

## MECHANISM OF THE REACTION OF 1-METHOXY- AND 1-CHLORO-2,4,6-TRINITROBENZENE WITH DIMETHYL MALONATE ANION

Vladimír MACHÁČEK<sup>a</sup>, Vojeslav ŠTĚRBA<sup>a</sup> and Antonín LYČKA<sup>b</sup>

<sup>a</sup> Department of Organic Chemistry,

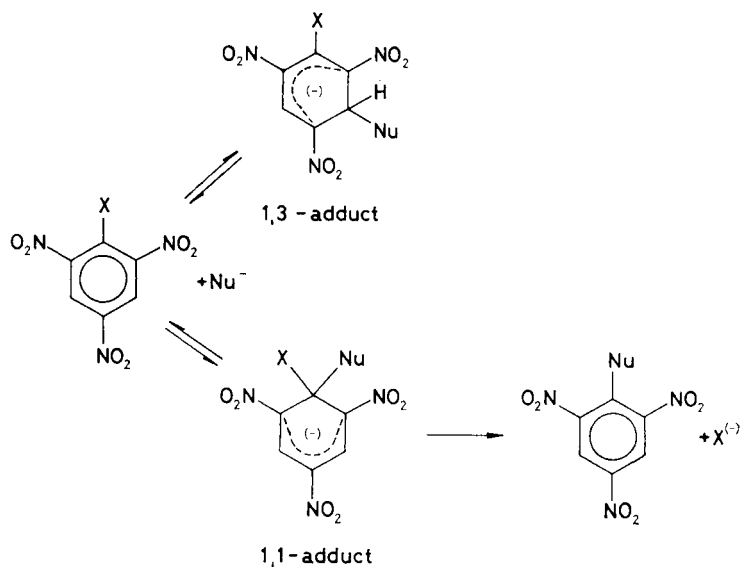
Institute of Chemical Technology, 532 10 Pardubice and

<sup>b</sup> Research Institute of Organic Syntheses, 532 18 Pardubice-Rybitví

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<sup>1</sup>H NMR spectra have been used to prove the formation of 1,3- and 1,1-adducts in the reaction of 1-methoxy-2,4,6-trinitrobenzene with dimethyl malonate anion and formation of 1,3-adduct in the analogous reaction of 1-chloro-2,4,6-trinitrobenzene. Dimethyl 2,4,6-trinitrophenylmalonate is formed from 1-chloro-2,4,6-trinitrobenzene at the same rate and by the same mechanism as the 1,1-adduct from 1-methoxy-2,4,6-trinitrobenzene. The two reactions only differ in their rate-limiting steps.

Reactions of 1-substituted 2,4,6-trinitrobenzenes with negatively charged nucleophiles proceed according to Scheme 1



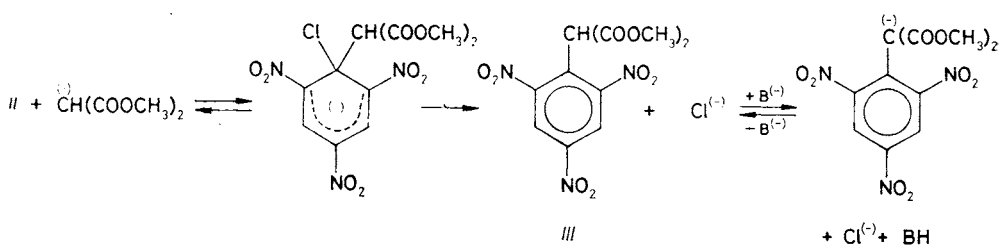
SCHEME 1

Kinetics of the reactions of 1-methoxy-2,4,6-trinitrobenzene (*I*) and 1-chloro-2,4,6-trinitrobenzene (*II*) with dimethyl malonate anion were studied in detail in methanol and in mixtures of methanol and dimethyl sulphoxide<sup>1,2</sup>. The following conclusions were made on the basis of the data measured.

a) In each of the systems mentioned, the reactions proceed by several steps which differ considerably in their rates. The reaction of compound *I* produces the 1,3-adduct in the first rapid step ( $t_{1/2} \sim \text{ms}$ ), and the adduct is very slowly transformed *via* the 1,1-adduct into dimethyl 2,4,6-trinitrophenylmalonate (*III*) or its anion<sup>1</sup>. The rate of reverse splitting off of the dimethyl malonate anion from the 1,1-adduct is at least by 1 order of magnitude greater than the rate of splitting off of methoxide ion with formation of the substitution product *III*. When the steady state is attained ( $[1,1\text{-adduct}]/[1,3\text{-adduct}] = \text{const.}$ , and the reaction obeys the first-order kinetics), the concentrations of the two adducts are comparable. The rate-limiting step of the substitution reaction consists in splitting off of methoxide ion from the 1,1-adduct.

b) In the reaction of compound *II*, the splitting off of chloride ion from the 1,1-adduct is substantially faster than that of the dimethyl malonate anion, hence the rate-limiting step of the substitution reaction consists in formation of the 1,1-adduct<sup>2</sup>.

Leffek<sup>3</sup> studied the reaction kinetics of 1-chloro-2,4,6-trinitrobenzene with dimethyl malonate anion in mixtures of dimethyl sulphoxide and benzene and suggested a mechanism for this reaction (Scheme 2). The rate-limiting step of the substitution reaction consists in slow splitting off of chloride ion from the 1,1-adduct. The rate constant of formation of the adduct was measured<sup>3</sup> by the stopped-flow method. The author<sup>3</sup> did not consider the 1,3-adduct to be formed in this reaction and he supported the mechanism suggested by him by the following arguments.



SCHEME 2

a) The 1,1-adducts are generally much more stable than the 1,3-adducts.

b) The reaction of 1,3,5-trinitrobenzene with dimethyl malonate anion is — at the conditions used — so fast that it cannot be followed even by means of the stopped-flow method. Leffek<sup>3</sup> presumed that the formation of 1,3-adduct from 1-chloro-2,4,6-

-trinitrobenzene with dimethyl malonate anion would have to be as fast as the reaction of 1,3,5-trinitrobenzene.

But in fact, the additions of negatively charged nucleophiles to 1-substituted 2,4,6-trinitrobenzenes are by about 1 order of magnitude slower than those to 1,3,5-trinitrobenzene itself<sup>1,2,4,5</sup>. At the conditions used<sup>3</sup>, also the half-lives of reactions of dimethyl malonate anion with compound *II* were close to the applicability limits of the stopped-flow method ( $t_{1/2} = 1-5$  ms), hence the reaction with 1,3,5-trinitrobenzene could not be followed by means of spectrophotometry at these conditions.

Although all the arguments support the mechanism suggested by us<sup>1,2</sup>, in ref.<sup>6</sup> it is stated that from kinetic data it is impossible to decide which of the mechanisms suggested<sup>1-3</sup> is correct. Therefore, we decided to determine structures and concentrations of the reaction intermediates by means of <sup>1</sup>H NMR spectra and thereby to solve the problem.

### EXPERIMENTAL

1-Methoxy-2,4,6-trinitrobenzene (*I*) (m.p. 57–58°C, ref.<sup>7</sup> m.p. 56–57°C) and 1-chloro-2,4,6-trinitrobenzene (*II*) (m.p. 82–83°C, ref.<sup>8</sup> m.p. 83°C) were prepared by the known procedures<sup>7,8</sup>. Sodium salt of dimethyl malonate was prepared by the reaction of dimethyl malonate with sodium hydride in dry benzene. The salt was collected by suction under argon, thoroughly washed with benzene, and dried by passing argon therethrough and by long-term standing in vacuum at room temperature. Dimethyl 2,4,6-trinitrophenylmalonate (*III*) was prepared by the reaction of compound *II* with dimethyl malonate and sodium methoxide<sup>1</sup>. <sup>1</sup>H NMR spectrum (hexadeuteriodimethyl sulphoxide):  $\delta(\text{Pi})$  9.16 (2 H, s),  $\delta(\text{CH})$  5.94 (1 H, s),  $\delta(\text{CH}_3)$  3.75 (6 H, s). <sup>13</sup>C NMR spectrum (hexadeuteriodimethyl sulphoxide):  $\delta(\text{CO})$  164.91,  $\delta_{2,6}$  150.52,  $\delta_1$  147.24,  $\delta_4$  128.76,  $\delta_{3,5}$  124.66,  $\delta(\text{CH}_3)$  53.29,  $\delta(\text{CH})$  50.83. Sodium salt of dimethyl 2,4,6-trinitrophenylmalonate — <sup>1</sup>H NMR spectrum (hexadeuteriodimethyl sulphoxide):  $\delta(\text{Pi})$  8.51 (2 H, s),  $\delta(\text{CH}_3)$  3.36 (6 H, s).

The <sup>1</sup>H and <sup>13</sup>C NMR spectra were measured with a JNM-FX 100 (JEOL) apparatus at 25°C at 99.602 and 25.047 MHz, respectively. For the <sup>1</sup>H NMR spectra measurement we used a 0.2 mol l<sup>-1</sup> solution of compound *I* and 0.2 mol l<sup>-1</sup> solution of sodium salt of dimethyl malonate in hexadeuteriodimethyl sulphoxide. The insoluble portion was removed from the solution of sodium salt by means of centrifugation. The precise concentration of the sodium salt solution was determined from the <sup>1</sup>H NMR spectrum of the adduct of this salt and 1,3,5-trinitrobenzene in a solution of known concentration<sup>9</sup>. Compound *II* was used in the form of concentrated (about 1.5 mol l<sup>-1</sup>) solution in hexadeuteriobenzene. The samples for the measurement were prepared by mixing equimolar amounts of the substrate and sodium salt of dimethyl malonate solutions at 25°C. A part of the mixture was transferred into a 5 mm NMR test tube, and a series of 24 pulses was carried out in a rapid sequence for each sample. The resulting FID's of each series were stored in a disc memory. The first measurement was started about 60 s after mixing the solutions. The first 10 series were measured at about 90 s time intervals, the intervals being gradually lengthened in further measurements. The measurement took 2 h. Then the individual FID's were submitted to Fourier's transformation, and the spectra obtained were integrated. For kinetic purposes, the time of the 12th pulse was considered in each series. The poor quality of spectra (Fig. 1) is due to considerable viscosity of the mixtures; no filtration of the samples was carried out before the measurement proper, and the shimming of the spectro-

meter on the sample measured was reduced to a minimum in order to trap the initial phase of the reaction. The accurate values of chemical shifts and coupling constants were read from the spectra of filtered samples with application of the line-narrowing method.

Kinetic experiments: 2 ml dimethyl sulphoxide was placed in a cell, and 40 (or 100)  $\mu\text{l}$  dimethyl malonate, 20  $\mu\text{l}$  of 0.1 (or 1, resp.)  $\text{mol l}^{-1}$  sodium methoxide solution, and one drop of  $4 \cdot 10^{-3} \text{ mol l}^{-1}$  solution of compound *II* in benzene were added thereto. The absorbance decrease was measured at 450 nm by means of a Specord UV VIS (Zeiss) spectrophotometer. The kinetic measurements were carried out at the temperature of 25°C.

Dimethyl sulphoxide was dried with calcium hydride and distilled in vacuum under inert atmosphere.

## RESULTS AND DISCUSSION

The  $^1\text{H}$  NMR spectra of the reaction mixtures of compound *I* with sodium salt of dimethyl malonate in hexadeuteriodimethyl sulphoxide are given in Fig. 1 for the time intervals of 100, 440, and 2 760 s after mixing the components (the concentrations of the starting compounds were  $0.1 \text{ mol l}^{-1}$  after the mixing). The spectra show signals of the 1,3-adduct ( $\delta_s$  8.34 (d),  $\delta_1$  5.55 (dd),  $^3J = 5.4 \text{ Hz}$ ,  $^4J \cong 1.5 \text{ Hz}$ ) and 1,1-adduct ( $\delta_{3,5}$  8.61 (s),  $\delta(\text{CH})$  5.10 (s)). The intensity of the signals of 1,1-adduct increases with time to the detriment of that of 1,3-adduct which proportionally decreases. At the time  $t = 100 \text{ s}$  the concentration ratio  $[\text{1,3-adduct}]/[\text{1,1-adduct}] = 10.4$ , at  $t = 440 \text{ s}$  it is 3.3. After about 3 000 s the ratio remained practically unchanged at a value of  $1.3 \pm 0.1$ . Even after 3 000 s the spectrum only contained the proton signals of the two adducts, the substitution product *III* being absent. After 20 h (from mixing the reactants) the reaction mixture contained besides the two

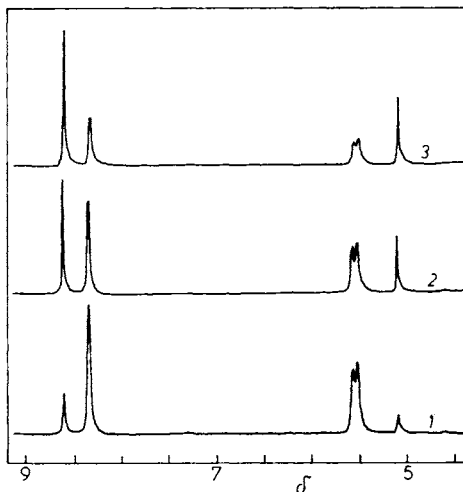
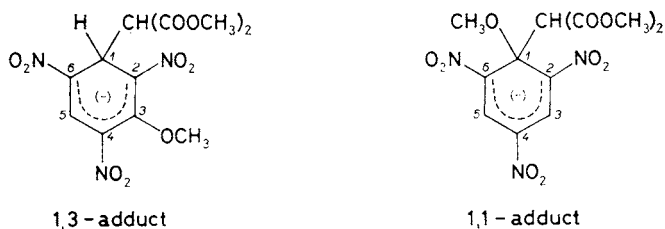


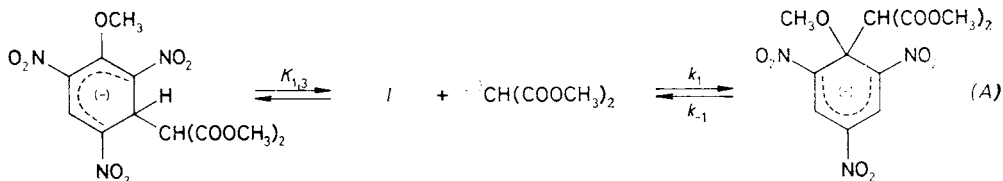
FIG. 1

Parts of  $^1\text{H}$  NMR spectra of the adducts formed in the reaction of 1-methoxy-2,4,6-trinitrobenzene with sodium salt of dimethyl malonate in hexadeuteriodimethyl sulphoxide recorded 100 s (1), 440 s (2), and 2 760 s (3) after mixing the solutions of starting components

adducts also about 5% of anion of compound *III*. The rate of formation of compound *III* is substantially lower in dimethyl sulphoxide than in methanol, because the rate constant of the rate-limiting step – splitting off of methoxide ion from the 1,1-adduct – rapidly decreases with increasing content of dimethyl sulphoxides in its mixture with methanol<sup>5</sup>.



The time dependences of  $\log [(I_{rel}^1)_t - (I_{rel}^1)_\infty]$  were linear. The  $(I_{rel}^1)_t$  and  $(I_{rel}^1)_\infty$  values are integral intensities of the  $H_1$  proton signal of the 1,3-adduct related to the sum of the integral intensities of the  $H_1$  proton of 1,3-adduct and the CH proton of 1,1-adduct at a time  $t$  and  $\infty$ , respectively. The calculated rate constant is  $k_{obs} = 0.693/t_{1/2} = (1.41 \pm 0.05) \cdot 10^{-3} \text{ s}^{-1}$ . The intensities of the proton signals of 1,1-adduct extrapolated to the zero time are equal to zero within experimental error, which means that only the 1,3-adduct is formed after mixing the starting components.

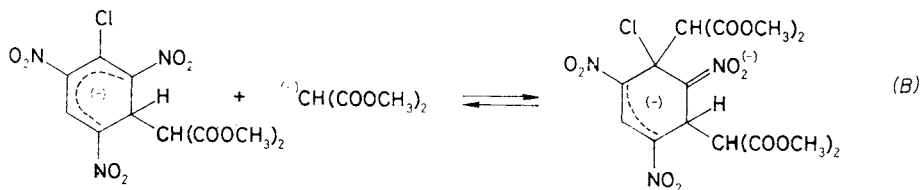


The  $k_{obs}$  value represents the rate constant of formation of the equilibrium mixture of 1,1- and 1,3-adducts (Eq. (A)) and is defined by Eq. (I). From Eq. (I) and from the overall equilibrium constant  $K$  of the reaction ( $K = K_{1,3} \cdot k_1/k_{-1} = 0.77$ ) we obtain, for the rate constant of formation of the 1,1-adduct, the value  $K_{1,3} \cdot k_1 = 6.1 \cdot 10^{-4} \text{ s}^{-1}$ .

$$k_{obs} = \vec{k} + \overleftarrow{k} = K_{1,3} \cdot k_1 + k_{-1} \quad (I)$$

After mixing a solution of compound *II* with a solution of sodium salt of dimethyl malonate in dimethyl sulphoxide, the 1,3-adduct is only formed ( $^1\text{H}$  NMR spectrum:  $\delta_5$  8.42 (d),  $\delta_1$  5.63 (d),  $^3J = 6.84 \text{ Hz}$ ,  $^4J \cong 2.2 \text{ Hz}$ ). The 1,3-adduct is gradually converted to the substitution product *III* and its anion. At the same time, compound *II* is hydrolyzed by the water present in hexadeuteriodimethyl sulphoxide, and the acids formed (HCl and 2,4,6-trinitrophenol) rapidly shift the equilibrium between

the adduct and the starting compounds back to compound *II* and dimethyl malonate. The proton signals of the 1,1-adduct were never observed in the  $^1\text{H}$  NMR spectra. With respect to the subsequent reaction described it was impossible from the NMR spectra to find the rate constant of formation of the substitution product *III*. Therefore, this constant was determined by means of spectrophotometry. The rate constant has the value  $k_{\text{obs}} = 6.8 \cdot 10^{-4} \text{ s}^{-1}$  and  $9.6 \cdot 10^{-4} \text{ s}^{-1}$  at the concentrations of the sodium salt of dimethyl malonate equal to  $10^{-3}$  and  $10^{-2} \text{ mol l}^{-1}$ , respectively. The increase in the  $k_{\text{obs}}$  rate constant at higher concentrations of the carbanion can be due to partial formation of the diadduct<sup>2</sup> according to Eq. (B) and its decomposition to the substitution product *III*.



The rate constants of the attack of 1 position of compounds *I* and *II* by negatively charged nucleophiles (methoxide anion, dimethyl malonate anion) are roughly the same, the same being also true of the attack at 3 position (Table I). The rate constant of formation of the product from compound *II* ( $k_{\text{obs}} = 6.8 \cdot 10^{-4} \text{ s}^{-1}$ ) is close to that of the 1,1-adduct from compound *I* and the same anion ( $k_1 K_{1,3} = 6.1 \cdot 10^{-4} \text{ s}^{-1}$ ). This fact represents another piece of evidence for the correspondence of the  $k_{\text{obs}}$  rate constant (of the reaction of compound *II* with the dimethyl malonate anion) with the formation of 1,1-adduct. Hence, the formation of 1,1-adduct represents the rate-limiting step of formation of the product *III* in this reaction.

TABLE I

The rate constants  $k$  ( $\text{l mol}^{-1} \text{ s}^{-1}$ ) of formation of 1,1- and 1,3-adducts in the reaction of 1-methoxy-2,4,6-trinitrobenzene (*I*) and 1-chloro-2,4,6-trinitrobenzene (*II*) with methoxide ion and dimethyl malonate anion in methanol at 25°C

| Substrate | Nucleophile                     | $k$ (1,1-adduct)                                      | $k$ (1,3-adduct)                       |
|-----------|---------------------------------|---|--|
| <i>I</i>  | $\text{CH}_3\text{O}^-$         | 17.3 (ref. <sup>10</sup> )                            | 950 (ref. <sup>11</sup> )              |
| <i>II</i> | $\text{CH}_3\text{O}^-$         | 17 (ref. <sup>2</sup> )<br>19.8 (ref. <sup>12</sup> ) | 912 (ref. <sup>13</sup> )              |
| <i>I</i>  | $^-\text{CH}(\text{COOCH}_3)_2$ | $\sim 86$ (ref. <sup>1</sup> )                        | $2.95 \cdot 10^4$ (ref. <sup>1</sup> ) |
| <i>II</i> | $^-\text{CH}(\text{COOCH}_3)_2$ | 82 (ref. <sup>2</sup> )                               | $3 \cdot 10^4$ (ref. <sup>2</sup> )    |

The reaction of both the compounds *I* and *II* with dimethyl malonate anion in dimethyl sulphoxide produces — in the first step — practically only the 1,3-adducts in accordance with the finding<sup>5</sup> that the formation of 1,3-adducts in the reaction of 1-methoxy-2,4,6-trinitrobenzene with nucleophiles is by about 2 orders of magnitude faster than the formation of 1,1-adducts. The equilibrium mixture obtained by the reaction of compound *I* with dimethyl malonate anion in hexadeuteriodimethyl sulphoxide contains comparable concentrations of the two adducts, and similar results are also obtained from the same reaction in methanol and in mixtures of methanol and dimethyl sulphoxide<sup>1</sup>.

In the reaction of compound *II* with dimethyl malonate anion, the formation of 1,1-adduct could not be proved by means of <sup>1</sup>H NMR spectra. The splitting off of chloride ion from the 1,1-adduct is much faster than that of dimethyl malonate anion, hence the formation of 1,1-adduct is rate-limiting.

The rate constant of formation of compound *III* from *II* and dimethyl malonate anion has almost the same value as that of formation of 1,1-adduct from 1,3-adduct in the reaction of compound *I* with dimethyl malonate anion. The reaction mechanisms of the two substrates with dimethyl malonate anion are the same, only different being the rate-limiting steps of the two reactions.

The structure of the intermediates formed in the reaction of compound *II* with dimethyl malonate anion in a benzene–dimethyl sulphoxide (7 : 1) mixture<sup>3</sup> could not be determined by means of <sup>1</sup>H NMR spectra owing to very low solubility of the salts in this medium. However, the kinetic data<sup>3</sup> indicate that the splitting off of Cl<sup>-</sup> does not represent the rate-limiting step. Generally, the 1,3-adducts are formed faster than 1,1-adducts by about 2 orders of magnitude, and the ratio of rate constants of formation and decomposition of the isomeric adducts does not depend on the medium<sup>5</sup>. If, in the benzene–dimethyl sulphoxide mixture, the splitting off of Cl<sup>-</sup> were the rate-limiting step, the substitution would have to proceed kinetically in 3 steps: *a*) the establishing of equilibrium between compound *II* and 1,3-adduct (*t*<sub>1/2</sub> ms); *b*) a slower establishing of equilibrium with the 1,1-adduct; *c*) the rate-limiting splitting off of Cl<sup>-</sup>. But in fact, only a single equilibrium was observed<sup>3</sup> to be established (*t*<sub>1/2</sub> ms), hence the intermediate observed spectroscopically must be the 1,3-adduct in this case, too.

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