

## Reaction of Some Terpenoids with Malononitrile in the Presence of Hydrotalcite

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**Abstract**— $\alpha$ -Ionone and 5,5,8-trimethyl-3,7-nonadien-2-one react with malononitrile in the presence of specially prepared hydrotalcite to afford the corresponding Knoevenagel condensation products with high yield and selectivity.

We previously showed [1, 2] that basic Cs- $\beta$  zeolite effectively catalyzes reactions of  $\alpha,\beta$ -unsaturated carbonyl compounds of the terpene series with CH acids and that the reactions follow either Michael addition or Knoevenagel condensation pattern or both these (tandem transformations), depending on the substrate structure. The reactions were carried out at room temperature without a solvent, a catalytic amount of Cs- $\beta$  zeolite was used, and the products were formed in good yields (with account taken of their complex structure).

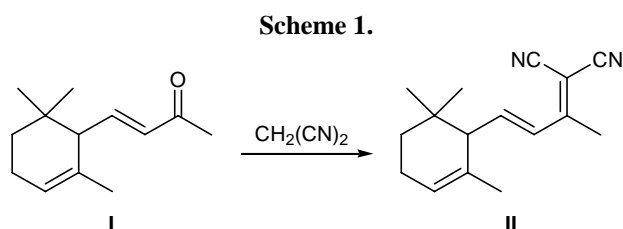
Although basic Cs- $\beta$  zeolite can readily be regenerated and repeatedly used without loss of catalytic activity, its wide application is limited due to high cost and difficulties in its preparation. Therefore, we continued search for heterogeneous catalysts suitable for promoting base-catalyzed transformations of terpenoids. Such catalysts may be, e.g., hydrotalcites and related materials, specifically layered basic minerals with the general formula  $[M_{(1-x)}^{2+}M_x^{3+}(\text{OH})_2]^{x+}(\text{A}_{x/m}^{m-}) \cdot n\text{H}_2\text{O}$  where  $M^{2+} = \text{Mg}^{2+}, \text{Ca}^{2+}, \text{Zn}^{2+}, \text{or Ni}^{2+}$  and  $M^{3+} = \text{Al}^{3+}, \text{Fe}^{3+}, \text{or Cr}^{3+}$  and compensating interlayer anions are  $\text{OH}^-, \text{Cl}^-, \text{NO}_3^-, \text{CO}_3^{2-}, \text{and SO}_4^{2-}$ . Previously, hydrotalcites were successfully used to catalyze epoxidation of activated olefins with hydrogen peroxide [3, 4], aldol condensations [5], Michael additions [6], Knoevenagel condensations [7], etc.

It should be noted that the efficiency of hydrotalcites and related catalysts in Knoevenagel and Michael reactions was estimated previously using

fairly simple substrates, for which the direction of the process was beyond doubts *a priori*. The possibility of using hydrotalcites as catalysts in CH acid reactions with such complex substrates as terpene-like  $\alpha,\beta$ -unsaturated carbonyl compounds was not studied.

Up to now, several simple procedures have been reported for the synthesis of hydrotalcites and related minerals from accessible and cheap reagents, e.g., from  $\text{MgCl}_2$  and  $\text{AlCl}_3$  [5], from  $\text{Mg}(\text{NO}_3)_2$  and  $\text{Al}(\text{NO}_3)_3$  [6], and from  $\text{MgO}$  and  $\gamma\text{-Al}_2\text{O}_3$  [3]. We have synthesized hydrotalcite according to the procedure described in [3] by heating a heterogeneous mixture of  $\text{MgO}$  and  $\gamma\text{-Al}_2\text{O}_3$  in aqueous  $\text{Na}_2\text{CO}_3$  under stirring. The layered structure of the product was confirmed by the presence of appropriate peaks in the X-ray powder pattern (see figure). In addition, the X-ray powder pattern showed broad reflexes (an impurity amount), the position of their maxima corresponding to the  $\text{Mg}(\text{OH})_2$  phase. We performed a control experiment in which  $\text{MgO}$  was kept under the same conditions as in the synthesis of hydrotalcites and analyzed the phase thus obtained. In fact, the observed peaks in the X-ray powder pattern (see figure) coincided with the foreign peaks in the X-ray powder pattern of hydrotalcite. In keeping with the analytical data, the obtained hydrotalcite has the formula  $\text{Mg}_{10.5}\text{Al}_2(\text{OH})_{25}\text{CO}_3 \cdot n\text{H}_2\text{O}$ . Its specific surface (determined by the BET method) was  $75 \text{ m}^2/\text{g}$ . A large excess of Mg over Al and a fairly small specific surface are likely to result from the presence of  $\text{Mg}(\text{OH})_2$  impurity.

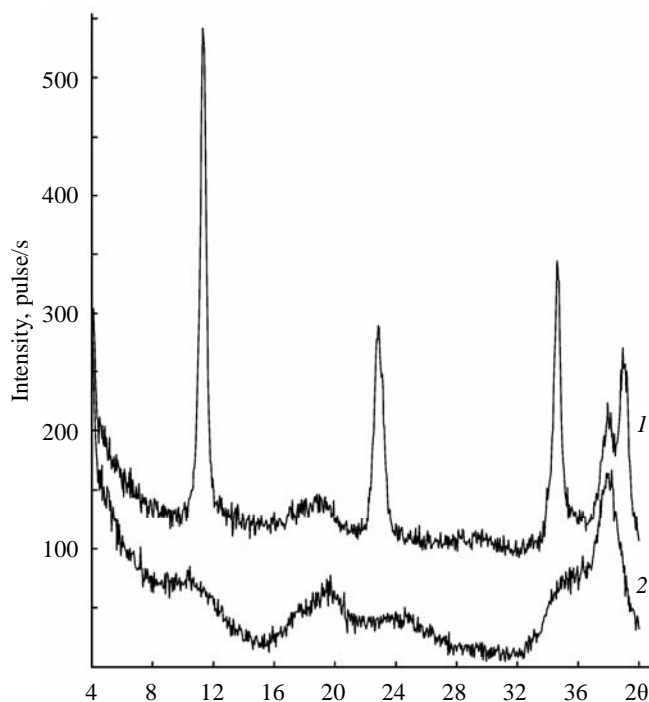
The ability of hydrotalcite to catalyze Knoevenagel condensation was estimated in the reaction of  $\alpha$ -ionone (**I**) with malononitrile (Scheme 1). We showed in [1] that in the presence of basic Cs- $\beta$  zeolite as catalyst this reaction gives the corresponding Knoevenagel condensation product, 2-methyl-4-(2,6,6-trimethyl-2-cyclohexenyl)-1,3-butadiene-1,1-dicarbonitrile (**II**) in 71% yield (calculated on the reacted ketone **I**; conversion 70%). The reaction was carried out without a solvent at room temperature (reaction time 120 h), and the catalyst was added in an amount of 20 wt % of the overall amount of the organic reactants.



In the reaction of  $\alpha$ -ionone (**I**) with malononitrile in the presence of hydrotalcite, the reactant ratio being the same as in the reaction catalyzed by Cs- $\beta$  zeolite, the conversion of **I** in 120 h was 43%, and the yield of dinitrile **II** was 56% calculated on the reacted **I** (Table 1). Increase of the amount of hydrotalcite from 20 to 33% allowed us to raise the conversion of  $\alpha$ -ionone (**I**) to 85%, and the yield of compound **II** was 67% (on the reacted **I**). Further raising the amount of the catalyst to 67% (with respect to the overall weight of the organic reactants) led to a slight increase in the conversion of **I** and a considerable increase in the yield of **II** (almost to quantitative, calculated on the reacted  $\alpha$ -ionone).

Thus the prepared hydrotalcite in an amount of 20 wt % was less effective than Cs- $\beta$  zeolite in the reaction of  $\alpha$ -ionone (**I**) with malononitrile, while the use of a larger amount of hydrotalcite led to considerably increased conversion of **I** and the yield of product **II**. It should be noted that in some cases, e.g., in Michael addition reactions [6], hydrotalcites were used in amounts comparable with the overall weight of the organic reactants. Increase in the relative amount of the catalyst results not only in increased conversion of the initial ketone and hence the theoretical yield of compound **II** but also in appreciable increase of the yield calculated on the reacted  $\alpha$ -ionone (**I**); presumably, this is the result of reduction of the contribution of side tarring processes.

As noted above, the prepared hydrotalcite contains an impurity of Mg(OH)<sub>2</sub> phase which was synthesized



X-Ray powder patterns of (1) hydrotalcite and (2) Mg(OH)<sub>2</sub> phase.

by a special experiment. We performed the reaction of  $\alpha$ -ionone (**I**) with malononitrile in the presence of that phase (reaction time 120 h). Despite an appreciable catalytic activity, Mg(OH)<sub>2</sub> turned out to be much less effective than hydrotalcite (Table 1). A mechanical mixture of MgO and Al<sub>2</sub>O<sub>3</sub>, hydrotalcite calcined at 500°C, and reprecipitated hydrotalcite obtained by the procedure described in [5] showed a poor catalytic activity in the reaction of  $\alpha$ -ionone (**I**) with malononitrile.

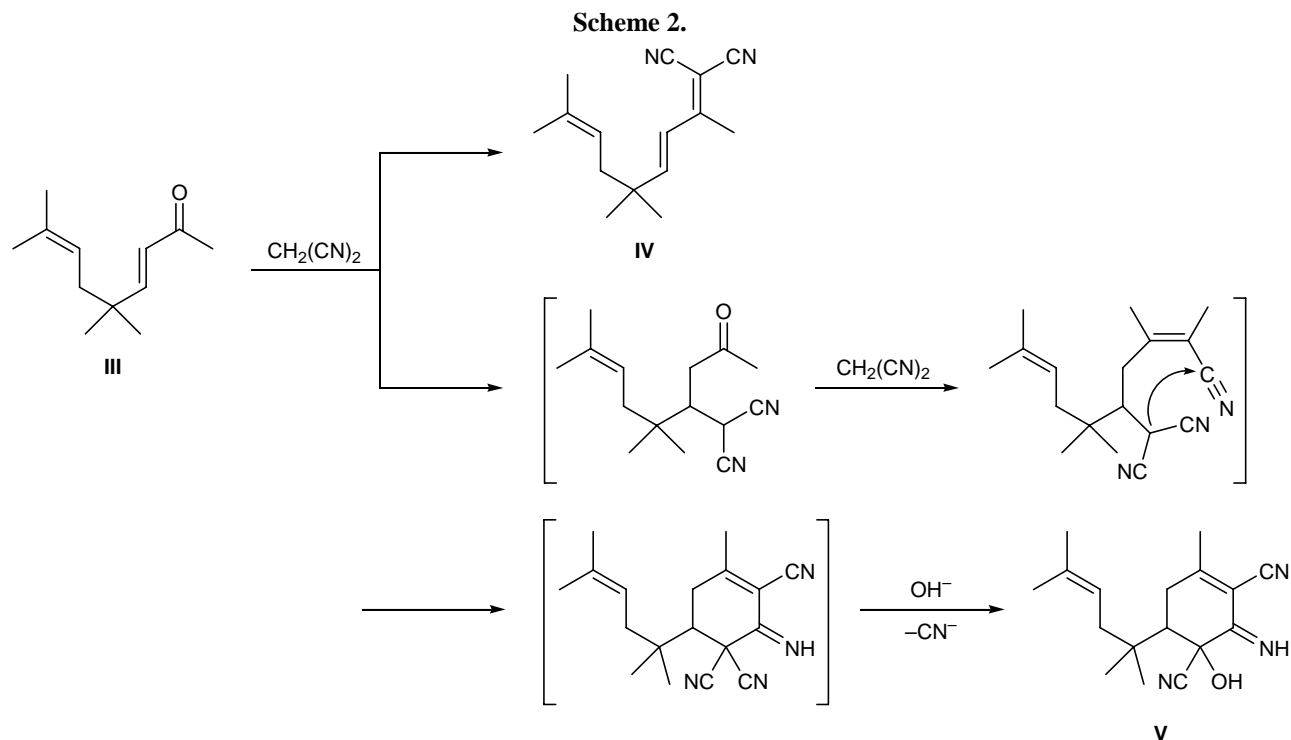
We also used hydrotalcite as base catalyst in the reaction of 5,5,8-trimethyl-3,7-nonadien-2-one (**III**) with malononitrile. The same reaction performed in

**Table 1.** Reaction of  $\alpha$ -ionone (**I**) with malononitrile in the presence of base catalysts

Catalyst	Amount of catalyst (wt %) <sup>a</sup>	Conversion of <b>I</b> , %	Yield of <b>II</b> , <sup>b</sup> %
Cs- $\beta$ zeolite	20	71	50 (70)
Hydrotalcite	20	43	24 (56)
Hydrotalcite	33	85	57 (67)
Hydrotalcite	66	90	89 (99)
Mg(OH) <sub>2</sub>	66	78	53 (68)

<sup>a</sup> With respect to the overall amount of the organic reactants.

<sup>b</sup> In parentheses is given the yield calculated on the reacted ketone **I**.



the presence of Cs- $\beta$  zeolite (16 wt % of the overall amount of the organic reactants) [1] involved concurrent Knoevenagel condensation and Michael addition processes leading to formation of compounds **IV** and **V**, the latter resulting from the tandem Michael–Knoevenagel transformation (Scheme 2). The reaction time was 48 h, the conversion of **III** was 73%, and the overall yield of products **IV** and **V** was 47% on the reacted ketone **III** (Table 2). The mechanism shown in Scheme 2 is confirmed by the fact that compound **IV** failed to react with malononitrile under analogous conditions and was recovered from the reaction mixture. Variation of the conditions in the reaction of ketone **III** with malononitrile in the presence of Cs- $\beta$  zeolite

(raising the temperature and ultrasonic activation) allowed us to considerably shorten the reaction time and change the product ratio [2]. More severe conditions favored formation of compound **V**.

When the reaction of **III** with malononitrile was performed in the presence of hydrotalcite (33 wt % of the overall amount of the organic reactants; reaction time 48 h), the overall yield of products **IV** and **V** was 87%, i.e., twice as high as in the presence of Cs- $\beta$  zeolite, and Knoevenagel condensation product **IV** was formed almost exclusively. As in the catalysis by Cs- $\beta$  zeolite, ultrasonic activation changed the product ratio toward increased fraction of polyfunctional compound **V**; however, this variation was not so strong as in the presence of Cs- $\beta$  zeolite.

We can conclude that in going from Cs- $\beta$  zeolite to hydrotalcite the ratio of the rates of the Michael and Knoevenagel reactions changes toward the latter process, leading to considerable increase in the fraction of product **IV**. The data in Table 2 show that the process may be forced to obtain almost exclusively dinitrile **IV** or strongly increase the fraction of compound **V** by varying the catalyst and reaction conditions.

Thus our results showed that hydrotalcites are capable of effectively catalyzing Knoevenagel reactions of  $\alpha,\beta$ -unsaturated carbonyl compounds of the

**Table 2.** Reaction of ketone **III** with malononitrile in the presence of base catalysts

Conditions	Conversion of <b>III</b> , %	Yield, <sup>a</sup> %		Ratio <b>IV</b> : <b>V</b>
		<b>IV</b>	<b>V</b>	
20°C, Cs- $\beta$ zeolite, 48 h	73	40	7	5.7
60°C, ultrasonic activation, Cs- $\beta$ zeolite, 4 h	77	25	16	1.6
20°C, hydrotalcite, 48 h	76	83	4	20.8
60°C, ultrasonic activation, hydrotalcite, 4 h	60	75	6	12.5

<sup>a</sup> Calculated on the reacted ketone **III**.

terpene series with malononitrile and that hydrotalcites may be regarded as a real alternative to Cs- $\beta$  zeolites used previously as catalysts to effect the same transformations.

### EXPERIMENTAL

The  $^1\text{H}$  NMR spectra were recorded on a Bruker WP-200SY spectrometer at a frequency of 200 MHz. The purity of the initial compounds and reaction products was checked by GLC on a Biokrom chromatograph (13000 $\times$ 0.22-mm quartz capillary column, stationary phase SE-54; flame ionization detector; carrier gas helium, inlet pressure 1 atm; oven temperature 70–180°C). The X-ray powder patterns were obtained on an HZG-4c diffractometer ( $\text{CuK}_\alpha$  irradiation). The elemental compositions were determined on a BLIRD ICP spectrometer. The specific surface was measured by nitrogen adsorption at 77 K. A Branson MTH-3510 ultrasonic bath (42 kHz, 130 W) was used for ultrasonic activation.

The catalyst was calcined for 3 h at 110°C just before use. The solvents were dried by passing through a column charged with calcined aluminum oxide. The products were isolated by column chromatography on silica gel (40–100  $\mu\text{m}$ ).

**Hydrotalcite.** To a solution of 13.5 g of  $\text{Na}_2\text{CO}_3$  in 250 ml of distilled water we added 2.15 g of  $\text{MgO}$  and 0.7 g of  $\gamma\text{-Al}_2\text{O}_3$ , and the resulting suspension was vigorously stirred for 24 h at 110°C. The precipitate was filtered off, washed with water until neutral washings, and dried overnight in air at room temperature and for 6 h at 110°C. Yield 3.78 g, white fine powder.

**$\text{Mg}(\text{OH})_2$  phase.** To a solution of 13.5 g of  $\text{Na}_2\text{CO}_3$  in 250 ml of distilled water we added 2.15 g of  $\text{MgO}$ , and the resulting suspension was vigorously stirred for 19 h at 110°C. The precipitate was filtered off, washed with water until neutral washings, and dried overnight in air at room temperature and for 5 h at 110°C. Yield 3.64 g, white fine powder.

**Reaction of  $\alpha$ -ionone (I) with malononitrile in the presence of hydrotalcite.** A solution of 0.060 g (0.9 mmol) of malononitrile in 1 ml of diethyl ether was added to 0.028 g of hydrotalcite. The solvent was removed under reduced pressure, and 0.080 g (0.4 mmol) of  $\alpha$ -ionone (I) was added. The mixture was kept for 120 h at 20°C, and the products were extracted into ethyl acetate. Separation by column chromatography (hexane, 2% of diethyl ether in

hexane) gave 0.046 g of initial  $\alpha$ -ionone (I) and 0.024 g of 1-methyl-4-(2,6,6-trimethyl-2-cyclohexenyl)-1,3-butadiene-1,1-dicarbonitrile (II) (57% on the reacted ketone I). The  $^1\text{H}$  NMR spectrum of II coincided with that given in [1].

In an analogous reaction with 0.046 g of hydrotalcite we isolated 0.012 g of initial  $\alpha$ -ionone (I) and 0.057 g of compound II (67% on the reacted I); in the presence of 0.092 g of hydrotalcite, 0.008 g of  $\alpha$ -ionone (I) and 0.089 g of II (99% on the reacted I) were isolated.

**Reaction of  $\alpha$ -ionone (I) with malononitrile in the presence of  $\text{Mg}(\text{OH})_2$  phase.** A solution of 0.059 g (0.9 mmol) of malononitrile in 1 ml of diethyl ether was added to 0.095 g of  $\text{Mg}(\text{OH})_2$  phase, the solvent was distilled off, and 0.085 g (0.4 mmol) of  $\alpha$ -ionone (I) was added. The mixture was kept for 120 h at 20°C, and the products were extracted into ethyl acetate. By column chromatography (hexane, 2.5% of diethyl ether in hexane) we isolated 0.019 g of initial  $\alpha$ -ionone (I) and 0.056 g of compound II (68% on the reacted ketone I).

**Reaction of 5,5,8-trimethyl-3,7-nonadien-2-one (III) with malononitrile in the presence of hydrotalcite.** *a.* A solution of 0.127 g (1.9 mmol) of malononitrile in 2 ml of diethyl ether was added to 0.071 g of hydrotalcite, the solvent was distilled off, and 0.085 g (0.47 mmol) of ketone III was added. The mixture was kept for 48 h at 20°C, and the products were extracted into ethyl acetate. By column chromatography (gradient elution, 0 to 100% of diethyl ether in hexane) we isolated 0.020 g of initial ketone III, 0.068 g (83%) of 2,5,5,8-tetramethyl-1,3,7-nonatriene-1,1-dicarbonitrile (IV) and 0.004 g (4%) of 1-hydroxy-2-imino-4-methyl-6-(1,1,4-trimethyl-3-pentenyl)-3-cyclohexene-1,3-dicarbonitrile (V). The  $^1\text{H}$  NMR spectra of compounds IV and V coincided with those given in [1].

*b.* A solution of 0.127 g (1.9 mmol) of malononitrile in 2 ml of diethyl ether was added to 0.074 g of hydrotalcite, the solvent was distilled off, and 0.100 g (0.56 mmol) of ketone III was added. The mixture was heated for 4 h at 60°C under ultrasonic irradiation, and the products were extracted into ethyl acetate. By column chromatography (gradient elution, 0 to 100% of diethyl ether in hexane) we isolated 0.040 g of initial ketone III, 0.057 g (75%) of compound IV and 0.006 g (6%) of compound V.

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