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Addition of adamantanes to acetylenic carboxylates catalyzed by *N*-hydroxyphthalimide (NHPI)

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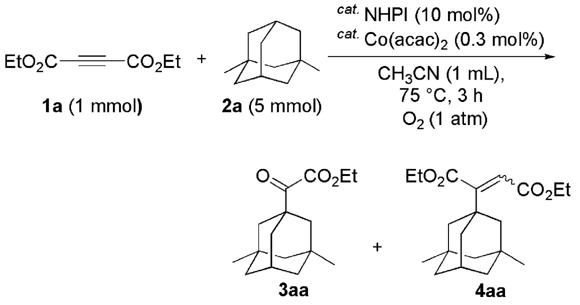
Abstract—Radical addition of 1,3-dimethyladamantane to diethyl acetylenedicarboxylate was catalyzed by NHPI combined with Co species under O_2 to give different adducts, ethyl 2-(3,5-dimethyladamantyl)-2-oxoethanoate and a normal adduct whose ratio was found to depend on the O_2 concentration of the reaction system.

1. Introduction

Although addition of alkyl radicals to alkynes has been studied to a lesser degree than that of alkenes, the addition of carbon radicals derived from alkyl halides and tellurides to alkynes has been modestly reported.[1] Eguchi et al. have reported the addition of 1-adamantyl bromide and iodide to alkenes and alkynes containing the electron-withdrawing group in the presence of tributyltin hydride and AIBN.[2] There have been several reports on the additions of carbon radicals generated from ketones and aldehydes to alkynes assisted by $Mn(OAc)_3$[3–5] or under γ-irradiation.[6] In these reactions, carbonyl compounds like aldehydes, ketones as well as acetic acid undergo the one-electron oxidation by Mn(III) ions to generate the corresponding α-carbon radicals which add to electron-rich alkenes like terminal aliphatic alkenes and allyl acetate. However, alkyl radicals are difficult to add to simple alkynes owing to the polar effect of the alkyl radicals which are favourable for electron-deficient alkynes. Therefore, the radical addition using Mn(III) ions is limited to the addition of carbonyl compounds to alkenes or alkynes.[7] Recently, we have developed a novel methodology for alkyl radical generation from alkanes using *N*-hydroxyphthalimide (NHPI) as a key catalyst.[8] Thus, oxyalkylation of alkenes by the addition of both oxygen and carbon radicals generated from alkanes,[9] alcohols,[10] and ethers was performed.[11] In this letter, we wish to report the NHPI-catalyzed radical addition of adamantanes to alkynes bearing electron-withdrawing substituent under molecular oxygen.

The reaction of diethyl acetylenedicarboxylate (**1a**) with 1,3-dimethyladamantane (**2a**) was chosen as a model reaction and carried out in the presence of a catalytic amount of NHPI combined with Co salts under various conditions (Eq. 1 and Table 1).

The reaction of **1a** with **2a** (5 equiv) was run in the presence of NHPI (10 mol %) and $Co(acac)_2$ (0.3 mol %) under dioxygen (1 atm) in CH_3CN at 75 °C for 3 h (run 1).



(1)

It was found that the reaction gives an unexpected cleaved adduct, ethyl 2-(3,5-dimethyladamantyl)-2-oxoethanoate (**3aa**), in 31% yield and expected normal addition products (20%), diethyl 2-(3,5-dimethyladamantyl)maleate (*Z*-**4aa**) and diethyl 2-(3,5-dimethyladamantyl)fumarate (*E*-**4aa**) consisting of about 6:4 mixture (run 1). In this reaction, about 10% of oxygenated products involving 3,5-dimethyladamantanol as a

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Table 1. Reactions of **1a** with **2a** under various conditions[a]

Run	O_2/N_2 (atm)	Conv. (%)	Yield (%)	
			3aa	**4aa** (*Z*/*E*)
1	1/0	>99	31	20 (62/38)
2[b]	1/0	90	38	10 (65/35)
3[b,c]	1/0	98	45	4 (53/47)
4[d]	1/0	85	27	5 (66/34)
5	0.5/0.5	>99	21	33 (64/36)
6	0.2/0.8 (air)	98	12	37 (66/34)
7	0.1/0.9	84	6	29 (67/33)
8[e]	0/1 (Ar)	18	n.d.	Trace
9[b]	0.2/0.8 (air)	88	13	19 (69/31)
10[c]	0.2/0.8 (air)	>99	10	40 (64/36)
11[c,f]	0.2/0.8 (air)	>99	15	46 (65/35)
12[g]	0.2/0.8 (air)	56	12	18 (65/35)
13[h]	0.2/0.8 (air)	98	17	29 (65/35)
14[i]	1/0	>99	31	24 (64/36)
15[i]	0.2/0.8 (air)	97	12	31 (68/32)

[a] **1a** (1 mmol) was reacted **2a** (5 mmol) in the presence of NHPI (0.1 mmol, 10 mol %) and $Co(acac)_2$ (0.003 mmol, 0.3 mol %) under dioxygen in CH_3CN (1 mL) at 75 °C for 3 h.

[b] In the absence of solvent.

[c] For 15 h.

[d] In the absence of $Co(acac)_2$.

[e] Under Ar (1 atm).

[f] **2a** (15 mmol) was reacted.

[g] Benzonitrile was used as a solvent.

[h] Acetic acid was used as a solvent.

[i] **1b** was used in place of **1a**. Products are **3ba** and **4ba**.

major component were formed. It is interesting to note that the cleaved adduct **3aa** is obtained in preference to normal addition products **4aa**. It is interesting to note that the cleaved adduct **3aa** is obtained in preference to normal adducts **4aa**. The reaction in the absence of a solvent resulted in the decrease of the yield of **4aa** (run 2). When the reaction was prolonged to 15 h under these conditions, the product **3aa** was slightly increased but the yield of **4aa** was decreased (run 3). A probable reaction path for the formation of the cleaved product **3aa** will be discussed later. The reaction by NHPI in the absence of $Co(acac)_2$ resulted in the decrease of the adducts (run 4). The formation of **3aa** and **4aa** was found to depend on the oxygen concentration in the reaction system. When the reaction was carried out under lower oxygen concentrations, the yield of the cleaved adduct **3aa** decreased in contrast to the increase of the yield of the adduct **4aa** (runs 5–7). Needless to say, no reaction took place under Ar atmosphere without O_2 (run 8). These results suggest that the oxygen concentration is an important factor, to control the reaction path to **3aa** and **4aa**. Even in the reaction under air for 15 h, the yields of **4aa** (40%) and **3aa** (10%) were not increased as expected (run 10). When the amount of **2a** was increased to 15 mmol, the yield of **4aa** was increased to 46% (run 11). Among several solvents examined, CH_3CN was found to be the best solvent (runs 12 and 13). The reaction using dimethyl acetylenedicarboxylate (**1b**) in place of **1a** afforded the corresponding adducts **3ba** and **4ba** in almost the same yields as those of **1a** except for the slight decrease of the yield of **4ba** (runs 14 and 15).

In order to obtain information on the reaction course, the time-dependence of **3aa** and **4aa** for the addition of **2a** to **1a** by the $NHPI/Co(acac)_2$ system and NHPI alone was followed (Fig. 1).

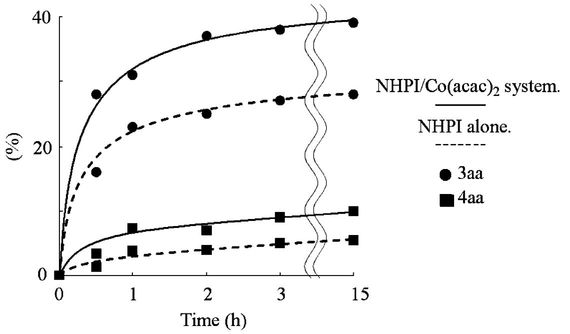
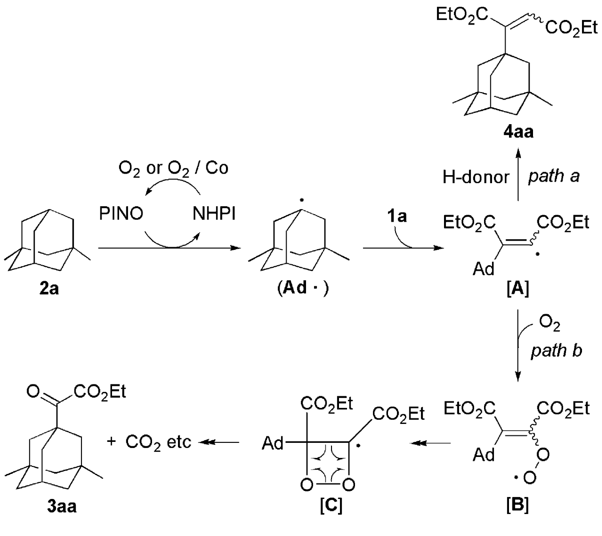


Figure 1. Reactions of **1a** with **2a** by NHPI or $NHPI/Co(acac)_2$ system.

As expected, the reaction by the $NHPI/Co(acac)_2$ system proceeded faster than that by the NHPI alone. In addition, this shows that the reaction was almost terminated for about 3 h. From the time-dependence curves of the adducts **3aa** and **4aa**, it was considered that these adducts are formed through the independent reaction pathway.

On the basis of these results, we can propose a following reaction path for the radical addition of **2a** to **1a** under molecular oxygen using NHPI as a key catalyst (Scheme 1).

The reaction is initiated by the hydrogen abstraction from **2a** by phthalimide *N*-oxyl radical (PINO) from NHPI to form adamantyl radical (Ad$^\bullet$) which then adds to **1a** leading to an adduct radical intermediate [**A**]. When NHPI or **2a** serves as a hydrogen donor of the radical [**A**], normal addition products, *E*- and *Z*-**4aa**, are formed (path a). Under the present reaction condition in which O_2 is present in the reaction system, however, the resulting radical **A** can easily react with O_2 to produce a peroxide **B** (path b). It is reasonable to assume that the



Scheme 1. A possible reaction path.

peroxide **B** may be converted into an ketocarboxylate **3aa** through a dioxetane radical intermediate **C**. Previously, we observed that a similar decarboxylation occurs in the NHPI-catalyzed radical addition of 1,3-dioxolanes to methyl vinyl ketone.[10] This type of intermediate is also postulated by Adam.[12] If the reaction was assumed to progress according to Scheme 1, the product ratio of **3aa** to **4aa** is dependent on the oxygen concentration. Thus, the reaction under higher dioxygen concentration leads to **3aa** in preference to **4aa**.

The addition of several cycloalkanes like cyclohexane and cyclooctane to **1a** was examined under several reaction conditions as shown in Table 1 to give a complex mixture involving normal addition products in 22–35% yields along with oxygenated products.

In conclusion, the NHPI-catalyzed radical addition of adamantanes to acetylenedicarboxylates under the influence of dioxygen was found to occur accompanied by the decarboxylation of acetylenedicarboxylates to give α-keto carboxylate and normal adducts.

2. Experimental

All starting materials were commercially available and used without any purification. GLC analysis was performed with a flame ionization detector using a 0.2 mm × 25 m capillary column (OV-1). ^{1}H and ^{13}C NMR were measured at 270 or 400 MHz and 67.5 MHz, respectively, in $CDCl_3$ with Me_4Si as the internal standard.

General procedure for reaction of **1a** *with* **2a**: To a mixture of NHPI (0.1 mmol) and $Co(acac)_2$ (0.003 mmol) in CH_3CN (1 mL) were added **1a** (1 mmol) and **2a** (5 mmol). The reaction mixture was stirred at 75 °C for 3 h under dioxygen. The product was isolated by column chromatography (230–400 mesh silica gel, *n*-hexane/ethyl acetate = 5–20:1). The yields of products were estimated from the peak areas based on the internal standard technique using GC.

Compound **3aa**: IR (NaCl) 2902, 1735, 1455, 1283 cm^{-1}; ^{1}H NMR δ 0.86 (s, 6H), 1.17–2.16 (m, 16H), 4.30 (q, 2H); ^{13}C NMR δ 14.0, 28.8, 30.3, 30.7, 35.9, 42.5, 43.2, 46.8, 50.4, 61.5, 164.0; MS (EI) *m/z* 264 $[M]^+$, 191 $[M–CO_2Et]^+$.

Compound *E*-**4aa**: IR (NaCl) 2900, 1720, 1455, 1220 cm^{-1}; ^{1}H NMR δ 0.81 (s, 6H), 1.13–2.08 (m, 19H), 4.18–4.24 (q, 4H), 6.06 (s, 1H); ^{13}C NMR δ 14.0, 14.1, 29.5, 30.5, 31.1, 38.2, 39.5, 42.6, 45.7, 50.4, 60.9, 122.1, 151.7, 167.0, 168.8; MS (EI) *m/z* 334 $[M]^+$, 305 $[M–Et]^+$.

Compound *Z*-**4aa**: IR (NaCl) 2900, 1725, 1460, 1180 cm^{-1}; ^{1}H NMR δ 0.84 (s, 6H), 1.13–2.04 (m, 19H), 4.15 (q, 2H), 4.30 (q, $2H_2$), 5.78 (s, 1H); ^{13}C NMR δ 14.0, 14.1, 29.2, 30.4, 30.5, 31.0, 39.1, 42.4, 46.6, 50.3, 60.4, 60.8, 115.7, 160.0, 165.0, 168.0; MS (EI) *m/z* 334 $[M]^+$, 305 $[M–Et]^+$.

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