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AN UNUSUALLY STABLE SALT FROM ISOPHORONE AND HYDROGEN BROMIDE

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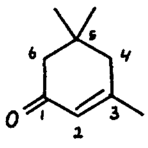
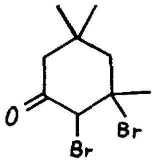
The addition of bromine to isophorone (I) in CCl_4 gives a solid white precipitate, originally reported[2,3] to be the normal Br_2 addition product (II), which readily loses a mole of HBr in the presence of moisture to give a product assumed to be 2-bromoisophorone.[3]

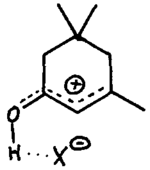
In connection with terpene syntheses, we have repeated this reaction, and find that although a complex mixture of bromination products remains in solution[4], the crystalline compound is actually the salt IIIa, which arises from the interaction of isophorone with HBr formed during the bromination. The salt IIIa can be formed quantitatively from anhydrous HBr and isophorone in CCl_4, but retains CCl_4 of crystallization.[6] Passage of HBr into neat isophorone gives IIIa as a somewhat discolored solid, m.p. 73-75° (sealed tube). Its structure follows from its mode of formation, the regeneration of isophorone on addition of water or other bases, and its spectral data, which are consistent with protonation on oxygen. It shows IR: ν_{CHCl_3} 1590 and 1510 cm^{-1} (isophorone: 1675 and 1645 cm^{-1}); $\lambda_{max}^{H_2SO_4}$ 282 mμ, $\varepsilon = 12,300$ (isophorone: λ_{max}^{EtOH} 232, $\varepsilon = 12,800$); and deshielding of all the peaks in the NMR (Table).



I.



II.



III. a. X = $Br^{\ominus}$
b. X = $HBr_2^{\ominus}$

In $CDCl_3$ solution, a mobile equilibrium between HBr and isophorone can readily be followed by the downfield shift in the NMR peaks with increasing HBr concentration, reaching the values quoted (Table) for IIIa when one mole of HBr has been added. The IR spectrum shows bands for both isophorone and the salt IIIa under these conditions. The solution will absorb a second mole of HBr, which doubtedlessly "solvates" the $Br^{\ominus}$ ion, to give the $HBr_2^{\ominus}$[7] salt IIIb. The further downfield shift of the NMR peaks (Table) and the loss of the carbonyl absorption in the IR show that protonation of isophorone is complete. *Both protons derived from the HBr are time-averaged* and appear at -0.90τ. The solid salt IIIb, m.p. ca 15° (sealed tube), could be made by passage of two moles of HBr into neat isophorone.

Table

NMR Spectra*(τ) of Salts IIIa and IIIb

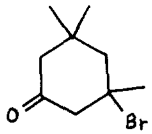
	C-2 H	C-4 H's	C-6 H's	C-3 Me	C-5 Me's	HBr
isophorone	4.13 (br)	7.80 (br)	7.80 (s)	8.04 (br)	8.96 (s)	____
IIIa	3.40 (br)	7.51 (br)	7.25 (s)	7.79 (br)	8.88 (s)	-3.75 (s)
IIIb	3.01 (br)	7.30 (br)	7.05 (s)	7.62 (br)	8.83 (s)	-0.90 (s)

*60 MHz spectra in $CDCl_3$ with internal TMS at 32°. All peaks are singlets. (br) = broadened by allylic coupling; (s) = sharp.

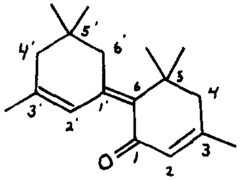
The NMR spectrum of isophorone in H_2SO_4 has been reported[8] and is very similar to that of the HBr salt IIIa in $CDCl_3$. Other acids, such as HI, $HClO_4$, and BF_3 essentially duplicate the spectrum, though anhydrous HCl is without effect. Isophorone in D_2SO_4-D_2O solution shows no tendency to polymerize or exchange deuterium at any position during a month at room temperature. This is in sharp contrast to the behavior of conjugated dienes in this medium.[8]

The pure salt IIIa is completely stable at room temperature when protected from moisture and light. However, the white crystals obtained from CCl_4 solution darken within a few days on storage, although they show no change in the NMR spectrum after months of storage. Heating the salt in a sealed tube to 70° for 24 hours causes a reaction to occur. The simple addition product IV does not seem to be present, since heating the total reaction product with collidine or in a gas chromatograph to 250° did not give any isophorone. The major product is a dimer, assigned structure V (*probably a mixture of double bond isomers*); IR: ν_{CHCl_3} 1660 and 1580 cm^{-1}; UV λ_{max}^{EtOH} 336 mμ, $\varepsilon = 22{,}000$; NMR($CDCl_3$), τ 9.06 (s) (C-5 methyls); 8.94 (s) (C-5' methyls); 8.19 (br) (C-3' methyl); 8.05(br)(C-3 methyl); 7.74 (s) (C-6' protons); 7.67(br) (C-4 and C-4' protons); 3.96(br) (C-2 and C-2' protons).

The assignment of the structure as V, derived from aldol condensation at C-6 (rather than C-2, C-4, or the C-3 methyl) rests mainly on the appearance of a shielded gem-dimethyl signal in the NMR at τ 9.06 (isophorone: 8.96) and a somewhat shielded methylene signal at τ 7.74. Inspection of a molecular model of V reveals that the C-5 methyls and the C-6' methylene should show mutual steric shielding, which is not possible in the other isomers except the C-4 condensation product, which is ruled out by the UV spectrum. The longest chromophore in V is calculated by the Woodward rules to absorb at λ_{max} 313 mμ. An addition of 15 mμ for strain in the system would give 328 mμ, in reasonable agreement with the observed value (336 mμ). The C-4 condensation product is calculated to absorb at 365 mμ. The only previously reported[9] condensation products of isophorone are all polycyclic compounds which result from base-catalyzed initial condensation at the C-3 methyl group, followed by further reactions.



IV.



V.

To our knowledge, salt III represents the first stable hydrogen halide salt to be reported for an aliphatic enone, although dibenzalacetone and related compounds form highly colored hydrohalic salts,[10] which readily add HX across the double bonds at room temperature. Stable HX salts are well known for cyclopropenone[11], tropone[11], and γ-pyrone[12] derivatives. However, the salts formed in these cases contain non-benzenoid aromatic ions and are expected to be much more stable.

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References.

(1) A preliminary account of this work was presented to the organic section of the 159th American Chemical Society Meeting, Houston, Texas, on February 24, 1970, Abstract # 33.

(2) W. Kerp and F. Müller, Ann., 299, 193 (1898)

(3) J. W. Baker, J. Chem. Soc., 633 (1926)

(4) Isophorone and 4-bromoisophorone[5] have been positively identified. A mixture of other monobromo and dibromo products were detected by NMR but were not separated. The "2-bromoisophorone" reported previously[3] was derived from the total CCl_4-soluble material and was not well characterized. If it is actually present at all, it is only a minor constitutient. The add-

ition compound II could not be detected, and probably never forms.

(5) A. J. B. Edgar, S. H. Harper, and M. A. Kazi, *J. Chem. Soc.*, 1083 (1957).

(6) Baker[3] reports m.p. *ca* 40°, but his material doubtlessly contained CCl_4 of crystallization. We obtain variable values depending on the exact method of formation, but usually about 64-66° (sealed tube). We have not been able to remove the CCl_4 without destroying the crystal formation.

(7) Rather unstable $HBr_2^{\ominus}$ salts of certain amines and related compounds are known: D. H. McDaniel and R. E. Vallee, *Inorg. Chem.* **2**, 996 (1963).

(8) N. C. Deno, H. G. Richey, N. Friedman, J. D. Hodge, J. J. Houser, and C. U. Pittman, *J. Am. Chem. Soc.*, **85**, 2991 (1963).

(9) E. Cyrot, N. Thoai, and J. Wiemann, *Tetrahedron Letters*, 83, (1970) and references therein.

(10) Cf. D. Vorlander and C. Tubandt, *Ber.*, **37**, 1644 (1904).

(11) Cf. B. E. Zaitsev, Yu. D. Koreshkov, M. E. Volp̂in, and Yu. N. Sheinker, *Doklady Akad. Nauk*, **139**, 1107 (1961).

(12) Cf. D. Cook, *Can. J. Chem.*, **41**, 505 (1963).