

Short Communication

Direct Carboxylation of Adamantane

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We have reported the one-step formation of *N*-(1-adamantyl)acetamide (1-Ad-NHCOCH₃) by reaction of adamantane with nitric acid and acetonitrile. The reaction was proposed to proceed by formation of the 1-adamantyl cation which reacted with acetonitrile in a Ritter reaction.¹

Derivatization of adamantane has previously been performed via 1-adamantyl bromide from bromination of adamantane or by formation of the 1-adamantyl cation (from adamantane and *tert*-butyl cation or by reaction with HNO₃–H₂SO₄–SO₃) followed by reaction with an appropriate nucleophile.^{2–7} The reported one-pot formation of 1-Ad-NHCOCH₃ by HNO₃ oxidation of adamantane appeared to be a convenient method for the preparation of that compound and we have now investigated the reaction with other nucleophiles.

The mechanism of the reaction has been investigated by Moiseev and is believed to proceed by a hydride abstraction of the nitronium ion (NO₂⁺).⁸ This is supported by the results of analogous oxidations by NO₂BF₄.⁹ However, adamantane is also ionized by the action of NO⁺BF₄[–].¹⁰ The presence of HNO₂ was not rigorously suppressed in the present work and ionization by NO⁺ cannot be excluded.

Results and discussion

The reactions were performed by mixing adamantane with 100% HNO₃, CCl₄ and the appropriate nucleophile. The products were worked up by CH₂Cl₂-extraction followed by washing with water and drying over Na₂SO₄. The products were identified by comparison of their spectroscopic properties (IR, ¹H and ¹³C NMR and MS) with those of authentic samples. The yields were determined by means of GC by the internal standard method.

With 1,1-dichloroethene and 1,1,2-trichloroethene as nucleophiles,^{5,6} no addition to the olefins was observed. The products identified were 1-Ad-OH (5%) and 1-Ad-ONO₂ (30%). Formic acid used in sulfuric acid as a carbon monoxide source⁴ gave no carboxylation with

adamantane and nitric acid. To increase the concentration of CO, the reaction was performed by application of CO gas at 20–30 atm. The main product was 1-Ad-COOH with 1-Ad-ONO₂ as a by-product. The maximum yield was 75% of 1-Ad-COOH with 9% of 1-Ad-ONO₂. The optimization and best reaction conditions are described in the Experimental. Adamantane has been carboxylated to 1-Ad-COOH (70% yield) by the use of *tert*-butyl alcohol–H₂SO₄ and HCOOH.⁴ Carboxylation with H₂SO₄–SO₃–HCOOH has also been reported.¹¹

To investigate the role of the organic solvent, the carboxylations were performed without CCl₄, with only CO–HNO₃ and adamantane. The first-formed product was 1-Ad-COOH. However, on further reaction, this was transformed into 3-carboxy-1-adamantyl nitrate (1,3-Ad-COOH-ONO₂) which became the major product (Table 1). By comparing the result at 30 min with that from the reaction with CCl₄ present (75% 1-Ad-COOH, 9% 1-Ad-ONO₂) it is evident that the result of the reaction depended on the presence of CCl₄.

The major product from the reaction without CCl₄ was 1,3-Ad-COOH-ONO₂. Prolonged reaction time resulted in a decrease in the yield of 1,3-Ad-COOH-ONO₂ and an increase in the yield of 1,3-Ad-(COOH)₂ (Table 1 at 1320 min). In a separate experiment it was established

Table 1. Product distribution (%) from the reaction of adamantane (1.18 mmol), 100% HNO₃ (3 ml) and CO (30 atm) at 20 °C. Analyses by GC (area % for 30 and 90 min, internal standard method for 1320 min) after methylation by CH₂N₂.

Products	Reaction time/min		
	30	95	1320
AdH	13	0	0
1-AdCOOH	48	8	0
1-Ad-ONO ₂	2	6	<1
1,3-Ad(COOH) ₂	0	8	32
1,3-Ad-COOH-ONO ₂	25	78	63
1,3-Ad-COOH-OH	0	0	10
AdOH	6	0	0

that 1,3-Ad-COOH-ONO₂ was converted into 1,3-Ad-(COOH)₂ under the reaction conditions. However, the conversion was slow and accompanied by some decomposition so that the combined yield of 1,3-Ad-(COOH)₂ and 1,3-Ad-COOH-ONO₂ decreased somewhat on increased reaction time: 19 h at 18 °C gave 64% 1,3-Ad-COOH-ONO₂ and 24% 1,3-Ad-(COOH)₂ starting from 100% 1,3-Ad-COOH-ONO₂. Nevertheless, this one-pot formation of 1,3-Ad-COOH-ONO₂ from adamantane is not without interest. There are several procedures for the transformation of 1-adamantyl nitrate into other adamantyl derivatives^{8,9} and we therefore have a general method for the preparation of 3-substituted adamantancarboxylic acids.

The results also indicate the role of CCl₄ in the monosubstitution of adamantane: the organic solvent, immiscible with HNO₃, dissolves the monosubstituted product formed and thereby makes it less accessible for further oxidation in the HNO₃ phase.

Experimental

All reagents were commercially available and were used as received. The reaction mixtures were analyzed by GLC (capillary column, J & W Scientific DB-1, non-polar 30 m × 0.32 mm; temperature program 80(0)–8–180(0)–20–250, internal standard *p*-nitrotoluene) after work-up. The reactions with CO were performed in a 10 ml glass vial placed inside a stainless steel reactor connected to a CO steel flask. Nitric acid (100%, *d* = 1.52, 3 ml) and CCl₄ (3 ml) were placed in the glass vial, AdH (160 mg, 1.18 mmol) was added and the CO pressure applied immediately. At this point the stirring

Table 2. Yields of AdH (recovered), AdONO₂ and AdCOOH (% GLC, internal standard method) under different reaction conditions.

Expt. No.	<i>p</i> _{CO} /bar	<i>T</i> /°C	Reaction time/min	[HNO ₂]/[AdH]	Yield (%)		
					AdH	AdONO ₂	AdCOOH
1	10	0	15	120	34	51	2
2	10	20	15	60	0	66	19
3	30	0	15	60	47	30	0
4	30	20	15	120	0	43	43
5	10	0	30	60	17	67	4
6	10	20	30	120	0	49	31
7	30	0	30	120	22	47	11
8	30	20	30	60	0	48	44

was started (by a magnetic bar in the vial) and the appropriate reaction temperature set.

1-Ad-COOH. The optimum conditions for the formation of 1-Ad-COOH was found by varying the conditions as shown in Table 2. The ratio of volume of CCl₄/volume HNO₃ was kept at 1. The optimization was performed as 1/2 fraction of a 2⁴-design, that is, as eight single experiments. The experiments are given in Table 2. From a multivariable regression analysis,¹² the following information was obtained:

$$\text{Yield of 1-Ad-COOH (\%)} = 19.1 + 15.0 \times X_1 + 5.4 \times X_2$$

$$\text{Yield of 1-Ad-ONO}_2 \text{ (\%)} = 32.3 - 5.4 \times X_2$$

where $X_1 = [\text{temperature (°C)} - 10]/10$ and $X_2 = [\text{CO pressure (bar)} - 20]/10$.

From this, the optimum conditions were reaction temperature, 30 °C; CO pressure, 4 MPa; [HNO₃]/[AdH], 60; reaction time 30 min with the volume ratio HNO₃/CCl₄ = 1. Under these conditions a yield of 75% AdCOOH with 9% AdONO₂ was obtained (GLC, internal standard method).

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