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N-Hydroxyphthalimide-Catalyzed Carboxylation of Polycyclic Alkanes with Carbon Monoxide in the Presence of Dioxygen

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Carbonylation as well as carboxylation of saturated hydrocarbons with carbon monoxide (CO) are challenging subjects in organic synthesis, since they are very difficult to carry out selectively.[1] The introduction of CO into unreactive carbon−hydrogen bonds has been reported to be achieved by transition metals,[2−5] Lewis and superacids,[6] and radical species.[7−10] For example, alkanes such as *n*-pentane were carbonylated with CO by a Rh complex under photochemical conditions.[2] Methane and ethane are carboxylated with CO by Pd/Cu[3] and $RhCl_3$[4] in the presence of molecular oxygen. Under the influence of superacids such as SbF_5/CF_3SO_3H[6b] and CH_2Br_2/2$AlCl_3$,[6e] adamantane was converted into adamantanecarboxylic acid and/or adamantanecarbaldehyde.

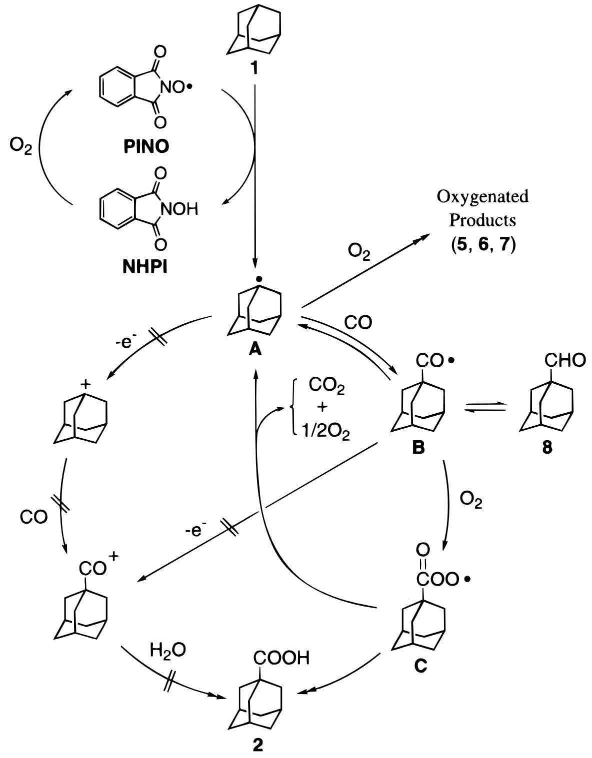
On the other hand, the carbonylation mediated by a free radical was first reported by Coffmann *et al.* in 1952,[11] but this type of reaction was not extensively studied for a long time probably because the reaction was conducted under extremely high CO pressure (200−3000 atm).[12] However, since the successful free-radical carbonylation of alkyl halides with CO mediated by tin hydride was reported by Ryu *et al.*, the radical carbonylation of alkanes has been examined in recent years.[13] Sen *et al.* have disclosed the free-radical carboxylation of methane to acetic acid by the use of peroxydisulfate as a radical source.[7] Benzophenone-[8] and polyoxotungstate-photocatalyzed[9] and mercury-photosensitized[10] carbonylations of cyclohexane afford cyclohexanecarboaldehyde in fair yields. These reactions, however, are limited to being carryied out on a synthetic scale, since the conversion of alkanes is not high.

Table 1. Carboxylation of Adamantane (1) Catalyzed by NHPI[a]

run	CO/atm	air/atm	conv/%	selectivity/% **2**	**3**[b]	**4**	**5**	**6**	**7**
1	15	1	69	55	7	4	8	2	2
2	15	1[c]	78	trace			54	5	4
3	15			no reaction					
4[d]	15	1	75	56	8	5	4	3	2
5[e]	15	1	79	40	7	3	8	3	2
6[f]	15	1	62	40	4	4	13	1	2
7	5	1	63	38	2	3	16	5	3
8[g]	15	1	69	35	4	3	9	3	4
9[h]	15	1	76	41	7	4	10	3	
10[i]	15	1		no reaction					

[a] Substrate (1 mmol) was allowed to react under carbon monoxide/air in the presence of NHPI (10 mol %) in acetic acid (3 mL) and 1,2-dichloroethane (3 mL) at 95 °C for 4 h. [b] Yield of **3** was estimated as dimethylester after esterfication with excess methanol. [c] O_2 was used in place of air. [d] In a mixed solvent of acetic acid (1 mL) and 1,2-dichloroethane (5 mL). [e] 60 °C, 15 h. [f] *N*-Hydroxysuccinimide was used in place of NHPI. [g] In acetic acid (6 mL). [h] In acetonitrile (6 mL). [i] In the presence of hydroquinone (0.1 mol %).

Scheme 1. Plausible Reaction Path for the NHPI-Catalyzed Free-Radical Carboxylation of Adamantane (1) with CO/Air



Recently, we showed that the aerobic oxidation of alkylbenzenes,[14a,f] alcohols,[14b] and alkanes[14c−e] was effi-

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[1] For recent reviews: (a) Barton, D. H. R.; Doller, D. *Acc. Chem. Res.* **1992**, *25*, 504. (b) Sommer, J.; Bukala, J. *Acc. Chem. Res.* **1993**, *26*, 370. (c) Arndtsen, B. A.; Bergman, R. G.; Mobley, T. A.; Peterson, T. H. *Acc. Chem. Res.* **1995**, *28*, 154. (d) Hill, C. L. *Synlett* **1995**, 127. (e) Ryu, I.; Sonoda, N. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1051.

[2] (a) Sakakura, T.; Sodeyama, T.; Sasaki, K.; Wada, K.; Tanaka, M. *J. Am. Chem. Soc.* **1990**, *112*, 7221. (b) Margl, P.; Ziegler, T.; Blöchl, P. E. *J. Am. Chem. Soc.* **1996**, *118*, 5412.

[3] (a) Satoh, K.-I.; Watanabe, J.; Takaki, K.; Fujiwara, Y. *Chem. Lett.* **1991**, 1433. (b) Nakata, K.; Miyata, T.; Jintoku, T.; Kitani, A.; Taniguchi, Y.; Takaki, K.; Fujiwara, Y. *Bull. Chem. Soc. Jpn.* **1993**, *66*, 3755. (c) Nakata, K.; Yamaoka, Y.; Miyata, T.; Taniguchi, Y.; Takaki, K.; Fujiwara, Y. *J. Organomet. Chem.* **1994**, *437*, 329. (d) Fujiwara, Y.; Takaki, K.; Taniguchi, Y. *Synlett* **1996**, 591 and references cited therein.

[4] (a) Lin, M.; Sen, A. *Nature* **1994**, *368*, 613. (b) Lin, M.; Hogan, T. E.; Sen, A. *J. Am. Chem. Soc.* **1996**, *118*, 4574.

[5] (a) Barton, D. H. R.; Csuhai, E.; Doller, D. *Tetrahedron Lett.* **1992**, *33*, 4389. (b) Barton, D. H. R. *Synlett* **1997**, 229.

[6] (a) Koch, H.; Haaf, W. *Organic Syntheses*; Wiley: New York, 1973; Collect. Vol. V, p 20. (b) Takeuchi, K.-I.; Akiyama, F.; Miyazaki, T.; Kitagawa, I.; Okamoto, K. *Tetrahedron* **1987**, *43*, 701. (c) Farooq, O.; Marcelli, M.; Prakash, G. K. S.; Olah, G. A. *J. Am. Chem. Soc.* **1988**, *110*, 864. (d) Akhrem, I. S.; Bernadyuk, S. Z.; Vol'pin, M. E. *Mendeleev Commun.* **1993**, 188. (e) Akhrem, I. S.; Churilova, I. M.; Orlinkov, A. V.; Vol'pin, M. E. *Russ. Chem. Bull.* **1997**, *46*, 491.

[7] Sen, A.; Lin, M. *J. Chem. Soc., Chem. Commun.* **1992**, 892.

[8] (a) Boese, W. T.; Goldman, S. *Tetrahedron Lett.* **1992**, *33*, 2119. (b) Boese, W. T.; Goldman, S. *J. Am. Chem. Soc.* **1992**, *114*, 350.

[9] Hill, C. L.; Jaynes, B. S. *J. Am. Chem. Soc.* **1995**, *117*, 4704.

[10] Ferguson, R. R.; Crabtree, R. H. *J. Org. Chem.* **1991**, *56*, 5503.

[11] Brubaker, M. M.; Coffman, D. D.; Hoehn, H. H. *J. Am. Chem. Soc.* **1952**, *74*, 1509.

[12] (a) Coffman, D. D.; Cramer, R.; Mochel, W. E. *J. Am. Chem. Soc.* **1958**, *80*, 2882. (b) Walling, C.; Savas, E. S. *J. Am. Chem. Soc.* **1960**, *82*, 1738. (c) Thaler, W. A. *J. Am. Chem. Soc.* **1966**, *88*, 4278. (d) Thaler, W. A. *J. Am. Chem. Soc.* **1967**, *89*, 1902. (e) Susuki, T.; Tsuji, J. *J. Org. Chem.* **1970**, *35*, 2982.

[13] (a) Ryu, I.; Kusano, K.; Ogawa, A.; Kambe, N.; Sonoda, N. *J. Am. Chem. Soc.* **1990**, *112*, 1295. (b) Ryu, I.; Sonoda, N. *Chem. Rev. (Washington, D.C.)* **1996**, *96*, 177. (c) Nagahara, K.; Ryu, I.; Komatsu, M.; Sonoda, N. *J. Am. Chem. Soc.* **1997**, *119*, 5465.

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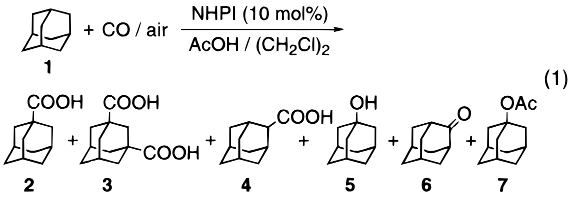
ciently promoted by *N*-hydroxyphthalimide (NHPI) combined with a small amount of transition metal salts to produce the corresponding oxygenated products. We have now developed a new type of catalytic free-radical carboxylation of polycyclic alkanes such as adamantanes with CO/air using *N*-hydroxyphthalimide (NHPI), which serves as an efficient radical catalyst. In this paper, we report the catalytic free-radical carboxylation of alkanes by NHPI without any photoactivation under mild conditions, *i.e.*, lower CO pressure (up to 15 atm) and temperature (below 100 °C).

A typical reaction was carried out as follows. To a solution of NHPI (0.1 mmol) in a mixed solvent of acetic acid (3 mL) and 1,2-dichloroethane (3 mL) in a glass-lining autoclave was added adamantane (**1**) (1 mmol), and then 1 atm of air and 15 atm of CO was charged. The reaction was carried out at 95 °C for 4 h. Table 1 shows the representative results for the carboxylation of **1** under various reaction conditions.



(1)

The carboxylation of **1** with CO/air in the presence of NHPI gave 1-adamantanecarboxylic acid (**2**), 1,3-adamantanedicarboxylic acid (**3**), 2-adamantanecarboxylic acid (**4**), and several oxygenated products such as 1-adamantanol (**5**) and 2-adamantanone (**6**) as well as 1-acetoxyadamantane (**7**). Although the selectivity of these products depended markedly on the reaction conditions, 1-adamantanecarbaldehyde (**8**) was not formed in all reactions examined. When the reaction was carried out using molecular oxygen in place of air, oxidative products were formed as major products (run 2). Needless to say, the reaction did not take place without air (run 3). Among the solvents examined, a mixed solvent consisting of acetic acid and 1,2-dichloroethane (1/5 v/v %) gave the best yield of **2** (56%) at 75% conversion (run 4). The present reaction proceeded even at 60 °C, although a prolonged reaction time was necessary to obtain satisfactory yield of **2** (run 5). The carboxylation of **1** using *N*-hydroxysuccinimide, an analogue of NHPI, under these conditions gave **2** in slightly lower selectivity (40%) (run 6).

The reaction did not take place in the presence of hydroquinone (0.1 mol %) (run 10). This shows that the NHPI-catalyzed carboxylation involves the radical process in the reaction step. In the present carboxylation of **1**, the relative reactivity of the tertiary hydrogen to the secondary hydrogen estimated from run 1 was ca. 12.[15] This value was almost the same as that by the NHPI-catalyzed aerobic oxidation of **1**,[14c] which may reflect a reaction path in the present carboxylation analogous to that of the aerobic oxidation reported previously.

In contrast to the NHPI-catalyzed aerobic oxidation of alkanes where the reaction is markedly enhanced by the addition of a transition metal salt such as Co(acac)$_2$, the present carboxylation of **1** was efficiently catalyzed by NHPI alone under mild conditions.

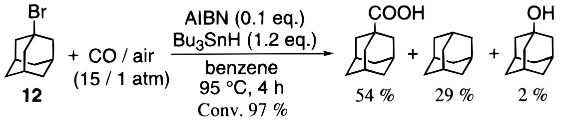
The carboxylation of **2** in the presence of NHPI (30 mol %) gave dicarboxylic acid **3** in 57% yield at 74% conversion (eq 2, Supporting Information). The formation of **3** is interesting from a synthetic point of view, because dicarboxylic acid **3** is difficult to obtain from the conventional carboxylation of **1** with CO.

Similarly, 1,3-dimethyladamantane was also carboxylated under these conditions to give the corresponding adamantyl monocarboxylic acid (55%) and dicarboxylic acid (7%) in 77% conversion (eq 3, Supporting Information). The carboxylation of *endo*-tricyclo[5.2.1.0^{2,6}]decane (**9**) by NHPI (30 mol %) combined with a slight amount of Co(acac)$_2$ (0.5 mol %) gave monocarboxylic acid **10** as the major product (55%) (eq 4, Supporting Information). The same reaction of **9** in the absence of Co(acac)$_2$ resulted in the lowering of the yield of **10**.

A plausible mechanism of the present NHPI-catalyzed radical carboxylation of **1** with CO/air system is outlined in Scheme 1. The first step is the generation of phthalimide-*N*-oxyl (PINO) from NHPI with O$_2$.[14d] The PINO abstracts a tertiary hydrogen from **1** to form an adamantyl radical (**A**), which is the key intermediate in this reaction. It is probable that the radical **A** is readily trapped with CO,[1e] giving adamantaneformyl radical (**B**), which on subsequent reaction with O$_2$, produces adamantanecarboperoxy radical (**C**) and eventually carboxylic acid **2**.

To clarify the participation of the acyladamantyl cation in the formation of carboxylic acid **2**, the carboxylation of **1** in the presence of H$_2{}^{18}$O was examined under the same conditions as run 1 in Table 1. The mass spectrum of the resulting **2** showed that the ratio of **2**/^{18}O labeled-**2** is 94/6. This suggests that most of the carboxyl oxygen contained in **2** comes from CO and air, but not from H$_2{}^{18}$O. If the NHPI-catalyzed carboxylation of **1** passes through the acyladamantyl cation as a transient intermediate, a considerable amount of **2** in which ^{18}O was incorporated in the molecule should be formed.

In addition, the reaction of 1-bromoadamantane (**12**) with CO/air by the Ryu system using AIBN/Bu$_3$SnH,[13] which can be excluded the formation of the acyladamantyl cation as the intermediate, gave also **2** in 54% yield (eq 5). These observations suggest that the NHPI-catalyzed carboxylation of **1** under the influence of CO/air proceeds through the acyladamantyl radical rather than the acyladamantyl cation. Although a part of the **C** seems to decompose to adamantyl radical **A**, carbon dioxide, and dioxygen, the resulting **A** can also react with CO to regenerate the **B**.



(5)

The fact that no aldehyde **8** was formed in the present reaction may indicate that the **8** formed is rapidly converted into carboxylic acid **2** under these conditions. In fact, the independent reaction of **8** under the influence of NHPI and CO/air gave **2** in 57% yield along with adamantane **1** (12%), 1-adamantanol **5** (5%), and 1-acetoxyadamantane **7** (1%) (eq 6). The formation of **1**, **5** and **7** from **8** suggests that the reaction between **1** and **8** is reversible path.

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Supporting Information Available: Equations 2–4 and 6 characterization data for all compounds (16 pages).

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[14] In a previous paper, we demonstrated that PINO is easily generated by exposing NHPI to molecular oxygen. (a) Ishii, Y.; Nakayama, K.; Takeno, M.; Sakaguchi, S.; Iwahama, T.; Nishiyama, Y. *J. Org. Chem.* **1995**, *60*, 3934. (b) Iwahama, T.; Sakaguchi, S.; Nishiyama, Y.; Ishii, Y. *Tetrahedron Lett.* **1995**, *36*, 6923. (c) Ishii, Y.; Kato, S.; Iwahama, T.; Sakaguchi, S. *Tetrahedron Lett.* **1996**, *37*, 4993. (d) Ishii, Y.; Iwahama, T.; Sakaguchi, S.; Nakayama, K.; Nishiyama, Y. *J. Org. Chem.* **1996**, *61*, 4520. (e) Ishii, Y. *J. Mol. Catal. A: Chem.* **1997**, 123. (f) Yoshino, Y.; Hayashi, Y.; Iwahama, T.; Sakaguchi, S.; Ishii, Y. *J. Org. Chem.* **1997**, *62*, 6810.

[15] The ratio of C$^{3°}$–H/C$^{2°}$–H was estimated from total yield of **2**, **3**, **5**, and **7**/total yield of **4** and **6**.