Organic Chemistry

Some aspects of selective ozonolysis of 5-allyl(allenyl)-4,4-dimethoxy-2,3,5-trichlorocyclopent-2-enones and their 3-morpholino derivatives

*N. S. Vostrikov, S. A. Torosyan, F. A. Akbutina, E. M. Vyrypaev, L. V. Spirikhin, and M. S. Miftakhov**

Institute of Organic Chemistry, Ufa Research Center of the Russian Academy of Sciences, 71 prosp. Oktyabrya, 450054 Ufa, Russian Federation. Fax: +7 (347 2) 35 6066

Ozonolysis of the title cyclopentenones proceeds selectively with the participation of exocyclic multiple bonds. In the case of 5-allyl derivatives, the corresponding ozonides were isolated along with the expected products.

Key words: 5-allylcyclopent-2-enone, 5-allenylcyclopent-2-enone, ozonolysis, enal, 1,2,4-trioxolane.

In this work, we demonstrate the possibility of the selective ozonolytic cleavage of double bonds of 5-allenyl and 5-allyl substituents of cyclopentenones (**1**—**4**).[1—4] The $RuCl_3$ (cat.)—$NaIO_4$ and OsO_4 (cat.)—$NaIO_4$ systems, which have been used for this purpose previously, made it possible to smoothly transform 3-morpholino derivatives **2** and **4** to acid **5** and a mixture of enals **6**, respectively.[5,6] However, the use of these reagents for performing analogous transformations of dichlorocyclopentenones **1** and **3** resulted in complex mixtures of products (Scheme 1).

Ozonolysis of compounds **1**—**4** was carried out in a CH_2Cl_2 solution at −78 °C followed by reduction of intermediate ozonides with Me_2S. Thus the reaction of 5-allenylcyclopentenone **1** with an excess of O_3 afforded trichlorocyclopentenone (**7**). We attribute the formation of compound **7** to smooth *in situ* decarbonylation of intermediate oxo aldehyde (**8**). To the contrary, ozonolysis of 3-morpholino derivative **2** afforded stable aldehyde (**9**) in high yield (Scheme 2).

Ozonolysis of 5-allylcyclopentenone **3** differently, this gave *Z*- and *E*-enals (**10**) and two diastereomeric 1,2,4-trioxolanes (**11**), separated by chromatography on SiO_2. The total yield of compounds **10** and **11**, which were formed in a ratio of 2 : 7, was more than 90%. According to the ^1H NMR spectroscopic data, the ratio of diastereomers **11** was ~1 : 2. Storage of the latter in methanolic HCl afforded tetramethoxy derivative **12** (Scheme 3).

The ratio of stereoisomers, *E*-**10** : *Z*-**10** ≈ 3 : 2, was established based on the data of ^1H NMR spectroscopy. In the spectrum of a mixture of isomers **10**, signals for the proton of the exocyclic double bond serve as diagnostic signals in the assignment. Due to the shifting effect of the carbonyl group,[7—10] the resonance of the olefinic proton of *E*-**10** was observed at lower field than that of *Z*-**10**. Undoubtedly, it is of interest that this reaction afforded ozonides **11**, which are rather stable with respect to Me_2S (under the action of Me_2S in CH_2Cl_2 at 20 °C, these compounds slowly converted

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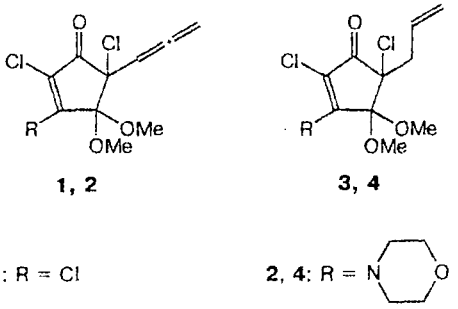
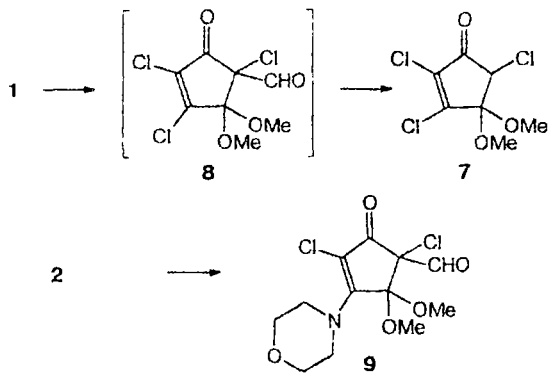
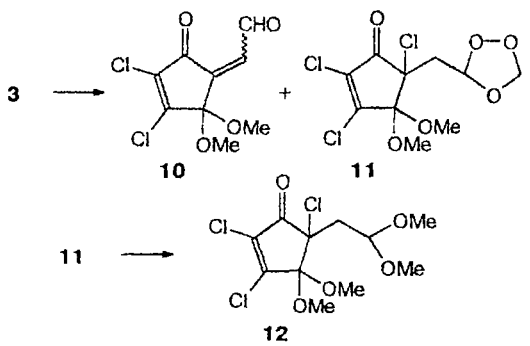
Scheme 1



Scheme 2



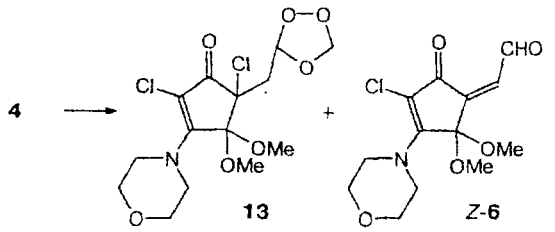
Scheme 3



into aldehydes **10**; complete conversion of **11** took more than 3 days). In this connection, it is of note that although a number of substituted ozonides of type **11** were reported in the literature,[11,12] only a few examples of 1,2,4-trioxolanes stable with respect to Me_2S are known.[13–15]

We also isolated a diastereomeric mixture of 1,2,4-trioxolanes (**13**), which is analogous to that of ozonides **11**, as a result of ozonolysis of cyclopentenone **4**. Aldehyde *Z*-**6** was obtained as a minor product. The total yield of compounds **13** and *Z*-**6** was 80%. The ratio **13** : *Z*-**6** = 3 : 1 (^{1}H NMR) (Scheme 4).

Scheme 4



To summarize, we demonstrated the possibility of selective ozonolysis of exocyclic double bonds of cyclopentenones **1**—**4**.

Experimental

The IR spectra were recorded on a UR-20 spectrophotometer in thin layers or as Nujol mulls. The NMR spectra were obtained on a Bruker AM-300 spectrophotometer (300 and 75.47 MHz for ^{1}H and ^{13}C, respectively) in $CDCl_3$ with Me_4Si as the internal standard. The mass spectra were measured on an Mkh-1320 instrument with the use of a system of direct inlet of the sample into the ion source; the energy of ionizing electrons was 70 eV; the temperature of the ionization chamber was 50—70 °C.

Ozonolysis of compounds 1—4 (general procedure). An ozone-oxygen mixture was bubbled through a solution of the compound under study (~1.5 mmol) in CH_2Cl_2 (20 mL) cooled to −78 °C until the solution turned pale-violet. The course of the reaction was monitored by TLC on Silufol. Passage of the ozone-oxygen mixture was discontinued when the initial compound disappeared. An excess of ozone was removed by purging with argon. Me_2S (4 mol.-equiv.) was added dropwise to the reaction mixture and stirred for 15 min. The test for peroxide compounds (starch iodide test) was negative (trioxolanes were detected by this method only after 30—40 min). Then the reaction mixture was warmed to room temperature, CH_2Cl_2 was evaporated *in vacuo*, and the residue was chromatographed on SiO_2.

2,3,5-Trichloro-4,4-dimethoxycyclopent-2-enone (7). The yield was 90%, colorless crystals, m.p. 52—54 °C (1 : 1 hexane—ethyl acetate). Found (%): C, 34.10; H, 2.82; Cl, 43.40. $C_7H_7Cl_3O_3$. Calculated (%): C, 34.25; H, 2.87; Cl, 43.32. IR, ν/cm^{-1}: 1596, 1620, 1636, 1696, 1752. ^{1}H NMR, δ: 3.30 (s, 3 H, OCH_3); 3.50 (s, 3 H, OCH_3); 4.64 (s, 1 H,

H(5)). ^{13}C NMR, δ: 52.03 (OCH_3); 52.07 (OCH_3); 62.19 (C(5)); 100.49 (C(4)); 133.77 (C(2)); 157.65 (C(3)); 186.17 (C(1)). MS, *m/z* (I_{rel} (%)): 250 (0.9); 248 (7.5); 246 (22.3); 244 $[M]^+$ (27.3); 217 (31.4); 215 (93.6); 213 $[M - OCH_3]^+$ (100); 211 (19.8); 209 $[M - Cl]^+$ (30.9); 190 (4.9); 188 (14.0); 186 $[M - CH_3O - CO]^+$ (15.5); 136 (6.1); 134 (13.8); 112 (2.5); 110 (9.7); 108 (13.3); 97 (31.9); 89 (7.4); 87 (22.8); 69 (11.9); 59 $[OCOCH_3]^+$ (17.7); 55 (11.1); 41 (8.0); 38 (5.5); 36 $[HCl]^+$ (14.8); 28 (23.9).

2,5-Dichloro-2-formyl-3,3-dimethoxy-4-morpholinocyclopent-4-enone (9). The yield was 85%, m.p. 167—169 °C (1 : 1 hexane—ethyl acetate). Found (%): C, 44.60; H, 4.70; Cl, 21.96; N, 4.40. $C_{12}H_{15}Cl_2NO_5$. Calculated (%): C, 44.46; H, 4.66; Cl, 21.87; N, 4.32. IR, ν/cm^{-1}: 1592, 1620, 1636, 1696, 1716, 1736, 1864. ^{1}H NMR, δ: 3.20 (s, 3 H, OCH_3); 3.35 (s, 3 H, OCH_3); 3.70—4.00 (m, 8 H, 2 NCH_2CH_2O); 9.23 (s, 1 H, CHO). ^{13}C NMR, δ: 49.45 (2 NCH_2); 51.57 (OCH_3); 53.67 (OCH_3); 66.81 (2 OCH_2); 81.78 (C(2)); 104.36 (C(4)); 104.42 (C(5)); 159.16 (C(3)); 179.98 (C(1)); 186.94 (CHO). MS, *m/z* (I_{rel} (%)): 327 (9.8); 325 (40.0); 323 $[M]^+$ (57.3); 299 (1.6); 297 (7.9); 295 $[M - CO]^+$ (15.0); 298 (1.8); 296 (10.4); 294 $[M - CHO]^+$ (19.6); 292 $[M - OCH_3]^+$ (12.7); 290 (38.0); 288 $[M - Cl]^+$ (100); 268 (3.0); 266 (13.7); 264 $[M - COOCH_3]^+$ (18.0); 234 (4.6); 232 (10.0); 230 (20.6); 138 $[O^+{\equiv}C{-}C{\equiv}C{-}N(CH_2CH_2)_2O]^+$ (17.2); 89 (10.0); 87 $[HN^+(CH_2CH_2)_2O]$ (19.2); 59 $[OCOCH_3]^+$ (28.1); 45 $[C_2H_2O]^+$ (30.2).

2,3-Dichloro-5-(*Z*)-formylmethylene-4,4-dimethoxycyclopent-2-enone (*Z*-10) and 2,3-dichloro-5-(*E*)-formylmethylene-4,4-dimethoxycyclopent-2-enone (*E*-10) were obtained as a (*Z*-**10**) : (*E*-**10**) mixture in a ratio of 3 : 2 in 20% yield, m.p. 80—90 °C (1 : 1 hexane—ethyl acetate). Found (%): C, 42.60; H, 3.29; Cl, 28.60. $C_9H_8Cl_2O_4$. Calculated (%): C, 43.06; H, 3.21; Cl, 28.24. IR, ν/cm^{-1}: 1610, 1700, 1730.

E-**10**. ^{1}H NMR, δ: 3.36 (s, 6 H, OCH_3); 6.60 (d, 1 H, CH=, *J* = 8.2 Hz); 10.30 (d, 1 H, CHO, *J* = 8.2 Hz). ^{13}C NMR, δ: 52.54 (2 OCH_3); 100.84 (C(4)); 128.57 (CH=); 139.17 (C(2)); 141.77 (C(5)); 157.65 (C(3)); 181.83 (C(1)); 190.61 (CHO).

Z-**10**. ^{1}H NMR, δ: 3.35 (s, 6 H, OCH_3); 6.30 (d, 1 H, CH=, *J* = 7.4 Hz); 10.70 (d, 1 H, CHO, *J* = 7.4 Hz). ^{13}C NMR, δ: 52.08 (2 OCH_3); 102.62 (C(4)); 132.21 (CH=); 138.97 (C(2)); 143.09 (C(5)); 157.71 (C(3)); 181.77 (C(1)); 190.61 (CHO).

2,3,5-Trichloro-4,4-dimethoxy-5-[(1,2,4-trioxolan-3-yl)methyl]cyclopent-2-enones (11). A mixture of 5,3′-diastereomers was obtained in a ratio of 2 : 1 (^{1}H NMR) in 70% yield. Found (%): $O_{act.}$ 9.46. $C_{10}H_{11}Cl_3O_6$. Calculated (%): $O_{act.}$ 9.63. IR, ν/cm^{-1}: 1630, 1680, 1710, 1750, 1770. MS, *m/z* (I_{rel} (%)): 336 (0.2); 334 (0.8); 332 $[M]^+$ (0.9); 306 (0.8); 304 (2); 302 $[M - CH_2O]^+$ (2); 290 (3); 288 (9.2); 286 $[M - CH_2O_2]^+$ (9); 261 (27); 259 (93); 257 $[M - CH_2O_2{-}CHO]^+$ (100); 255 $[M - CH_2O_2 - OCH_3]^+$ (15); 253 (16); 251 $[M - CH_2O_2 - Cl]^+$ (10); 248 (1); 246 (4); 244 $[M - CH_2O_2 - CH_2{=}C{=}O]^+$ (4); 227 (12); 225 (19); 223 (28); 195 (14); 193 (50); 191 (70); 167 (3); 165 (14); 163 (27); 143 (9); 141 (8); 137 (5); 135 (10); 133 (15); 115 (4); 113 (10); 91 (6); 89 (27); 87 (45); 85 (17.5); 75 (4); 73 (6); 63 (4); 61 (6); 59 $[COOCH_3]^+$ (30); 53 (10); 46 (8); 43 (6); 38 (6.5); 36 [HCl] (20); 30 (10); 29 (24); 28 (20).

Major diastereomer (**11**). ^{1}H NMR, δ: 2.45 (dd, 1 H, CH_2, J_{AB} = −15.7 Hz, J_{AX} = 5.0 Hz); 2.49 (dd, 1 H, CH_2, J_{AB} = −15.7 Hz, J_{BX} = 4.8 Hz); 3.46 and 3.52 (both s, 3 H, OCH_3); 4.98 (s, 1 H, OCH_2O); 5.09 (s, 1 H, OCH_2O); 5.48 (dd, 1 H, OCHO, J_{XA} = 5.0 Hz, J_{XB} = 4.8 Hz). ^{13}C NMR, δ: 39.54 (CH_2); 51.88 (OCH_3); 52.23 (OCH_3); 72.44 (C(5)); 93.47 (OCH_2O); 99.97 (OCHO); 102.11 (C(4)); 133.57 (C(2)); 156.06 (C(3)); 187.43 (C(1)).

Minor diastereomer (**11**). ^{1}H NMR, δ: 2.45 (dd, 1 H, CH_2, J_{AB} = 15.7 Hz, J_{AX} = 5.0 Hz); 2.49 (dd, 1 H, J_{AB} = 15.7 Hz, J_{BX} = 4.8 Hz); 3.46 and 3.70 (both s, 3 H, OCH_3); 4.90 (s, 1 H, OCH_2O); 5.07 (s, 1 H, OCH_2O); 5.61 (dd, 1 H, OCHO, J_{XA} = 5.0 Hz, J_{XB} = 4.8 Hz). ^{13}C NMR, δ: 40.76 (CH_2); 52.11 (OCH_3); 52.23 (OCH_3); 72.91 (C(5)); 93.65 (OCH_2O); 99.83 (OCHO); 102.16 (C(4)); 133.21 (C(2)); 156.44 (C(3)); 187.52 (C(1)).

2,3,5-Trichloro-4,4-dimethoxy-5-(2,2-dimethoxyethyl)cyclopent-2-enone (12) was obtained upon storage of a mixture of diastereomers **11** in a 5% solution of HCl in MeOH (20 °C, 12 h), in 60% yield. Found (%): C, 39.60; H, 4.40; Cl, 31.25. $C_{11}H_{15}Cl_3O_5$. Calculated (%): C, 39.61; H, 4.53; Cl, 31.88. IR, ν/cm^{-1}: 1600, 1670, 1730. ^{1}H NMR, δ: 2.29 (dd, 1 H, CH_2, J_{AB} = 14.7 Hz, J_{AX} = 3.3 Hz); 2.40 (dd, 1 H, CH_2, J_{AB} = 14.7 Hz, J_{BX} = 6.7 Hz); 3.18 and 3.20 (both s, 3 H, OCH_3); 3.42 and 3.53 (both s, 3 H, OCH_3); 4.45 (dd, 1 H, OCHO, J_{XA} = 3.3 Hz, J_{XB} = 6.7 Hz). ^{13}C NMR, δ: 43.97 (CH_2); 51.76 (OCH_3); 52.82 (2 OCH_3); 54.45 (OCH_3); 76.32 (C(5)); 100.81 (OCHO); 101.85 (C(4)); 134.34 (C(2)); 154.16 (C(3)); 187.87 (C(1)). MS, *m/z* (I_{rel} (%)): 336 (0.1); 334 (0.4); 332 $[M - H]^+$ (0.4); 306 (1); 304 (7); 302 $[M - OCH_3]^+$ (7); 274 (3.5); 272 (10); 270 $[M - CH_3O - CH_3OH]^+$ (13); 268 (7.5); 266 $[M - CH_3O - HCl]^+$ (12.5); 196 (3.6); 194 (8); 192 (11.3); 168 (2), 166 (6); 164 (7.8); 135 (4); 133 (9.4); 89 (8); 87 (19); 85 (8); 76 (20); 75 $[CH_3O^+{=}CH{-}OCH_3]$ (100); 59 $[CH_3OCO]^+$ (26.3); 47 $[CH_3 - O^+(H) - CH_3]$ (62); 38 (8); 36 $[HCl]^+$ (22); 31 (30); 29 (14); 28 (43).

2-Chloro-5-(*Z*)-formylmethylene-4,4-dimethoxy-3-morpholinocyclopent-2-enone (*Z*-6). The yield was 20%, oil. Found (%): C, 51.67; H, 5.30; Cl, 11.94; N, 4.55. $C_{13}H_{16}ClNO_5$. Calculated (%): C, 51.75; H, 5.35; Cl, 11.75; N, 4.64. ^{1}H NMR, δ: 3.25 (s, 6 H, OCH_3); 3.80—4.10 (m, 8 H, OCH_2CH_2N); 6.05 (d, 1 H, CH=, *J* = 7.6 Hz); 11.00 (d, 1 H, CHO, *J* = 7.6 Hz). ^{13}C NMR, δ: 49.63 (CH_2N); 52.26 (2 OCH_3); 67.22 (CH_2O); 103.90 (C(4)); 111.24 (C(2)); 128.10 (CH=); 142.66 (C(5)); 157.42 (C(3)); 180.70 (C(1)); 191.45 (CHO).

2,5-Dichloro-4,4-dimethoxy-3-morpholino-5-[(1,2,4-trioxolan-3-yl)methyl]cyclopent-2-enones (13). The yield was 60%; the ratio of the diastereomers was 1 : 3 (^{1}H NMR). IR, ν/cm^{-1}: 1590, 1690.

Minor diastereomer (**13**). ^{1}H NMR, δ: 2.39 (dd, 1 H, CH_2, J_{AB} = −14.8 Hz, J_{AX} = 4.7 Hz); 2.42 (dd, 1 H, CH_2, J_{AB} = −14.8 Hz, J_{BX} = 3.8 Hz); 3.25 and 3.54 (both s, 3 H, OCH_3); 3.70—4.30 (m, 8 H, OCH_2CH_2N); 5.06 (s, 1 H, OCH_2O); 5.08 (s, 1 H, OCH_2O); 5.60 (dd, 1 H, OCHO, J_{XA} = 4.7 Hz, J_{XB} = 3.8 Hz). ^{13}C NMR, δ: 43.07 (CH_2); 49.40 (CH_2N); 51.65, 53.53 (OCH_3); 67.14 (OCH_2); 72.15 (C(5)); 93.83 (OCH_2O); 100.20 (OCHO); 103.05 (C(4)); 104.57 (C(2)); 157.89 (C(3)); 186.36 (C(1)).

Major diastereomer (**13**). ^{1}H NMR, δ: 2.39 (dd, 1 H, CH_2, J_{AB} = −14.8 Hz, J_{AX} = 4.7 Hz); 2.42 (dd, 1 H, CH_2, J_{AB} = −14.8 Hz, J_{BX} = 3.8 Hz); 3.24 and 3.55 (both s, 3 H, OCH_3); 3.70—4.30 (m, 8 H, OCH_2CH_2N); 4.98 (s, 1 H, OCH_2O); 5.12 (s, 1 H, OCH_2O); 5.60 (dd, 1 H, OCHO, J_{XA} = 4.7 Hz, J_{XB} = 3.8 Hz). ^{13}C NMR, δ: 43.59 (CH_2); 51.40 (CH_2N); 51.59 (OCH_3) and 53.58 (OCH_3); 67.14 (OCH_2); 72.54 (C(5)); 93.83 (OCH_2O); 100.20 (OCHO); 103.12 (C(4)); 104.57 (C(2)); 157.89 (C(3)); 186.36 (C(1)).

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