Synthesis of *N*-substituted amides by the Ritter reaction with heteropoly acids as catalysts

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Reactions of a number of nitriles with camphene in the presence of the heteropoly acids $H_3PW_{12}O_{40}$, $H_7PMo_{12}O_{42}$, and $H_4SiW_{12}O_{40}$ as catalysts were studied. In all cases, *N*-substituted amides were obtained in sufficiently high yields.

Key words: Ritter reaction, heteropoly acids, nitriles, camphene, *N*-substituted amides.

Acid-catalyzed reactions of nitriles with some alkenes and alcohols known as the Ritter reaction[1,2] is widely used to synthesize various (in both properties and structures) *N*-substituted amides. This reaction has been usually catalyzed by strong mineral acids such as H_2SO_4, $PhSO_3H$, $MeSO_3H$, HSO_3F, anhydrous HF, and some others.[2,3]

In the present work, we studied the possibility of employing heteropoly acids (tungsten and molybdenum oxo complexes) as catalysts for the Ritter reaction.[4] The structures, features, and advantages of heteropoly acids as homogeneous and heterogeneous catalysts have been discussed earlier.[4,5] Heteropoly acids are strong Brensted acids; due to their other practically valuable properties, they have found applications not only in fine organic synthesis but also in some industrial processes.[2,4—6]

Acetonitrile (**1a**), benzonitrile (**1b**), acrylonitrile (**1c**), propionitrile (**1d**), and 1-naphthonitrile (**1e**) were used as nitrile substrates; camphene (**2**) served as an alkylating reagent.

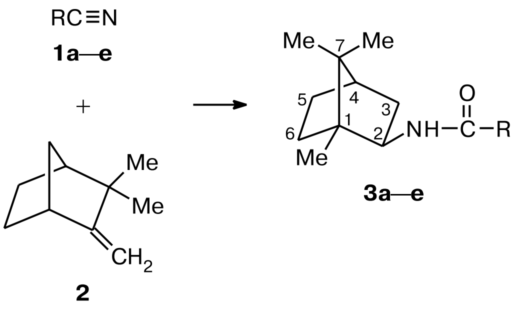
It should be noted that reactions of camphene with various nitriles in the presence of mineral acids and other catalytic systems have been studied earlier[1,3,6—9] and found to yield *N*-substituted amides as the result of the Wagner—Meerwein rearrangement.

Here we showed that heteropoly acids such as $H_3PW_{12}O_{40}$, $H_4SiW_{12}O_{40}$, and $H_7PMo_{12}O_{42}$ are also efficient catalysts for the Ritter reaction. For instance, the reactions of compound **2** with the aforementioned nitriles **1a**—**e** used in excess in the presence of water and $H_3PW_{12}O_{40}$ as a catalyst gave the expected *N*-substituted amides of the norbornane series **3a**—**e** in sufficiently high yields (Scheme 1, Table 1).

The optimum molar camphene : catalyst ratio was 2 : 1.

As expected, the yields of substituted amides depend on the catalyst loading, the temperature, and the reaction duration (Figs 1—3). However, these dependences are complicated: at temperatures and catalyst loadings that differ from those specified in Table 1, the yields decreased substantially.

Scheme 1



R = Me (**a**), Ph (**b**), CH=CH$_2$ (**c**), Et (**d**), 1-C$_{10}$H$_7$ (**e**)

The reaction between compounds **1a** and **2** was also studied in AcOH. The camphene : catalyst ratio was 1 : 1.1

Table 1. Conditions for the $H_3PW_{12}O_{40}$-catalyzed reactions of nitriles **1a**—**e** with camphene (**2**)

Nitrile	$n \cdot 10^3$/mol[a]	t/°C[b]	τ/h[c]	Yield of the product[d] (%)
1a	1.7	80	8	65
1b	1.5	65	4	70
1c	0.3	80	6	64
1d	1.1	65	8	66
1e	0.1	92	6	60

[a] The catalyst loading.
[b] The reaction temperature.
[c] The reaction duration.
[d] Upon the recrystallization.

Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 2, pp. 374—376, February, 2006.

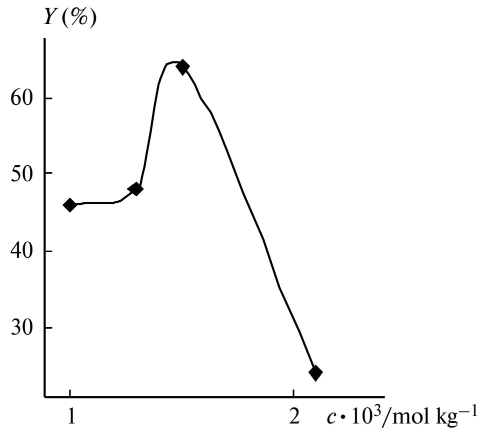


Fig. 1. Plot of the yield of product **3a** (Y) *vs.* the concentration (c) of the catalyst $H_3PW_{12}O_{40}$ (80 °C, 4 h).

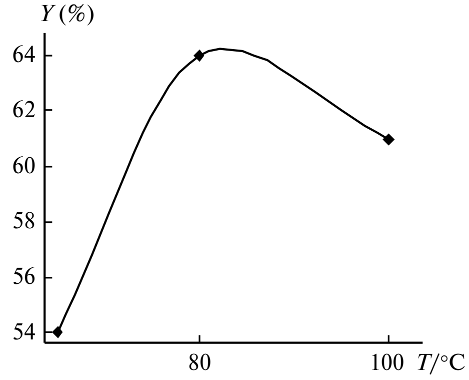


Fig. 2. Plot of the yield of product **3c** (Y) *vs.* the reaction temperature.

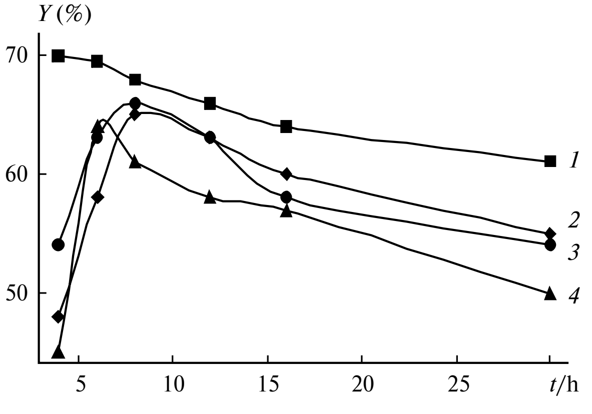


Fig. 3. Plots of the yield of product (Y) *vs.* the duration (τ) of the reaction of nitrile **1a** (*1*), **1b** (*2*), **1c** (*3*), and **1d** (*4*) with compound **2** at 80 (*1*, *3*) and 65 °C (*2*, *4*).

and the amount of the catalyst was $1.7 \cdot 10^{-3}$ mol. Heating of the reaction mixture at 80 °C for 10 h gave product **3a** in 60% yield.

Other heteropoly acids also proved to be efficient catalysts for these reactions. For instance, in the reaction between compounds **1a** and **2** in the presence of $H_7PMo_{12}O_{42}$, the yield of the target product was 72%; a close yield was reached with $H_4SiW_{12}O_{40}$ as the catalyst. The near-optimum yield of product **3c** (60%; see Table 1) was obtained with $H_7PMo_{12}O_{42}$ as the catalyst. In the reaction of compound **1b** with camphene **2**, the yield of product **3b** was 67%.

The structure of compound **3c** was confirmed by comparing its physicochemical parameters with the known data.[6] The structures of other *N*-substituted amides **3a**, **3b**, **3d**, and **3e** were determined by mass spectrometry and ^{1}H and ^{13}C NMR spectroscopy.

Experimental

^{1}H and ^{13}C NMR spectra (200 and 50 MHz, respectively) were recorded on a Bruker AC-200 spectrometer; ^{1}H and ^{13}C chemical shifts were measured relative to Me_4Si. Mass spectra were recorded on a Finnigan MATINCOS 50 instrument. The composition of the reaction mixture was analyzed and the course of the reaction was monitored by GLC on a Chrom 5 instrument (stationary phase PFMS-4 (15%) on Chromaton N-AW-DMSC (0.20—0.25), column 3000×10 mm, evaporator temperature 230 °C, nitrogen as a carrier gas).

High-purity commercial heteropoly acids were used as catalysts without additional purification. Nitriles **1b—e** were prepared according to known procedures. Acetonitrile **1a** was purified according to a known procedure.[10] Commercial camphene was purified (≥99%) by recrystallization from EtOH, m.p. 50 °C (*cf.* Ref. 11: m.p. 50 °C).

***N*-(1,7,7-Trimethylnorbornyl)acetamide (3a).** A mixture of acetonitrile (**1a**) (14 mL), camphene (**2**) (0.454 g, 3.3 mmol), water (1 mL, 55.6 mmol), and $H_3PW_{12}O_{40}$ (4.9 g, 1.7 mmol) was kept at 80 °C for 8 h. After the reaction was completed, the reaction mixture was poured into water and the product was extracted with $CHCl_3$. The organic fraction was washed with 10% aqueous NaOH to neutral pH, dried with $CaCl_2$, and concentrated. Recrystallization of the residue from C_6H_{14}—AcOEt (3 : 1 v/v) gave compound **3a** (0.43 g; the yields of the products are given in Table 1), m.p. 135 °C. Found (%): C, 73.96; H, 10.80; N, 7.22. $C_{12}H_{21}NO$. Calculated (%): C, 73.85; H, 10.77; N, 7.18. MS (EI, 70 eV), m/z (I_{rel} (%)): 195 $[M]^+$ (13); 136 (11); 121 (23); 95 (44); 86 (11); 77 (10); 67 (16); 55 (13); 43 (100). ^{1}H NMR ($CDCl_3$), δ: 0.91 (s, 3 H, C(1)Me); 3.84—3.96 (m, 1 H, C(2)H); 1.09—1.35 (m, 2 H, C(3)H); 1.76—1.97 (m, 1 H, C(4)H); 1.48—1.76 (m, 2 H each, C(5)H, C(6)H); 0.84 (s, 3 H each, C(7)Me); 1.92—2.02 (t, 3 H, COMe); 5.41 (s, 1 H, NH). ^{13}C NMR ($CDCl_3$), δ: 48.4 (C(1)); 56.7 (C(2)); 38.9 (C(3)); 44.8 (C(4)); 27.0 (C(5)); 35.9 (C(6)); 47.0 (C(7)); 20.3 (2 CH_3, $\underline{C}H_3C(7)$); 11.7 ($CH_3C(1)$); 23.5 (Me, COMe); 169.4 (CO, $\underline{C}OMe$).

Compounds **3b—e** were obtained analogously.

***N*-(1,7,7-Trimethylnorbornyl)benzamide (3b)** was obtained by heating a mixture of benzonitrile (**1b**) (8 mL), camphene (**2**) (0.3 g, 2.2 mmol), water (0.5 mL, 27.8 mmol), and $H_3PW_{12}O_{40}$ (3.3 g, 1.5 mmol) at 65 °C for 4 h; m.p. 126 °C (from C_6H_{14}—AcOEt (4 : 1 v/v)). Found (%): C, 79.49; H, 8.97; N, 6.24. $C_{17}H_{23}NO$. Calculated (%): C, 79.37; H, 8.95; N, 6.22.

MS (EI, 70 eV), *m/z* ($I_{\rm rel}$ (%)): 257 [M]$^+$ (24); 173 (1); 136 (16); 121 (21); 105 (100); 95 (27); 77 (58); 67 (9); 51 (12); 41 (21). ^{13}C NMR (DMSO—CCl_4), δ: 49.2 (C(1)); 56.4 (C(2)); 36.3 (C(3)); 44.3 (C(4)); 26.8 (C(5)); 35.4 (C(6)); 46.3 (C(7)); 19.7, 20.3 (2 CH_3, $CH_3C(7)$); 11.3 (CH_3, $CH_3C(1)$); 127.1, 127.4, 130.1(C_o, C_p, C_m); 135.4 (C_{ipso}); 166.8 (CO, $\underline{C}$OPh).

***N*-(1,7,7-Trimethylnorbornyl)acrylamide (3c)** was obtained by heating a mixture of acrylonitrile (**1c**) (3 mL), camphene (**2**) (0.09 g, 0.7 mmol), water (0.2 mL, 11.1 mmol), and $H_3PW_{12}O_{40}$ (1 g, 0.3 mmol) at 80 °C for 6 h; m.p. 132 °C (from C_6H_{14}—AcOEt (4 : 1 v/v); *cf.* Ref. 6: m.p. 133 °C).

***N*-(1,7,7-Trimethylnorbornyl)propionamide (3d)** was obtained by heating a mixture of propionitrile (**1d**) (10 mL), camphene (**2**) (0.3 g, 2.2 mmol), water (0.7 mL, 38.9 mmol), and $H_3PW_{12}O_{40}$ (3.13 g, 1.1 mmol) at 65 °C for 8 h; m.p. 100 °C (from C_6H_{14}). Found (%): C, 74.76; H, 11.02; N, 6.70. $C_{13}H_{23}NO$. Calculated (%): C, 74.64; H, 11.00; N, 6.69. MS (EI, 70 eV), *m/z* ($I_{\rm rel}$ (%)): 209 [M]$^+$ (15); 166 (2); 136 (19); 121 (21); 108 (8); 95 (84); 79 (18); 67 (33); 57 (86); 41 (100). ^{13}C NMR (DMSO—CCl_4), δ: 48.4 (C(1)); 55.5 (C(2)); 37.1 (C(3)); 44.2 (C(4)); 26.7 (C(5)); 35.5 (C(6)); 46.2 (C(7)); 20.2, 20.2 (2 CH_3, $CH_3C(7)$); 11.1 (CH_3, $CH_3C(1)$); 28.3 (CH_2, $CH_3\underline{C}H_2CO$); 22.3 (CH_3, $\underline{C}H_3CH_2CO$); 172.2 (CO, $CH_3CH_2\underline{C}O$).

***N*-(1,7,7-Trimethylnorbornyl)-1-naphthamide (3e)** was obtained by heating a mixture of 1-naphthonitrile (**1e**) (1.5 g), camphene (**2**) (0.5 g, 3.6 mmol), water (1 mL, 55.5 mmol), and $H_3PW_{12}O_{40}$ (0.41 g, 0.1 mmol) at 92 °C for 6 h; m.p. 121 °C (from C_6H_{14}—AcOEt (2 : 1 v/v)). Found (%): C, 82.21; H, 8.16; N, 4.57. $C_{21}H_{25}NO$. Calculated (%): C, 82.08; H, 8.14; N, 4.56. MS (EI, 70 eV), *m/z* ($I_{\rm rel}$ (%)): 307 [M]$^+$ (35); 264 (5); 238 (4); 184 (5); 172 (11); 155 (100); 127 (89); 109 (5); 95 (18); 55 (14); 41 (27). ^{13}C NMR (DMSO—CCl_4), δ: 49.4 (C(1)); 56.6 (C(2)); 36.4 (C(3)); 44.4 (C(4)); 26.9 (C(5)); 35.7 (C(6)); 46.4 (C(7)); 19.8, 20.4 (2 CH_3, $CH_3C(7)$); 11.7 (CH_3, $CH_3C(1)$); 124.6, 124.9, 125.5, 125.8, 126.2, 127.9, 129.2, 129.9, 133.0, 135.3 (10C, $C_{10}H_7$); 168.4 (CO, $\underline{C}OC_{10}H_7$).

We are grateful to A. A. Michurin for providing samples of nitriles **1b—e**.

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Received July 15, 2005;
in revised form November 22, 2005