

Acid-Catalyzed Reactions of Thiocyanates with Camphene

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Abstract—The reactions of thiocyanates with camphene catalyzed by the heteropoly acids $\text{H}_3\text{PW}_{12}\text{O}_{40}$ and $\text{H}_4\text{SiW}_{12}\text{O}_{40}$ were studied. The optimal reaction conditions were found, and the formation of N-substituted thiocarbamates in comparatively high yields was established. It was shown that the heteropoly acids exhibit a higher catalytic activity than sulfuric acid.

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The chemical transformations of terpenes, which are highly active and readily available compounds, have recently attracted considerable attention. Of special interest are acid-catalyzed reactions of terpenes since they are accompanied by a reconstruction of the carbon backbone. This makes it possible to carry out unusual transformations and to selectively obtain valuable products or new compounds. Until recently, the literature has reported only sparse examples of the use of thiocyanates in terpene chemistry, apparently because thiocyanates are difficult to investigate. It was demonstrated that the Ritter reaction between a thiocyanate and camphene followed by hydrolysis can occur in homogeneous acid media in the presence of concentrated sulfuric acid [1]. This method can be used in the preparation of N-substituted thiocarbamates, but, in some cases, the product yield is too low. The reactions of camphene with benzylthiocyanate and phenylthiocyanate do not occur under these conditions.

We studied the possibility of preparing thiocarbamates via the Ritter reaction catalyzed by the most typical heteropoly acids (HPAs), namely, $\text{H}_3\text{PW}_{12}\text{O}_{40}$ and $\text{H}_4\text{SiW}_{12}\text{O}_{40}$. From the standpoint of catalysis, the high Brønsted acidity of these HPAs is important, which far exceeds the acidity of ordinary mineral acids and conventional acid catalysts.

The structure and unique physicochemical properties of the HPAs, as well as the advantages of homogeneous and heterogeneous catalysts, are discussed in [2–4]. In this study, we investigated the reactions of methylthiocyanate (**Ia**) and ethylthiocyanate (**Ib**) with the natural terpene camphene (**II**) in the presence of the above HPAs. The resulting N-substituted thiocarbamates exhibit bactericidal and fungicidal properties, as was demonstrated by microbiological tests. The test organisms were *Streptococcus*, *Proteus*, and *Staphylococcus* bacteria and *Aspergillus*, *Alternaria*, *Penicillium*, and other fungi.

EXPERIMENTAL

Starting chemicals. The commercially available 12-HPAs $\text{H}_3\text{PW}_{12}\text{O}_{40} \cdot 15\text{H}_2\text{O}$ and $\text{H}_4\text{SiW}_{12}\text{O}_{40} \cdot 19\text{H}_2\text{O}$ (pure grade) were used as catalysts. Their water of crystallization was removed in vacuo at 100–150°C for 2 h. The initial, optically active camphene ($[\alpha]_{580}^{22} = +12.5^\circ$ ($c = 11.6$, CHCl_3)), which contained 10% tricyclene (according to GLC data), was purified to 99% purity by recrystallization from ethanol. The melting point of the purified substance was 50°C, which is in agreement with the reference data for camphene (mp 50°C [5]). Commercial **Ia** (reagent grade, 99%) was used as received. Thiocyanate **Ib** was synthesized by a known procedure [6]; its relative density at 16°C (versus water at 4°C) was 1.02. Isoborneol (commercial-purity grade) was purified to 96% (GLC data) by fractional recrystallization from ethanol. Diethyl ether, ethanol, and *n*-hexane (reagent grade) were purified by standard procedures [7].

Methods of analysis. The verification of the purity of the initial compounds and the analysis of the reaction products were performed by GLC on a Chrom-5 chromatograph with a flame-ionization detector. The column (30000 × 10 mm) was filled with the stationary phase PFMS-4 (15%) on Chromaton N-AW-DMSC (0.20–0.25 mm). The column temperature was 180–190°C. The carrier gas (nitrogen) pressure was 2.5 atm. *N*-(1,7,7-Trimethylnorbornyl)propionamide was used as the internal standard. The thin-layer chromatographic analysis was performed on silica gel LSL 5/40. The structure of the compounds was determined by ^1H NMR and ^{13}C NMR spectroscopy. ^1H NMR (200 MHz) and ^{13}C NMR (32 MHz) spectra were recorded on a Bruker AC-200 spectrometer. The signal from CDCl_3 was used as the internal standard ($\delta = 7.24$ ppm, $\delta_{\text{C}} = 76.90$ ppm). The elemental analysis of the compounds obtained was carried out by high-resolution mass spectrometry using a Finnigan MATINCOS 50 instrument. The samples to be analyzed were prepared as KBr pel-

lets or as mineral-oil mulls. The product yields were calculated with respect to the initial camphene.

General experimental procedure. All reactions were conducted in a thermostatically controlled glass vessel fitted with a backflow condenser [3] at various temperatures for 2–30 h. After the completion of the reaction, the reaction mixture was extracted with diethyl ether, whose volume was half the volume of the aqueous phase. The organic phase was washed with a 10% NaOH solution and water until the aqueous extract had a neutral pH. Next, samples of the organic phase were dried over anhydrous Na_2SO_4 for 1 day. The organic layer was analyzed by GLC. The solvent was removed at a reduced pressure to obtain the pure samples. The crystalline residue was recrystallized from *n*-hexane until a constant melting point.

Synthesis of *N*-(1,7,7-trimethylnorbornyl)methylthiocarbamate (IIIa**).** A solution of **Ia** (4 ml, 57.9 mmol) and **II** (0.246 g, 1.79 mmol) was added to $\text{H}_3\text{PW}_{12}\text{O}_{40}$ (2.68 g, 0.93 mmol) wetted with water (0.4 ml, 22.24 mmol). The mixture, which was a homogeneous system with pH 2, was held at 65°C for 4 h. Compound **IIIa** (0.16 g, 40%, mp 80°C) was thus obtained.

Found (%): C 63.37, H 9.28, N 6.26 ($\text{C}_{12}\text{H}_{21}\text{NOS}$)

Calculated (%): C 63.44, H 9.25, N 6.17

Mass spectrum (70 eV):

<i>m/z</i>	227 (M^+)	175	137	122	106	93	79	54	41
<i>I</i> _{rel} (%)	25	10	18	68	12	96	35	8	10

^1H NMR (CDCl_3). δ (ppm): 0.93 (s, 3H, C(1)Me); 3.90–3.92 (m, 1H C(2)H); 1.08–1.38 (m, 2H, C(3)H); 1.78–1.92 (m, 1H, C(4)H); 1.52–1.78 (m, 2H, C(5)H, C(6)H); 0.84 (s, 3H, C(7)Me); 1.92–2.02 (t, 3H, SMe); 5.21 (s, 1H, NH).

^{13}C NMR (CDCl_3). δ , ppm: 48.9 C(1); 59.1 C(2); 39.1 C(3); 44.9 C(4); 27.0 C(5); 35.9 C(6); 47.1 C(7); 20.3 (2CH_3 , $\text{CH}_3\text{C}(7)$); 11.8 ($\text{CH}_3\text{C}(1)$); 12.5 (CH_3 , COSCH_3); 167.0 (CO, COSCH_3).

Synthesis of *N*-(1,7,7-trimethylnorbornyl)ethylthiocarbamate (IIIb**).** A solution of **Ib** (3 ml, 21.2 mmol) and **II** (0.12 g, 0.88 mmol) was added to $\text{H}_3\text{PW}_{12}\text{O}_{40}$ (1.34 g, 0.46 mmol) wetted with water (0.2 ml, 11.11 mmol). The mixture, which was a homogeneous system with pH 2, was kept at 65°C for 4 h. Compound **IIIb** (0.09 g, 42%, mp 91°C) was thus obtained 91°C.

Found (%): C 65.7, H 9.52, N 5.5 ($\text{C}_{13}\text{H}_{23}\text{NOS}$)

Calculated (%): C 64.7, H 9.54, N 5.8

Mass spectrum (70 eV):

<i>m/z</i>	241 (M^+)	177	137	121	105	93	75	54	41
<i>I</i> _{rel} (%)	25	18	38	69	12	95	33	12	19

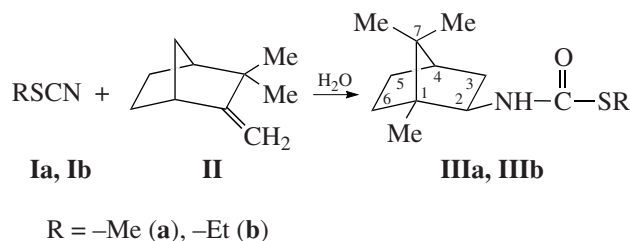
^1H NMR (CDCl_3). δ , ppm: 0.94 (s, 3H, C(1)Me); 3.89–3.91 (m, 1H C(2)H); 1.08–1.38 (m, 2H, C(3)H); 1.77–1.91 (m, 1H, C(4)H); 1.53–1.77 (m, 2H, C(5)H,

C(6)H); 0.84 (s, 3H, C(7)Me); 1.91–2.02 (t, 3H, SCH_2CH_3); 5.21 (s, 1H, NH).

^{13}C NMR (CDCl_3). δ , ppm: 48.8 C(1); 59.3 C(2); 39.2 C(3); 44.7 C(4); 27.1 C(5); 35.8 C(6); 47.2 C(7); 20.3 (2CH_3 , $\text{CH}_3\text{C}(7)$); 11.8 ($\text{CH}_3\text{C}(1)$); 28.5 (CH_2 , $\text{CH}_3\text{CH}_2\text{SCO}$); 22.3 (CH_3 , $\text{CH}_3\text{CH}_2\text{SCO}$); 168.0 (CO, $\text{CH}_3\text{CH}_2\text{SCO}$).

RESULTS AND DISCUSSION

Experimental data demonstrated that the homogeneous catalytic reactions examined indeed produce *N*-substituted thiocarbamates **IIIa** and **IIIb** in rather high yields (Scheme 1).



Scheme 1.

The resulting compounds were identified by comparing the ^{13}C and ^1H NMR spectra of the purified products with the same spectra of various camphene derivatives [8]. The *N*-substituted thiocarbamates are white crystalline compounds; their physicochemical parameters are in agreement with the reference data for **IIIa** and **IIIb** [1].

With $\text{H}_3\text{PW}_{12}\text{O}_{40}$ as the catalyst, the yields of **IIIa** and **IIIb** after recrystallization were 40 and 42%, respectively. When sulfuric acid was used as the catalyst, the product yields were equal to 34 and 19%, respectively.

The heteropoly acid $\text{H}_4\text{SiW}_{12}\text{O}_{40}$ is among the efficient catalysts of the reactions examined. However, its catalytic performance does not exceed that of $\text{H}_3\text{PW}_{12}\text{O}_{40}$. This is likely due to the fact that the acidity of tungstic acids depends only slightly on the nature of the central atom [9]; that is, the strengths of the two acids are nearly equal.

The reactions were conducted in excess **Ia** and **Ib**, which were used both as reactants and as solvents (camphene : thiocyanate molar ratio was 1 : 32 and 1 : 24, respectively). The amount of thiocyanates required for the complete dissolution of the catalysts was found experimentally. Water was added to the reaction mixture because HPA would precipitate without water (water : catalyst molar ratio was 24 : 1). The addition of small amounts of water also allowed us to conduct the reaction at comparatively low temperatures.

We found the optimal reaction conditions, namely, the required concentrations of the acids, reactants ratios, and reaction times and temperatures. Figure 1 shows the dependences of the yields of thiocarbamates **IIIa** and **IIIb** at 65°C on the catalyst concentration. The

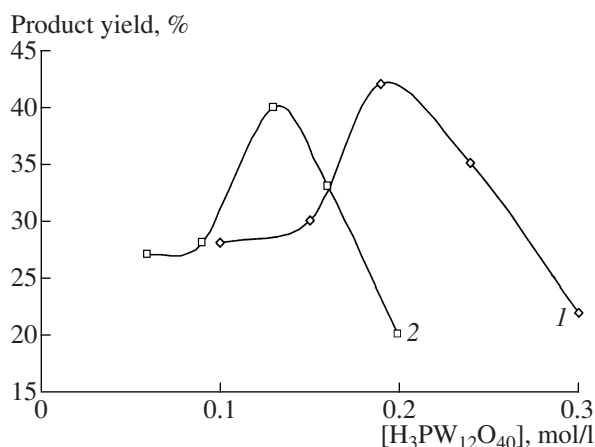


Fig. 1. Yields of (1) **IIIa** and (2) **IIIb** as a function of the concentration of the $\text{H}_3\text{PW}_{12}\text{O}_{40}$ catalyst (reaction time, 4 h; $T = 65^\circ\text{C}$).

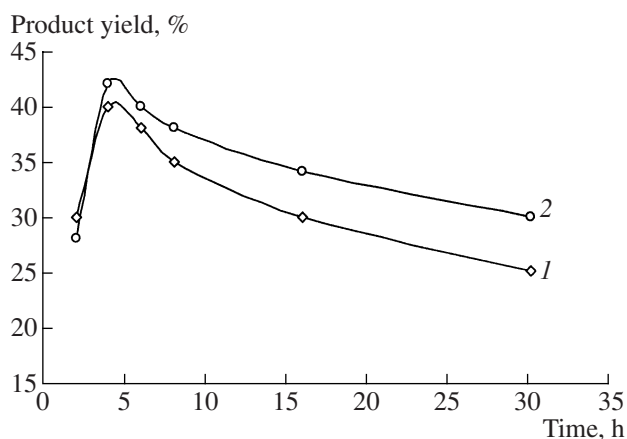
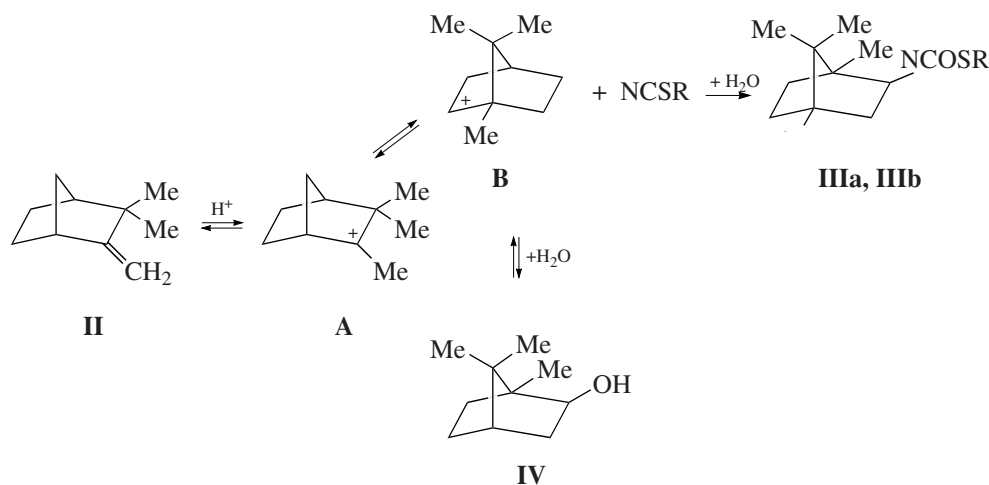


Fig. 2. Yields of (1) **IIIa** and (2) **IIIb** as a function of the reaction time at 65°C .

maximum carbamate yield is attained at a catalyst concentration of 0.19 and 0.13 mol/l, respectively. Further raising the catalyst concentration decreases the carbamate yield and selectivity. Extending the reaction time also reduces the thiocarbamate yield (Fig. 2) because of the significant changes in the composition of the reaction mixture (GLC data). Above 80°C , the reaction

mixture undergoes resinification, as judged from its color and from the formation of slop. This resinification markedly reduces the yield of the desired product.

In view of the recent data for camphene reactions in the presence of acid catalysts [10], the interaction between camphene and isocyanates can be represented as follows:



Scheme 2.

Adding a hydrogen ion, camphene forms the camphenylhydro cation **A**, which undergoes the Wagner-Meerwein rearrangement to turn into the ion **B**. The interaction between **B** and the thiocyanate yields the final products **IIIa** and **IIIb**.

Isoborneol (**IV**) can form simultaneously. Minor amounts of **IV** were actually detected in the reaction mixture. The identification of isoborneol was carried out by GLC using an isoborneol standard. At modest temperatures, this reaction pathway is dominant. At moderately high temperatures, the step $\text{B} \rightleftharpoons \text{IV}$ is fast and the product formation is controlled by the rate of

the reaction between the cation **B** and the thiocyanate [11, 12].

CONCLUSIONS

(1) *N*-(1,7,7-Trimethylnorbornyl)methylthiocarbamate and *N*-(1,7,7-trimethylnorbornyl)ethylthiocarbamate were synthesized in rather high yields by the reactions of camphene with thiocyanates in the presence of heteropoly acids.

(2) The by-product of these reactions is isoborneol.

(3) The use of an HPA in the Ritter reaction enabled us to carry out the process under substantially milder conditions.

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