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OXIDATIVE REARRANGEMENT OF CYANOHYDRINS WITH MIGRATION

OF CYANO GROUP: MECHANISM OF INITIATION BY

S₂O₈²⁻-Ag⁺ SYSTEM

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The oxidative rearrangements of cyanohydrins (CH) with 1,4-migration of the cyano group are known, which proceed under the influence of the systems: $Pb(OAc)_4-I_2$ [1] and $S_2O_8^{-}-Ag^{+}$ [2]. The mechanism of the first system was discussed in [3-5], and that of the second system in [2]. In the latter case it was postulated that only the Ag ions take direct part in the oxidation of the CH and the generation of radicals from it, although the possible involvement of the intermediately formed sulfate ion-radicals SO_4^{-} in this reaction cannot be excluded without experimental verification. The purpose of the present paper was to check the correctness of this assumption and refine the mechanism of initiating the oxidative rearrangement of CH by the $S_2O_8^{-}-Ag^+$ system.

To solve the given problem the cyanohydrins of 2-hexanone (Ia), 2-heptanone (Ib), and 2-octanone (Ic) were oxidized with sodium peroxydisulfate in the absence of Ag⁺ ions at 60° (Table 1). It proved that the oxidative rearrangement of CH also proceeds without the involvement of Ag⁺, but in the case of CH (Ib) and (Ic) it is nonregioselective, and specifically it proceeds with 1,4- and 1,5-migration of the cyano group. Under analogous conditions CH (Ia) undergoes regioselective oxidative isomerization to 5-cyano-2-hexanone (IIa):

It should be mentioned that the oxidative rearrangement of CH with 1,5-migration of the CN group was observed for the first time.

The nonregioselective character of the oxidation of CH (Ib) and (Ic) under the influence of the sulfate ion-radicals generated from $S_2 O_8^{2-}$ testifies to a different mechanism

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TABLE 1. Oxidation of Cyanohydrins of 2-Hexanone (Ia), 2-Heptanone (Ib), and 2-Octanone (Ic) with $Na_2S_2O_8$ and $Na_2S_2O_8$ -AgNO₃ System*

| Cyanohydrin | Oxidizing agent | Time, h | CH conver- sion, % | Yield of cyano- alkanone, % | |
|--|---|----------------------------|----------------------------------|----------------------------------|-------------------------|
| | | | | (II) | (III) |
| (Ia) † (Ia) (Ib) (Ib) (Ic) † (Ic) | $\begin{array}{c} S_{2}O_{8}^{2-}-Ag^{+}\\ S_{2}O_{8}^{2-}\\ S_{2}O_{8}^{2-}-Ag^{+}\\ S_{2}O_{8}^{2-}\\ S_{2}O_{8}^{2-}-Ag^{+}\\ S_{2}O_{8}^{2-}-Ag^{+}\\ S_{2}O_{8}^{2-}\end{array}$ | 3 6 3 6 3 6 | 95 87 88 80 84 85 | 60 55 90 40 80 23 | - - 45 - 23 |

*20 mmoles of CH, 30 mmoles of $Na_2S_2O_8$, 3 mmoles of AgNO₃, 20 mmoles of NaHSO₄ (CH stabilizer), and 300 ml of water, at 60°C. +Data from [2].

for their reaction with CH when compared with the oxidative system $S_2O_8^{2-}-Ag^+$, where reaction is regioselective and only 5-cyano-2-heptanone (IIb) is formed from CH (Ib), and 5-cyano-2-octanone (IIc) from CH (Ic) [2]. This important difference in the results of oxidizing CH (Ib) and (Ic) by $S_2O_8^{2-}$ ions and the $S_2O_8^{2-}-Ag^+$ system also permits concluding that in the reaction catalyzed by Ag^+ ions the sulfate ion-radicals practically do not take part in the direct oxidation of CH and the generation of radicals from them. Otherwise, together with the 5-cyano-2-alkanones, the 6-cyano-2-alkanones would be formed in this reaction.

The conversion of CH (Ia-c) to ketonitriles (IIa-c) and (IIIb, c) under the influence of SO4⁻⁻ most probably proceeds by the scheme



Most of the steps indicated in this scheme have been substantiated and confirmed previously, for example, the transformations of type (A) \rightarrow (B) \rightarrow (C) \rightarrow (II) in [3-7], and (D) \rightarrow (E) \rightarrow (F) \rightarrow (III) in [6, 7], which permits limiting ourselves here to a discussion of the steps (Ia-c) \rightarrow (A) and (Ia-c) \rightarrow (D). It is known that SO₄⁺ has a strongly expressed electrophilic character [8] and when reacted with organic substrates it efficiently cleaves H from hydrocarbon groupings [8, 9]. In the case of nitriles the electron-acceptor cyano group, due to the electrostatic repulsion of the electrophilic sulfate ion-radicals, hinders the cleavage of H from the hydrocarbon groupings of CH (Ia-c) adjacent to the cyano group. As a result the cleavage of H by the SO_4 ion-radicals probably occurs mainly from the CH_2 groups at the end of the alkyl chains of these cyanohydrins. Such an assumption in the case of CH (Ic) postulates the formation of three radicals, namely (A), (D) ($R = C_2H_5$), and MeCH(CH2)4C(OH)(CN)Me (G). However, the oxidation product of CH (Ic) contained only cyanooctanones that are derivatives of radicals (A) and (D) (R = Et) (see scheme). 7-Cyano-2octanone was not detected, which is apparently related mainly to the substantially slower cyclization rate of radical (G) when compared with (A) and (D) (R = Et), since a sevenmembered iminyl radical should be formed in this case. The much slower cyclization rate of the 6-cyanoalkyl radicals when compared with the 4- and 5-cyanoalkyl radicals was mentioned earlier in [10].

| anu | ولاندندني | 0) | | | | | |
|--------------|------------------------|-----------------------------------|------------------------|---------------------|-----------------------|---|--|
| noal- | b₊p₊, °C | Empiri- cal | Found Calculated, % | | , % | PMR spectrum (δ,ppm) | Mass spectrum (m/z, relative in- |
| Cyai kanc | mm Hg | formula | С | Ħ | N | | tenarcy, 10) |
| (IIa) | 115–116 (15) | C7H11NO | <u>66,60</u> 67,20 | <u>8,71</u> 8,80 | <u>11,32</u> 11,20 | 1,40 d (3H, CH ₂), 1,75 m (2H, CH ₂), 2,16 s (3H, CH ₃ CO), 2,65 m (2H, CH ₂ CO), 2,85 m (1H, CHCN) | $\begin{array}{c} 125(56,M^+),\\ 124(26),110(72),\\ 82(73),68(68),\\ 55(73),44(78),\\ 43(100),39(64) \end{array}$ |
| (II b) | 105 (5) | C8H13NO | <u>69,60</u> 69,06 | 9,20 9,35 | <u>10,40</u> 10,07 | 1,02 t (3H, CH ₃), 1,4-1,85 m (4H, CH ₂), 2,05 s (3H, CH ₃ CO), 2,5 ^t (2H, CH ₂ CO), 2,80 m (1H, CHCN) | $\begin{array}{c} 139(20,M^+),\\ 124(9),111(6),\\ 96(10),82(20),\\ 71(10),69(55),\\ 68(30),58(100),\\ 57(10),55(29),\\ 54(35) \end{array}$ |
| (IIIb) | 1 05–110 (5) | | | | | 1,23 d (3H, CH₃), 1,4-1,73 m (4H, CH₂), 2,05 s (3H, CH₃CO), 2,5 t (2H, CH₂CO), 2,8 m (1H, CHCN) | $\begin{array}{c} 139(20,M^+),\\ 124(8),111(8),\\ 97(18),96(40),\\ 83(8),82(25),\\ 69(55),68(31),\\ 58(100),55(42),\\ 54(38) \end{array}$ |
| (11 c) | 117-118 (8) | C ₉ H ₁₅ NO | <u>69,80</u> 70,59 | 9,76 9,80 | 9,58 9,15 | 0,9 t (3H, CH ₃), 1,3-1,85 m (6H, CH ₂), 2,05 s (3H, CH ₃ CO), 2,55 t (2H, CH ₂ CO), 2,8 m (1H, CHCN) | $\begin{array}{c} 153(14,M^+),\\ 138(8),111(9),\\ 110(7),96(22),\\ 83(31),82(10),\\ 71(23),69(19),\\ 68(15),67(8),\\ 59(9),58(100),\\ 55(35),54(45) \end{array}$ |
| (1110 | 130–135 (6) | | | | | 1,0 t (3H, CH ₃) 1,4-1,7 m (6H, CH ₂), 2,05 s (3H, CH ₂ CO), 2,42 t (2H, CH ₂ CO), 2,8 m (1H, CHCN) | $ \begin{array}{c} 153 (5, \mathrm{M^+}), \\ 138 (25), 125 (17), \\ 110 (11), 96 (17), \\ 93 (5), 85 (6), \\ 84 (7), 83 (42), \\ 82 (31), 71 (13), \\ 69 (28), 68 (18), \\ 67 (9), 58 (100), \\ 55 (33), 54 (21) \end{array} $ |

TABLE 2. Properties of 5- and 6-Cyano-2-alkanones (IIa-c) and (IIIb. c)

EXPERIMENTAL

The GLC analysis was run on an LKhM-8MD chromatograph equipped with a flame-ionization detector, in an N₂ stream, and using a 150×0.3 cm stainless steel column packed with 10% Carbowax 20M deposited on Celite 545 (0.16-0.20 mm), treated with H₃PO₄ as described in [11]. For the preparative separation of the compounds we used a preparative attachment to the indicated chromatograph, a 200×1 cm copper column packed with 10% PMPS deposited on Chromosorb A, and He as the carrier gas (60 ml/min). The PMR spectra were measured on a Tesla BS-497 spectrometer (100 Hz) using CCl₄ as the solvent and HMDS as the internal standard. The mass spectra were respectively taken on Varian MAT CH-6 and MAT CH-111 (Gnom) instruments with direct and chromatographic insertion of the sample into the ion source, and an ionizing electron energy of 70 and 80 eV.

The oxidizing agent $(Na_2S_2O_8)$ and catalyst $(AgNO_3)$ were of analytical grade. The solvent was monodistilled water.

<u>2-Hexanone Cyanohydrin (Ia).</u> Cyanohydrin (Ia) was obtained by reacting a mixture of 2-hexanone and aqueous KCN solution with conc. HCl [12], and was purified by vacuum-distillation. Prior to distillation a small amount of H_3PO_4 was added to the crude (Ia) for its thermal stabilization. The yield of (Ia) was 70%, bp 107° (17 mm), n_D^{20} 1.4217 (cf. [13]) based on the titration data using standard NiSO₄ solution as described in [14] the purity was 95%.

<u>2-Heptanone-Cyanohydrin (Ib) and 2-Octanone Cyanohydrin (Ic).</u> The cyanohydrins were synthesized by reacting KCN, MeCOOH, and the ketone in a two-phase ether-water system [15], and were purified by vacuum-distillation in the presence of H_3PO_4 . We obtained: (Ib),

70% yield, bp 105° (5 mm), n_D^{20} 1.4265, purity 97% (Ic), 65% yield, bp 128° (8 mm), n_D^{20} 1.4321, purity 90% [16].

Oxidation of CH (Ia-c). With efficient stirring, a mixture of the reactants and water (see Table 1) was heated for 6 h (3 h in the presence of AgNO₃) at 60°. Based on the iodometric titration data, a part of the cooled Na2S208 mixture decomposes to the extent of 85% under these conditions, and completely in the presence of AgNO3. Then the mixture was extracted with ether (100 ml×3), and the amount of unreacted CH in the extract was determined by titration with standard NiSO4 solution and its conversion was calculated (see Table 1). The remainder of the extract was evaporated. The residue was treated with 10 drops of Et₃N and after 16 h the amount of ketonitriles (IIa-c) and (IIIb, c) in it was determined by GLC, using their nearest homologs as the internal standard.

For the preparative preparation of (IIa-c) and (IIIb, c) we took 60 mmoles of the CH, 90 mmoles of Na₂S₂O₈, either 0 or 9 mmoles of AgNO₃, 60 mmoles of NaHSO₄, and 100 ml of water. In these experiments the CH conversion was 40%. The formed ketonitriles were isolated by vacuum-distillation, cyanoalkanones (IIb) and (IIIb), and also (IIc) and (IIIc), as their mixtures, which were then separated by preparative GLC (Table 2).

CONCLUSIONS

1. The oxidation of cyanohydrins by the $S_2O_8^{2-}$ -Ag⁺ system begins with the reaction of the OH group of the cyanohydrin with silver ions, which results in the formation of 1-cyanoalkoxyl radicals. The sulfate ion-radicals practically do not take part in the direct oxidation of cyanohydrins.

2. The initiation of the oxidation of cyanohydrins by peroxydisulfate in the absence of Ag⁺ ion proceeds via the cleavage of H atoms from the hydrocarbon groupings of the cyanohydrin by the sulfate ion-radicals. The 4(5)-hydroxy-4(5)-cyanoalkyl radicals, formed as a result of the 1,4- and 1,5-migration of the cyano group and subsequent oxidation, are converted to 5- and 6-cyanoalkanones. The oxidative rearrangement of alkanone cyanohydrins to 6-cyanoalkanones was observed for the first time.

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