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Improved Approach Towards Synthesis of Adamantane-1,3,5-triol

E. A. Ivleva[a], I. A. Platonov[b], and Yu. N. Klimochkin[a]

[a] *Samara State Technical University, ul. Molodogvardeiskaya 244, Samara, 443100 Russia*
e-mail: elena.a.ivleva@yandex.com

[b] *Korolev Samara State Aerospace University (National Research University), Samara, Russia*

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Abstract—1-Adamantanol can be converted into adamantane-1,3,5-triol in the presence of *N*-hydroxylphthtalimide, cobalt(II) acetylacetonate, and manganese dioxide under oxygen atmosphere in glacial acetic acid.

Keywords: polyhydric alcohol, oxidation, transition metal salt, *N*-hydroxyphthtalimide

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Selective functionalization of C–H bonds in the cage hydrocarbons is a topical task of modern organic chemistry [1–6]. In particular, functionalization of adamantane is an important challenge, since its derivatives are widely used as building blocks in the synthesis of drugs [7–10], supramolecular polymer materials [11], ligands in metal complexes [12], and synthetic bases of working fluids for avionics [13]. The prospects of adamantane derivatives application for advanced material development are due to their set of unique properties: high lipophilicity, conformational rigidity, and excellent thermal and oxidative stability. Polyol derivatives of adamantane, in particular adamantane-1,3-diol and adamantane-1,3,5-triol are of special interest in view of functional materials design.

The known methods of adamantane-1,3,5-triol synthesis include oxidation of adamantane or adamantane-1,3-diol in the presence of transition metal salts [14–16]. In particular, oxidation of adamantane with chromic anhydride [17] and methyl(trifluoromethyl) dioxirane [18] has been described. Adamantane-1,3,5-triol can be prepared via hydrolysis of 1,3,5-tribromoadamantane as well [19].

In this work we investigated the features of 1-adamantanol **I** oxidation in the presence of *N*-hydroxylphthalimide (NHPI) and transition metal salts in glacial acetic acid under oxygen atmosphere. The choice of *N*-hydroxyphthalimide as a catalyst was due to its recognized high activity in the reactions of C–H bonds of various organic compounds [20, 21]. It is well known that the addition of salts of transition metal such as Cu(II), Mn(II), Fe(II), Co(II), Ni(II), etc. catalyze the oxidative transformations [22, 23].

According to gas chromatography–mass spectrometry analysis, the performed reaction afforded adamantane-1,3-diol **II**, adamantane-1,3,5-triol **III**, hydroxyketones, and diketones of adamantane series. The outcome of 1-adamantanol **I** oxidation under different conditions is shown in Table 1.

The reaction proceeded via a radical mechanism to form highly reactive phthalimide-*N*-oxyl radical (PINO) [24]. The PINO radical was generated in situ from *N*-hydroxyphthalimide and peroxide radical **A**, the latter formed via a single-electron reduction of molecular oxygen with the transition metal salt (Scheme 2).

Scheme 1.

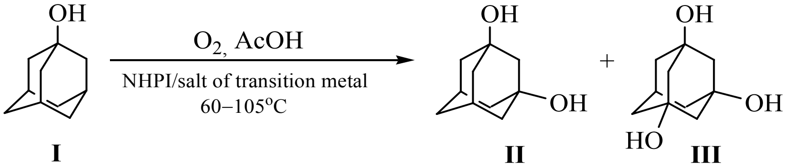


Table 1. Oxidation of 1-adamantanol **I** with oxygen catalyzed by *N*-hydroxyphthalimide in the presence of transition metal salts

Exp. no.	Metal salt	Salt amount, mol %	*T*, °C	Time, h	1-Adamantanol conversion, %[a]	Yield, %[a]	
						II	**III**
1	$Co(acac)_2$	1	105	10	97	46	28
2	$Fe(acac)_3$	1	105	15	86	40	14
3	$Co(OAc)_2$	1	105	15	94	41	17
4	$FeSO_4$	1	105	15	90	42	16
5	$Mn(OAc)_2$	1	105	15	15	9	2
6	$Cu(OAc)_2$	1	105	15	7	3	<1
7	$K_2Cr_2O_7$	1	105	15	No reaction	–	–
8	$NiCl_2$	1	105	15	15	4	<1
9	Ti(O-*i*Pr)$_4$	1	105	15	No reaction	–	–
10	$Co(acac)_2$	0.25	105	10	65	25	12
11	$Co(acac)_2$	0.5	105	10	87	37	21
12	$Co(acac)_2$	2	105	10	98	52	29
13	$Co(acac)_2$	1	80	10	98	54	31
14	$Co(acac)_2$	1	60	10	95	67	27

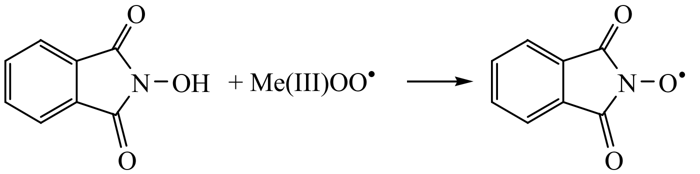
[a] According to GC–MS data.

The reaction mechanism involved the intermediate formation of hydroperoxide **B** via rupture of the C–H bond in 1-adamantanol **I** and generation of peroxide radical. The hydroperoxide is formed via rupture of the O–H bond in *N*-hydroxyphthalimide. The intermediate hydroperoxide **B** was further converted into the corresponding alcohol via formation of the alkoxide radical **C** (Scheme 3).

We first investigated the effect of transition metals salts on 1-adamantanol **I** oxidation under oxygen atmosphere (*p* = 1 atm) in the presence of NHPI (10 mol %) (Table 1, exp. 1–9). The best result was achieved with Co(acac)$_2$ (Table 1, exp. 1). When using other salts, the oxidation of 1-adamantanol **I** proceeded with poorer selectivity (Table 1, exp. 2–4) or lower substrate conversion (Table 1, exp. 5, 6, and 8); the

Scheme 2.

$$\mathrm{Me(II)} + \mathrm{O_2} \longrightarrow \underset{\mathbf{A}}{\mathrm{Me(III)OO^{\bullet}}}$$



Scheme 3.

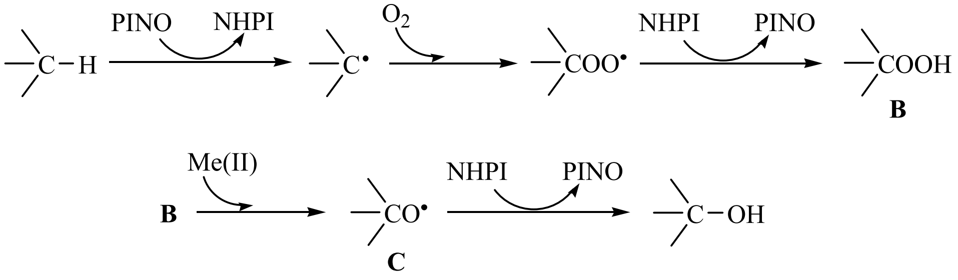


Table 2. Oxidation of 1-adamantanol **I** with oxygen catalyzed by *N*-hydroxyphthalimide in the presence of pairs of salts

Exp. no.	Metal salts (1 mol % + 0.5 mol %)	Time, h	1-Adamantanol conversion, %[a]	Yield, %[a]	
				II	**III**
1	$Co(OAc)_2 + FeSO_4$	15	94	40	17
2	$Co(acac)_2 + Fe(acac)_3$	15	95	38	22
3	$Co(acac)_2 + FeSO_4$	15	No reaction	–	–
4	$Co(acac)_2 + Mn(OAc)_2$	10	6	<1	1
5	$Co(acac)_2 + Cu(OAc)_2$	10	7	<1	<1
6	$Co(OAc)_2 + Mn(OAc)_2$	15	95	42	17
7	$Co(OAc)_2 + Cu(OAc)_2$	15	90	42	13

[a] According to GC–MS data.

Table 3. Oxidation of 1-adamantanol **I** with oxygen catalyzed by NHPI–$Co(acac)_2$ system in the presence of various oxidizers

Exp. no.	Additive	Time, h	1-Adamantanol conversion, %[a]	Yield, %[a]	
				II	**III**
1	Chloranil	20	92	44	24
2	$NaNO_2$	20	88	50	21
3	AIBN	20	91	55	20
4	I_2	30	No reaction	–	–
5	MnO_2	30	100	42	56

[a] According to GC–MS data.

reaction did not occur in the presence of potassium dichromate or titanium(IV) isopropoxide (Table 1, exp. 7 and 9).

We hypothesized that simultaneous use of two salts could increase the oxidation selectivity due to synergetic effect; however, that was not confirmed experimentally (Table 2, exp. 1–7). In certain cases (Table 2, exp. 3–5) addition of the second salt nearly stopped the reaction in the presence of $Co(acac)_2$. The attempt to perform the oxidation upon portionwise addition of NHPI failed as well (Table 1, entry 1).

Concentration of $Co(acac)_2$ affected the reaction outcome. At relatively low concentration of the salt (Table 1, exp. 10 and 11), the substrate **I** conversion and the product **III** yield were moderate. The best result was achieved at 1 mol % of $Co(acac)_2$ (Table 1, exp. 1), further increase of the salt concentration to 2 mol % gave no significant improvement of the reaction selectivity (Table 1, exp. 12). Importantly, decrease of the reaction temperature significantly suppressed the side products formation (Table 1, exp. 13 and 14).

The above-discussed data revealed that typically the reaction gave adamantane-1,3-diol **II** and adamantane-1,3,5-triol **III** in the ratio of about 2.5 : 1. We attempted to aid further in situ oxidation of adamantane-1,3-diol **II** into adamantane-1,3,5-triol **III**; to do so, catalytic amount of an oxidizer was added to the reaction mixture: sodium nitrite, chloranil, molecular iodine, 2,2'-azoisobutyronitrile (AIBN), or manganese dioxide.

Using chloranil, sodium nitrite, and AIBN (Table 3, exp. 1–3) did not noticeably improve the results, whereas iodine inhibited the oxidation of 1-adamantanol **I** (Table 3, exp. 4). The best result was achieved in the presence of manganese dioxide (Table 3, exp. 5).

In summary, the optimized catalytic system NHPI–$Co(acac)_2$–MnO_2 in glacial acetic acid allowed selective oxidation of 1-adamantanol with oxygen to yield adamantane-1,3-diol and adamantane-1,3,5-triol, key building blocks for new functional materials design [25].

EXPERIMENTAL

Mass spectra were obtained using a Thermo-Finnigan DSQ gas chromatography–mass spectrometry device equipped with a ZB5MS silica capillary column (70 eV, stationary phase thickness 0.25 mm, 1.5 mL min^{-1} of helium as carrier gas, heating from 150°C to 340°C at 20 K min^{-1}, evaporator temperature 300°C).

Oxidation of 1-adamantanol *(optimized procedure).* A mixture of 25 g (0.164 mol) of 1-adamantanol **I**, 2.68 g (0.0164 mol) of NHPI, 0.482 g (1.64 mmol) of Co(acac)$_2$, 0.715 g (0.0082 mol) of MnO_2, and 250 mL of glacial acetic acid was heated under vigorous stirring to 60°C and then stirred at that temperature upon stirring and bubbling with oxygen during 30 h. After cooling, acetic acid was removed. The residue was dissolved in 250 mL of chloroform and heated at reflux during 2 h. Solid adamantane-1,3,5-triol **III** was filtered off and recrystallized from ethyl acetate. Yield 15.7 g (52%), mp 202–204°C (mp 203–205°C [17]). Adamantane-1,3-diol **II** precipitated from chloroform was filtered off and dried. Yield 10.7 g (39%), mp 296–297°C (mp 298–300°C [26]). Mass spectrum, m/z (I_{rel}, %): **1**, 152 (35) $[M]^+$, 109 (10), 95 (100); **II**, 168 (28) $[M]^+$, 150 (4), 111 (100), 95 (14); **III**, 184 (10) $[M]^+$, 166 (6), 150 (50), 127 (100), 111 (46), 92 (28).

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REFERENCES

1. Wanka, L., Cabrele, C., Vanejews, M., and Schreiner, P.R., *Eur. J. Org. Chem.*, 2007, vol. 9, p. 1474. DOI: 10.1002/ejoc. 200600975.
2. Fokin, A.A., Shubina, T.E., Gunchenko, P.A., Isaev, S.D., Yurchenko, A.G., and Schreiner, P.R., *J. Am. Chem. Soc.*, 2002, vol. 124, p. 10718. DOI: 10.1021/ja0265512.
3. Ivleva, E.A., Gnusarev, D.I., Osyanin, V.A., and Klimochkin, Yu.N., *Russ. J. Gen. Chem.*, 2014, vol. 84, no. 11, p. 2262. DOI: 10.1134/S107036321411036X.
4. Akhrem, I.S., Avetisyan, D.V., and Afanas'eva, L.V., *Tetrahedron Lett.*, 2012, vol. 53, p. 3493. DOI: 10.1016/j.tetlet.2012. 04.125.
5. Ivleva, E.A., Skomorokhov, M.Yu., and Klimochkin, Yu.N., RU Patent 2488577, 2012.
6. Lu, H. and Zhang, X.P., *Chem. Soc. Rev.*, 2011, vol. 40, p. 1899. DOI: 10.1039/c0cs00070a.
7. Madhra, M.K., Sharma, M., and Khanduri, C.H., *Org. Proc. Res. Dev.*, 2007, vol. 11, no. 5, p. 922. DOI: 10.1021/op700138p.
8. Savage, S.A., Jones, G.S., Kolotuchin, S., Ramrattan, S.A., Vu, T., and Waltermire, R.E., *Org. Proc. Res. Dev.*, 2009, vol. 13, no. 6, p. 1169. DOI: 10.1021/op900226j.
9. Deng, Y., Wang, A., Tao, Z., Chen, Y., Pan, X., and Hu, X., *Asian J. Chem.*, 2014, vol. 26, no. 18, p. 6275. DOI: 10.14233/ajchem.2014.17621.
10. Zoidis, G., Fytas, C., Papanastasiou, I., Foscolos, G.B., Fytas, G., Padalko, E., de Clercq, E., Naesens, L., Neyts, J., and Koloco- uris, N., *Bioorg. Med. Chem.*, 2006, vol. 14, p. 3341. DOI: 10.1016/j.bmc.2005.12.056.
11. Ohshita, J., Hino, K., Inata, K., Kunai, A., and Maehara, T., *Polymer*, 2007, vol. 48, p. 4301. DOI: 10.1016/j.polymer. 2007.05.052.
12. Tominaga, M., Masu, H., and Azumaya, I., *J. Org. Chem.*, 2009, vol. 74, p. 8754. DOI: 10.1021/jo9018842.
13. Ivleva, E.A., Baimuratov, M.R., Zhuravleva, Yu.A., Klimochkin, Yu.N., Kulikova, I.A., Pozdnyakov, V.V., Sheikina, N.A., and Tyshchenko, V.A., *Russ. J. Gen. Chem.*, 2014, vol. 84, no. 12, p. 2464. DOI: 10.1134/S1070363214120226.
14. Hitomi, Y., Arakawa, K., and Kodera, M., *Chem. Eur. J.*, 2013, vol. 19, p. 14697. DOI: 10.1002/chem.201302111.
15. Ishii, Y., Kato, S., Iwahama, T., and Sakaguchi, S., *Tetrahedron Lett.*, 1996, vol. 37, no. 28, p. 4993. DOI: 10.1016/0040- 4039(96)00992-6.
16. Ishii, Y., Nakayama, K., Takeno, M., Sakaguchi, S., Iwahama, T., and Nishiyama, Y., *J. Org. Chem.*, 1995, vol. 60, p. 3934. DOI: 10.1021/jo00118a002.
17. Zhu, H., Guo, J., Yang, C., Liu, S., Cui, Y., and Zhong, X., *Synth. Commun.*, 2013, vol. 43, p. 1161. DOI: 10.1080/00397911. 2011.625134.
18. Mello, R., Cassidei, L., Fiorentino, M., Fusco, C., and Curci, R., *Tetrahedron Lett.*, 1990, vol. 31, no. 21, p. 3067. DOI: 10.1016/S0040-4039(00)89027-9.
19. Stetter, H. and Wulff, C., *Chem. Ber.*, 1960, vol. 93, no. 6, p. 1366. DOI: 10.1002/cber.19600930619.
20. Recupero, F. and Punta, C., *Chem. Rev.*, 2007, vol. 107, p. 3800. DOI: 10.1021/cr040170k.
21. Biliuta, G., Fras, L., Drobota, M., Persin, Z., Kreze, T., Stana-Kleinschek, K., Ribitsch, V., Harabagiu, V., and Coseri, S., *Carbohyd. Polym.*, 2013, vol. 91, p. 502. DOI: 10.1016/j.carbpol.2012.08.047.
22. Punniyamurthy, T., Velusamy, S., and Iqbal, J., *Chem. Rev.*, 2005, vol. 105, p. 2329. DOI: 10.1021/cr050523v.
23. Dick, A.R. and Sanford, M.S., *Tetrahedron*, 2006, vol. 62, p. 2439. DOI: 10.1016/j.tet.2005.11.027.
24. Coseri, S., *Catal. Rev.*, 2009, vol. 51, p. 218. DOI: 10.1080/01614940902743841.
25. Ivleva, E.A., Baimuratov, M.R., and Klimochkin, Yu.N., RU Patent 2530777, 2013.
26. Cui, L.Q., Liu, K., and Zhang, C., *Org. Biomol. Chem.*, 2011, vol. 9, no. 7, p. 2258. DOI: 10.1039/C0OB00722F.