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Application of NO_2/supercritical CO_2 system for safe and selective nitration of adamantanes and tertiary alkyl bromides

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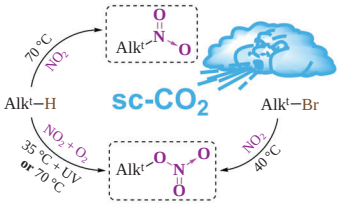
A concise safe approach for selective nitration and nitroxylation of *tert*-alkanes, in particular adamantane, and *tert*-alkyl bromides utilizing NO_2 in supercritical CO_2 medium has been established. Major reaction products were *tert*-alkyl nitro compounds and *tert*-alkyl nitrates depending on the reaction conditions.



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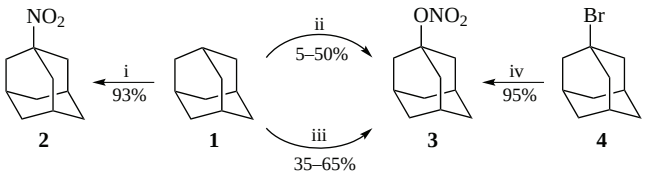
Functionalization of alkanes remains a challenge[1] because of their extremely low reactivity and, in case of *tert*-alkanes, owing to the steric repulsion between substituents linked to the same carbon atom. The common approach is based on the reactions employing free radicals capable of initiating the homolytic cleavage of the *tert*-C–H bond. Modern methods of radical functionalization[2] usually involve the use of expensive organic catalysts which increase the cost of the processes, or high temperatures which make the reactions less selective and increase technological risks.[3] Non-catalytic low-temperature routes, *e.g.*, halogenation, are environmentally dangerous.[2,4] Thus, safe, reliable, and efficient methods for radical functionalization of *tert*-alkanes, with available radical sources are still in demand.

A versatile approach to alkane functionalization is nitration and nitroxylation reactions giving nitroalkanes and alkyl nitrates, valuable semi-products and products of organic synthesis.[5,6] Previously,[7] we proposed a novel approach to *sec*-C–H functionalization of alkanes based on the 'NO_2–supercritical CO_2 ($scCO_2$)' or 'NO_2–O_2–$scCO_2$' reaction systems employing UV irradiation. Herein, we report the first application of these fire and explosion safe reaction systems for effective nitration of tertiary hydrocarbons.

We have found that adamantane **1** reacted with an excess of NO_2 in a $scCO_2$ medium at 70 °C affording 1-nitroadamantane **2** in nearly quantitative yield (Scheme 1, reaction i).† The addition of oxygen to the reaction system 'NO_2–O_2 (3 equiv.)–$scCO_2$' resulted in selective transformation of **1** to 1-nitroxyadamantane **3** (reaction ii). The yield of **3** depended on the reaction temperature and NO_2 excess. Thus, over 16 h with 2.2 equiv. of NO_2 it reached <5, 37, and 50% at 35, 50, and 70 °C, respectively, while with 4 equiv. of NO_2 the yield of **3** was 17% even at 35 °C (^{1}H NMR data).

UV irradiation of the 'NO_2–O_2–$scCO_2$' reaction system (see General procedure†) facilitated the process: with the use of 1.1 equiv. NO_2 the desired nitrate **3** was selectively obtained in 35% and 50% yield over 4 and 16 h, respectively; while with 2.2 equiv. of NO_2 the 65% yield of **3** was reached over 16 h (see Scheme 1, reaction iii). In all experiments no traces of di- or polyfunctional adamantane derivatives were recorded.

Similar processing of methylcyclopentane, methylcyclohexane, or 1,3,5-trimethylcyclohexane with NO_2 in $scCO_2$ medium led to the formation of complex inseparable mixtures of

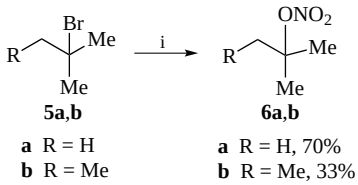


Scheme 1 *Reagents and conditions*: i, NO_2 (6 equiv.), 70 °C, 16 h, $scCO_2$, 150 bar; ii, NO_2 (1–2 equiv.), O_2 (3 equiv.), 35–70 °C, 16 h, $scCO_2$, 80–150 bar; iii, NO_2 (2–4 equiv.), O_2 (3 equiv.), 35 °C, 4–16 h, UV (375–380 nm), $scCO_2$, 80 bar; iv, NO_2 (2 equiv.), 40 °C, 4 h, $scCO_2$, 90 bar.

† *General procedure for nitration.* A 22 cm^3 steel autoclave with a magnetic stirrer and sapphire windows was loaded with the substrate (and oxygen, if needed), filled with CO_2 in a third and cooled down to 10 °C in a thermostat. The calculated amount of cooled to 0 °C NO_2 was loaded into a separate cylinder and dissolved in liquid CO_2 (3–5 cm^3). The obtained solution was warmed up to room temperature and added to the autoclave by capillary with valve due to the pressure difference between the warm cylinder and the cooled autoclave. The residual NO_2 was transferred from the cylinder to the autoclave with fresh CO_2 until the latter was filled by ~3/4 volume. Then the autoclave with the reaction mixture was kept at the required temperature for the planned time. If UV irradiation was needed, the autoclave was equipped with photodiodes (375–380 nm, two pieces of 3 W) in front of the sapphire windows. After completion of the reaction, the autoclave was cooled to room temperature and carefully decompressed *via* the outlet valve releasing gaseous CO_2 and keeping the reaction products at the bottom of the autoclave. The purification of the products **2**, **3**, **6a**,**b** was performed by column chromatography (silica gel, *n*-hexane).

products that may be attributed to concurrent non-selective functionalization of *sec*-carbon centers or to the instability of the produced nitroalkanes under the reaction conditions. Interestingly, substituted adamantanes, *e.g.*, 1-carboxyadamane, 1,1′-biadamantane, as well as adamantan-2-one, do not react with NO_2 under similar or even harsher conditions (70 °C, 16 h, O_2 excess, UV irradiation, $scCO_2$). The exception is 1-bromoadamantane **4** which almost quantitatively underwent debrominative nitroxylation to 1-adamantyl nitrate **3** under the action of NO_2 in only 4 h under rather mild conditions (40 °C, no UV, no O_2) (see Scheme 1, reaction iv).

The similar processing of *tert*-alkyl bromides **5a**,**b** afforded *tert*-butyl nitrate **6a** and *tert*-amyl nitrate **6b** (Scheme 2). Although the conversion of both substrates **5a**,**b** exceeded 90%, the yields of the products were significantly lower, which may be attributed to short term of living (pure compounds **6a**,**b** degraded in less than overnight period). The lower yield of *tert*-amyl nitrate **6b** (33% *vs*. 70% for compound **6a**) indicates that the *sec*-carbon atom facilitates the consequent unwanted transformations, apparently comprising an HNO_3 elimination stage.

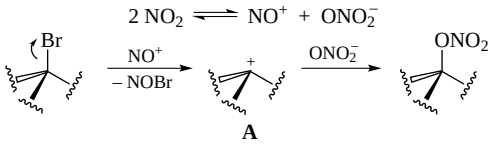


5a,**b** **6a**,**b**

a R = H **a** R = H, 70%
b R = Me **b** R = Me, 33%

Scheme 2 *Reagents and conditions*: i, NO_2 (2.5 equiv.), 40 °C, 4 h, $scCO_2$, 90 bar.

The formation of the nitrates **3** and **6a**,**b** in the absence of extra oxygen is in accordance with previously reported ability of N_2O_4 to produce ionic pair $[NO^+][ONO_2^-]$ in the non-polar condensed carbon dioxide medium.[8] Apparently,[9,10] highly reactive nitrosonium cation abstracts bromide anion from compounds **4** and **5a**,**b** affording corresponding carbocations **A** (Scheme 3) of increased stability.[11] Higher stability of adamantyl cation with respect to acyclic *tert*-alkyl cations[11,12] facilitates the formation of 1-adamantyl nitrate **3** in excellent yield. The evolved nitrosonium bromide decomposes during the workup procedure. To our knowledge, the nitroxylation of alkyl bromides with NO_2 has not been reported so far.



A

Scheme 3

To sum up, the obtained results indicate that, regardless of the substrates restrictions, the developed approach based on reactions of adamantane or tertiary alkyl bromides with available NO_2, in some cases may be useful for the preparation of corresponding nitro and nitroxy derivatives due to mild reaction conditions and lower environmental impact.

Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi: 10.1016/j.mencom.2023.06.006.

References

1 K. I. Goldberg and A. S. Goldman, *Acc. Chem. Res.*, 2017, **50**, 620.
2 *Alkane Functionalization*, eds. A. J. L. Pombeiro and M. F. C. Guedes da Silva, Wiley, 2019.
3 M. Shiri, M. A. Zolfigol, H. G. Kruger and Z. Tanbakouchian, *Tetrahedron*, 2010, **66**, 9077.
4 Y. Sasson, *Formation of Carbon–Halogen Bonds (Cl, Br, I)*, in *Patai's Chemistry of Functional Groups*, ed. I. Marek, Wiley, Chichester, 2009.
5 S. G. Zlotin, I. L. Dalinger, N. N. Makhova and V. A. Tartakovsky, *Russ. Chem. Rev.*, 2020, **89**, 1.
6 S. G. Zlotin, A. M. Churakov, M. P. Egorov, L. L. Fershtat, M. S. Klenov, I. V. Kuchurov, N. N. Makhova, G. A. Smirnov, Yu. V. Tomilov and V. A. Tartakovsky, *Mendeleev Commun.*, 2021, **31**, 731.
7 R. E. Ivanov, M. N. Zharkov and S. G. Zlotin, *ChemPhotoChem*, 2022, **6**, e202200084.
8 R. E. Ivanov, M. N. Zharkov and S. G. Zlotin, *Dokl. Chem.*, 2021, **500**, 209 (*Dokl. Ross. Akad. Nauk, Khim., Nauki Mater.*, 2021, **500**, 40).
9 Yu. N. Klimochkin, M. V. Leonova and E. A. Ivleva, *Russ. J. Org. Chem.*, 2020, **56**, 1702 (*Zh. Org. Khim.*, 2020, **56**, 1516).
10 A. McKillop and M. E. Ford, *Tetrahedron*, 1974, **30**, 2467.
11 E. M. Arnett and T. C. Hofelich, *J. Am. Chem. Soc.*, 1983, **105**, 2889.
12 I. Lengyel, D. B. Uliss and R. V. Mark, *J. Org. Chem.*, 1970, **35**, 4077.

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