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$Ba(OH)_2$ as Catalyst in Organic Reactions IV. Reaction Between Coumarin and Diethyl Malonate

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The reaction of diethyl malonate and coumarin catalyzed by an activated barium hydroxide catalyst (C-200) in a solid-liquid-system is described. No *Michael* addition takes place. An unusual nucleophilic addition-elimination process to the C=O bond of coumarin is observed and the new compound is described the first time. The process is explained by the microcrystalline structure of the solid, the nature of the active sites of the catalyst and the chelating action of coumarin on Ba^{II} of the lattice.

(Keywords: Coumarin; Basic catalyst; Barium hydroxide catalyst)

$Ba(OH)_2$ *als Katalysator organischer Reaktionen, 4. Mitt.: Die Reaktion zwischen Cumarin und Diethylmalonat*

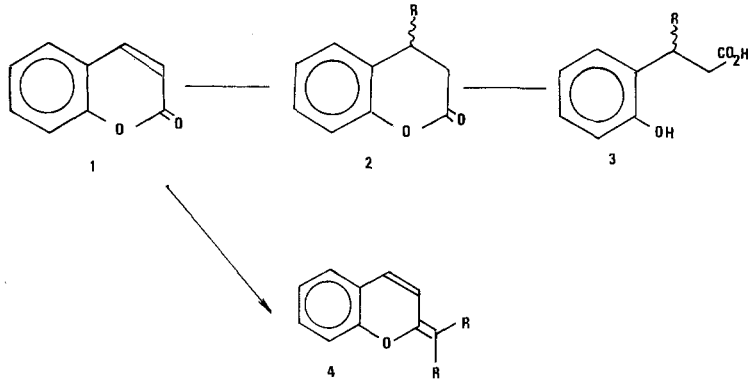
Es wird die Reaktion von Diethylmalonat mit Cumarin unter der katalytischen Wirkung von aktiviertem Bariumhydroxid (C-200) in einem Fest-flüssig-System beschrieben. Es ist keine *Michael*-Addition zu beobachten. Es tritt eine ungewöhnliche Addition-Eliminierung an der C=O-Bindung des Cumarin ein und die dabei entstehende Verbindung wird erstmals beschrieben. Der Prozeß wird auf der Basis der mikrokristallinen Struktur des Festkörpers, der Natur der aktiven Stellen am Katalysator und der chelierenden Wirkung von Cumarin auf die Gitter-Ba^{II}-Ionen erklärt.

Introduction

The coumarin skeleton (**1**) is related to many natural products and drugs, e.g. antifungi, carcinogenics, anticoagulatives, etc; consequently, synthesis and reactivity of coumarins have been extensively studied in the literature. Recently a new barium hydroxide catalyst (C-200) has been described as a catalyst in *Michael* addition in the heterogeneous phase[1]. Thus we tried to obtain 4-substituted 3,4-dihydrocoumarins (**2**) by

Michael addition of nucleophils to **1**, catalyzed by C-200 in the solid-liquid system. This heterogeneous catalytic process could be of some interest because with the conventional *Michael* catalysts the alcaline hydrolysis of the δ-lactone **2** predominates (see Scheme 1).

Scheme 1



With diethyl malonate an unusual 1,2-addition-elimination process at the C=O bond was observed leading to **4**.

In the present paper the reaction of diethyl malonate with coumarin is discussed* and compared with the *Michael* addition to chalcone[1]. The different behaviour of coumarin and chalcone is explained by the structure of the solid catalyst which plays the main role in this process. The influence of the solvent, the reaction time and the amount of catalyst on the yield of **4** are discussed.

Results and Discussion

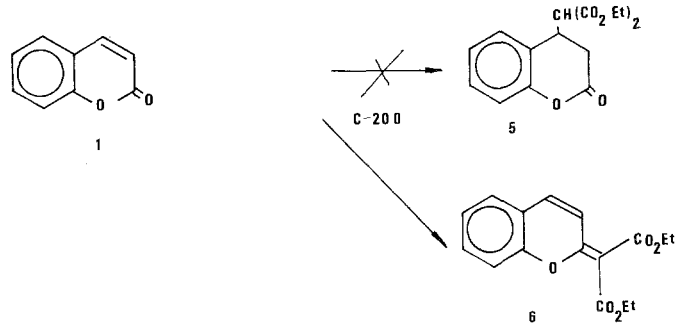
The Reaction Product

If the *Michael* reaction of diethyl malonate and coumarin was carried out with 0.2 g of C-200, compound **5** was expected (Scheme 2).

However, a different compound was obtained (30% yield) as the only reaction product. Its elemental analysis differed considerably from that calculated for **5**: found C 66.9, H 5.9, O 27.2; calc. for **5** C 62.8, H 5.9,

* Similar results were obtained in the reaction of coumarin with other active methylene compounds with similar *pKa*, e. g. $CH_2(CN)_2$, $CN—CH_2—CO_2Et$, etc.

Scheme 2



O 31.4. From the experimental data the empirical formula $C_{16}H_{16-18}O_5$ was deduced.

In the IR spectrum the γ,δ-unsaturated δ-lactone band was not present but a 1 730 cm^{-1} band was observed. This can be attributed to an α,β-unsaturated ester. No OH band was observed, thus no alcaline hydrolysis had occured*.

In the PMR spectrum, peaks at 7.8 (d) and 6.45 (d) ppm ($J = 9.8$ Hz) were observed. They must be due to the two olefinic protons in the coumarinic skeleton. The —CH_2—CH < group was not observed (**5**) and only the ethylester group is present. Therefore structure **6** ($C_{16}H_{16}O_5$) has been assigned to the reaction product**.

Table 1. *Influence of the amount of catalyst; molar ratio* $CH_2(CO_2Et)_2$: **1** = 1 *(4 h in refluxing Et*OH*)*

Catalyst weight (g)	yield of 6 (% on wt)*
2.0	17
0.5	12
0.2	30
0.1	2

* Experimental error 10%.

Experimental Conditions

From the results in Table 1 we can deduce that an amount of catalyst greater than 0.2 g gives lower yields. This is due to the alcoholysis of

* This catalyst hydrolyzes esters[3,14].

** In a previous note[2] **6** was described for the first time.

Table 2. X-ray *powder diagram for* C-200

C-200		$Ba(OH)_2 \cdot H_2O$[6]		$Ba(OH)_2$[6]	
d(Å)	Intensity	d(Å)	I/I_0	d(Å)	I/I_0
6.35	v. s.	6.37	65	—	—
4.69*	v. s.	4.70*	100	4.67	35
3.86	s	3.87	40	3.96	15
3.67	w	—	—	3.67	20
3.46	s	3.48	40	3.61	60
				3.41*	100
3.29	m	3.32	20	3.37	95
				3.33	85
				3.26	35
3.03	w	3.05	8	—	—
2.98	s	2.998	55	2.95	35
2.88	s	2.893	45	2.91	25
2.58	m	2.594	45	2.54	30
2.38	s	2.403	35	2.33	25
2.31	v. s.	2.323	55	2.30	30
2.17	w	2.179	14	2.15	10

Intensities were stimated visually and are expressed as follows vs = very strong, s = strong, m = medium, w = weak.

* The most intense peak.

coumarin[3]. The optimal reaction time was 4 h in refluxing ethanol. The *Michael* reaction catalyzed by the C-200 catalyst is very sensitive to the nature of the solvent[1,4]. Nevertheless the synthesis of **6** takes place in solvents with different dielectric constants, e.g. 1,4-dioxane ($\varepsilon = 2.2$), cyclohexane ($\varepsilon = 1.89$, 17% **6**), and *Et*OH ($\varepsilon = 24.5$, 30% **6**). The reaction in 1,4-dioxane gives a mixture of **6** and **1** but the purification of **6** from **1** and from $BaCl_2$ is tedious*; therefore this is not convenient from a synthetic point of view.

Structure of the Catalyst

A study of the solid was carried out to explain the different behaviours of coumarin and chalcone in the reaction with diethyl malonate in the presence of the heterogeneous C-200 catalyst.

The C-200 catalyst is $Ba(OH)_2 \cdot 0.8\,H_2O$ as deduced from TGA analysis. The surface area was $(1.9 \pm 0.1)\,m^2g^2$ by the *BET* method[5]. This low value of the surface area shows that the solid has probably a microcrystalline structure which was confirmed by an X-ray powder diagram. The X-ray diagram (Table 2) was compared to the ASTM

* The presence of **1** and **6** were detected by IR and PMR.

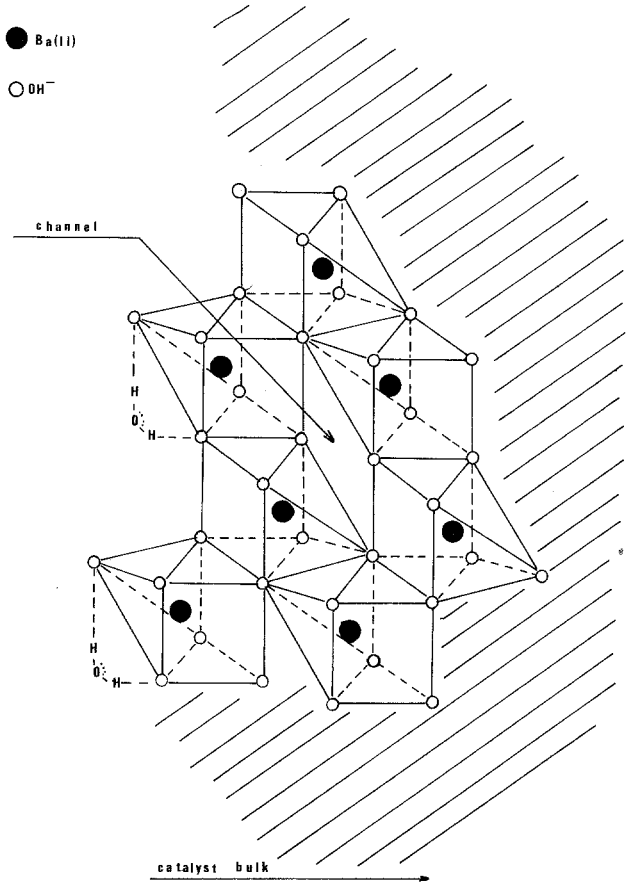


Fig. 1. Schematical presentation of the structure of the active site of the C-200 catalyst

cards[6]. From this study[7] we could deduce that the catalyst is a mixture of $Ba(OH)_2 \cdot H_2O$ and $\beta\, Ba(OH)_2$. This agrees with the TGA analysis. The cell unity of the main product: $Ba(OH)_2H_2O$ is orthorhombic:

$$a_0 = 6.366\,\text{Å},\ b_0 = 6.955\,\text{Å},\ c_0 = 3.894\,\text{Å}.$$

The X-ray structure was accomplished by determination of the coordination number of Ba^{II}. By means of the X-ray results and those of barium and strontium hydroxides monohydrates in the literature[8—10] a tentative structure is proposed in Fig. 1.

This main structure is that of $Ba(OH)_2 \cdot H_2O$ in the surface. The

average distance Ba^{II}—OH^- is 2.6 Å and OH^-—OH^- is 3.5 Å. The distance H_2O—OH^- cannot be determined because the water molecule is only weakly bound to the lattice and there is an equlibrium

$$Ba(OH)_2 \cdot H_2O_{(s)} \rightleftharpoons \beta\, Ba(OH)_{2(s)} + H_2O_{(g)}$$

related to the water vapor pressure of the atmosphere.

In order to complete our knowledge of the catalyst, the nature and amount of active sites of the catalytic surface were determined by the spectrophotometric method[11].

Phenotiazine (*PHEN*) and *m*-dinitrobencene (*DNB*) were used as the titrating agents of oxidant and reducing sites, respectively. Benzoic acid ($pKa = 4.2$) (*BA*) and 2,6-ditertbutyl-4-methyl-phenol (*TBMPHE*) ($pKa > 10$) were used to determine number and strength of basic sites. Pyridine (*Py*) ($Pka = 5.3$) was used to titrate the acid sites. The value of X_m (mmol · ads) · (g · cat)$^{-1}$ equivalent to the number of titrated sites[11] are shown in Table 3.

Table 3. *Acid, basic and red-ox properties of the* C-200 *catalyst*

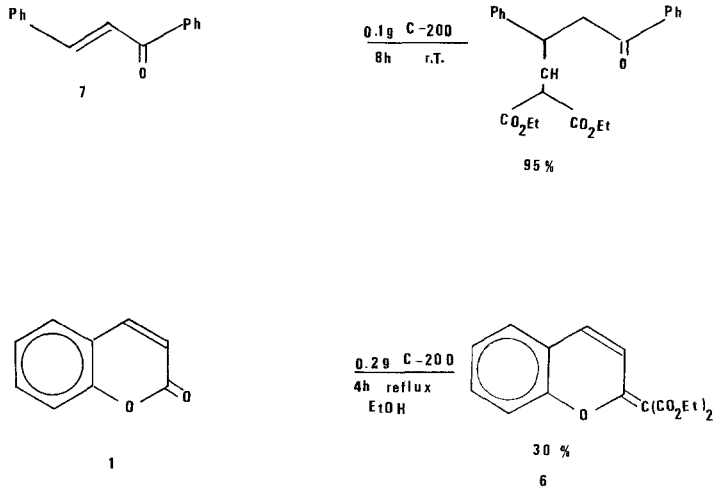
Titrating agent	X_m (mmol. ads.) (g. cat.)$^{-1}$
DNB (E. A. = 2.21 eV)	$(3.5 \pm 0.3)\, 10^{-2}$
PHEN (I. P. = 7.13 eV)	—
Pyridine	—
BA	$(9 \pm 1)\, 10^{-2}$
TBMPHE	$(6.3 \pm 0.2)\, 10^{-3}$

From these values it can be deduced that no oxidant and no acid sites of $pKa < 5.3$ are present in the catalyst. This is due to the nature of the barium ion. The catalyst has basic sites exclusively titrated by *BA* and very strong acid sites without steric hinderance titrated only by *TBMPHE*. The nature of reducing sites is not clear although several studies of selective poisoning have been carried out. Nevertheless we can say that they do not act in the carbanion formation in diethyl malonate because no selective poisoning is observed with *DNB*.

Mechanistic Considerations

The different behaviour observed for coumarin (**1**) and chalcone (**7**) in the reaction with diethyl malonate in the presence of the C-200 catalyst may be explained by means of the different behaviour of **1** and **7** against the crystalline structure of the solid catalyst.

Scheme 3



It is evident that diethyl malonate ($pKa = 13$) will react with the strong basic sites titrated by *TBMPHE* (Fig. 2 and Scheme 3).

These very strong basic sites are responsible for the carbanion formation from diethyl malonate[12] in the *Michael* addition to chalcone[12]. In this process (similar to the first step of the reaction studied), the carbanion is placed where the apical OH^- had been in the lattice (Fig. 2). The basic sites only titrated by *BA* have a weak basic character versus diethyl malonate and cannot react with it. A polymeric supported reagent Ⓟ—CH=CH—CO-*Ph* was used to analyze if the carbanion leaves the solid and if the process is a phase transfer catalysis. When the polymeric supported reagent is added to a mixture of diethyl malonate and C-200 catalyst, no *Michael* addition was observed*. Therefore we can deduce that the carbanion does not leave the solid surface. Thus the reaction takes place at the catalytic surface and the microcrystalline structure of the solid plays a very important role in the process.

When the reactions of adsorbed carbanion with **1** or **7** are analyzed we can assume two differences between **1** and **7** from the catalytic point of view: i) **7** has a flexible structure and **1** a rigid one; ii) **1** has two oxygen atoms that can easily chelate the Ba^{II} of the lattice, but not **7**. Thus, **7** does not interact with the Ba^{II} of the lattice and can approach the catalytic surface giving a *Michael* addition.

* No ester bands were observed in the IR of the polymer supported reagent.

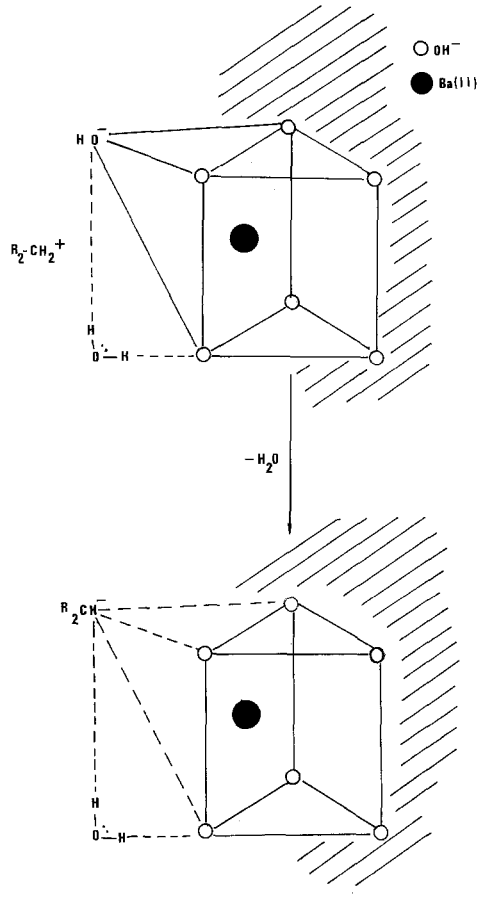


Fig. 2. Carbanion formation on the lattice of the $Ba(OH)_2$ catalyst (proposed mechanism); $R = CO_2Et$

1 goes to the catalytic surface to chelate Ba^{II} where the water molecule had been in the lattice (see Fig. 2). This water molecule is weakly linked to the lattice[13] and can be replaced by organic molecules[11] giving a structure such as Fig. 3. The distance between the ^-CH and the coumarinic ring would be ≈ 3.5 Å to stabilize the crystal lattice. With this structure the carbanion of diethyl malonate replaces OH^- and the two oxygens of the coumarinic ring replace the water molecule. The overlapping between the p_z^2 orbital of the carbanion and the p_z orbital of the carbon atom of the C=O bond would be very good and the Ad_N would take place giving the

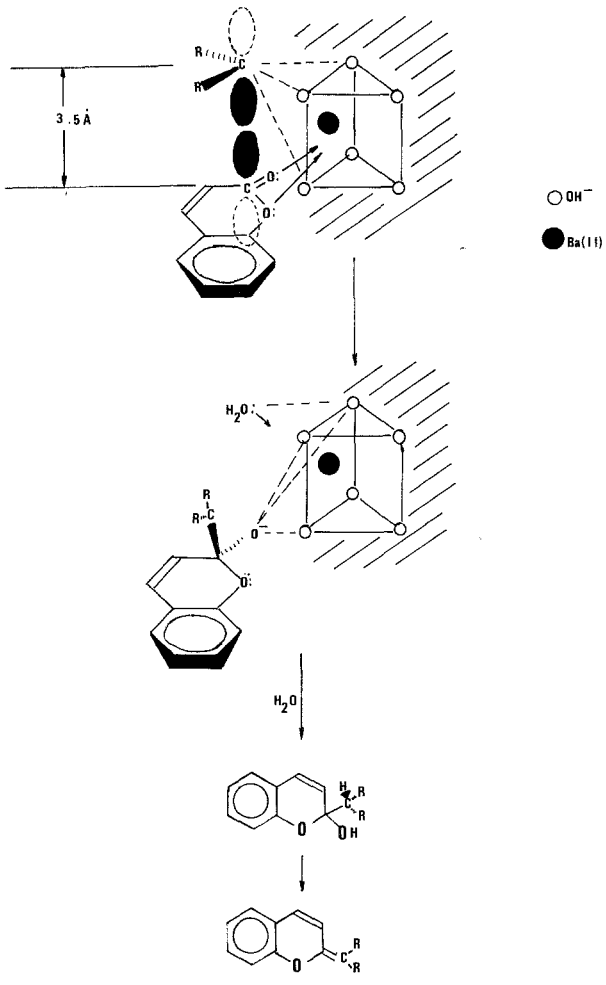


Fig. 3. Mechanism postulated for the process; $R = CO_2Et$

second structure of Fig. 3 where the anion O^- plays a role similar to OH^- and the water molecule goes to the solid surface.

The process should occur rather difficult compared to a *Michael* addition[1] because three very restrictive conditions are necessary: i) a strong basic character of the active site; ii) no steric hindrance in the active site; iii) a microscopical structure where the crystal of C-200 allows the two oxygens of **1** to approach Ba^{II} for chelation.

Experimental

Preparation of the catalyst

The activated barium hydroxide catalyst C-200 has been prepared by calcination of commercial Probus S. A. barium described previously[14]. The surface area was $(1.9 \pm 0.1)\,m^2\,g^{-1}$ as determined by the *BET* method[5].

The active sites of the catalyst were determinated according to the method previously described[11,15].

The TGA analysis was carried out in a Dupont 990 thermalanalyzer. The X-ray powder diagram was carried out in a Philips PW 1130 (35 kV, 35 mA) X-ray diffraction unit with CoK_α ($\lambda = 1.790260$ Å) filtered radiation, $15° < 2\theta < 42°$, scan rate $1°\ 2\theta\,min^{-1}$.

Synthesis of **6** *[2-(di-ethoxycarbonylmethyliden)-chromene]*

To a stirred solution of coumarin (1.46 g, 0.01 mol) and diethyl malonate (1.52 ml, 0.01 mol) in *Et*OH (96%, 56 ml) the barium hydroxide catalyst (0.2 g) was added. The mixture was stirred at reflux for 4 h. Then cold HCl—H_2O solution was added (to $pH = 6$) to destroy the catalyst. The mixture was cooled to 4 °C and the product **6** filtered and washed with cold water. No recrystallization of **6** was necessary.

$C_{16}H_{16}O_5$ (*M*, 288); found C 66.9, H 5.9; calculated C 66.6, H 5.6. Yield 30%; m. p. = 56 °C.

IR (KBr, $\alpha\,cm^{-1}$) = 1 730 (—**CO**—O*Et*), 1 200 (broad, —**O**—**CH**$_2$CH$_3$), 1 260 (v. arylic ether), 760 (ortho subst.).

^{1}H-NMR ($CDCl_3$, *TMS* int.) δ ppm = 1.22 (t, 6 H), 4.3 (q, 4 H), 6.5 (d, 9.8 Hz, 1 H), 7.3–7.6 (m, 4 H), 7.8 (d, 9.8 Hz, 1 H).

Reaction with polymeric supported reagent

The supported reagent Ⓟ—CH=CH—CO-*Ph* was obtained from functionalized polystyrene Ⓟ—CHO (1.3 meq g^{-1})[16] by reaction with acetophenone under standard *Claisen-Schmidt* conditions. The supported reagent was added to a mixture of diethyl malonate and C-200 catalyst (this mixture was equilibrated for 10 h) and stirred for 24 h. The resin was washed and dried and the IR spectrum recorded. The C=C—C=O band of polymeric supported reagent remained in the polymer.

Acknowledgements

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