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Amidation of norbornene with organic nitriles in the presence of water catalyzed by iron compounds

Ravil I. Khusnutdinov *, Tatyana M. Oshnyakova

Institute of Petrochemistry and Catalysis, Russian Academy of Sciences, 141 Prospekt Oktyabrya, Ufa 450075, Russian Federation

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ABSTRACT

The amidation of norbornene with various nitriles was performed in the presence of water under the action of $FeCl_3{\cdot}6H_2O$ to give *N*-(*exo*-2-norbornyl)acylamides in 76–95% yield.

The reaction of nitriles with olefins using the Ritter reaction is widely used to synthesize *N*-substituted amides.[1–5] For example the amidation of olefins with acetonitrile has been reported to be catalyzed by mineral acids such as H_2SO_4, $PhSO_3H$, HF, and oleum as well as heteropoly acids.[2–5] Specifically, the reaction of norbornene **1** with acetonitrile in the presence of a large excess of H_2SO_4 has previously been reported for the formation of *N*-(*exo*-2-norbornyl)acetamide **2** in 70% yield.[5]

In this Letter we report the amidation of norbornene **1** with organic nitriles in the presence of water and iron-containing catalysts.

Initially the reaction was examined using norbornene **1**, acetonitrile, and water, stirring at 130 °C for 6 h in the presence of various iron compounds as the catalyst. The reaction led to a mixture of three products, namely, *N*-(*exo*-2-norbornyl)acetamide **2**, *exo*-bicyclo[2.2.1]heptan-2-ol **3**, and tricyclo[$2.2.1.0^{2,6}$]heptane **4** (Scheme 1) and their yields and the ratios obtained were shown to be dependent upon the catalyst used (Table 1). The compounds were all identified using NMR (^1H, ^{13}C) spectroscopy and mass-spectrometry.

The reaction of norbornene with acetonitrile and water in the presence of $FeCl_3{\cdot}6H_2O$ as the catalyst gave a 10:1 mixture of *N*-(*exo*-2-norbornyl)acetamide **2** and the minor reaction product *exo*-bicyclo[2.2.1]heptan-2-ol **3** in 84% total yield (Table 1, entry 1). Compound **2** could be separated from the mixture of products in 76% isolated yield.[6]

Increasing the temperature to 140 °C did not result in an increase in yield but promoted the norbornene isomerization side reaction affording tricyclo[$2.2.1.0^{2,6}$]heptane **4** (Table 1, entry 2).

When $FeCl_3{\cdot}6H_2O$ was replaced by anhydrous $FeCl_3$, the total yield of products **2**–**4** decreased to 41% (Table 1, entry 3). Other iron catalysts, namely, $Fe(acac)_3$, $Fe(C_5H_5)_2$, $Fe(OAc)_2{\cdot}4H_2O$, and $Fe_2(CO)_9$ were found to catalyze the reaction only upon addition of an equimolar amount of HBr to give a mixture of products **2** and **3** (Table 1, entries 4–7).

Increasing the amount of HBr to 9 mol % (Table 1, entry 8) resulted in a small increase in the conversion of norbornene **1**, but gave a 1:1 mixture of **2** and tricyclo[$2.2.1.0^{2,6}$]heptane **4** as a result of the isomerization of **1**.

Next the scope of the reaction was examined using other nitriles such as propionitrile, acrylonitrile, benzonitrile, and *o*-tolunitrile which all actively participated in the amidation reaction (Table 2, entries 1–4).[6]

Reactions involving these nitriles required higher temperature (140–145 °C) in comparison with acetonitrile (130 °C), giving the desired amides **5**–**8** in isolated yields of 80–95% with by-products **3** and **4** only being formed in trace amounts (Scheme 2).

Other transition and rare earth metal complexes were also tested as catalysts for the amidation of **1** with organic nitriles under the optimized reaction conditions. Notably, $NiCl_2$, $Ni(acac)_2$, $RuCl_3{\cdot}nH_2O$, $PrCl_3$, $EuCl_3{\cdot}6H_2O$, $MnCl_2$, $Mn(acac)_3$, $CuCl_2{\cdot}2H_2O$,

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* Corresponding author. Tel./fax: +7 347 2842750.
E-mail address: khusnutdinovri47@gmail.com (R.I. Khusnutdinov).

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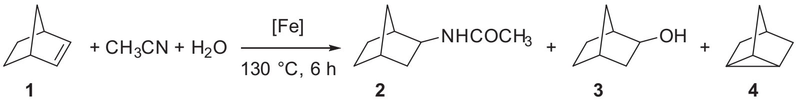


Scheme 1. Amidation of norbornene with acetonitrile catalyzed by iron compounds.

Table 1
The effect of the nature of the catalyst on the yield and ratio of the reaction products in the amidation reaction of norbornene **1** with acetonitrile and water

Entry	Catalyst	Total yield of **2**–**4** (%)	Ratio of **2**:**3**:**4**[a]
1	$FeCl_3·6H_2O$	84	10:1:0
2	$FeCl_3·6H_2O$	81[b]	2:1:1
3	$FeCl_3$	41	3:0:1
4	$Fe(acac)_3$–HBr (1:1)	20	6:1:0
5	$Fe(C_5H_5)_2$–HBr (1:1)	16	9:1:0
6	$Fe(OAc)_2·4H_2O$–HBr (1:1)	50	5:1:0
7	$Fe_2(CO)_9$–HBr (1:1)	38	20:1:0
8	$Fe_2(CO)_9$–HBr (1:3)	57	1:0:1

Reaction conditions: catalyst (0.032 mmol), **1** (1.06 mmol), CH_3CN (8.53 mmol), H_2O (1.06 mmol), 130 °C, 6 h.

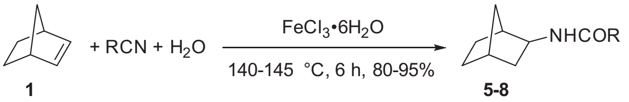
[a] Ratio determined by GLC using undecane as an internal standard.

[b] Reaction temperature 140 °C.

Table 2
The effect of the structure of nitrile on the yield of the reaction product

Entry	R	Product	Isolated yield (%)
1	Et	5	90
2	$H_2C{=}CH{-}$	6	80
3	Ph	7	90
4	*o*-Tol	8	95

Reaction conditions: $FeCl_3·6H_2O$ (0.032 mmol), **1** (1.06 mmol), RCN (5.3 mmol), H_2O (1.06 mmol), 140–145 °C, 6 h.



Scheme 2. Reaction of norbornene with organic nitriles and water catalyzed by $FeCl_3·6H_2O$.

$MoO_2(acac)_2$, and $Mo(CO)_6$ did not show marked activity toward this reaction.

In conclusion, we have developed a new catalytic method for the amidation of norbornene **1** using organic nitriles in the presence of water and $FeCl_3·6H_2O$.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2015.09.131.

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6. General procedure for the preparation of *N*-(*exo*-2-norbornyl)acylamides: the amidation of norbornene with organic nitriles was carried out in a 10 mL glass ampoule. The ampoule was charged with norbornene (0.1 g, 1.06 mmol), catalyst (0.032 mmol), CH_3 CN (8.53 mmol) [or RCN (5.3 mmol)], and water (0.02 g, 1.06 mmol). The ampoule was sealed, placed into a steel microautoclave, and heated at 130 °C (140–145 °C for RCN) for 6 h. After reaction completion, the ampoule was cooled to rt. The reaction mixture was filtered through Al_2O_3 (eluted with $CHCl_3$), the solvent was removed by distillation, and the residue recrystallized from CH_3CN. *N-(exo-2-norbornyl)acetamide* (**2**): mp 140–141 °C (CH_3CN) (Lit. 7 mp 141–142 °C). ^1H NMR (400 MHz, $CDCl_3$): δ 1.18 (m, 6H), 1.67 (m, 2H), 1.87 (m, 3H), 2.12 (m, 1H), 1.18 (m, 1H), 3.62 (m, 1H), 6.38 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 23.17, 26.47, 28.16, 35.40, 35.59, 39.87, 42.25, 169.50. MS (EI, 70 eV) m/z (%): 153 $[M]^+$ (31), 138(10), 124(13), 94(64), 43(100). *N-(exo-2-norbornyl)propanamide* (**5**): mp 88–89 °C (CH_3 CN). ^1H NMR (400 MHz, $CDCl_3$): δ 1.02–1.03 (m, 3H), 1.09–1.68 (m, 8H), 2.09 (s, 1H), 2.16 (s, 1H), 3.61 (s, 1H), 6.04 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 9.94, 26.39, 28.07, 29.57, 35.37, 35.53, 39.96, 42.26, 52.51, 173.14. MS (EI, 70 eV) m/z (%): 167 $[M]^+$ (70), 152(2), 139(6), 138(42), 111(42), 110(39), 101(44), 94(100). IR (vaseline oil): ν_{max} 3275, 1661, 1634, 1555 cm^{-1}. Found (%): C, 71.83; H, 10.23; N, 8.36. $C_{10}H_{17}NO$. Calcd. (%): C, 71.81; H, 10.25; N, 8.37. *N-(exo-2-norbornyl)acrylamide* (**6**): mp 143–144 °C (CH_3 CN). ^1H NMR (400 MHz, $CDCl_3$): δ 0.88–1.49 (m, 8H), 2.18–2.21 (m, 2H), 3.70–3.75 (m, 1H), 5.50–5.53 (m, 2H), 6.09–6.21 (m, 1H), 6.40 (s, 1H).^{13}C NMR (100 MHz, $CDCl_3$): δ 26.56, 28.62, 35.54, 35.69, 39.97, 42.38, 52.89, 125.66, 131.39, 164.97. MS (EI, 70 eV) m/z (%): 165$[M]^+$ (23), 150(4), 137(3), 109(50), 108(47), 98(100), 95(5), 94(59). IR (vaseline oil): ν_{max} 3290, 1673, 1654, 1625, 1545 cm^{-1}. Found (%): C, 72.68; H, 9.14; N, 8.50. $C_{10}H_{15}NO$. Calcd. (%): C, 72.69; H, 9.15; N, 8.48. *N-(exo-2-norbornyl)benzamide* (**7**): mp 151 °C (CH_3CN) (Lit. 8 mp 150–150.5 °C). ^1H NMR (400 MHz, $CDCl_3$)[9]: δ 1.12–1.57 (m, 8H), 1.82–1.87 (m, 1H), 2.29 (s, 1H), 3.88–3.90 (m, 1H), 6.16 (s, 1H), 7.35–7.46 (m, 3H), 7.72 (d, J = 7.6 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$)[9]: δ 26.60, 28.23, 35.72, 35.82, 40.47, 42.49, 53.41, 126.94, 128.50, 131.24, 135.05, 166.90. MS (EI, 70 eV) m/z (%): 215 $[M]^+$(20), 148(8), 135(6), 134(8), 122(16), 105(100), 94(6). *N-(exo-2-norbornyl) methylbenzamide* (**8**): mp 145–146 °C (CH_3 CN). ^1H NMR (400 MHz, $CDCl_3$): δ 1.15–1.94 (m, 8H), 2.31–2.33 (m, 1H), 2.43 (s, 3H), 2.55 (s, 1H), 3.87–3.92 (m, 1H), 5.75 (s, 1H), 7.16–7.32 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 19.75, 26.56, 28.22, 35.70, 35.81, 40.45, 42.57, 52.15, 125.71, 126.71, 129.67, 130.92, 135.88, 136.92, 169.38. MS (EI, 70 eV) m/z (%): 229$[M]^+$(27), 136(6), 134(12), 120(14), 119(100), 94(6), 91(50). IR (vaseline oil): ν_{max} 3280, 1632, 1599, 1536 cm^{-1}.). Found (%): C, 78.55; H, 8.35; N, 6.13. $C_{15}H_{19}NO$. Calcd. (%): C, 78.56; H, 8.35; N, 6.11.
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