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Ceric(IV) Ammonium Nitrate In the Selective Conversion of Hydrazides to Esters

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Abstract: Hydrazides were treated with ceric(IV) ammonium nitrate (CAN) in the presence of the appropriate alcohol as a nucleophile to afford esters in good yields. Reactions took place exclusively at the hydrazino moiety even when other sensitive groups were present in either of the partners.
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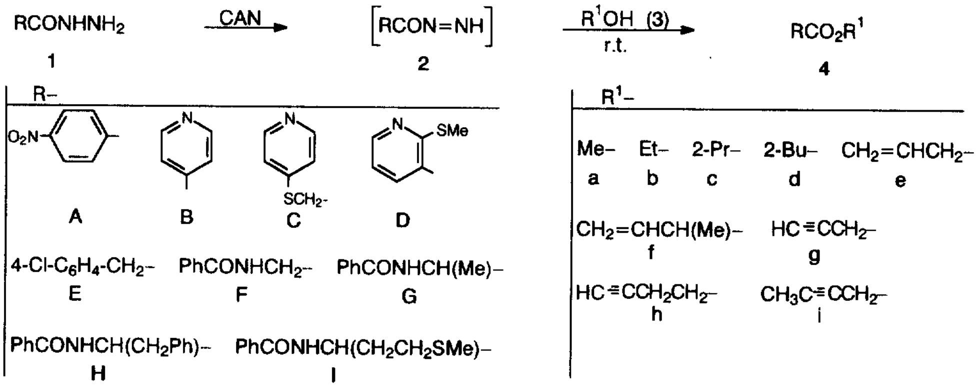
In connection with our endeavours to explore the synthetic potential of hydrazides and their derivatives,[1] we recently demonstrated an application of thallium(III) nitrate trihydrate (TTN) for the oxidation of the hydrazino group in the presence of the appropriate nucleophile leading to esters and other compounds.[2] Due to the high toxicity of TTN we were looking for an alternative oxidant of the hydrazino moiety. Sodium hexanitrocobaltate(III), $Na_3Co(NO_2)_6$, reacted with hydrazides, but the final products were acyl azides.[3] On the other hand, ceric(IV) ammonium nitrate (CAN),[4] which has already been used for the conversion of hydrazides to acids,[5] showed similar reactivity to TTN in the oxidation of 1,4-disubstituted semicarbazides to diazenes[6] and therefore seemed to be promising candidate for the present study. Thus, hydrazide **1** was treated with CAN in the presence of alcohols **3**,[7] giving the corresponding ester **4** (Scheme 1) in good yield.

Scheme 1



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The reaction probably proceeds *via* the acyl diimide **2**, although the formation of the acyl cation cannot be excluded.[8] In a typical experiment, the hydrazide **1** (1 mmol) was added at room temperature within the period of 30–40 min to CAN (4 mmol) in the appropriate alcohol **3** (5–7 mL). The reaction mixture was stirred at r.t. for the additional time indicated in Table 1, evaporated to dryness below 40 °C, treated with water (10 mL) and neutralised with sodium hydrogen carbonate. After extraction with chloroform or methylene chloride (8 x 20 mL), the organic phase was dried over anhydrous sodium sulfate and concentrated under reduced pressure to give the ester **4** in good to excellent yield. Selected examples are reported in Table 1.

Table 1. Preparation of Esters from Hydrazides with CAN in the presence of Alcohols.

Entry	Hydrazide	Alcohol	Reaction Time (h)[a]	Product[9]	Yield (%)[b]
1	**1A**	**3a**	0.25	**4Aa**	97
2	**1A**	**3c**	0.5	**4Ac**	80
3	**1A**	**3d**	1.5	**4Ad**	76
4	**1A**	**3f**	3.5	**4Af**	80
5	**1A**	**3i**	7.5	**4Ai**	84
6	**1B**	**3b**	0.25	**4Bb**	89
7	**1B**	**3h**	8.5	**4Bh**	89
8	**1C**	**3a**	0.75	**4Ca**	81
9	**1D**	**3a**	0.75	**4Da**	98
10	**1D**	**3e**	1	**4De**	83
11	**1D**	**3g**	0.75	**4Dg**	77
12	**1E**	**3e**	2.5	**4Ee**	80
13	**1F**	**3a**	0.2	**4Fa**	92
14	**1F**	**3h**	6	**4Fh**	83
15	**1G**	**3g**	1.5	**4Gg**	81
16	**1H**	**3e**	2	**4He**	89
17	**1H**	**3g**	5	**4Hg**	93
18[c]	**1I**	**3a**	0.75	**4Ia**	80

[a] Reaction time after the addition of the entire amount of the hydrazide **1** to the reaction mixture.

[b] Yields of isolated products are given.

[c] Addition of the reagents was slightly modified: the solution of the hydrazide **1I** (1 mmol) in MeOH (4 mL) and the solution of CAN (4 mmol) in MeOH (4 mL) were added simultaneously over the period of 30 min to the flask containing MeOH (2 mL).

It should be noted that the oxidation of various sulfides with CAN, leading to sulfoxides, occurs; easily in aqueous acetonitrile,[10] under phase transfer conditions,[11] in methylene chloride on hydrated silica gel[12] and in the combination with CAN either with sodium bromate[13] or with oxygen.[14] Contrary to these results, the sulfide functionality remained intact under the conditions we used for the transformation of hydrazides to esters (Table 1: entries 8–11, and 18). Furthermore, we did not detect any oxidation of the alcohols themselves, in spite of the fact that CAN has already been described as a reagent for the conversion of alcohols to aldehydes or ketones,[4b,15] and, in the combination with sodium bromate, even for the selective oxidation of secondary alcohols in the presence of primary ones.[16] Under the reaction conditions we employed, the esters deriving from either primary or secondary alkanols, alkenols or alkynols were obtained as the only products. The esters did not suffer any cleavage to the corresponding acids, although this reaction has already been described, but was shown to require treatment of the esters with CAN in aqueous acetonitrile under reflux.[17]

In conclusion, we have developed a simple method for the conversion of hydrazides to esters with CAN. This transformation involves selective oxidation of the hydrazino group, followed by reaction with various saturated or unsaturated alcohols as nucleophiles, and is not interrupted by the presence of other functional groups. Our approach seems to be useful for the preparation of esters possessing a wide variety of fragments R and R^1.

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9. New compounds were characterised by IR, NMR, MS spectra and by elemental analysis or HRMS. Selected data: **4Ai**: ^{1}H NMR (300 MHz, CDCl$_3$) δ 1.89 (t, 3H, J = 2.3 Hz), 4.94 (q, 2H, J = 2.3 Hz), 8.27 (m, 4H). ^{13}C NMR (75 MHz, CDCl$_3$) δ 3.6, 54.2, 72.6, 84.1, 123.5, 130.9, 135.1, 150.7, 164.1. MS (EI) *m/z* 219 (M$^+$, 29), 150 (100), 104 (8). Anal. Calcd for $C_{11}H_9NO_4$: C, 60.28; H, 4.14; N, 6.39. Found: C, 60.27; H, 4.08; N, 6.26. **4Bh**: ^{1}H NMR (300 MHz, CDCl$_3$) δ 2.05 (t, 1H, J = 2.6 Hz), 2.69 (dt, 2H, J_1 = 6.7 Hz, J_2 = 2.6 Hz), 4.47 (t, 2H, J = 6.7 Hz), 7.86 (m, 2H), 8.79 (m, 2H). ^{13}C NMR (75 MHz, CDCl$_3$) δ 19.0, 63.3, 70.3, 79.6, 122.9, 137.1, 150.7, 164.9. MS (EI) *m/z* 175 (M$^+$, 14), 123 (37), 106 (100), 78 (93). HRMS calcd for $C_{10}H_9NO_2$ 175.0633, found 175.0640. **4De**: ^{1}H NMR (300 MHz, CDCl$_3$) δ 2.49 (s, 3H), 4.80 (td, 2H, J_1 = 5.6 Hz, J_2 = 1.3 Hz), 5.27 (dtd, 1H, J_1 = 10.4 Hz, J_2 = 2.6 Hz, J_3 = 1.3 Hz), 5.43 (dtd, 1H, J_1 = 17.1 Hz, J_2 = 2.6 Hz, J_3 = 1.3 Hz), 6.01 (m, 1H), 7.00 (dd, 1H, J_1 = 7.8 Hz, J_2 = 4.7 Hz), 8.18 (dd, 1H, J_1 = 7.8 Hz, J_2 = 1.9 Hz), 8.53 (dd, 1H, J_1 = 4.7 Hz, J_2 = 1.9 Hz). ^{13}C NMR (75 MHz, CDCl$_3$) δ 13.7, 65.7, 117.7, 118.6, 122.7, 131.7, 138.4, 151.8, 162.7, 164.6. MS (EI) *m/z* 209 (M$^+$, 65), 168 (100), 152 (65), 150 (59), 79 (70). HRMS calcd for $C_{10}H_{11}NO_2S$ 209.0511, found 209.0517. **4Dg**: ^{1}H NMR (300 MHz, CDCl$_3$) δ 2.53 (t, 1H, J = 2.5 Hz), 4.94 (d, 2H, J = 2.5 Hz), 7.06 (dd, 1H, J_1 = 7.8 Hz, J_2 = 4.7 Hz), 8.26 (dd, 1H, J_1 = 7.8 Hz, J_2 = 1.9 Hz), 8.60 (dd, 1H, J_1 = 4.7 Hz, J_2 = 1.9 Hz). ^{13}C NMR (75 MHz, CDCl$_3$) δ 13.8, 52.6, 75.4, 77.3, 117.9, 122.1, 138.9, 152.3, 163.3, 164.4. MS (EI) *m/z* 207 (M$^+$, 77), 192 (29), 168 (100), 138 (61), 130 (75), 78 (98). HRMS calcd for $C_{10}H_9NO_2S$ 207.0354, found 207.0360. **4Ee**: ^{1}H NMR (300 MHz, CDCl$_3$) δ 3.61 (s, 2H), 4.59 (td, 2H, J_1 = 5.8 Hz, J_2 = 1.3 Hz), 5.22 (dtd, 1H, J_1 = 10.4 Hz, J_2 = 2.7 Hz, J_3 = 1.3 Hz), 5.27 (dtd, 1H, J_1 = 17.1 Hz, J_2 = 2.7 Hz, J_3 = 1.3 Hz), 5.90 (m, 1H), 7.28 (m, 4H). MS (EI) *m/z* 210 (M$^+$, 21), 125 (100), 89 (21). HRMS calcd for $C_{11}H_{11}ClO_2$ 210.0448, found 210.0451. **4Fh**: ^{1}H NMR (300 MHz, CDCl$_3$) δ 2.02 (t, 1H, J = 2.7 Hz), 2.60 (dt, 2H, J_1 = 6.8 Hz, J_2 = 2.7 Hz), 4.29 (d, 2H, J = 4.9 Hz), 4.32 (t, 2H, J = 6.8 Hz), 6.65 (broad, 1H), 7.49 (m, 3H), 7.82 (m, 2H). ^{13}C NMR (75 MHz, CDCl$_3$) δ 18.9, 41.7, 63.1, 70.2, 79.5, 127.1, 128.6, 131.8, 133.7, 167.4, 169.8. MS (EI) *m/z* 231 (M$^+$, 6), 134 (40), 105 (100). Anal. Calcd for $C_{13}H_{13}NO_3$: C, 67.52; H, 5.67; N, 6.06. Found: C, 67.44; H, 5.73; N, 5.99.

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