

FORMATION OF SPIRO ADDUCT FROM N-METHYL-N-(2,4,6-TRINITROPHENYL)GLYCINE ANION

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The intramolecular nucleophilic addition of N-methyl-N-(2,4,6-trinitrophenyl)glycine anion in methanol-dimethyl sulfoxide mixtures produces spiro[(3-methyl-5-oxazolidinone)-2,1'-(2',4',6'-trinitrobenzenide)]. The spiro adduct has been identified by means of ^1H and ^{13}C NMR spectroscopy. This is the first case when the formation of a Meisenheimer adduct with carboxylate ion is observed. Logarithm of the equilibrium constant of adduct formation increases linearly with the mole fraction of dimethyl sulfoxide in its mixture with methanol.

Reactions of electron-deficient aromatics with strong nucleophilic reagents produce the Meisenheimer adducts. Typical examples are adducts of 1,3,5-trinitrobenzene and 1-X-2,4,6-trinitrobenzenes with alkoxides, nitrogen- and sulfur-containing nucleophiles, and anions of weaker C-acids ($\text{p}K > 10$) which are stable also in methanolic solutions¹. The stability of these adducts in mixtures of methanol and some aprotic solvent (most often dimethyl sulfoxide) increases with increasing content of the aprotic solvent². Carboxylate ions belong to the most usual nucleophiles in organic chemistry. However, so far no case of formation of Meisenheimer adducts of carboxylate ions with electron-deficient aromatics has been described, not even in neat dimethyl sulfoxide. The stability of these adducts is increased by many orders of magnitude, if their formation is connected with ring closure (most often a five-membered ring)³. The main reason of this increased stability of the spiro adducts formed by the intramolecular attack — as compared with the adducts formed by an intermolecular nucleophilic addition — consists in the high rate of formation of the spiro adducts. Therefore, we have studied the reactions of N-methyl-N-(2,4,6-trinitrophenyl)glycine with bases where it is possible to expect the formation of spiro adducts by the intramolecular attack by the carboxylate ion.

EXPERIMENTAL

The ^1H and ^{13}C NMR spectra were measured with a JNM FX-100 spectrometer (Jeol) at 99.602 and 25.047 MHz, respectively, using c. 10% solutions of the substances in hexadeuteriodimethyl sulfoxide. The chemical shifts are related to the signal of hexamethyldisiloxane ($\delta(^1\text{H})$ 0.05) and to the middle signal of the solvent multiplet ($\delta(^{13}\text{C})$ 39.6), respectively.

N-Methyl-N-(2,4,6-trinitrophenyl)glycine (I). A solution of 2.4 g (22 mmol) sodium salt of sarcosine in a mixture of 15 ml methanol and 3 ml water was stirred and treated with 2.5 g (10 mmol) 1-chloro-2,4,6-trinitrobenzene. After c. 20 min the solution was acidified with 4.5 ml 2M-HCl. The compound *I* precipitated on standing, it was collected by suction, and washed with a mixture methanol-water (3 : 1). Yield 2.1 g (70%), m.p. 126–128°C. For $C_9H_8N_4O_8$ (300.2) calculated: 36.01% C, 2.69% H, 18.66% N; found: 36.11% C, 2.81% H, 18.60% N. 1H NMR (hexadeuteriodimethyl sulfoxide): 12.6 b, 1 H (COOH); 8.92 s, 2 H (Pi); 3.93 s, 2 H (CH₂); 2.97 s, 3 H (NCH₃). ^{13}C NMR (hexadeuteriodimethyl sulfoxide): 169.12 (CO), 138.35 (C-1), 143.68 (C-2, 6), 125.24 (C-3, 5), 142.56 (C-4), 55.75 (CH₂), 41.41 (NCH₃).

Spiro[(3-methyl-5-oxazolidinone)-2,1'-(2',4',6'-trinitrobenzenide)], sodium salt (III) was prepared in solution by mixing c. 20% solutions of 300 mg (1 mmol) compound *I* and 90 mg (1.1 mmol) anhydrous sodium acetate in hexadeuteriodimethyl sulfoxide.

Measurements of Equilibrium Constants

The pK_A value of *N*-methyl-*N*-(2,4,6-trinitrophenyl)glycine was determined spectrophotometrically in methanolic chloroacetate buffers [$ClCH_2COONa$] 0.025 mol l^{-1} , [$ClCH_2COOH$] 0.0025 to 0.025 mol l^{-1} at 25°C, I 0.025 mol l^{-1} , concentration of compound *I* $1 \cdot 10^{-4} \text{ mol l}^{-1}$, at the wavelengths of 384 and 400 nm. The absorbances of the acid *I* alone and of its anion *II* alone were determined by the measurements in 0.01M methanolic HCl and 0.01M methanolic CH_3COONa , respectively. The absorbance value of the anion *II* was corrected for the presence of the spiro adduct in pure methanol (about 3%) which was determined from the value of equilibrium constant $K = [III]/[II]$ in methanolic solution (the K value for the methanolic solution was found by extrapolation of the dependence of $\log K$ vs mole fraction of dimethyl sulfoxide). The pK_A value was determined by the standard graphical method.

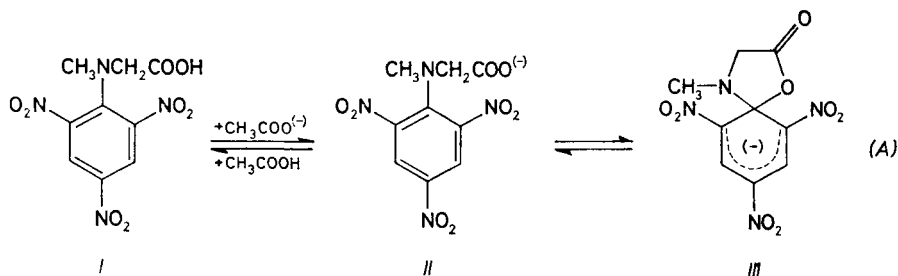
The equilibrium constant of formation of the spiro adduct *III* from the anion *II* was determined spectrophotometrically in methanol-dimethyl sulfoxide mixtures at 25°C in the following way: 2 ml solution of compound *I* in methanol-dimethyl sulfoxide mixture (0–70% by vol. dimethyl sulfoxide, $[I] = 5 \cdot 10^{-4} \text{ mol l}^{-1}$ for 0–50% by vol. dimethyl sulfoxide, $[I] = 5 \cdot 10^{-5} \text{ mol l}^{-1}$ for 40–70% by vol. dimethyl sulfoxide) was treated with 20 μl methanolic acetate buffer ($[CH_3COONa]/[CH_3COOH] = 4$, $[CH_3COONa] = 0.1 \text{ mol l}^{-1}$), and the absorbance A of the solution was measured at 505 nm. The absorbance of the pure adduct *III* (A_{III}) was determined in the same way using solution of compound *I* in 95% by vol. dimethyl sulfoxide, that of the acid *I* (A_I) was determined after addition of 20 μl 0.1M methanolic HCl to $5 \cdot 10^{-5} \text{ mol} \cdot \text{l}^{-1}$ solution of compound *I* in 95% by vol. dimethyl sulfoxide. The calculation of the equilibrium constant $K = [III]/[II]$ according to the equation $K = (A - A_I)/(A_{III} - A)$ is based on the presumption that the molar absorption coefficient of the spiro adduct does not depend on the composition of the methanol-dimethyl sulfoxide mixture, and the molar absorption coefficients of acid *I* and its anion *II* have practically the same values at 505 nm.

RESULTS AND DISCUSSION

An addition of 20 μl methanolic acetate buffer ($[CH_3COONa]/[CH_3COOH] = 4$, $[CH_3COONa] = I = 0.2 \text{ mol l}^{-1}$) to the solution of *N*-methyl-*N*-(2,4,6-trinitrophenyl)glycine (*I*) in methanol (2 ml, $10^{-4} \text{ mol l}^{-1}$) causes a change in electronic spectrum of compound *I*: the maximum is shifted from 367 to 375 nm, and the absorbance at λ_{max} is increased by c. 35%. These spectral changes are caused by the

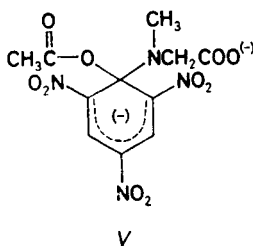
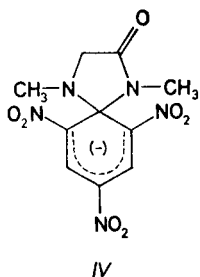
dissociation of carboxylic group in compound *I*. The dissociation constant of compound *I* measured in methanolic chloroacetate buffers (pK_A 7.96, ref.⁴) has the value pK_A 8.30.

When dimethyl sulfoxide is added to methanolic solution of the anion of compound *I*, new absorption maxima appear in the electronic spectrum at 415 and 505 nm, and the absorbance values at these wavelengths increase with increasing content of dimethyl sulfoxide in the mixture. The character of the newly formed spectra is typical of σ adducts of 1-X-2,4,6-trinitrobenzenes with nucleophiles. It can be presumed that in the methanol–dimethyl sulfoxide mixtures spiro[(3-methyl-5-oxazolidinone)-2,1'-(2',4',6'-trinitrobenzenide)] (*III*) is formed according to Eq. (A), because acetate ion in acetate buffers does not form adducts with 1,3,5-trinitrobenzene or 1-methoxy-2,4,6-trinitrobenzene. Structure of spiro adduct *III* was confirmed by means of 1H and ^{13}C NMR spectra. The 1H NMR spectrum of the spiro adduct *III* prepared by mixing the solutions of acid *I* and sodium acetate in hexadeuteriodimethyl sulfoxide contains, beside the signals of methyl groups of the mixture $CH_3COOH + CH_3COO^-$ (δ 1.92) and $COOH + H_2O$ (δ 10.44), only the proton signals of the spiro adduct: 8.67 s, 2 H (Ar); 3.66 s, 2 H (CH_2); 2.45 s, 3 H (NCH_3). The analogous spiro[(1,3-dimethyl-5-imidazolidinone)-2,1'-(2',4',6'-trinitrobenzenide)] (*IV*) (ref.⁵) exhibits the following chemical shifts: 8.65 s, 2 H (Ar); 3.37 s, 2 H (CH_2); 2.48 s, 3 H (NCH_3).



The ^{13}C NMR spectrum of spiro adduct *III* (hexadeuteriodimethyl sulfoxide): 171.58 (CO), 130.92 (C-2, 6), 126.71 (C-3, 5), 121.39 (C-4), 103.84 (C-1), 55.98 (CH_2), 35.50 (NCH_3). The chemical shifts of carbon atoms of the acetate buffer present in the mixture have the values of 21.76 (CH_3) and 173.04 ($COO^- + COOH$). The analogous spiro adduct⁵ *IV* has the following $\delta(^{13}C)$ values: 170.76 (CO), 129.34 (C-2, 6), 128.41 (C-3, 5), 118.40 (C-4), 83.83 (C-1), 57.09 (CH_2), 34.39 (NCH_3). Except for the C-1 carbon atom of the cyclohexadienide system, the other carbon atoms exhibit very similar chemical shifts. The difference between the $\delta(C-1)$ values is caused by the different structural environment: N—C—N in adduct *IV* and N—C—O in adduct *III*.

The basicity of triethylamine in dimethyl sulfoxide is not high enough to transform acid *I* into its anion quantitatively. Attempts at the preparation of triethylammonium salt of spiro adduct *III* by adding triethylamine to a solution of compound *I* in hexa-deuteriodimethyl sulfoxide resulted in obtaining spectra in which both the ^1H and ^{13}C signals appeared (due to rapid chemical exchange) between the chemical shifts of the corresponding atoms in acid *I* and spiro adduct *III*. With increasing excess of triethylamine the signals approached to the chemical shifts of the atoms in the spiro adduct, but in no case it was possible to observe the signal of C-1 carbon atom of cyclohexadienide system, his shape being affected by the chemical exchange to the greatest extent (the greatest difference between the $\delta(\text{C-1})$ chemical shifts of compounds *I* and *III*, $\Delta\delta \sim 34$ ppm). The formation of the triethylammonium salt of adduct *III* excludes the possibility of formation of adduct *V* in the reaction of compound *I* with acetate ion.



When sodium methoxide is added to the solution of compound *I* in the methanol–dimethyl sulfoxide mixture, the absorbance increase is greater than that obtained from the reaction with acetate in the same medium, and, at the same time, λ_{max} is slightly shifted to shorter wavelengths as compared with the spectrum of spiro adduct *III*. Probably the reaction of compound *I* with the base produces, beside the spiro adduct, also 1,1- or 1,3-adducts with methoxide. Therefore, we used the basic acetate buffer ($[\text{CH}_3\text{COO}^-]/[\text{CH}_3\text{COOH}] = 4$) only when determining the equilibrium constant of the reaction $\text{II} \rightleftharpoons \text{III}$ in methanol–dimethyl sulfoxide mixtures. The dissociation constant of acetic acid in methanol⁴ is 9.52, i.e. in the methanolic 4 : 1 acetate buffer there is 1.5% of compound *I* present in the nondissociated form and 98.5% in the form of anion *II*. Increasing content of aprotic solvents in their mixtures with methanol is connected with increasing value of the ρ constant of dissociation of carboxylic acids⁶, hence the difference $\Delta\text{p}K_{\text{A}}$ between compound *I* and acetic acid increases, too. The proportion of non-dissociated acid *I* in the buffer must decrease and has no effect of the equilibrium constant of formation of spiro adduct *III*. This result was confirmed by using, beside the basic 4 : 1 acetate buffer, also 1 : 1 acetate buffer in the mixtures containing 70 and 80% of dimethyl sulfoxide: the calculated values of the equilibrium constant of reaction $\text{II} \rightleftharpoons \text{III}$ were the same.

The logarithms of the found equilibrium constants of the reaction $II \rightleftharpoons III$ show a linear dependence on the mole fraction of dimethyl sulfoxide (x_{DMSO} ; Table I, Eq. (1)), which is typical of the equilibrium constants of reactions of electron-deficient aromatics with nucleophiles⁷. The slope value 5.61 of this dependence is by c. 20% greater than that found for the formation of adduct between 2,4,6-trinitroanisole and phenoxide in water–dimethyl sulfoxide mixtures⁸ and by c. 30% smaller than that for the formation of 1,1-adduct of 2-chloro-4,6-dinitroanisole with methoxide in methanol–dimethyl sulfoxide mixtures⁹. The magnitude of slopes of the $\log K$ vs x_{DMSO} dependences of the three above-mentioned additions is in accordance with the solvation requirements of phenoxide, methoxide, and carboxylate. Methoxide has a localized charge, and its activity coefficient increases fastest with addition of dimethyl sulfoxide, whereas the changes are smallest for phenoxide with its delocalized charge.

We tried to measure the rate constants of formation and decomposition of spiro adduct III by means of the stopped-flow method using a Durrum Gibson D-110 spectrophotometer (mixing of solutions of compound I and acetate buffer $[\text{CH}_3\text{COO}^-]/[\text{CH}_3\text{COOH}] = 4$ in 60% by vol. dimethyl sulfoxide in methanol). In this medium the equilibrium constant K has a value near to 1, and the half-life of the reversible reaction should be relatively the longest. However, also in this case we only recorded the absorbance of the equilibrium mixture after the dead time of the spectrophotometer. As the dead time is c. 2 ms, the reaction half-life must have been shorter than 0.5 ms. We tried, at least, to measure the decomposition rate of spiro adduct III in 95% dimethyl sulfoxide in which medium its stability is the highest and the reverse reaction should be slower by at least one order of magnitude than the reaction in 60% dimethyl sulfoxide. However, in this case, too, we only recorded the absorbance of the equilibrium mixture. This means that $k_{-1} \gg 10^3 \text{ s}^{-1}$ and $k_1 \gg 10^6 \text{ s}^{-1}$ (in 95% dimethyl sulfoxide). The low stability of spiro adduct III is thus caused by high rate of its decomposition. The rapid reverse decomposition was also observed with spiro adducts containing the dioxolane ring (as compared

TABLE I
The equilibrium constants K of the reaction $II \rightleftharpoons III$ in methanol–dimethyl sulfoxide mixtures

x_{DMSO}	0.060	0.125	0.197	0.236	0.276	0.319	0.364	0.462	0.572
$K \cdot 10^3$	2.75	6.92	18.2	32.4	53.7	89.1	148	550	2 140

$$\log K = -(2.85 \pm 0.02) + x_{\text{DMSO}}(5.61 \pm 0.06) \quad (1)$$

$$r = 0.9995 \quad s = 0.029 \quad n = 9$$

with 1,1-dialkoxy-1,1-dihydrocyclohexadienides), the stability of spiro adducts being higher than that of 1,1-dialkoxy adducts due to their high rate of formation¹⁰.

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