Kinetics and Mechanism of the Change of the 4-Nitrobenzylthio-System into 4,4′-Diformylazoxybenzene in Alkaline Dioxane-Water Media

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Sodium hydroxide reacts with α-(4-nitrobenzylthio)-acetic acid in aqueous-dioxane media to give 4,4′-diformylazoxybenzene as the main product besides 4,4′-dicarboxyazoxybenzene and a nitrone acid. This reaction was kinetically studied in presence of excess of alkali in different dioxane-water media at different temperatures. It started by a fast reversible α-proton abstraction step followed by two consecutive irreversible first-order steps forming two intermediates (α-hydroxy, 4-nitrosobenzylthio)-acetic acid and 4-nitrosobenzaldehyde. The latter underwent a Cannizzaro's reaction, the products of which changed in the reaction medium into 4,4′-diformylazoxybenzene and 4,4′-dicarboxyazoxybenzene. The rate constants and the thermodynamic parameters of the two consecutive steps were calculated and discussed. A mechanism was put forward for the formation of the nitrone acid.

Other six 4-nitrobenzyl, aryl sulphides were qualitatively studied and they gave mainly 4,4′-diformylazoxybenzene beside 4,4′-dicarboxyazoxybenzene or its corresponding azo acid.

Introduction

The preparation of azoxy- and azo-compounds directly from nitro aromatics under mildly reducing conditions has for long being attractive for chemists [1–7].

The present report is a kinetic study of the action of alkali on α-(4-nitrobenzylthio)-acetic acid (**I**), and the like, in order to reach a factual mechanism for its transformation into 4,4-diformyazoxybenzene.

Experimental

Action of alkali on α-(4-nitrobenzythio)-acetic acid [8, 9]

a) In 50% aqueous dioxane

The acid (3 g) was dissolved in 25 ml dioxane and 25 ml 10% aqueous sodium hydroxide. Boiling for one minute, cooling, dilution and filteration gave a solid (1.27 g) that crystallized from benzene, m.p. 190° undepressed when mixed with an authentic specimen of 4,4′-diformylazoxybenzene. Acidification of the Alkaline filtrate evolved hydrogen sulphide and gave a precipitate (0.53 g), which was a mixture of two acids, one soluble in boiling ethanol (0.37 g) while the insoluble part was (0.16 g).

(i) The soluble part in boiling ethanol decomposed at 360° and was identified as a nitrone having a molecular formula $C_{18}H_{16}N_2O_8S_2$ (452): requires: N, 6.2%; found N, 6.2%. Its molecular weight according to Rast's method [10] was found to be 450 ± 3. IR (KBr disk): 1600 (aromatic rings), 1580 (C=N) [11, 12] and 1280 Cm^{-1} (N → O) [13]; UV 1×10^{-4} in 2×10^{-4} M NaOH (50% aq. dioxane) $\lambda_{max} = 340$ nm $\log \varepsilon = 4.5$ ($\pi - \pi^*$ transition) [11, 13, 14]; ^{1}H-NMR (DMSO): $\delta = 1.2$ (s, 4H, $2CH_2$), 1.85 (s, 2H, CHOH), 7.4–8.4 (m, 8H, aromatic) and 10.15 (s, 2H, acidic).

(ii) The insoluble acid in boiling ethanol was crystallized from dilute acetic acid, did not melt up till 360° was identified as 4,4′-dicarboxyazoxybenzene [5]. $C_{14}H_{10}N_2O_5$ requires: C, 58.7; H, 3.5; N, 9.8%. Found: C, 58.9; H, 4.0; N, 9.67%. IR (KBr disk): 3100 – 2550 (OH), 1698 (C=O), 1425 (N=N) [15] and 1290 Cm^{-1} (N → O) [15]. UV 1×10^{-4} in 2×10^{-4} M NaOH (50% aq. dioxane) $\lambda_{max} = 334$ nm $\log \varepsilon = 4.3$. ^{1}H-NMR (DMSO): $\delta = 7.9 - 8.5$ (m, 8H, aromatic) and 10.15 (d, 2H, acidic).

b) In deuterium oxide medium

I (1.5 g) was dissolved in 25 ml of a 5% solution of sodium hydroxide in deuterium oxide, and left at

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room temperature for 30 min. The reaction was interrupted by acidification, the unreacted acid was recovered, crystallized from dilute ethanol and its ^{1}H-NMR (DMSO) spectrum was compared with that of pure starting acid. For **I** $\delta = 3.15$ (s, 2H, $-CH_2COO^-$), 3.95 (s, 2H, benzylic) while for the recovered acid there was about 15% decrease in the intensity of the signal corresponding to the benzylic hydrogens, which meant that H/D exchange took place.

*Action of sodium methoxide on **I** in absolute methanol*

The acid (0.58 g) was dissolved in dry methanol (25 ml), treated with 0.2 N sodium methoxide (25 ml). The mixture was refluxed for 24 h. No reaction took place. Acidification and dilution precipitated the starting acid.

Action of sodium hydroxide on 4-nitrosobenzaldehyde [16]

The reaction did not give the expected products, namely, 4-nitrosobenzyl alcohol and 4-nitrosobenzoic acid, but gave equimolecular quantities of 4,4′-diformylazoxybenzene and 4,4′-dicarboxyazoxybenzene.

Action of sodium hydroxide on some 4-nitrobenzyl, aryl sulphides

Each of the following compounds was treated with sodium hydroxide in 50% aqueous dioxane medium in a similar way to **I**. The reactions products are given in Table 1.

The procedure used to purify the 1,4-dioxane has been described elsewhere [17].

Kinetic procedure

The reaction of **I** and sodium hydroxide was followed by measuring the ultraviolet-visible absorption of the reaction at 420 nm using a Unicam 1805 SP spectrophotometer coupled with an ultrathermostate. One ml of each of the reactant solutions, **I** (2×10^{-3} M in appropriate dioxane-water mixture) and sodium hydroxide (2×10^{-1} M in water) were separately introduced into the two parts of the two compartment cell whose thickness was 0.437 Cm (Hellma, 238-QS) and thermostated for 15 min. After shaking the cell contents, 5 – 10 s, the absorption of the reaction mixture was recorded at suitable time intervals.

Results and Calculations

The reaction of aqueous sodium hydroxide on **I** was found to give, besides the already known 4,4′-diformylazoxybenzene (73.3%), two other acids, namely, 4,4′-dicarboxyazoxybenzene (8.41%) and a nitrone acid (**IV**) (12.74%).

The reaction was studied kinetically in different aqueous-dioxane media containing 5, 10, 20, 30, 40, and 50% (v/v) dioxane at 35, 45, 55 and 65°. The

Table 1. Products of the action of sodium hydroxide on some 4-nitrobenzyl, aryl sulphide in aqueous or in 50% aqueous dioxane.

Aryl group	Percipitate after heating and dilution	Material set free after acidification
phenyl [18]	4,4′-diformylazoxybenzene	thiophenol and 4,4′-dicarboxyazobenzene
4-methyl phenyl	4,4′-diformylazoxybenzene	4-methyl thiophenol and 4,4′-dicarboxyazobenzene
2-carboxy phenyl [20]	4,4′-diformylazoxybenzene	disulphide of 2-thiolbenzoic acid [21]
4-methoxy phenyl [19]	4,4′-diformylazoxybenzene	4-methoxy thiophenol and 4,4′-dicarboxyazoxybenzene
4-chloro phenyl [19]	4,4′-diformylazoxybenzene	4-chloro thiophenol and 4,4′-dicarboxyazoxybenzene
4-nitrobenzyl [22]	4,4′-diformylazoxybenzene	disulphide of 4-nitrobenzylthiol [23]

Table 2. Rate constants k_1 and k_2 for the consecutive reaction between sodium hydroxide and α-(4-nitrobenzylthio)-acetic acid in dioxane-water mixtures.

t [°C]	$k \cdot 10^4$ [s^{-1}]	dioxane [vol %]				
		10	20	30	40	50
35	k_1	2.47 ± 0.14	3.28 ± 0.29	1.81 ± 0.13	1.81 ± 0.15	1.45 ± 0.08
	k_2	0.90 ± 0.05	1.07 ± 0.08	2.65 ± 0.28	2.33 ± 0.24	1.91 ± 0.15
45	k_1	6.76 ± 1.24	5.97 ± 0.28	3.78 ± 0.21	3.54 ± 0.21	2.41 ± 0.16
	k_2	1.87 ± 0.39	2.42 ± 0.11	8.47 ± 0.73	6.44 ± 0.58	2.69 ± 0.21
55	k_1	12.19 ± 0.94	12.71 ± 1.25	9.05 ± 0.12	7.92 ± 0.37	5.82 ± 0.51
	k_2	3.48 ± 0.31	5.61 ± 0.54	12.06 ± 0.22	9.00 ± 0.61	3.71 ± 0.30
65	k_1	–	18.60 ± 0.82	20.28 ± 2.78	17.42 ± 2.59	9.10 ± 0.21
	k_2	–	7.05 ± 0.29	14.02 ± 1.80	11.03 ± 1.44	5.56 ± 0.61

Table 3. Thermodynamic parameters of activation at 35 °C.

Parameter	dioxane [vol %]				
	10	20	30	40	50
$\Delta G_1^{\ddagger}$ [kJ mol^{-1}]	97.00	96.34	97.83	97.85	98.34
$\Delta H_1^{\ddagger}$ [kJ mol^{-1}]	34.05	27.01	38.82	32.99	28.09
$-\Delta S_1^{\ddagger}$ [J mol^{-1} deg^{-1}]	204.27	225.09	191.51	210.51	227.97
$\Delta G_2^{\ddagger}$ [kJ mol^{-1}]	99.30	98.79	96.32	96.67	101.82
$\Delta H_2^{\ddagger}$ [kJ mol^{-1}]	24.66	29.91	23.04	24.70	18.95
$-\Delta S_2^{\ddagger}$ [J mol^{-1} deg^{-1}]	242.21	223.54	237.81	235.51	269.06

reaction course was followed by determining the absorption at 420 nm, at which there is no absorption by the starting acid but all the reaction products do absorb.

Although the ratio acid: alkali was 1:100, yet the kinetic results did not conform to a first-order rate equation. The reaction, by virtue of its complex nature, was considered to involve two consecutive irreversible first-order reactions of the type $\mathbf{I} \xrightarrow{k_1} \mathbf{II} \xrightarrow{k_2} \mathbf{III}$, where **I**, **II** and **III** represent starting material, intermediate and 4-nitrosobenzaldehyde, respectively, and k_1 and k_2 represent the rate constants of these two steps. **III** undergoes a Cannizzaro's disproportionation exhibiting third-order kinetics, second order in aldehyde and first order in base [16]. To calculate the rate constants from a set of experimental data, the time ratio method, developed by Swain [24] and then by Frost and Schwemer [25], was used. The steady state approximation treatment was applied to the intermediate **II**. The values of k_1 and k_2 are collected in Table 2 at the indicated temperatures.

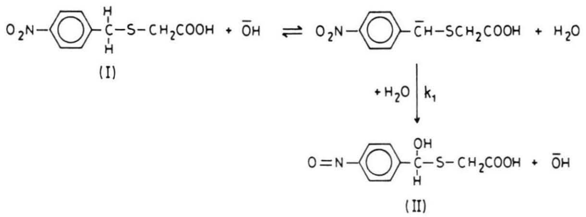
The calculated thermodynamic parameters of activation [26], $\Delta H^{\ddagger}$, $\Delta G^{\ddagger}$ and $\Delta S^{\ddagger}$ are collected in Table 3.

Discussion

In 1951 Iskander and Riad [8] reported a schematic mechanism for the action of aqueous sodium hydroxide on **I**, where 4-nitrosobenzyl alcohol or (α-hydroxy, 4-nitrosobenzylthio)-acetic acid (**II**) was expected to be formed according to either C-S fission or aci-formation taking the lead.

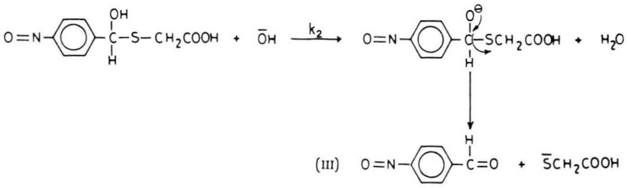
In the present work it was proved that **I** reacted with aqueous sodium hydroxide via a fast and reversible α-proton abstraction step as indicated by H/D exchange. A similar α-proton abstraction was reported to take place in 4-nitrobenzyl-halides [27], pyridinium salts [28], and sulphides [28] under similar conditions.

When **I** was boiled under reflux for a long time with sodium methoxide in anhydrous methanol, no reaction took place. Water is therefore essential for the reaction to give the intermediate **II**.



The same observation was noticed when 4-nitrophenyl acetic acid was boiled with sodium methoxide in anhydrous methanol, whereby no reaction took place, while in presence of water α-hydroxy, 4-nitrosophenyl acetic acid was postulated to be formed [6]. Values of k_1 (s^{-1}) for this step under different conditions are compiled in Table 2.

II undergoes a base promoted elimination reaction displacing $^-SCH_2COOH$ and giving rise to 4-nitrosobenzaldehyde.

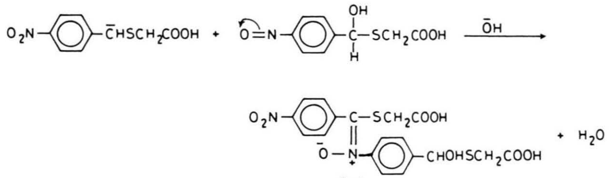


Values of k_2 (s^{-1}) for this step under different conditions are compiled in Table 2.

4-Nitrosobenzaldehyde, being soluble in aqueous dioxane in the presence of alkali, undergoes a Cannizzaro's disproportionation reaction to give rise to 4-nitrosobenzyl alcohol and 4-nitrosobenzoic acid. The latter acid is known to change in an alkaline medium very rapidly into 4,4′-dicarboxyazoxybenzene [16].

The kinetic behaviour of 4-nitrosobenzaldehyde with sodium hydroxide in aqueous-dioxane media under similar conditions as of the present investigation was found to exhibit third-order kinetics, not involving free-radicals, radical anions or radical chain mechanism [16]. The values of k_3 ($l^2\,mol^{-2}\,s^{-1}$) [16] are greater than those of k_1 and k_2 under the same conditions, meaning that the Cannizzaro's step is not rate determining in the present reaction.

4-Nitrobenzyl alcohol, formed via Cannizzaro's reaction, changes rapidly in the alkaline medium into 4-hydroxylaminobenzaldehyde, and this may either dimerise [29] or react with 4-nitrosobenzaldehyde to form 4,4′-diformylazoxybenzene [16]. The nitrone acid, isolated from the reaction between **I** and sodium hydroxide, is expected to be formed from the interaction between the anion of **I** and the intermediate **II** in the presence of alkali, thus affording evidence for the existence of **II**.



(IV)

The structure of this nitrone acid was confirmed by estimation of its nitrogen content, molecular weight determination, ^{1}H-NMR, IR and UV spectra. Such a nitrone is unable to react further with another molecule of **II** to give more complex structures, because this nitrone has no longer methylene group. Nitrone is known to be formed by different procedures, among which is the reaction between nitroso compounds and compounds having an active methylene group [11].

No free radicals nor radical anions are involved in the present mechanism since the reaction rate was not changed in the presence of benzoyl peroxide.

The values of the thermodynamic parameters of activation, i.e., the free energies $\Delta G^{\ddagger}$, the enthalpies $\Delta H^{\ddagger}$ and the entropies $\Delta S^{\ddagger}$ for the two steps are given in Table 3. $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ do not change much as the dioxane content of the solvent mixture is increased, and the compensation effect between $\Delta H^{\ddagger}$ and $T\,\Delta S^{\ddagger}$ plays an important role in keeping $\Delta G^{\ddagger}$ more or less constant, in other cases [30, 31]. Moreover the values of the entropy of activation of the second step, $\Delta S_2^{\ddagger}$, are lower than those for the first step, $\Delta S_1^{\ddagger}$, indicating that the activated complex produced during the elimination of $^-SCH_2COOH$ from intermediate **II** is more solvated than that formed from **I**.

The six 4-nitrobenzyl, aryl sulphides, described in Table 1, were treated with sodium hydroxide in 50% aqueous dioxan medium. All of them gave 4,4′-diformylazoxybenzene as the main product, which was precipitated from the reaction medium either alone or after dilution. After filteration and acidification of the alkaline filtrate either 4,4′-dicarboxyazoxybenzene or the corresponding azo-acid was precipitated besides a mercaptan which was set free, or its sulphide.

The mechanism presented for the reaction between sodium hydroxide and **I**, in aqueous dioxane can be applied to the present cases. Thus alkaline aqueous dioxane media change the 4-nitrobenzylthio-system into 4,4′-diformylazoxybenzene and 4,4′-dicarboxyazoxybenzene.

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