THE STRUCTURES OF THE HYDROGEN HALIDE SALTS OF SUCCINONITRILE AND RELATED COMPOUNDS

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Abstract- The constitutions of the hydrogen halide salts of succinonitrile are shown to be 2-amino-5.5dihalo-1-pyrrolinium halides (II) and are thus the next lower homologs of the corresponding salts of glutaronitrile.¹ On the other hand the homologous 2,3-diphenyl-succinonitrile when treated with hydrogen bromide leads to 5-amino-2-bromo-3,4-diphenyl-3<u>H</u>-pyrrole hydrobromide (IX) which is tautomerically different from the analogous salt obtained previously from 2,5-diphenylglutaronitrile. The hydrolysis of IX has been examined and the products completely characterized. 2,2,3,3-Tetramethylsuccinonitrile in ether affords 5-imino-3,3,4,4-tetramethyl-2-pyrrolidone hydrobromide when treated with anhydrous hydrogen bromide whereas 1,1'-dicyano-1,1'-bicyclohexyl is unreactive towards this gas, in aprotic solvents.

Succinonitrile-hydrogen halide adducts

In the preceding publication¹ we discussed in some detail the structures of the glutaronitrile-hydrogen halide salts. These proved to be derivatives of 2,3,4,5-tetrahydropyridine having structure I (X=Cl, Br, or I). In this paper we present the results of our studies on the hydrogen halide salts derived from succinonitrile and certain of its derivatives.

The salts of succinonitrile itself were obtained in precisely the same way as we had obtained those of glutaronitrile. In stoichiometry we found that they corresponded



to the latter salts having the empirical formula $(CH_2 \cdot CN)_2 \cdot 3HX$, (X = Cl, Br, or I)in contradistinction to recent Russian work² which claimed the chlorides to be complexes containing only two molecules of hydrogen chloride. Their IR spectra (Fig. 1) by comparison with those of I, were such that, at an educated guess, they could tentatively be assigned the same general structure with, of course, one less methylene



¹ L. G. Duquette and F. Johnson, Tetrahedron 23, 4517 (1967).

² E. N. Zil'berman and P. S. Pyryalova, Zh. Org. Chem. 1, 983 (1965); See also H. Blitz, Ber. Disch. Chem. Ges. 25, 2533 (1892).

group in the ring. Again, as with I, the free bases of these salts could not be obtained by treatment with mild alkali because of concomitant hydrolysis. In the presence of moisture they afforded the iminoimide hydrohalides III, or the free base of these compounds if mild alkali were present. The latter compound itself also proved to be



FIG. I. IR spectra of (a) IIa (b) IIb (c) IIc and (d) IId in Nujol mull.

unstable on long standing in the presence of moisture releasing ammonia and being converted to succinimide. No trace of a compound corresponding to IV or V could be found in the initial hydrolysis. Even more disappointing was the fact that treatment of any one of these salts with acetic anhydride did not lead to a hydrohalide of IV or V. On long stirring with this reagent the salts simply deteriorated producing a considerable amount of an intractable greenish-brown powder. Thus in this sense IIa-c did not correspond to Ia-c because the latter with this reagent gave good yields of the dehydrohalogenation products VI (X = Cl, Br, or I). This difference in the chemical behavior of the two sets of salts prompted a more detailed investigation of the structures of II, since it was felt that the loss of hydrogen halide from these compounds should be facile because of the potentially aromatic nature of the product.

We approached this problem as we had done in the case of I, again using only the chloro and bromo compounds IIa and IIb in the investigation since the iodo homolog (IIc) was insoluble in all of the solvents suitable for spectroscopic work.

Addressing ourselves to the problem of organically-bound versus inorganicallybound halogen in these compounds. IIb was treated with liquid hydrogen fluoride.¹ The resulting salt IId, gave an elemental analysis which corresponded well with the formula $(CH_2CN)_2$ ·4HF, thus implying that IIb contained two organically-bound bromine atoms and one ionic bromine atom.¹ Treatment of IIb with liquid hydrogen chloride confirmed this; the salt that was obtained analysed for the formula $(CH_2CN)_2$ 2HBr·HCl, while its infrared spectrum was barely distinguishable from that of IIb.

The fluorine resonance spectrum³ of IId in liquid SO₂ showed a simple triplet centered at +70.6 ppm (J = 11 c/s) typical of the $-CH_2CE_2$ - group, and a broad singlet at 111.1 ppm for the HE₂ anion, thus again indicating a structure analogous to I for these compounds.

The PMR spectra of these salts in liquid SO₂ at -60° showed some interesting features. In the high field area, IIa showed a singlet sharp peak⁴ at 3.40 ppm which integrated for four protons thus indicating the hydrogens of the methylene groups to have the same chemical shift. However, in the spectrum of IIb, these four protons



FIG. 2. NH proton resonance of (a) IIa and (b) IIb in liquid SO₂ at -60°

- ³ Details of the methods used in obtaining the fluorine and proton resonance spectra discussed here are contained in footnote 20 of the previous paper.
- In all samples of the chloro compound (IIa) a small peak was also present at 6:34 ppm (-60°). We consider this is due to an impurity since it integrated for less than half of one proton and unlike other peaks in the spectrum, its location was very temperature dependent (e.g. 5:96 at -30°). It also became very much sharper as the temperature increased.

showed a symmetrical octet centered at 3.5 ppm (J = 5 c/s). The fluoro compound on the other hand exhibited a complex multiplet in the PMR spectrum centered roughly at 3.0 ppm. These three spectra thus fall approximately into line with the relative deshielding effects of CX_2 (X = halogen) adjacent to a methylene group (Br > Cl > F).¹

In the NH proton resonance region of the spectra of IIa and IIb the patterns (Fig. 2) are similar, in one respect, to those of I (X = Cl or Br). They both show a low field singlet (at 10.26 and 9.63 ppm; X = Cl and Br resp.). However they are dissimilar in the sense that in the upfield region of this area these spectra possess only a singlet⁵ (at 8.50 and 8.17 ppm; X = Cl and Br resp.) which integrates for two protons, vis à vis the corresponding salts of I which show two singlets that coalesce with rising temperature. An increase in the temperature merely causes broadening of both NH peaks in the case of IIa and IIb, which is undoubtedly due to more rapid proton exchange.

Despite the differences in the 5- and 6-membered series the NMR patterns as they stand still support a formulation such as II-I for these salts rather than II-II or II-III.



because of the relative dispositions of the NH peaks and the ratio of their integrals. If II-III were the correct structure one would expect the positions of the peaks to be reversed, whereas II-II would lead to a singlet corresponding in area to three protons, or a triplet $(J \sim 60 \text{ c/s})^6$. The only point of structural difference then between the hydrogen halide salts of glutaronitrile and succinonitrile is that in the latter the exocyclic C-N group has much less double bond character than that in the former, at any one temperature in the range -60 to -30° . The question as to why acetic anhydride causes the elimination of hydrogen halide from I but not from II, remains unanswered.

Substituted succinonitrile-hydrogen halide adducts

The reaction of hydrogen bromide with two alkylated derivatives of succinonitrile namely the 2,2,3,3-tetramethyl succinonitrile and the 1,1'-dicyano-1,1'-bicyclohexyl compounds was also examined. The latter could not be induced to react at all in benzene or ether, starting material alone, being recovered. The former on long standing in ether solution gave, in good yield, a highly crystalline precipitate which proved to be, not a homolog of II, but merely the hydrolysis product to which, on the basis of analytical and spectroscopic data, we loosely assign structure VII. The oxygen in this molecule undoubtedly originates in the solvent, being transferred by way of water from the hydrogen bromide cleavage of the diethyl ether. Neutralization of VII gave the free

³ It should be noted that at very high concentrations both IIa IIb do show three peaks in the NH region each integrating for one proton. However, the upfield pair in this case does not coalesce at all with rising temperature (-60 to -30°) but does so with decreasing concentration. Under these conditions we believe we are dealing with association timers of II.

⁶ J. D. Roberts, J. Am. Chem. Soc. 78, 4495 (1956); R. J. Gillespie and T. Birchall, Canad. J. Chem. 41, 148 (1963).

base identical in melting point with that obtained by Dougherty⁷ by the action of alkali on 2,2'azobisisobutyramidine hydrochloride. No further work was done with these nitriles.



We next turned our attention to the previously described⁸ hydrogen bromide salt (IX) derived from 2,3-diphenyl succinonitrile (VIII). Hot dichloroacetic acid turned out to be a much more suitable medium for the preparation of IX rather than the diethyl ether used by Osborn.⁸ and in this solvent also, the corresponding salts derived from both 2,3-bis(4'-chlorophenyl) and 2,3-bis(3',4'-dimethoxylphenyl)succinonitrile were easily prepared. All structural investigations were carried out with IX since its immediate precursor was the most readily available dinitrile.

Elemental analysis confirmed the formula $C_{16}H_{12}N_2 \cdot 2HBr$ assigned to IX by Osborn.⁸ and our infrared spectrum was identical to that reported by him. However, further physicochemical investigations were hindered by the lack of solubility



FIG 3. NMR Spectrum of IX in Trifluoroacetic Acid

* J. H. Osborn, Ph.D. Thesis, University of Minnesota 1958; Diss. Abstr. 19, 2475 (1959).

⁷ T. J. Dougherty, J. Am. Chem. Soc. 83, 4849 (1961); see also N. O. Brace [J. Org. Chem. 28, 3093 (1963)] who obtained the hydroiodide corresponding to VII when attempting the free radical addition of 2-iodo-perfluoropropane to cyclohexene in the presence of azobisisobutyronitrile.

of IX in anything but strong acids. Even the NMR spectrum (Fig. 3) of IX in trifluoroacetic acid was uninformative. Assuming the small broad peaks at lower field to represent one proton apiece, the multiplet at ~ 7.3 ppm then integrates for 11–12 protons. The former can, on the basis of past experience, be assigned to NH protons. The latter while it represents largely the ten aromatic protons, must also contain at least one other proton absorption perhaps of the NH type. The possibility also exists that the doublet at 7.13 ppm is not part of the aromatic absorption but represents a highly deshielded CH proton.



Possible structures for IX are IX-I, IX-II, IX-III and IX-IV. All would satisfy the NMR requirements except IX-I which would be expected to show two coupled doublets. Another feature which makes IX-I unlikely is the bright yellow color of IX. Although true examples of this bisimine chromophore are apparently unknown, one would not expect it to be colored.⁹

Using IR evidence alone Osborn⁸ had selected structure IX-II for IX. Our own investigations, however, suggest that IX-IV is a much more acceptable formulation, the most useful evidence in our case, coming from hydrolysis experiments.

Treatment of IX with water led exothermically, to a colorless salt X, which analysed well for $C_{16}H_{14}N_2O.2H_2O.HBr$. Its NMR spectrum, taken in $(CD_3)_2SO$, showed three broad peaks of equal area at 8.51, 9.43 and 10.50 ppm, which must be ascribed to three NH protons, and a complex multiplet having a major peak at 7.33 ppm, for the ten aromatic protons. Of greater interest was the singlet at 6.45 ppm (one proton) and a very broad symmetrical band centered at 3.42 ppm (five protons). The latter obviously represented the protons of the water of hydration together with another OH or NH proton. This was confirmed by the quenching of IX with D₂O. The NMR spectrum of the product showed the almost complete absence of this feature. Essentially only the aromatic protons and that proton exhibiting a peak at 6.45 ppm remained intact. This last point is highly significant because if no C- D bond is formed in this hydrolysis, then the system reacting with the water must be a

Br -C=N - group! This thus eliminates structural possibilities IX-II and IX-III. The other implication is that the hydrolysis product X must be represented as shown below and not as a dihydrate of the free base of IX-II as claimed originally by Osborn.⁸



⁹ The closely related 3-amino-1,3-dibromoacryliminium bromide is colorless. [E. Allenstein and P. Quis. Ber Disch. Chem. Ges. 97, 1857 (1964)].

Treatment of X with mild base gave a material XI whose NMR spectrum in $(CD_3)_2SO$ surprisingly displayed a pair of coupled doublets (J = 4.5 c/s) at 3.64 and 4.16 ppm, respectively (total area = two protons). In the low field region the multiplet integrated for twelve protons and thus must represent both the aromatic protons and the two NH protons. Consequently XI can be formulated as shown below, although the exact tautomeric disposition of the amidine function is unknown. As expected, when either IX or XI was boiled with water, the imide XII resulted. Its NMR spectrum showed a singlet peak at 4.35 ppm due to the benzylic protons.



Unexpectedly, treatment of XI with dry hydrogen bromide gas did not regenerate anhydrous X but afforded a new non-crystalline hydrobromide (XIII). Even the subsequent addition of water did not produce X^{10} XIII must be represented as shown above since the elemental analysis was roughly in agreement with this formula and its NMR spectrum in CDCl₃ like that of XI, showed a pair of coupled doublets (J = 6 c/s) at 4.07 and 4.79 ppm, respectively, for two protons. Aromatic protons¹¹ appeared as a sharp band at 7.29 ppm (10 protons) and at lower field three broad peaks could be observed at 9.61, 10.31 and 12.04 ppm, each of which integrated for a single hydrogen atom. The latter pattern was very similar to that seen^{1.10} for the



 $N\underline{H}$ protons of I and XIV. Although XI gave an amorphous hydrobromide, its crystalline picrate, analysed well, and gave an NMR spectrum which closely resembled that of XIII, disregarding the aromatic protons due to the picrate anion.

The evidence then, while not absolutely conclusive, supports IX-IV for the hydrogen bromide adduct of 2,3-diphenylsuccinonitrile, and X for its initial hydrolysis product. Only a discussion of their fine structure remains.

¹⁰ This implies that X represents the kinetic, and XIII the thermodynamic product of hydrolysis of IX. In the case of X there appears to be no mechanism available for its facile isomerization to XIII, in a strongly acid medium.

¹¹ H. T. Miles, R. B. Bradley and E. D. Becker, *Science* 142, 1569 (1963); E. D. Becker, H. T. Miles and R. B. Bradley, J. Am. Chem. Soc. 87, 5575 (1965).

Considering X first, the simplest structure suggested by the facts is X-I.



We presume that X is formed by protonation of the oxygen atom of the hypothetical

free base XV, and that it is this $H = \dot{O}^{-1}C_{\frac{1}{2}}$ system which is solvated by the water

of hydration. If this proton is rapidly exchanging with the water this would account for the appearance in the NMR spectrum (*vide supra*) of the broad band at 3.42 ppm representing five protons. The positions of the N<u>H</u> proton peaks could also be accommodated by this structure. The one at lowest field corresponding to the more acidic proton of the lactam, and the other two being due to the NH₂- proton function which experiences restricted rotation.

The exact distribution of the NH protons in IX is difficult to pin down. However, if it is presumed (a) that in trifluoroacetic acid solution the NMR absorptions of the benzylic proton and one of the NH protons both lie in the aromatic proton region (where, as we have noted above, the peaks integrate for 11–12, and not 10 protons)



and (b) that the rate of rotation about the exocyclic C = N bond is very slow (which is reasonable because of the proximity of the phenyl ring), then one possible and logical structural choice to fully describe IX is IX-V.

An alternate choice, namely IX-VI, seems equally admissable since the separation of the two visible NH proton peaks is 65 c/s, close to that expected for N^{14} quadrupole splitting of protons of an ammonium group.⁶ The third component of this triplet is easily accommodated as being 65 c/s upfield, buried under the aromatic protons.

Further work on the structure and reactions of these interesting compounds will be reported in future publications.

EXPERIMENTAL

M.ps were determined on a Fisher-Johns m.p. block and are uncorrected. IR spectra were measured as Nujol mulls on a Baird instrument model No. 4-55. NMR spectra were recorded using a Varian A56-60 spectrometer.

Cyclization of the dinitriles. Unless otherwise stated these were carried out as described for glutaronitrile in the preceding paper.¹

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2-Amino-5,5-dibromo-1-pyrrolinium bromide (11b). Succinonitrile (40 g; 0.05 mole) in dry benzene (200 ml) was treated with dry HBr until precipitation of solid ceased. The material was removed, washed with dry ether, then dried under a stream of dry N_2 . The resulting white solid, 11b, (14-78 g; 0.0457 mole; 91-5°, yield) had no definite m.p. It turned dark grey at 120-125° then decomposed to a black viscous liquid at 135°. (Found: C, 150; H, 2:2; Br, 74-1; N, 8-7. Calc. for C₄H₇Br₃N₂: C, 149; H, 2:2; Br, 74-3; N, 8-7°,)

2-Amino-5,5-diiodo-pyrrolinium iodide (11c). This was prepared in the same way as the bromide above, except that the final product was washed with benzene rather than ether. The dry salt was an off-yellow colored powder m.p. ~ 117 120° (becoming orange colored at 90°), yield, 83.5°, (Found: C. 10.6; H. 1.8; 1, 82.2; N. 6.1. Calc. for C₄H₇N₂I₃: C. 10.4; H. 1.5; I. 82.1; N. 6.0°,)

2-Amino-5,5-dichloro-t-pyrrolinium chloride (IIa). This salt was prepared according to the method of Zil'berman and Pyryalova.² It was obtained in 98°_{\circ} yield as a highly crystalline solid which turned to a grey color at ~75°, but did not melt up to 200°. (Found : C, 25:0; H, 4:1; Cl. 56:2; N, 14:5; Calc. for C₄H₇Cl₃N₂: C, 25:4; H, 3:72; Cl. 56:1; N, 14:8°₀.)

2-Amino-5,5-difluoro-1-pyrrolinium bifluoride (11d). 2-Amino-5,5-dibromo-1-pyrrolinium bromide (3:1 g; 7:34 mmole) was treated with an excess of dry liquid HF for about 1 hr. The soln was allowed to evaporate to dryness and the resulting glass was then triturated with ether to give 11d as a white crystalline salt (1:0 g; 6:25 mmole; 85°_{\circ} yield). This compound proved to be very hygroscopic and heat sensitive. At 47–49 it began to yellow, melted to an opalescent liquid at 52-54°, resolidified at 65–67° and blackened with gas evolution above 185°. (Found: C, 30:0; H, 5:30; F, 47:2; N, 17:4. Calc. for C₄H₈F₄N₂: C, 30:0; H, 5:04; F, 47:5; N, 17:5°₀.)

2-Amino-5,5-dibromo-1-pyrrolinium chloride. A sample of IIb (4.3 g; 13.3 mmole) was treated with a large excess of liquid HCl and the soln kept at $\sim -100^{\circ}$ for 2 hr. Evaporation of the HCl left a quantitative yield of the desired product as a white crystalline salt. (Found: C, 17.6; H, 2.7; halogen, 68.0; N, 9.8. Calc. for C₄H-Br₂ClN₂: C, 17.3; H, 2.5; halogen, 70.1; N, 10.1°₆.)

5-Imino-3.3.4.4-tetramethyl-2-pyrrolidone hydrobromide (VII). Treatment of tetramethylsuccinonitrile (2.0 g; 1.47 mmole) in ether with dry HBr did not lead to any immediate ppt. The mixture was then stored at -10° for one week during which time crystals of the title compound slowly deposited. The colorless product (2.14 g; 0.91 mmole; 62 $^{\circ}$, yield) had m.p. 283–286° (subliming slowly over 200°). Its IR spectrum showed bands at 5.56, 5.86, 6.21, 7.11, 7.66, 8.54, 8.80, 8.94, 9.13, 12.27, 13.16, 13.90, 14.80, 15.82 and 18.40 μ . (Found: C, 40.5; H, 6.50; Br, 34.0; N, 11.9. Calc for C₈H₁₃BrN₂O: C, 40.9; H, 6.40; Br, 34.0; N, 11.9 $^{\circ}$, N



5-Amino-2-bromo-3,4-diphenyl-3H-pyrrole hydrobromide (1X). 2,3-Diphenylsuccinonitrile (7.0 g; 31.7 mmole) was dissolved in dichloroacetic acid (100 ml) at 70°. The hot soln was then added dropwise to a saturated soln (45 ml) of HBr in AcOH. When the mixture had attained room temp, ether (300 ml) was added, and thereafter a yellow ppt began to form. Stirring was continued for 30 min and the crystalline product was then removed by filtration, washed with ether and dried. The material (11.1 g; 28.2 mmole; 89°_{o} yield) obtained in this way was pure m.p. 180–190° (dec). (Found: C, 48.9; H, 3.6; Br, 40.6; N, 70. Calc for C₁₀H₁₄Br₂N₂: C, 48.8; H, 3.6; Br, 40.6; N, 71.°_o)



5-Amino-2-bromo-3,4-bis(4'-chlorophenyl)-3H-pyrrole hydrobromide. By the use of the procedure for the preparation IX, 2,3-bis(4'-chlorophenyl)succinonitrile afforded a 62.6% yield of the title compound. The latter was obtained as a bright yellow crystalline material m.p. 178° (dec). (Found: C, 41.4; H, 2.70; Br, 34.4; CL, 15.3; N, 6.1. Calc. for $C_{16}H_{12}Br_2Cl_2N_2$: C, 41.5; H, 2.6; Br, 34.5; CL, 15.3; N, 6.1°%)

5-Amino-2-bromo-3,4-bis(3',4'-dimethoxyphenyl-3H-pyrrole hydrobromide. Using the procedure for the preparation of IX, 2,3-bis(3',4'-dimethoxyphenyl)succinonitrile afforded the title compound in quantitative yield as a bright yellow crystalline powder m.p. 140–145 (dec). (Found: C, 46:5; H, 4:5; Br, 31:2; N, 5:6. Calc. for $C_{20}H_{22}Br_2N_2O_4$: C, 46:7; H, 4:3; Br, 31:1; N, 5:5°). This compound showed IR bands at 3:28. 5:96, 6:32, 6:60, 6:99, 7:08, 7:88 -7:94, 8:17, 8:42, 8:50, 8:70, 8:76, 9:75, 11:53, 12:05, 12:27, 12:91, 13:35 μ .

2-Amino-3,4-diphenyl-5-oxo-2-pyrroline hydrobromide dihydrate (X). 5-Amino-2-bromo-3,4-diphenyl-3<u>H</u>-pyrrole hydrobromide (0.5 g; 1.27 mmole) was added to water (5 ml). The material turned from yellow to white almost immediately. After a few min the crystalline product (0.3 g; 0.82 mmole; 64° , yield) was removed by filtration, washed with ether and dried. A sample of the material was recrystallized from MeOH ether and had m.p. 158 161° (reported⁸ 159.5 161.5°). The IR spectrum of this product was identical with a previously published spectrum.

3.4-Diphenyl-5-imino-2-pyrrolidinone (X1), its hydrobromide (X111) and picrate. A fresh sample of X (2g; 6:05 mmole) was allowed to stand in a warm soln (10 ml) of NaHCO₃ (1 equiv) for 20 min. The suspended material was then removed, washed with water, then ether and finally dried. The product, XI (1:78 g), was recrystallized from MeOH and afforded the pure substance (0:82 g; 3:28 mmole; 54°_{\circ} yield) m.p. 180-195' (dec) [reported[#] 200-203 (dec)]. Its IR spectrum was identical with that previously published by Osborn.[#]

A soln of XI (0-13 g) in MeOH (8 ml) was treated with a saturated aqueous solution (5 ml) of picric acid. Almost immediately a yellow crystalline salt precipitated. The material was collected and recrystallized from MeOH to give the pure picrate of XI, m.p. 200–203°. (Found: C, 55·2; H, 4·0; N, 14·5; Calc. for $C_{22}H_{13}N_5O_8$: C, 55·1; H, 3·6; N, 14·6°.)

XI (0.2 g) in chloroform (2.5 ml) was treated with a fine stream of HBr gas. After the soln was saturated, the chloroform was removed under reduced press at 40°. The resulting solid froth m.p. \sim 105–110° could not be induced to crystallize. (Found: Br, 24.9; N, 8.2. Calc. for C₁₆H₁₅BrN₂O: Br, 24.1; N, 8.5°_o.)

2,3-Diphenylsuccinimide (XII). A sample of X (0.7 g) was refluxed for 19 hr with water (20 ml) containing cone HCl (3 ml). The crystalline material (0.38 g) was recrystallized from MeOH to give pure XII, m.p. 2:8 208:5' (reported[®] 200:202). Its IR spectrum showed bands at 3:02, 5:56, 5:84, 6:66, 7:37, 7:47, 7:52, 7:66, 7:71, 8:49, 10:21, 10:28, 11:21, 12:80, 13:20, 14:10, 14:35 and 15:60 μ .

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