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Backside Activation of $\sigma_{C\text{-}C}$-Bonds with Cr(VI) - Reagents

Andrey A. Fokin,* Pavel A. Gunchenko, Borislav A. Tkachenko, Ekaterina D. Butova, Alexander G. Yurchenko

Department of Organic Chemistry, Kiev Polytechnic Institute, 37 Pobedy Avenue, 252056 Kiev, Ukraine

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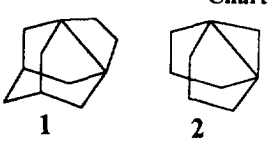
Abstract: The transformations of stable propellanes 3,6-dehydrohomoadamantane (**1**) and 1,5-dehydrobicyclo[3.3.1]nonane (**2**) on treatment with chromyl oxidants in different solvents were studied. Hydrocarbon **1** with CrO_2Cl_2 in nonpolar solvents forms 3,6-dichloro- (**3**) and 3-chloro-6-hydroxy- (**4**) homoadamantanes in the course of *backside* oxidative addition to the strained C-C bond and 3-oxobicyclo[3.3.1]nonane-7-spirocyclopropane (**5**) as a result of the oxidative cyclobutane ring contraction. $CrO_2(OAc)_2/Ac_2O$ and $CrO_2(OCOCF_3)_2/(CF_3CO)_2O$ result only in oxidative addition with the formation of the mixtures of the corresponding 6-hydroxy-3-acetates (**7**,**9**) and 3,6-diacetates (**6**,**8**). In the case of **2** the only oxidative addition takes place. Possible mechanisms of the *backside* oxidative addition to the C-C bond are discussed.

The activation and functionalization of hydrocarbons by metal oxo species is a subject of both synthetic and mechanistic studies.[1] The reactivity of alkane C-H bonds with Co(III), Mn(VII), Fe(IV) and Cr(VI)-containing reagents has been examined by many.[2a-d] The synthetic utility of these processes in chemistry of alkanes is limited because of low selectivity and complexity of these reactions. A general mechanistic picture of these transformations is also understood not well enough; recent mechanistic studies have been applicable to the reaction of CrO_2Cl_2 with different hydrocarbons.[3] The reagent was suggested to act as H-abstractor at the rate-limiting step with an alkyl radical and $HOCrOCl_2$ formation. The abstraction step of these reactions is still dimmed because one is unable to identify the nature of the leaving group. In order to gain additional information on the mechanisms of alkane activation by Cr(VI)-reagents, well-understood model systems should be used. It was previously shown that some propellanes[4] could be used as relevant models for studying the mechanisms of alkane activation by stable electrophiles. We have recently reported[5] a detailed study on the *backside* oxidation of the propellanic $\sigma_{C\text{-}C}$-bond by NO_2^+-containing reagents. In the present paper we will discuss the reactivity of some propellanes *viz.* 3,6-dehydrohomoadamantane (**1**) and 1,5-dehydrobicyclo[3.3.1]nonane (**2**) (**Chart 1**) towards low-electrophilic chromyl oxidants {CrO_2Cl_2, $CrO_2(OAc)_2$ and $CrO_2(OCOCF_3)_2$[6]} in different media. In accordance with the data obtained earlier,[5,7] hydrocarbons **1** and **2** add various reagents without the rearrangement of the cage structure, and their choice as model compounds for the target study seems to be most promising.

Chart 1



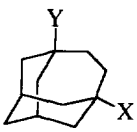
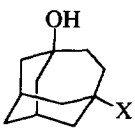
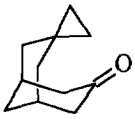
1 **2**

Table summarizes GC/MS data for typical experiments on hydrocarbon **1** interacting with Cr(VI)-reagents. The reaction of **1** with 2.5 equivalents of CrO_2Cl_2 in nonpolar solvents (exp. 1 and exp. 2) is accompanied by the formation of a dark green solution and brown precipitate. After the quenching of the reaction mixture with saturated $NaHSO_3$ followed by a standard workup,[3] reaction products **3**,**4** and, surprisingly,[8] **5** were separated by column chromatography with good preparative yields. Ketone **5** does form the complex with a reduced chromium reagent (Étard complex[9a]) in the course of the reaction. On separate workup of the

liquid phase and precipitate, compounds **3** and **4** were separated from the former (preparative yields of 33% and 20%, respectively) and ketone **5** was obtained only from the latter (25% yield). The structure of the Étard complex of **5** is of special interest[9] and its separation and titration according to a procedure[3a] show the +4.5(±0.2) oxidation state[9b] of chromium (for a possible structure of the complex, see[9b] and below).

The same situation holds for the reaction of **1** with $CrO_2(OAc)_2/CCl_4$ (exp. 3) and $CrO_2(OCOCF_3)_2/CCl_4$ (exp. 5). Under the same conditions (2.5 molar excess of the reagent, 0°C, 0.5 h) compounds **5-9**[10] were formed with good preparative yields. In contrast with the transformations in weakly nucleophilic solvents, in the reaction with $CrO_2(OAc)_2/Ac_2O$ and $CrO_2(OCOCF_3)_2/(CF_3CO)_2O$ ketone **5** is formed only in trace amounts (exp. 4 and exp. 6).

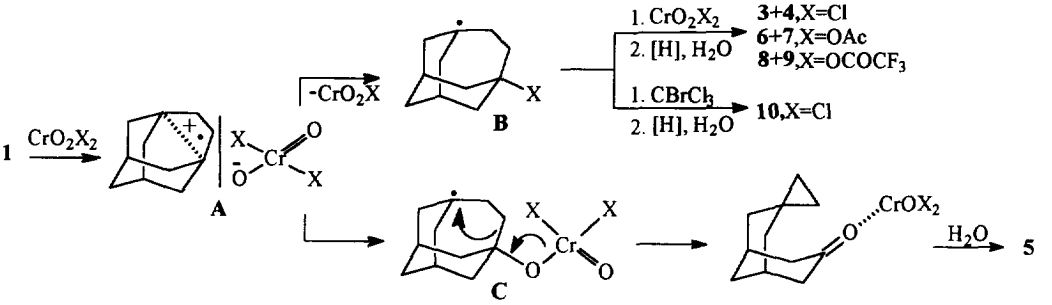
Table. Distribution of product in the reaction of 3,6-dehydrohomoadamantane (**1**) with Cr(VI)-reagents (GC/MS data).

Exp #	Reagent	Solvent			
1	CrO_2Cl_2	CCl_4	**3**, X=Y=Cl (39%)	**4**, X=Cl (25%)	**5** (28%)
2	CrO_2Cl_2	n-C_5H_{12}	**3**, X=Y=Cl (40%)	**4**, X=Cl (25%)	**5** (27%)
3	$CrO_2(OAc)_2$	CCl_4	**6**, X=Y=OAc (15%)	**7**, X=OAc (45%)	**5** (35%)
4	$CrO_2(OAc)_2$	Ac_2O	**6**, X=Y=OAc (47%)	**7**, X=OAc (43%)	**5** (3%)
5	$CrO_2(OCOCF_3)_2$	CCl_4	**8**, X=Y= $OCOCF_3$ (17%)	**9**, X= $OCOCF_3$ (42%)	**5** (34%)
6	$CrO_2(OCOCF_3)_2$	$(CF_3CO)_2O$	**8**, X=Y= $OCOCF_3$ (85%)	**9**, X= $OCOCF_3$ (5%)	**5** (3%)
7	CrO_2Cl_2	$CBrCl_3$	**3**, X=Y=Cl (31%) **10**, X=Cl, Y=Br (16%)	**4**, X=Cl (20%) **11**, X=Br (3%)	**5** (19%)

Thus, we can consider that the transformation of **1** on treatment with Cr(VI)-reagents (addition of two nucleophiles to the $\sigma_{C\text{-}C}$ -bond) has important common features with the reaction of **1** with NO_2^+-containing reagents.[5] Moreover, the formation of compounds **3,6** and **8** can be explained only within the frame of the CET-mechanism proposed earlier[5] for the oxidation of **1**. The electrophilic way of the reaction can be excluded because of an extremely high stability of **1** towards electrophiles[5b] and low electrophilicity of the reagents.[11] Besides, the electrophilic pathway cannot explain the formation of ketone **5**, formed parallel with **3** and **4** (monitoring the reaction by GC/MS). The free-radical chlorination of the C-C bond by Cl$^{\bullet}$, formed as a result of CrO_2Cl_2 homolysis, also seemed unfavorable because of independence of reaction rates and the product distribution on light irradiation and in the presence of peroxide initiators or Hg as the Cl_2 capturer.[12] Additionally the starting compound **1** was shown to be stable towards t-BuOO$^{\bullet}$ in the model reaction of oxo chromyl radical activation[13] even on heating in CCl_4. The series of the products can be rationalized on the basis of one-electron *backside* oxidative addition (**Scheme 1**) with the cleavage of the $\sigma_{C\text{-}C}$-bond and the formation of the cation radical **A** which may further undergo ion-pair or radical-pair collapse. In nonpolar solvents the ion collapse of **A** with the formation of radicals **B** and **C** is more probable than the radical one. The product selection at the level of **A** transformation was confirmed using $CBrCl_3$ as an efficient free radical trapping agent.[14] A partial trapping of **B** and **C** by $CBrCl_3$ leads to the formation of substantial amounts of bromide **10** and only trace amounts of alcohol **11** (exp. 7). At the same time **3/4** ratio in this experiment remained unchanged in comparison with the data of exp. 1. The fact that **10** is the main product in radical trapping experiment might be concerted with **B** formation as a common intermediate on the way to **3** and **4**. In addition, the product distributions were examined in depending on the initial excess of CrO_2Cl_2. With increasing the excess of the reagent over the range of 1 to 10 eqv., the ratio of **3/4** remains unchanged {1.55(±0.05)} and the

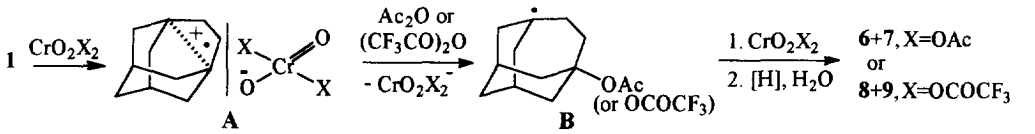
relative amounts of **5** in the reaction mixture decreased. These observation may be a manifestation of **B** interaction with CrO_2Cl_2 at the final step of the reaction.

Scheme 1



In contrast with the reactions in CCl_4 and n-pentane the second step of the reaction in the nucleophilic solvents (exp. 4 and exp. 6) consists in the trapping of **A** by a side nucleophile[15] (**Scheme 2**) and that explains why in these cases **5** is formed only in trace amounts.

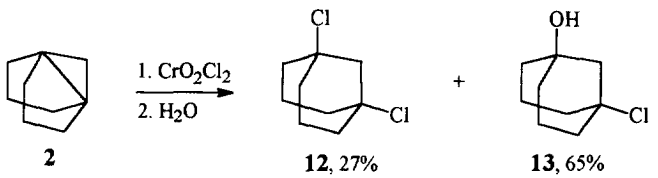
Scheme 2



It should be noted that the formation of the radical **C** can also occur by a direct *backside* attack of CrO_2X_2 on the strained C-C bond as it was previously suggested for small-ring propellane reactions with radical reagents.[4] But this reaction pathway omits the formation of compounds **3,6** and **8** which are the main reaction products and such mechanism seems less probable, moreover **1** is stable towards the radical reagent (t-BuOO˙) attack (see above).

We have also carried out similar experimental studies on the reaction of hydrocarbon **2** with chromyl reagents. In these reactions **2** gives a series of products that can be rationalized on the basis of oxidative cleavage of the $\sigma_{C\text{-}C}$-bond, *i.e.* the case of **2** is similar to that of **1**. The only difference is the absence of ketones among the reaction products in the case of **2** interacting with CrO_2Cl_2 (**Scheme 3**) where **12** and **13** are formed[10] with high preparative yields.

Scheme 3



One can conclude that the *backside* oxidative addition of Cr(VI) reagents proves to be a general reaction of stable propellanes. The application of our model substrates revealed a new route of the nonelectrophilic $\sigma_{C\text{-}C}$-bond activation. It is impossible to say at this stage how well the oxidative addition of such reagents will perform for other alkane systems with the reactive $\sigma_{C\text{-}C}$ bond. It should be pointed out that the conclusions drawn from this work are mainly based on the synthetic data and a more detailed mechanistic study of these transformations will be reported elsewhere.

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REFERENCES AND NOTES

1. *Activation and Functionalization of Alkanes*; Hill, C.L., Ed.; John Wiley and Sons, Inc.: New York, **1989**. Shilov, V.A. *Activation of Saturated Hydrocarbons by Transition Metal Complexes*; D. Reidel: Dordrecht, **1984**. *Selective Hydrocarbon Activation, Principles and Progress*; Davies, J.A.; Watson, P.L.; Liebman, J.F.; Greenberg, A., Eds.; VCH: New York, **1990**.
2. (a) Co(III): Colussi, A.J.; Ghibaudi, E.; Yuan, Z.; Noyes, R.M. *J.Am.Chem.Soc.* **1990**, 112, 8660. Roelofs, M.G.; Wasserman, E.; Jensen, J.H. *ibid.* **1987**, 109, 4207. (b) Mn(VII): Fatiadi, A.J. *Synthesis (Stuttgart)* **1987**, 85. Arndt, D. *Manganese Compounds as Oxidizing Agents in Organic Chemistry*; Open Court Publishing: La Salle, IL, **1981**. (c) Fe(IV): Bach, R.D.; Schlegel, H.B.; Andres, J.L.; Sosa, C. *J.Am. Chem. Soc.* **1994**, 116, 3475. Ortiz de Montellano, P.R. *Acc.Chem. Res.* **1987**, 20, 289. (d) Cr(VI): *Comprehensive Organic Synthesis*; Trost, B.M., Ed.; Pergamon: New York, **1991**; v. 7. *Oxidation in Organic Chemistry*; Wiberg, K.B., Ed.; Academic Press: New York, **1965**.
3. (a) Cook, G.K.; Mayer, J.M. *J.Am.Chem.Soc.* **1994**, 116, 1855. (b) Cook, G.K.; Mayer, J.M. *ibid.* **1995**, 117, 7139.
4. Ginsburg, D. *Acc.Chem.Res.* **1972**, 5, 249. Wiberg, K.B. *Chem.Rev.* **1989**, 89, 975. Wiberg, K.B.; Waddell, S.T. *Tetrahedron Lett.* **1987**, 151. Tobe, Y. *Propellanes*, in: *Carbocyclic Cage Compounds; Chemistry and Applications*. Osawa, E.; Yonemitsu, O., Eds.; VCH: New York, **1992**.
5. (a) Fokin, A.A.; Gunchenko, P.A.; Yaroshinsky, A.I.; Krasutsky, P.A.; Yurchenko, A.G. *Tetrahedron Lett.* **1995**, 4479. (b) Fokin, A.A.; Gunchenko, P.A.; Kulik, N.I.; Iksanova, S.V.; Krasutsky, P.A.; Gogoman, I.V.; Yurchenko, A.G. *Tetrahedron* **1996**, 5857.
6. $CrO_2(OCOCF_3)_2$ was obtained as described in: Suggs, I.W.; Ytuarte, L. *Tetrahedron Lett.* **1986**, 437.
7. Warner, P. *Tetrahedron Lett.* **1974**, 1409. Warner, P.; LaRose, R.; Scleis, T. *ibid.* **1976**, 4443.
8. The formation of cyclopropylketone **5** by the reaction of **1** with CrO_2Cl_2 represents a new type of oxidative cyclobutane ring contraction. Ketone **5** is identical with the material obtained independently *via* dibromocyclopropanation of 3-methylenebicyclo[3.3.1]nonan-7-one (as described in: Fokin, A.A. et al. *Teoret. i Experim. Khimiya* **1984**, 20, 427) followed by the reduction of the dibromoadduct with $LiAlH_4$ in ether and Jones oxidation of the obtained alcohol in acetone at O°C.
9. (a) The nature of the complexes derived from CrO_2Cl_2 by oxidation of organic substrates is still open to question. For the detailed studies see[3a] and references therein. (b) The oxidation level of chromium in the Étard complex has been found more than IV because substantial amounts of the reagent are captured by the precipitate. A precise determination of the oxidation level of chromium in the precipitate is troublesome because of its complexity (GS/MS data on the mixture obtained after the quenching of the precipitate: **3**-1%, **4**-5%, **5**-90% and unidentified compounds - 4%).
10. Diacetate **6** is identical to material described earlier[5b] as a main product of **1** oxidation with NO_2OAc. The structure of other products was proved by the microanalytical data as well as ^1H,^{13}C, ^{19}F NMR, IR, and MS spectra. **^{1}H NMR (δ, ppm, TMS, $CDCl_3$) - 3**: 1.45 (bs,2H), 2.75 (bs,4H), 1.80-2.40 (m,10H); **4**: 1.50 (bs,2H), 1.65-1.95 (m,6H), 2.00-2.50 (m, 8H), 3.10 (bs,1H); **5**: 0.68 (m,2H), 1.72 (AB-sys., 11 Hz,2H), 1.95-2.25 (m,6H), 2.30-2.42 (bs,6H); **7**: 1.45 (bs,2H), 1.60-1.75 (m, 4H), 1.85 (s,3H), 1.95-2.30 (m,10H), 3.1 (bs,1H);**8**: 1.60 (bs,2H), 1.75-2.25 (m,10H), 2.3 (bs,4H); **9**: 1.50 (bs,2H), 1.70-2.00 (m,4H), 2.15-2.30 (m,8H), 2.40-2.75 (m,2H), 3.20 (bs,1H); **12**: 1.50-2.00 (m,12H), 2.30 (s,2H); **13**: 1.50-2.00 (m,12H), 2.10 (bs,2H), 4.60 (bs,1H). **{^{13}C-H} NMR (δ, ppm, TMS, $CDCl_3$) - 3**: 32.07, 34.99, 42.64, 40.93, 72.30; **4**: 31.12, 35.32, 40.38, 40.88, 46.74, 49.18, 72.56, 73.32; **5**: 11.34, 12.27, 19.58, 32.13, 32.45, 41.66, 47.61, 210.81; **7**: 23.11, 29.58, 33.51, 35.30, 38.13, 43.17, 46.50, 72.70, 85.01, 170.67; **8**: 29.17, 32.78, 34.47, 42.21, 90.42, 114.80 (q,287 Hz), 156.28 (q,41.32 Hz); **9**: 29.51, 33.16, 34.83, 37.49, 42.55, 46.26, 72.50, 91.58, 114.76 (q, 287 Hz), 156.22 (q,41 Hz); **12**: 24.82, 40.46, 55.59, 70.58; **13**: 23.29, 38.27, 41.07, 54.38, 71.89, 72.99. **^{19}F NMR (δ, ppm, $CFCl_3$, $CDCl_3$) - 8**: -76.91 (s); **9**: -76.85 (s).
11. Mardsen, C.J.; Hedberg, K. *Inorg. Chem.* **1982**, 21, 1115.
12. Hartford, W.H.; Darrin, M. *Chem.Rev.* **1958**, 58, 1.
13. See Korzekwa, K.R.; Jones, J.P.; Gillette, J.R. *J.Am.Chem.Soc.* **1990**, 112, 7042 and correlation between the reactivity of CrO_2Cl_2 and oxygen radicals[3b] in the alkane activation reactions.
14. Danen, W.C. In: *Methods in Free Radical Chemistry*, 5Th ed. Huyser, R.S., Ed.; M.Dekker: New York, **1974.**
15. Nucleophile capturing is the typical first step of hydrocarbon radical cation transformations in nucleophilic solvents (see Weng, H.; Du, X.-M.; Roth H.D. *J.Am.Chem.Soc.* **1995**, 117, 135).

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