

## REACTION OF ADAMANTANONE, DIAMANTANONE, AND THEIR DERIVATIVES WITH THIONYL CHLORIDE

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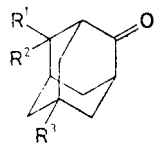
In reaction of adamantanone, diamantanone, and their chloro or oxo derivatives with thionyl chloride the oxo group is replaced with two chlorine atoms under formation of geminal dichloro derivatives. The presence of a chlorine atom or an oxo group in both ketones reduces the reaction rate. The reaction rate decreases with decreasing distance between the substituent and the carbonyl group. Ketones with chlorine atom in  $\alpha$ - or  $\beta$ -axial position do not react with thionyl chloride. The reaction is accelerated by hydrogen chloride whereas in the presence of pyridine no reaction was observed.

In our previous study on reaction of 5-oxo-4-oxahomoadamantane with thionyl chloride 2,2,4-trichloroadamantane has been found<sup>1</sup> among the reaction products. This compound was assumed to arise from the primary reaction product – 4-chloro-2-adamantanone<sup>1</sup>. Our assumption has been confirmed by reaction of isomeric 4-chloro-2-adamantanones, as well as adamantanone itself, with thionyl chloride.

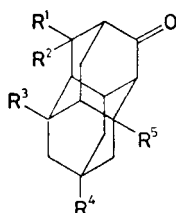
Our present paper concerns the reaction of compounds *I–XII* with thionyl chloride. The chloro ketones *II–IV* and *VI–X* were prepared *in situ* by reaction of thionyl chloride with the corresponding hydroxy ketones *XIII–XVIII*. Hydroxy derivatives with axial hydroxyl (*XIII* and *XV*) afforded a mixture of axial and equatorial chloro ketones in approximate ratio 4 : 6. This fact indicates that the replacement of hydroxyl by chlorine atom in adamantanone and diamantanone derivatives (at least in those with secondary hydroxyl) proceeds by  $S_N1$  mechanism.

The reaction of carbonyl group with thionyl chloride was catalyzed with hydrogen chloride. With the slowly reacting diketones *XI* and *XII*, we observed an apparent induction period. Whereas the reaction rate was markedly enhanced on addition of hydrochloric acid, no reaction occurred in the presence of pyridine. The induction period was not well perceptible with chloro ketones which had been prepared from the corresponding hydroxy ketones and thionyl chloride and which therefore contained hydrogen chloride from the beginning of the reaction.

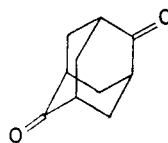
All the studied carbonyl compounds cannot exist in the enol form (Bredt rule). The reaction with thionyl chloride proceeds probably *via* the ester chloride *C* which further decomposes into the dichloro derivative *D* (Scheme 1). The carbonyl group



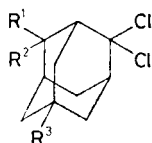
I-IV, XIII, XIV



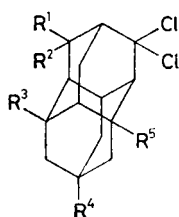
V-X, XV-XVIII



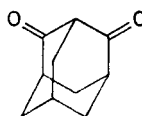
XI



XIX-XXII



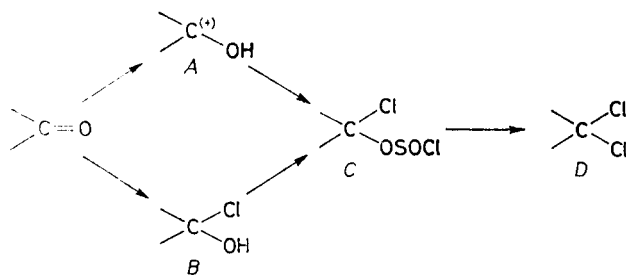
XXIII-XXVIII



XII

- |   |  |
|---|--|
| I, XIX, R <sup>1</sup> = R <sup>2</sup> = R <sup>3</sup> = H  | IX, XXVII, R <sup>4</sup> = Cl ; R <sup>1</sup> = R <sup>2</sup> = R <sup>3</sup> = R <sup>5</sup> = H |
| II, XX, R <sup>1</sup> = Cl ; R <sup>2</sup> = R <sup>3</sup> = H                                       | X, XXVIII, R <sup>5</sup> = Cl ; R <sup>1</sup> = R <sup>2</sup> = R <sup>3</sup> = R <sup>4</sup> = H |
| III, XXI, R <sup>2</sup> = Cl ; R <sup>1</sup> = R <sup>3</sup> = H                                     | XIII, R <sup>1</sup> = OH ; R <sup>2</sup> = R <sup>3</sup> = H  |
| IV, XXII, R <sup>3</sup> = Cl ; R <sup>1</sup> = R <sup>2</sup> = H                                     | XIV, R <sup>3</sup> = OH ; R <sup>1</sup> = R <sup>2</sup> = H   |
| V, XXIII, R <sup>1</sup> = R <sup>2</sup> = R <sup>3</sup> = R <sup>4</sup> = R <sup>5</sup> = H        | XV, R <sup>1</sup> = OH ; R <sup>2</sup> = R <sup>3</sup> = R <sup>4</sup> = R <sup>5</sup> = H        |
| VI, XXIV, R <sup>1</sup> = Cl ; R <sup>2</sup> = R <sup>3</sup> = R <sup>4</sup> = R <sup>5</sup> = H   | XVI, R <sup>3</sup> = OH ; R <sup>1</sup> = R <sup>2</sup> = R <sup>4</sup> = R <sup>5</sup> = H       |
| VII, XXV, R <sup>2</sup> = Cl ; R <sup>1</sup> = R <sup>3</sup> = R <sup>4</sup> = R <sup>5</sup> = H   | XVII, R <sup>4</sup> = OH ; R <sup>1</sup> = R <sup>2</sup> = R <sup>3</sup> = R <sup>5</sup> = H      |
| VIII, XXVI, R <sup>3</sup> = Cl ; R <sup>1</sup> = R <sup>2</sup> = R <sup>4</sup> = R <sup>5</sup> = H | XVIII, R <sup>5</sup> = OH ; R <sup>1</sup> = R <sup>2</sup> = R <sup>3</sup> = R <sup>4</sup> = H     |

can react with thionyl chloride either in the protonated form *A*, or the first reaction intermediate can be the chlorohydrin *B* formed by reaction of the carbonyl with hydrogen chloride. No unequivocal distinction between these two ways is possible at present.



SCHEME 1

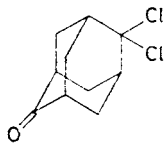
The reaction rate is substantially influenced by substituents attached to the adamantane skeleton. No precise kinetic studies have been done; approximate reaction rates were obtained by comparing the time of 10% conversion into the geminal dichloride with that found for adamantanone (Table I). Steric hindrance in the substituted adamantanones may arise only when the substituents are in position  $\alpha$ - or  $\beta$ -axial to the carbonyl group and, in case of very bulky substituents, also in the  $\gamma$ -axial position. Substituents in  $\beta$ -equatorial and more distant positions cannot give rise to any hindrance. Accordingly, diamantanone (formally adamantanone with two  $\beta$ -equatorial and one  $\delta$  substituents) reacts practically at the same rate as adamantanone.

A greater influence on the reaction velocity has the inductive effect. Derivatives with substituents in position  $\alpha$  were not available. In the reaction of 1-chloro-3-diamantanone (X) in which the chlorine atom is  $\beta$ -axial and the steric and induction effects operate in the same direction, no trichloro derivative XXIX was found even after 30 hours' reflux with thionyl chloride. The reaction of 4-chloro-2-adamantanones (II and III) gave only one of the possible trichloro derivatives – 2,2,4<sup>e</sup>-trichloroadamantane (XXI), showing that only the equatorial chloroadamantanone III reacts. The isomer II, containing (like 1-chloro-3-diamantanone (X)) a  $\beta$ -axial chlorine atom, did not react with thionyl chloride and was equilibrated to the isomer III. The same situation was also found with 5-chloro-3-diamantanone (VI and VII). Introduction of a  $\beta$ -equatorial chlorine atom decreased the reaction rate by about two orders of magnitude. 1-Chloro-4-adamantanone (IV) with a  $\gamma$ -chlorine atom reacted at about the same rate as chloro ketones with  $\beta$ -equatorial chlorine substi-

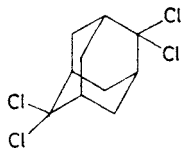
TABLE I  
Relative reaction rates of substituted adamantanones and diamantanones

| Compound                                   | Position of 2 <sup>nd</sup> substituent | Relative rate       |
|--|---|---------------------|
| Adamantanone(I)                            | —                                       | 1                   |
| Diamantanone(V)                            | —                                       | $8.3 \cdot 10^{-1}$ |
| 11-Chloro-3-diamantanone(VIII)             | $\delta$                                | $1.8 \cdot 10^{-1}$ |
| 9-Chloro-3-diamantanone(IX)                | $\delta$                                | $1.6 \cdot 10^{-1}$ |
| 1-Chloro-4-adamantanone(IV)                | $\gamma$                                | $2.9 \cdot 10^{-2}$ |
| 4 <sup>e</sup> -Chloro-2-adamantanone(III) | $\beta$ -equatorial                     | $1.4 \cdot 10^{-2}$ |
| 5 <sup>e</sup> -Chloro-3-diamantanone(VII) | $\beta$ -equatorial                     | $2.7 \cdot 10^{-2}$ |
| 2,6-Adamantanedione(XI), method A          | $\delta$                                | $2.5 \cdot 10^{-2}$ |
| 2,6-Adamantanedione(XI), method B          | $\delta$                                | $1.2 \cdot 10^{-1}$ |
| 2,4-Adamantanedione(XII), method A         | $\beta$                                 | $1.1 \cdot 10^{-2}$ |
| 2,4-Adamantanedione (XII), method B        | $\beta$                                 | $1.9 \cdot 10^{-2}$ |

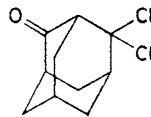
tuent. 11-Chloro- and 9-chloro-3-diamantanone (*VIII* and *IX*) contain a  $\delta$ -chlorine atom. Their reaction rates are very similar and, as expected, least reduced compared with *I* and *V* (about one order of magnitude).



XXIX



XXX



XXXI

The presence of a second carbonyl group in the diones lowered the reaction rate by about 2 orders of magnitude. In 2,4-adamantanedione (*XII*) only one of the carbonyl groups reacted: The arising 4,4-dichloro-2-adamantanone (*XXXI*), in which one of the chlorine atoms is  $\beta$ -axial, did not react further with thionyl chloride. In the case of 2,6-adamantanedione (*XI*), the originally formed 6,6-dichloro-2-adamantanone (*XXIX*) with both chlorine atoms in  $\delta$ -position reacted further, affording 2,2,6,6-tetrachloroadamantane (*XXX*) as the final reaction product.

## EXPERIMENTAL

### Analytical Methods

Gas-liquid chromatographic analyses were performed on a Chrom 5 chromatograph (Laboratorní přístroje, Prague) on a  $3 \times 1$  200 mm glass column packed with XF-1 150 (3% on Chromaton N-AW-DMCS) at 120–180°C (FID, carrier gas nitrogen). The elution data are given as relative elution times,  $t_r$ , related to the starting ketone, dione or chloro ketone. The samples for analysis were prepared in the following manner: After withdrawal of the sample (50  $\mu$ l) with a micropipette, thionyl chloride was evaporated *in vacuo*, the residue was dissolved in chloroform (100  $\mu$ l), washed with water (200  $\mu$ l) and injected into the chromatograph. Mass spectra of pure compounds were measured on an LKB 9 000 instrument (direct inlet), IR spectra (KBr pellets) on a Perkin-Elmer 325 spectrometer.

### Reaction of Ketones and Diones with Thionyl Chloride

A. A solution of the carbonyl compound in thionyl chloride ( $c = 0.5 \text{ mmol ml}^{-1}$ ) was refluxed and samples were withdrawn during the reaction and analyzed by gas-liquid chromatography. The results are given in Table I. In the end, thionyl chloride was distilled off *in vacuo*, the residue was dissolved in chloroform, the solution was washed with water, dried and the solvent was evaporated. The product was separated or purified by chromatography on silica gel (50 g/1 g of product; elution with hexane and a gradient of hexane-ether).

B. Concentrated hydrochloric acid (10  $\mu$ l/1 mmol of ketone) was added to a solution of the carbonyl compound in thionyl chloride ( $c = 0.5 \text{ mmol ml}^{-1}$ ) and the mixture was refluxed. The monitoring and work-up of the reaction mixture were the same as ad A.

C. Dry pyridine (100  $\mu\text{l}$ /1 mmol of ketone) was added to a solution of the carbonyl derivative in thionyl chloride ( $c = 0.5 \text{ mmol ml}^{-1}$ ) and the mixture was refluxed. The monitoring and work-up of the reaction mixture were the same as ad A.

*Adamantanone (I)*: 0.5 g (3.3 mmol) of *I*, reaction time 8 h, yield 0.63 g (93%) of 2,2-dichloro-adamantane (*XIX*),  $t_r$  (150°C) 0.90, m.p. 208.5–209°C (reported<sup>2</sup> 203–204°C). Mass and IR spectra identical with those of a standard<sup>1</sup>.

*Diamantanone (V)*: 0.5 g (2.5 mmol) of *V*, reaction time 8 h, yield 0.6 g (94%) of 3:3-dichloro-diamantane (*XXIII*),  $t_r$  (160°C) 0.78, m.p. 118–119°C (hexane). For  $\text{C}_{14}\text{H}_{18}\text{Cl}_2$  (257.2) calculated: 65.38% C, 7.05% H, 27.57% Cl; found: 65.44% C, 7.00% H, 27.28% Cl. Mass spectrum  $m/z$  (%): 256 (7,  $\text{M}^+$ ), 221 (44), 220 (100), 185 (20). IR spectrum  $\nu$ ,  $\text{cm}^{-1}$ : 610, 639, 643, 691, 748, 767, 775, 804.

*2,6-Adamantanedione (XI)*: Methods A, B, C: 0.3 g (1.8 mmol) of *XI*, reaction time 40 h, yield A 0.44 g, B 0.46 g, C 0.28 g. In the presence of pyridine (method C) only the starting dione *XI* was recovered. Chromatography of the combined products obtained by methods A and B afforded 0.36 g of *XXX*, 0.26 g of *XXIX*, and 0.18 g of *XI*.

*2,2,6,6-Tetrachloroadamantane (XXX)*:  $t_r$  (160°C) 0.67, m.p. (acetone) 133.5–134°C. For  $\text{C}_{10}\text{H}_{12}\text{Cl}_4$  (274.0) calculated: 43.83% C, 4.42% H, 51.75% Cl; found: 43.71% C, 4.31% H, 51.48% Cl. Mass spectrum  $m/z$  (%): 239 (93), 237 (100), 201 (57), 165 (54), 129 (52), 113 (28), 77 (39). IR spectrum  $\nu$ ,  $\text{cm}^{-1}$ : 632, 684, 773, 799.

*6,6-Dichloro-2-adamantanone (XXIX)*:  $t_r$  (160°C) 0.85, m.p. 244.5–245°C (hexane). For  $\text{C}_{10}\text{H}_{12}\text{Cl}_2\text{O}$  (219.1) calculated: 54.82% C, 5.52% H, 32.36% Cl; found: 54.83% C, 5.44% H, 32.07% Cl. Mass spectrum  $m/z$  (%): 220 (65), 218 (100), 183 (74), 165 (44), 147 (67), 119 (98), 117 (58), 91 (72). IR spectrum  $\nu$ ,  $\text{cm}^{-1}$ : 623, 632, 725, 774, 790, 806, 1 728.

*2,4-Adamantanedione (XII)*: Method A: 0.16 g (1 mmol) of *XII*, method B: 0.5 g (3 mmol) of *XII*, reaction time 40 h, yield: A 0.19 g, B 0.63 g. Chromatography of combined products of both experiments afforded 0.57 g of unreacted dione *XII* and 0.21 g of 4,4-dichloro-2-adamantanone (*XXXI*),  $t_r$  (140°C) 0.78, m.p. 203–204°C (hexane). For  $\text{C}_{10}\text{H}_{12}\text{Cl}_2\text{O}$  (219.1) calculated: 54.82% C, 5.52% H, 32.36% Cl; found: 54.75% C, 5.44% H, 32.17% Cl. Mass spectrum  $m/z$  (%) 218 (20,  $\text{M}^+$ ), 183 (50), 182 (42), 155 (75), 154 (50), 119 (100), 91 (70). IR spectrum  $\nu$ ,  $\text{cm}^{-1}$ : 622, 648, 687, 730, 762, 783, 797, 1 735.

#### Reaction of Chloro Ketones with Thionyl Chloride

A mixture of the hydroxy derivative and thionyl chloride (1 ml/0.5 mmol of substrate) was allowed to stand at room temperature. After 1 h a sample was withdrawn and analyzed by gas-liquid chromatography. The reaction mixture was refluxed, analyzed and worked up as described above. The results are given in Table I.

*4<sup>a</sup>-Chloro-2-adamantanone (II, III)*: From 4<sup>a</sup>-hydroxy-2-adamantanone (*XIII*; 0.6 g; 3.6 mmol), reaction time 40 h, yield 0.65 g. Chromatography of the reaction product gave *XXI* (0.11 g), *III* (0.21 g), *II* (0.15 g), and intermediate fractions (0.15 g).

*2,2,4<sup>e</sup>-Trichloroadamantane (XXI)*:  $t_r$  (180°C) 0.81; m.p. 151.5–154°C. Mass and IR spectra identical with those of a standard<sup>1</sup>.

*4<sup>e</sup>-Chloro-2-adamantanone (III)*:  $t_r$  (180°C) 1.00, m.p. 202.5–204°C (reported<sup>3</sup> 201–203°C). Mass spectrum identical with the published one<sup>4</sup>.

*4<sup>a</sup>-Chloro-2-adamantanone (II)*:  $t_r$  (180°C) 2.17, m.p. 217–219°C (reported<sup>5</sup> 214.5–216°C). Mass spectrum identical with the published one<sup>4</sup>.

5<sup>a,e</sup>-Chloro-3-diamantanone (VI, VII): From 0.5 g (2.3 mmol) of 5<sup>a</sup>-hydroxy-3-diamantanone (XV), reaction time 30 h, yield 0.58 g. Chromatography of the reaction product afforded XXV (0.19 g), VII (0.24 g), VI (0.16 g), and intermediate fractions (0.19 g).

3,3,5<sup>e</sup>-Trichlorodiamantane (XXV):  $t_r$  (180°C) 0.70, m.p. (hexane) 114.5–115.5°C. For C<sub>14</sub>H<sub>17</sub>Cl<sub>3</sub> (291.6) calculated: 57.66% C, 5.88% H, 36.47% Cl; found: 57.59% C, 5.74% H, 36.29% Cl. Mass spectrum  $m/z$  (%): 290 (2, M<sup>+</sup>), 255 (33), 254 (100), 220 (7), 219 (30), 183 (9). IR spectrum  $\nu$ , cm<sup>-1</sup>: 609, 638, 679, 692, 728, 757, 793, 807.

5<sup>e</sup>-Chloro-3-diamantanone (VII):  $t_r$  (180°C) 1.00, m.p. (hexane) 233–234.5°C. For C<sub>14</sub>H<sub>17</sub>ClO (236.7) calculated: 71.03% C, 7.24% H, 14.97% Cl; found: 70.90% C, 7.28% H, 14.66% Cl. Mass spectrum  $m/z$  (%): 236 (30, M<sup>+</sup>), 201 (33), 173 (100), 91 (80). IR spectrum  $\nu$ , cm<sup>-1</sup>: 604, 638, 682, 713, 763, 799, 1720.

5<sup>a</sup>-Chloro-3-diamantanone (VI):  $t_r$  (180°C) 2.19, m.p. (hexane) 171–172°C. For C<sub>14</sub>H<sub>17</sub>ClO (236.7) calculated: 71.03% C, 7.24% H, 14.97% Cl; found: 70.88% C, 7.16% H, 14.73% Cl. Mass spectrum  $m/z$  (%): 236 (63, M<sup>+</sup>), 201 (58), 200 (24), 173 (55), 172 (26), 91 (90), 80 (100). IR spectrum  $\nu$ , cm<sup>-1</sup>: 612, 633, 664, 695, 738, 753, 800, 1714.

1-Chloro-4-adamantanone (IV): From 0.4 g (2.4 mmol) of 1-hydroxy-4-adamantanone (XIV); reaction time 30 h, yield 0.51 g. Chromatography of the reaction product afforded 0.23 g of XXII, 0.19 g of IV, and 0.06 g of an intermediate fraction.

1,4,4-Trichloroadamantane (XXII):  $t_r$  (120°C) 0.93, m.p. (acetone) 152–152.5°C (reported<sup>6</sup> 153–154°C). Mass spectrum  $m/z$  (%): 238 (1, M<sup>+</sup>), 203 (100), 202 (19), 167 (32), 131 (28), 113 (16), 91 (24). IR spectrum  $\nu$ , cm<sup>-1</sup>: 662, 694, 780, 800.

1-Chloro-4-adamantanone (IV):  $t_r$  (120°C) 1.00, m.p. (hexane) 194–194.5°C (reported<sup>7</sup> 197–200°C). Mass spectrum  $m/z$  (%): 184 (89, M<sup>+</sup>), 136 (10), 149 (23), 131 (49), 113 (39), 91 (48), 79 (100).

1-Chloro-3-diamantanone (X): From 0.25 g (1.15 mmol) of 1-hydroxy-3-diamantanone (XVIII); reaction time 30 h, yield 0.24 g (89%) of 1-chloro-3-diamantanone (X), m.p. (hexane) 266.5°C – (decomp.). For C<sub>14</sub>H<sub>17</sub>ClO (236.7) calculated: 71.03% C, 7.24% H, 14.97% Cl; found: 69.78% C, 7.17% H, 14.74% Cl. Mass spectrum  $m/z$  (%): 236 (70, M<sup>+</sup>), 201 (100), 173 (22), 131 (14), 91 (27). IR spectrum  $\nu$ , cm<sup>-1</sup>: 632, 655, 662, 710, 746, 753, 788, 810, 1715.

11-Chloro-3-diamantanone (VIII): From 0.3 g (1.4 mmol) of 11-hydroxy-3-diamantanone (XVI); reaction time 25 h, yield 0.37 g (93%) of 1,5,5-trichlorodiamantane (XXVI),  $t_r$  (160°C) 0.72, m.p. (hexane) 129–129.5°C. For C<sub>14</sub>H<sub>17</sub>Cl<sub>3</sub> (291.6) calculated: 57.66% C, 5.88% H, 36.47% Cl; found: 57.64% C, 5.93% H, 36.39% Cl. Mass spectrum  $m/z$  (%): 290 (2, M<sup>+</sup>), 255 (100), 254 (66), 219 (68), 183 (27), 165 (11), 129 (21), 91 (36). IR spectrum  $\nu$ , cm<sup>-1</sup>: 618, 636, 657, 668, 705, 758, 775, 807.

9-Chloro-3-diamantanone (IX): From 0.3 g (1.4 mmol) of 9-hydroxy-3-diamantanone (XVII), reaction time 30 h, yield 0.38 g (95%) of 3,3,9-trichlorodiamantane (XXVII),  $t_r$  (160°C) 0.71, m.p. (hexane) 123–123.5°C. For C<sub>14</sub>H<sub>17</sub>Cl<sub>3</sub> (291.6) calculated: 57.66% C, 5.88% H, 36.47% Cl; found: 57.59% C, 5.80% H, 36.19% Cl. Mass spectrum  $m/z$  (%): 290 (5, M<sup>+</sup>), 255 (100), 254 (90), 219 (38), 218 (44), 183 (17). IR spectrum  $\nu$ , cm<sup>-1</sup>: 620, 640, 655, 714, 755, 770, 780, 801, 810.

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