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Electrochemical behavior of bridged 1,2,4-dioxazolidine derivative in acetonitrile medium on the smooth gold

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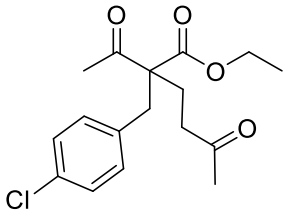
Caution: Although we have not encountered any difficulties in working with the peroxides described below, proper precautions should be taken whenever possible, such as using protective screens, fume hoods, and avoiding transition metal salts, heat, and shaking.

^{1}H and ^{13}C spectra were registered on a «Bruker AM-300» instrument, operating at 300 (^{1}H) or 75 (^{13}C) MHz. Internal standard is $CHCl_3$. ^{1}H NMR chemical shifts are given relative to the residual solvent signal ($CDCl_3$) 7.27 ppm for ^{1}H nuclei and 77.0 ppm for ^{13}C nuclei.

Chromatography of the products was performed on silica gel (0.060–0.200 mm, 60°, CAS 7631-86-9). Dichloromethane, chloroform, acetonitrile, petroleum ether (PE) (40:70), ethyl acetate (EA), methyl vinyl ketone, H_2O_2 (35% aqueous solution), $MgSO_4$, $NaHCO_3$, NaI, $CeCl_3 \cdot 7H_2O$, $BF_3 \cdot Et_2O$ and $Na_2S_2O_3$ were purchased from Acros. Ethyl 2-acetyl-2-(4-chlorobenzyl)-5-oxohexanoate (**3**) and ethyl 2-(4-chlorbenzyl)-1,5-dimethyl-6,7-dioxa-8-azabicyclo[3.2.1]octane-2-carboxylate (**1**) were obtained by known methods[S1,S2].

Synthesis of ethyl 2-acetyl-2-(4-chlorobenzyl)-5-oxohexanoate, 3



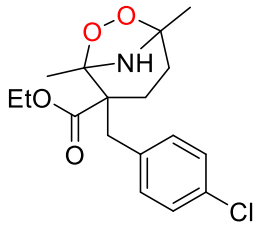
Methyl vinyl ketone (0.90 g, 12.87 mmol), cerium(III) chloride (0.88 g, 2.34 mmol) and sodium iodide were added successively to ethyl 2-acetyl-2-(4-chlorbenzyl)-5-oxohenoate **2** (3 g, 11.7 mmol) with stirring at room temperature. The solution was stirred at 20-25 °C for 24 hours. Then EtOAc (5 ml) was added, and the suspension was stirred for another 30 minutes. After that the sediment was filtered off. The filtrate was washed with aqueous sodium thiosulfate until discoloration. Then the organic phase was separated and the aqueous phase was extracted with EtOAc (3x15 ml). The combined organic phases were washed with water (2x10 ml), dried over $MgSO_4$, filtered, and the solvent was removed under vacuum using a water-jet pump. Product **3** (3.23 g, 9.95 mmol) was obtained, yield 85%.

White crystals. R_f = 0.57 (TLC, PE : EA, 2:1), T_m= 64-65 °C.

^{1}H NMR (300.13 MHz, δ, ppm, *J*/Hz, $CDCl_3$): 7.21 (d, *J* = 8.4 Hz, 2H), 6.99 (d, *J* = 8.4 Hz, 2H), 4.23 – 4.08 (m, 2H), 3.18 (d, *J* = 14.2 Hz, 1H), 3.05 (d, *J* = 14.2 Hz, 1H), 2.48 – 2.26 (m, 2H), 2.17 – 2.00 (m, 8H), 1.23 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (75.48 MHz, δ, ppm, J/Hz, $CDCl_3$): 206.9, 205.1, 171.7, 134.5, 133.2, 131.3, 128.7, 63.9, 61.7, 38.3, 37.8, 30.1, 27.7, 25.7, 14.1.

Synthesis of ethyl 2-(4-chlorbenzyl)-1,5-dimethyl-6,7-dioxa-8-azabicyclo[3.2.1]-octane-2-carboxylate (1)



To a solution of 1,5-diketone **3** (0.300 g; 0.924 mmol) in methyl alcohol (10 ml) with stirring on a magnetic stirrer at room temperature, ammonium acetate (5 eq., 0.356 g, 4.62 mmol) and 35% aqueous solution of hydrogen peroxide (1.5 eq., 0.471 g, 0.112 ml, 1.386 mmol) were added successively. The obtained solution was stirred for 90 minutes. After stirring, the solution was extracted three times with 20 ml of chloroform and 10 ml of water. The organic phase was dried using $MgSO_4$. Then the solvent was removed under vacuum using a water-jet pump, thus a light yellow liquid was obtained. The liquid was purified by column chromatography on silica gel. Firstly, the silica gel layer was pre-washed with a solution of 50 ml of chloroform and 1 ml of triethylamine. After that chloroform was used as an eluent. A crystalline product was obtained as a mixture of two isomers of **1** (0.27 g, 0.79 mmol), yield 86%.

White crystals. Mixture of diastereomers 79:21. R_f = 0.46 (TLC, PE : EA, 5:1).

^{1}H NMR (300.13 MHz δ, ppm, *J*/Hz, $CDCl_3$): 7.20 (d, *J* = 8.4 Hz, 2H), 7.05 (d, *J* = 8.4 Hz, 0.42H), 6.99 (d, *J* = 8.4 Hz, 1.58H), 4.21 – 4.08 (m., 2H), 3.29 (d, *J* = 12.8 Hz, 0.79H), 3.24 – 3.17 (m., 0.42H), 3.16 (br. s, 0.79H), 3.11 (br. s, 0.21H), 2.64 (d., *J* = 12.8 Hz, 0.79H), 2.59 – 2.43 (m., 0,21H), 2.03 – 1.59 (m., 1.79H), 1.78 (s., 2.37H), 1.58 (s., 0,63H), 1.49 – 1.39 (m., 0,21H), 1.48 (s., 0,63H), 1.40 (s., 2.37H), 1.24 (t., 3H, *J* =7.1 Hz).

^{13}C NMR (75.48 MHz, δ, ppm, *J*/Hz, $CDCl_3$): 173.1, 135.1, 132.7, 131.5, 131.2, 128.4, 128.4, 101.1, 100.5, 98.0, 97.4, 40.4, 34.0, 32.5, 26.7, 23.0, 21.3, 21.1, 20.1, 19.5, 14.2.

Cyclic voltammograms were recorded with an IPC-Pro MF potentiostat controlled by a personal computer. The studies were carried out in a three-electrode cell at a temperature of 293 K in the -2800 to 2800 mV range of potential *E*. The potential scan rate was varied in the range of 200 to 500 mV/s. A gold wire 0.3 mm in diameter, soldered into glass and immersed 5 mm in an

electrolyte solution, was used as a working electrode. A platinum wire of the same size served as an auxiliary electrode. To study the processes occurring in the anodic region in detail, we used a gold disk electrode with a working area of 43.55 mm^2. A silver chloride electrode with a double membrane (Ag|AgCl|KCl (3.5 $mol \cdot L^{-1}$)) served as a reference electrode. Before each experiment, the platinum and gold electrodes were etched in aqua regia and subjected to cathodic polarization in в 0.1 N solution of H_2SO_4 at j = 20.9 mA/cm^2.

Working solutions were prepared using acetonitrile (MeCN) preliminarily dehydrated over P_2O_5. A 0.05 M solution of tetrabutylammonium hexafluorophosphate (Bu_4NPF_6) in acetonitrile was used as the supporting electrolyte. The concentration of the studied compound **AP** was 0.03 M during the studies. Before recording of CVs, working solutions were purged with argon to create an inert atmosphere.

Electrolysis of **1** was performed for 5.5 hours at room temperature in a two-electrode cell with no separation of the anodic and cathodic spaces at a current I = 2 mA and a potential E = 6 V using a gold wire (d = 0.3 mm) as the cathode and a platinum wire (d = 0.3 mm) as the anode with immersion of both electrodes 10 mm in a solution of compound **1** (100 mg) in 5 mL of acetonitrile in the presence of Bu_4NBF_4 (0.05 M). Charge passed Q is 39.6 C. The product **3** was purified by column chromatography on silica gel using the solution of petroleum ether and (PE) ethyl acetate (EA) (PE:EA, 2:1). The weight of product **3** was 39 mg.

Corrosion of a gold anode during electrolysis was studied for 8.5 hours at room temperature in a two-electrode cell at a current I = 5 mA. A potential E gradually decreased from 8 V to 6.5 V during the experiment. A platinum wire (d = 0.3 mm) was used as the cathode, and the anode was a gold wire (d = 0.3 mm), both electrodes were immersed 10 mm in the solution. The concentration of compound **AP** was 0.05 M in a solution of Bu_4NPF_6 (0.05 M) in acetonitrile, and the volume of working solution was 5 mL. To estimate the loss (or gain) of the electrodes' mass, they were weighed at certain intervals on an ABJ220-4NM electronic analytical balance («Kern», United States) (d = 0.0001 г).

The presence of gold particles in the solution was determined *via* X-ray fluorescence spectrometry with calibration according to the fundamental parameters an ARL PFX-101 X-ray fluorescence spectrometer (Thermo ARL, Switzerland).

The solution containing colloidal gold after completion of electrolysis was examined by transmission electron microscopy (TEM) on an electron microscope «Hitachi HT7700» (Japan). The images were taken in the transmitted electron recording mode (bright field mode) at an accelerating voltage of 100 kV. Before shooting, the working solution was applied to a thin carbon film and dried in a vacuum. The carbon film was attached to a 3 mm diameter copper grid, which was fixed in a special holder.

Calculation of electrochemical parameters

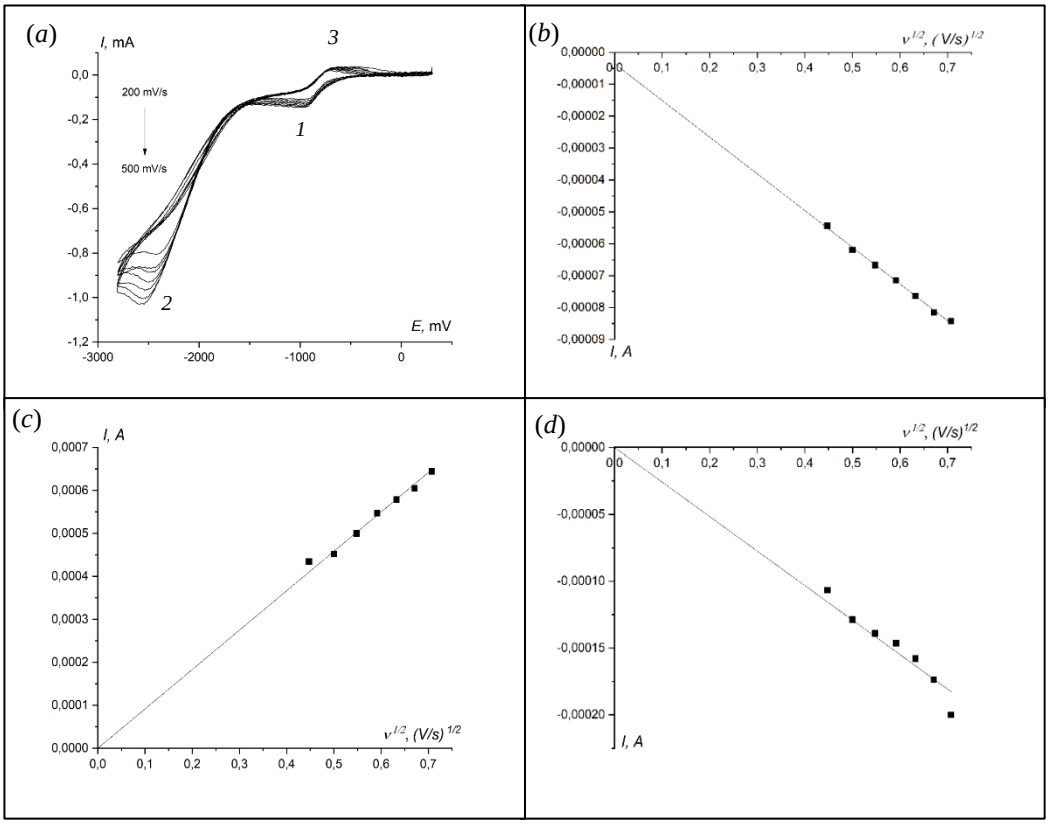


Figure S1. *(a)* CVs of the **AP** solution in the cathode region on the Au-electrode, ν = 200, 250, 300, 350, 400, 450, 500 mV/s. *(b)* Dependency of $I_c^p - \nu^{0.5}$ for the peak *1*. *(c)* Dependency of $I_c^p - \nu^{0.5}$ for the peak *3*. *(d)* Dependency of $I_c^p - \nu^{0.5}$ for the peak *2*.

Figure S1, parts *b-d* show the linear dependences $I_c^p - \nu^{0.5}$ for the peaks on the cathode region of the CVs, passing close to the origin of coordinates, indicating that the reduction in both cathodic processes in the studied ranges of potentials is limited by the stage of diffusion when supplying the substrate to the surface of the electrode[S3,S4]. In this case it is possible to apply the next equation:

$$I_{p,c} = 0.496 S \alpha^{0.5} n_\alpha^{0.5} n F c_0 (\frac{FD}{RT})^{0.5} v^{0.5}, \quad (1)$$

where S is the surface area of the working electrode immersed in the solution, cm^2; c_0 is the concentration of the studied substance in the cell, mol/cm^3; F is the Faradey constant, C/mol; R is the universal gas constant, $\frac{J}{K\ mol}$; T is the absolute temperature during the experiment, K; D is the coefficient of diffusion, cm^2/s; α is the coefficient of electron transfer; n_α is the number of electrons involved in the limiting stage of charge transfer; n is the total number of electrons transferred by the diffusing particle. As a rule, $n_a = 1$.

We calculated the values of αn_a for cathode processes. The arithmetic mean values of αn_a were then found for each potential rate of each cathode peak, using equation 2:

$$\alpha n_a = \frac{1.857RT}{F\Delta E_{\frac{p}{2}}} \quad (2)$$

where $E_{p/2}$ is the potential value for $0.5I_{p,c}$, V.

According to calculations based on the data in Figure S1 and Eq. 2, $\alpha_1 n_\alpha$=0.5 for the first cathode peak, $\alpha_2 n_a$=0.35 for the second cathode peak and $\alpha_3 n_a$=0.40 for the third peak, which is *quasi*-reversible peak of the first one. All these values are within the range $0<\alpha<0.5$, so we may assume that n_a=1 and n=1.

The substrate's coefficients of diffusion were calculated using Eq. (1), with allowance for the already established value of coefficient α. Surface area S was 4.78×10^{-6} m^2, since the diameter of the working electrode was 0.3 mm and the immersion in the solution was 5 mm. Allowing for the slopes of the lines in Fig. S1b, S1c and S1d, coefficients of diffusion D were calculated using Eq. (1), assuming, that one electron was transferred in each process (n=1). The slopes of the lines were $\frac{dI}{dv^{0.5}} = -1.21 \times 10^{-4}$ As$^{1/2}$/V$^{1/2}$ for the first cathode peak (1), $\frac{dI}{dv^{0.5}} = 2.582 \times 10^{-4}$ As$^{1/2}$/V$^{1/2}$ for the second cathode peak (2) and $\frac{dI}{dv^{0.5}} = 9.17 \times 10^{-4}$ As$^{1/2}$/V$^{1/2}$ for the *quasi*-reversible cathode peak (3). The calculated coefficients of diffusion were respectively $D_1 = 1.57 \times 10^{-7}$ cm^2/s, $D_2 = 1.02 \times 10^{-6}$ cm^2/s and $D_3 = 1.126 \times 10^{-5}$ cm^2/s.

References

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S2. I. A. Yaremenko, Y. Y. Belyakova, P. S. Radulov, R. A. Novikov, M. G. Medvedev, N. V. Krivoshchapov, A. A. Korlyukov, I. V. Alabugin and A. O. Terent'ev, *J. Am. Chem. Soc.*, 2021, **143**, 6634; https://doi.org/10.1021/jacs.1c02249.

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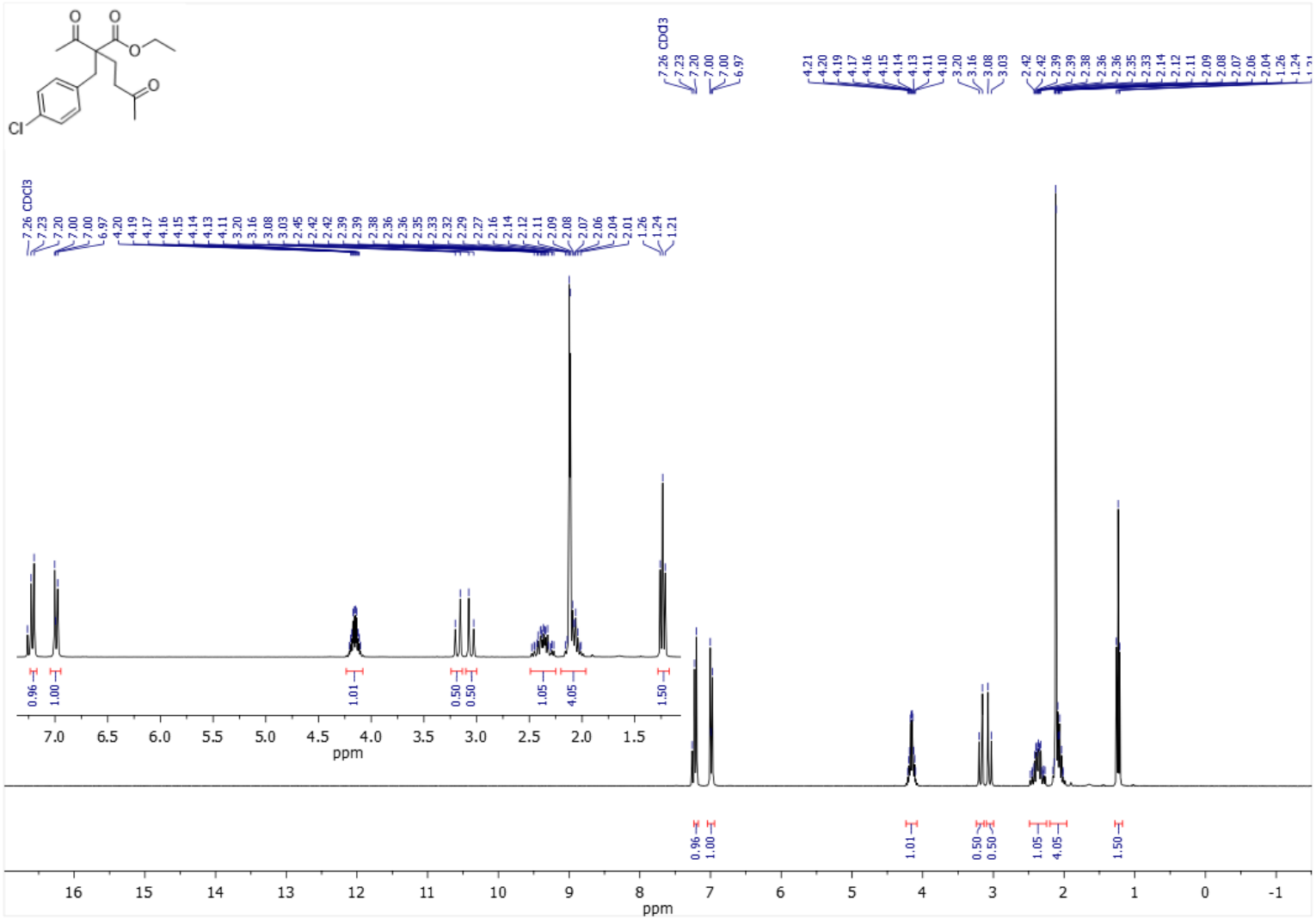
^{1}H NMR (300.13 MHz, $CDCl_3$). Ethyl 2-acetyl-2-(4-chlorobenzyl)-5-oxohexanoate, 3



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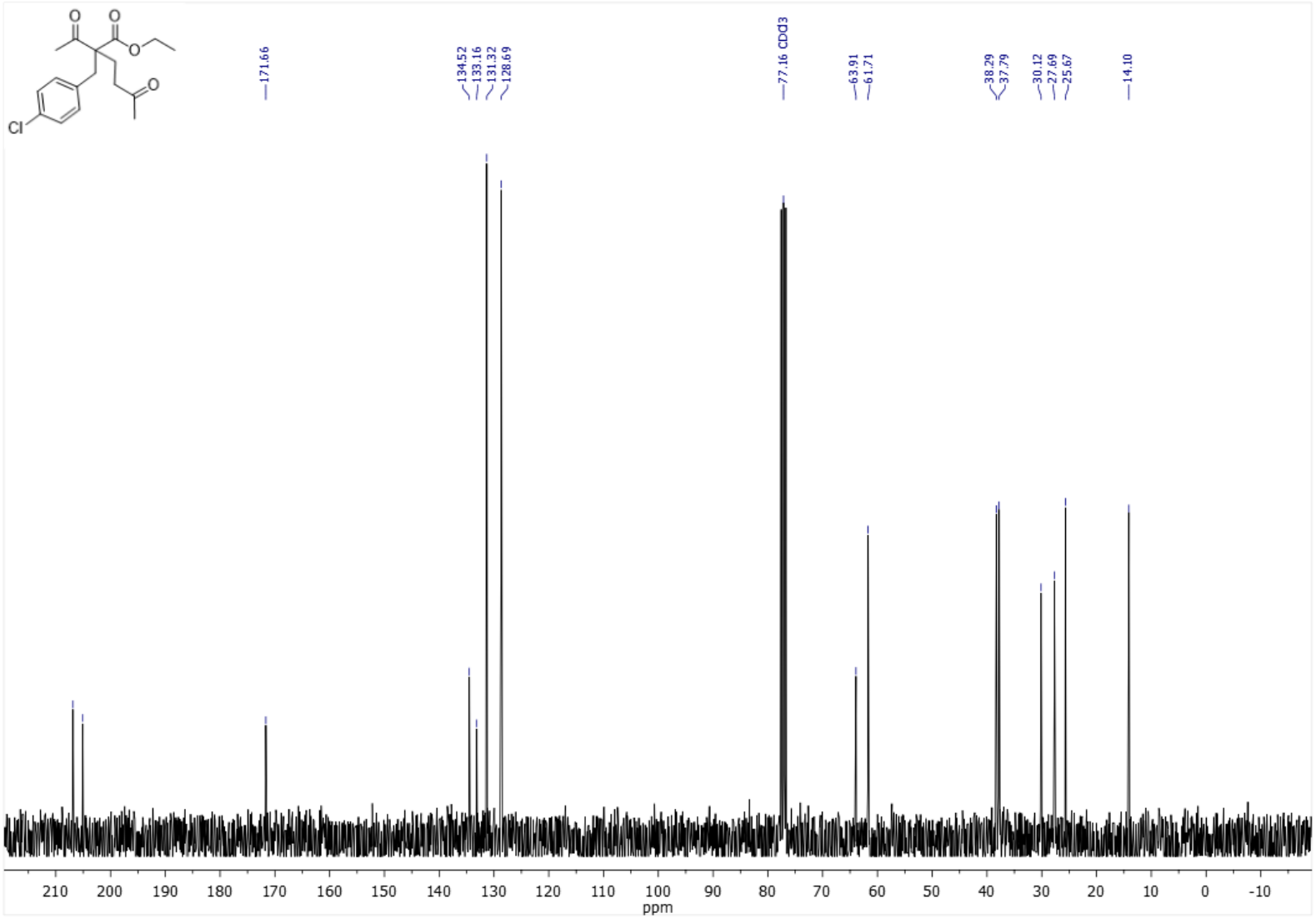

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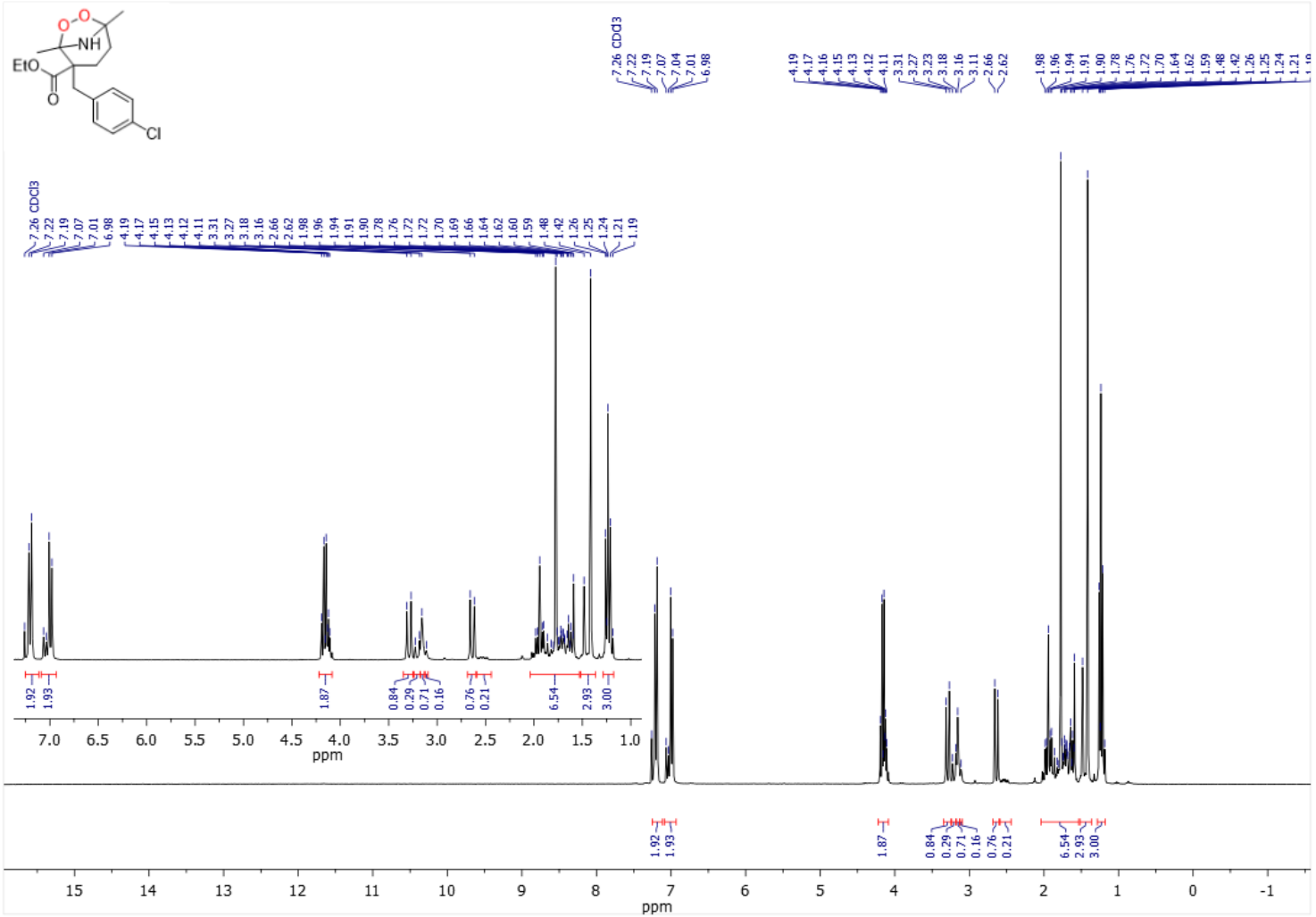

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