize excess sodium hydride, the solvent was distilled off, and the solid residue was dissolved in 300 ml of chloroform. The solution was washed in succession with water, 1 N hydrochloric acid (2×25 ml), water, a solution of sodium carbonate, water, a solution of sodium metabisulfite, and water. The organic layer was separated and dried over $MgSO_4$, the solvent was distilled off under reduced pressure, and the crude product was purified by recrystallization first from ethanol and then from methanol–chloroform. Yield 78%, mp 143–145°C. 1H NMR spectrum, δ , ppm: 0.45 t (6H, CH_3), 1.25 m (4H, OCH_2CH_2), 3.2 d (4H, $ArCH_2Ar$, $J = 12.9$ Hz), 3.6 t (4H, CH_2CH_3), 4.32 d (4H, $OCH_2CH=$, $J = 6.4$ Hz), 4.5 d (4H, $ArCH_2Ar$, $J = 12.9$ Hz), 5.14 m (4H, $CH=CH_2$), 6.2 m (2H, $CH=CH_2$), 6.9–7.3 m (12H, H_{arom}).

25,27-Dihydroxy-5,17-bis(prop-2-en-1-yl)-26,28-dipropoxycalix[4]arene (IV) (cone conformer). A solution of 4.54 g (7.74 mmol) of compound **III** in 20 ml of *N,N*-dimethylaniline was heated for 6 h under reflux with stirring. The resulting suspension was cooled and poured into a 100 ml of a 1:1 mixture of hydrochloric acid with ice. The precipitate was filtered off and dissolved in 150 ml of methylene chloride, and the solution was washed in succession with 6 N hydrochloric acid (3×20 ml), water, a solution of sodium carbonate, and water. The organic phase was separated and dried over $MgSO_4$, the solvent was distilled off under reduced pressure, and the crude product was purified by recrystallization from methylene chloride–propan-2-ol. Yield 95%, mp 196–198°C. 1H NMR spectrum, δ , ppm: 0.38 t (6H, CH_3), 1.12 m (4H,

OCH₂CH₂), 3.29 d (4H, OCH₂CH=, *J* 6.65 Hz), 3.54 t (4H, CH₂CH₃), 3.75 d (4H, ArCH₂Ar), 3.96 d (4H, ArCH₂Ar, *J* = 13.29 Hz), 5.06 m (4H, CH=CH₂), 5.89–6.05 m (2H, CH=CH₂), 6.89 s (4H, H_{arom}), 7.01 t (2H, H_{arom}), 7.16 d (2H, H_{arom}), 7.19 d (2H, H_{arom}), 7.37 s (2H, OH).

5,17-Bis(prop-2-en-1-yl)-26,28-dipropoxy-25,27-(3,6,9,12-tetraoxatetradecane-1,14-diylldioxy)calix[4]arene (V). *a.* A mixture of 3.8 g (6.46 mmol) of compound **IV** and 8.4 g (25.84 mmol) of cesium carbonate in 900 ml of anhydrous acetonitrile was stirred for 1.5 h at 60°C, a solution of 3.26 g (7.106 mmol) of 1,14-diiodo-3,6,9,12-tetraoxatetradecane in 100 ml of anhydrous acetonitrile was added dropwise, and the mixture was heated for 10–12 h under reflux. The mixture was cooled and filtered from inorganic precipitate, the solvent was distilled off under reduced pressure, the solid residue was dissolved in methylene chloride, the solution was washed in succession with water, 1 N nitric acid (3×50 ml), water, a solution of sodium carbonate, a solution of sodium metabisulfite, and water. The organic phase was evaporated under reduced pressure, and the crude product was purified by fractional crystallization from propan-2-ol, propan-2-ol-acetonitrile, and heptane. Yield 75%.

b. Compound **VIII**, 3.8 g (6.46 mmol), was added in portions to a suspension of 0.62 g (25.84 mmol) of sodium hydride (80%) in 800 ml of anhydrous THF, cooled to 0°C, the mixture was stirred for 1 h at room temperature, a solution of 3.26 g (7.106 mmol) of 1,14-diiodo-3,6,9,12-tetraoxatetradecane in 100 ml of anhydrous THF was added, and the mixture was heated for 13 h under reflux with stirring. When the reaction was complete, 15 ml of methanol was added to decompose excess sodium hydride, the solvent was distilled off, the solid residue was dissolved in 300 ml of chloroform, the organic phase was washed in succession with water, 1 N hydrochloric acid (2×25 ml), a solution of sodium carbonate, and water. Yield 90%, mp 95°C. ¹H NMR spectrum, δ, ppm: 0.38 t (6H, CH₃), 1.28–1.33 m (4H, OCH₂CH₂), 3.24 d (4H, OCH₂CH=, *J* = 6.6 Hz), 3.34 d (4H, ArCH₂Ar), 3.69 s [4H, ArO(CH₂CH₂O)CH₂], 3.45–3.51 m and 3.65–3.79 m [20H, O(CH₂CH₂), OCH₂CH₂CH₃], 3.96 t (4H, ArOCH₂), 4.29 d (4H, ArCH₂Ar, *J* = 13.26 Hz), 5.0–5.08 m (4H, CH=CH₂), 5.88–5.94 m (2H, CH=CH₂), 6.76 t (2H, H_{arom}), 6.85 s (4H, H_{arom}), 6.93 d (4H, H_{arom}). ¹³C NMR spectrum, δ_C, ppm: 10.8 s (OCH₂-CH₂CH₃); 23.3 s (OCH₂CH₂CH₃); 35.0 s (ArCH₂Ar); 40.1 s (ArCH₂Ar); 41.1 s (CH₂CH=CH₂); 68.6 s, 71.06 s, and 71.2 s (OCH₂CH₂O); 72.8 s (OCH₂CH₂-

CH₃); 116.5 s (CH₂CH=CH₂); 123.1 s (C^o); 128.8 s and 129.7 s (C^o); 131.2 s, 134.2 s (C^m); 138.2 s (CH₂-CH=CH₂); 140.4 s (C^p); 153.5 s and 155.7 s (Cⁱ). Mass spectrum (FAB), *m/z*: 813 [M + Na]⁺, 791 [M + H]⁺.

26,28-Dipropoxy-25,27-(3,6,9,12-tetraoxatetradecane-1,14-diylldioxy)-5,17-bis[3-(triethoxysilyl)propyl]calix[4]arene (VI). Compound **V**, 1 g (1.2 mmol), was dissolved in 30 ml of anhydrous toluene, 1.2 ml of a solution of H₂PtCl₆ in THF was added (1 mg/ml), the mixture was stirred for 30 min at room temperature, 1.18 g (7.2 mmol) of triethoxysilane was added, and the mixture was heated for 35 h under reflux. The solvent was distilled off under reduced pressure in a stream of dry nitrogen, the dry residue was heated in boiling anhydrous heptane to remove unreacted compound **V**, the mixture was filtered, and the crude product was purified by recrystallization first from anhydrous acetonitrile and then from a mixture of anhydrous acetonitrile and anhydrous THF. ¹H NMR spectrum, δ, ppm: 0.76–1.0 m (10H, SiCH₂, CH₃), 1.19 t (18H, OCH₂CH₃), 1.24–1.28 m (4H, CH₂CH₂-CH₂), 1.8 m (4H, SiCH₂CH₂CH₂), 2.45 m (4H, SiCH₂-CH₂CH₂), 3.1–4.2 br.m [ArCH₂Ar, ArO(CH₂CH₂O)₅, OCH₂CH₃, OCH₂CH₂CH₃], 6.9 t (2H, H_{arom}), 7.18 d (4H, H_{arom}), 7.23 s (4H, H_{arom}). ¹³C NMR spectrum, δ_C, ppm: 10.7 s (OCH₂CH₂CH₃); 11.0 s (CH₂CH₂CH₂Si); 17.6 s and 18.4 s (SiOCH₂CH₃); 23.5 s (OCH₂CH₂-CH₃); 24.5 s (CH₂CH₂CH₂Si); 35.8 s and 37.4 s (ArCH₂Ar); 39.6 s (CH₂CH₂CH₂Si); 57.8 s and 58.1 s (SiOCH); 68.7 s, 69.4 s, 71.0 s, and 71.5 s (OCH₂-CH₂O); 75.4 s (OCH₂CH₂CH₃); 123.0 s (C^o); 127.8 s and 128.2 s (C^o); 131.1 s and 131.16 s (C^p); 132.3 s, 138.15 s, and 138.2 s (C^m); 156.4 s and 157.5 s (Cⁱ). Mass spectrum (FAB), *m/z*: 1141 [M + Na]⁺, 1118 [M + H]⁺.

25,27-Bis(prop-2-en-1-yloxy)-26,28-dipropoxy-calix[4]arene (VII) (1,3-alternate). A suspension of 5.1 g (11 mmol) of compound **II** and 14.3 g (44 mmol) of cesium carbonate in 300 ml of anhydrous acetonitrile was stirred for 1.5 h at 60°C, 7.75 g (45.6 mmol) of propyl iodide was added, and the mixture was heated for 24 h under reflux with stirring. The mixture was cooled and filtered from inorganic precipitate, the solvent was distilled off under reduced pressure, the solid residue was dissolved in methylene chloride, the solution was washed in succession with water, 1 N nitric acid (3×50 ml), water, a solution of sodium carbonate, a solution of sodium metabisulfite, and water. The organic phase was separated and dried over MgSO₄, the solvent was distilled off under reduced pressure, and the crude product was purified by recryst-

tallization from hexane. Yield 85%, mp 170–172°C. ^1H NMR spectrum, δ , ppm: 0.6 t (6H, CH_3), 1.3 m (4H, OCH_2CH_2), 3.5 d (4H, ArCH_2Ar , $J = 12.9$ Hz), 3.7 t (4H, CH_2CH_3), 3.9 d (4H, $\text{OCH}_2\text{CH}=\text{CH}_2$, $J = 6.3$ Hz), 4.3 d (4H, ArCH_2Ar , $J = 13$ Hz), 5.3 m (4H, $\text{CH}=\text{CH}_2$), 6.4 m (2H, $\text{CH}=\text{CH}_2$), 7.0–7.2 m (6H, H_{arom}), 7.31–7.46 m (6H, H_{arom}). Mass spectrum, m/z : 588 $[M]^+$, 547 $[M - \text{CH}_2\text{CH}=\text{CH}_2]^+$, 545 $[M - \text{CH}_2 - \text{CH}_2\text{CH}_3]^+$, 506 $[M - \text{CH}_2\text{CH}=\text{CH}_2 - \text{CH}_2\text{CH}=\text{CH}_2]^+$, 504 $[M - \text{CH}_2\text{CH}=\text{CH}_2 - \text{CH}_2\text{CH}_2\text{CH}_3]^+$.

25,27-Dihydroxy-5,17-bis(prop-2-en-1-yl)-26,28-dipropoxycalix[4]arene (VIII) (1,3-alternate conformer). mp 203–205°C. ^1H NMR spectrum, δ , ppm: 0.45 t (6H, CH_3), 1.2 m (4H, OCH_2CH_2), 3.2 d (4H, $\text{OCH}_2\text{CH}=\text{CH}_2$, $J = 6.6$ Hz), 3.34 t (4H, CH_2CH_3), 3.6 d (4H, ArCH_2Ar), 4.0 d (4H, ArCH_2Ar , $J = 13.4$ Hz), 5.1 m (4H, $\text{CH}=\text{CH}_2$), 6.12–6.0 m (2H, $\text{CH}=\text{CH}_2$), 7.18–6.9 m (6H, H_{arom}), 7.23 s (4H, H_{arom}), 7.4 s (2H, OH). Mass spectrum, m/z : 588 $[M]^+$, 545 $[M - \text{CH}_2 - \text{CH}_2\text{CH}_3]^+$, 502 $[M - \text{CH}_2\text{CH}_2\text{CH}_3 - \text{CH}_2\text{CH}_2\text{CH}_3]^+$.

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