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# ON THE MECHANISM OF THE BROMONITROCAMPHANE-ANHYDROBROMONITROCAMPHANE REARRANGEMENT

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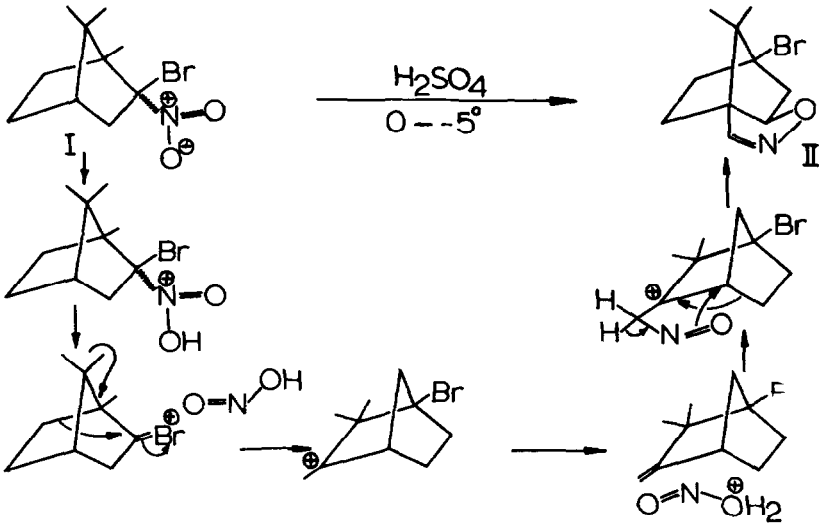
Reactions involving fragmentation and subsequent recombination of these fragments in a different manner are uncommon(1). The sulfuric acid transformation of bromonitrocamphane*(I) to anhydrobromonitrocamphane**(II)(yield 30%) has been explained on basis of such a mechanism, involving initial loss of the nitro group with subsequent reunion as a nitrosating agent(see below)***(2). This communication presents convincing proof for the plausibility of this path, as well as some novel reactions encountered in the process.

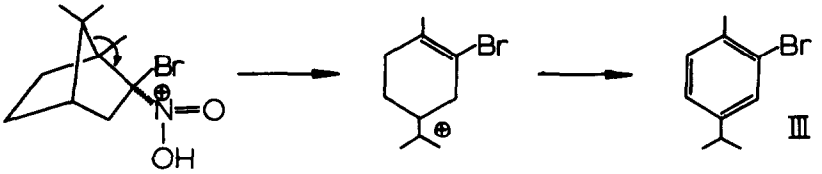



* Bromonitrocamphane is prepared by oxidation of camphor oxime with KOBr. The reaction gives the mechanistically unexpected, exo bromo isomer I(D.A.Brueckner, T.A.Hamer, J.M.Robertson and G.A. Sim, J.Chem.Soc.,799(1962). The mechanism of this reaction is under study.

** The transformation has been considered as unusual and Fascinating; see Problems in Advanced Organic Chemistry, T.Goto, Y.Hirata and G.H.Stout, Holden-Day, Inc., San Francisco, 1968, p 303; Fascinating Problems in Organic Reaction Mechanisms, S. Ranganathan, Holden-Day, Inc., San Francisco, 1967, p 72.

*** In the case of the exo nitro bromonitrocamphane, it is possible to visualize an intramolecular transformation to II, via transannular interaction with 7-methyl group. The original mechanism(2) has been slightly modified to accomodate the real stereochemistry of I.

Reaction of I with sulfuric acid at room temperature gave no II, but yielded 2-bromo-p-cymene(III) in 55% yield;NMR($\delta CDCl_3$ 7.3,7(m,aromatic), 2.87(t proton), 2.3($-CH_3$),1.22( $\overset{Me}{Me}$>)*. At 10°, the major product was still the cymene;however under the conditions usually employed for the I→II change(-5°) no cymene is produced**. The ready formation of III is best explained on basis of loss of nitro group from a protonated intermediate, assisted by the stereochemically favourably disposed 1,7 bond. To our knowledge such a ready loss of a nitro group has no parallel; further the remarkable temperature dependence of 1,7 vs 1,6 participation is without precedent:




Having established that the nitro group could be removed by protonation, efforts were made to determine the further course of the nitrogen-free species. We have demonstrated the involvement of the bromocamphene intermediate in several ways***. In expectation of a mechanism involving fragmentation-recombination, added $NaNO_2$ increased the yield by nearly two-fold. In another experiment I was reacted with $HNO_3/H_2SO_4$ (nitrating mixture) to intercept the camphene with $NO_2^+$ species. This reaction, conducted under conditions employed in the I→II change, gave, in addition to II(12%) a crystalline, highly insoluble compound, mp 259-260° for which the bromotricyclene acid structure IV is given(yield 5%)****;analysis(3),IR($\lambda$ max KBr 5.97(-COOH)$\mu$ ), NMR($\delta CF_3COOH$ 2.2(b,2 protons),2.06(m,4 protons),1.15(s, $\overset{Me}{Me}$>))*****,

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* The structure III was confirmed by direct comparison (IR,NMR,VPC-5 ft silicone-rubber at column temperatures 200° and 150°) with authentic sample(R.J.W.Le Fevre, J.Chem.Soc.,980(1933)).

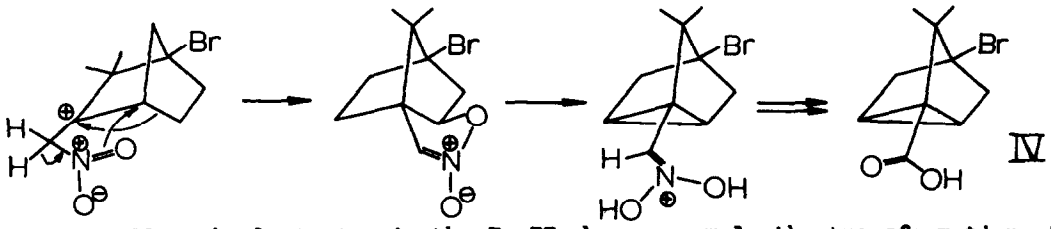
** Forster(J.Chem.Soc., 75, 1141(1899)) reported the formation of III in minor yields in the course of preparation of II, starting from large amounts of I.

*** Initial attempts to isolate this compound by extracting out with large amounts of hexane were unsuccessful; subsequently in model experiments, when camphene itself was subjected to treatment with $H_2SO_4$, under conditions employed in I→II change, no camphene could be recovered.

**** The isolation of IV was possible, solely because of the very high insolubility of the acid in usual solvents.

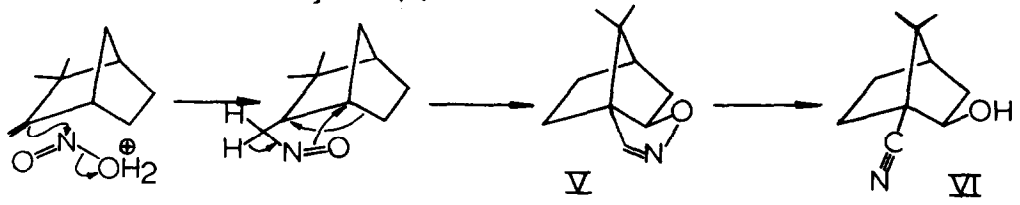
***** The IR and NMR are very similar to that of the corresponding bromine-free tricyclene acid;IR($\lambda$max KBr 6.03(-COOH)$\mu$ ),NMR($\delta CCl_4$ 1.93(b,2 protons),1.6(m, 5 protons),1.1(s,6 protons)).

mass spectrum(m/e 245). The acid could be easily precipitated from aqueous NaOH solutions on addition of dilute HCl. Careful model experiments confirmed that II is not involved in the formation of IV and also that IV is not present during the usual sulfuric acid I→II change. The formation of IV is accounted on basis of acceptance of $NO_2^+$ by the camphene intermediate followed by changes outlined*:




IV

Finally, the last step in the I→II change, namely the transformation of the camphene intermediate to II by acceptance of elements of $NO^+$ was proved possible by addition of a hexane solution of camphene(10g,25 ml) to stirred and cooled(-5°) hexane-sulfuric acid(100:12 ml) to which solid $NaNO_2$ (11.2 g) has been added. This reaction gave after precipitation and sublimation, as the sole isolable product, a white crystalline compound, mp 210°(dec),for which the isoxazoline structure V is given(yield 34%)**; analysis(3), IR(λ max KBr 6.4(-C=N-O-)μ ), NMR(δ $CCl_4$ 7.00 (s,H-C=N- ), 4.2(q,non-bridgehead t-proton)); further the NMR of V is strikingly similar to that of II(δ $CDCl_3$ 7.07(s,H-C=N- ), 4.12(q,non-bridgehead t-proton))***:




V VI

The isoxazoline ring in V is easily ruptured by brief warming with ethanolic HCl, giving rise to, in quantitative yields, the cyano hydroxy compound VI****.

* This mechanistic sequence is similar to that proposed for the sulfuric acid transformation of ω-nitrocamphene to tricyclene acid(S.Ranganathan,A.Goel and B.B.Singh,Tetrahedron Letters,3299(1968); primary nitro groups could be converted to carboxylic acids by mineral acids(M.J.Kamlet,L.A.Kaplan and J.C.Dacons,J.Org.Chem., 26,4371(1961)).

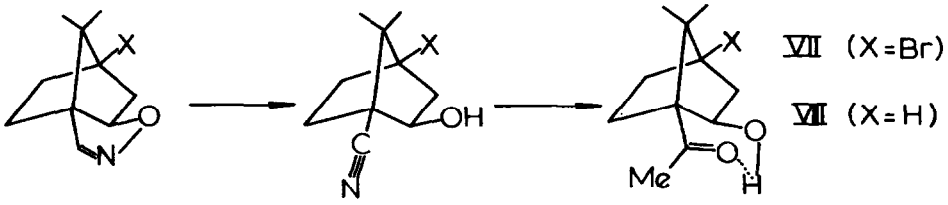
** Attempted debromination of II using Li in cyclohexane gave no V;the product was a bromocyano compound related to VI.

*** The isoxazoline is formed only under very narrowly defined reaction conditions. Reaction of camphene with $NaNO_2$ in AcOH,addition of $N_2O_3$ to camphene, reduction of ω-nitrocamphene with Zn/AcOH, all failed to yield V.

**** Reaction of camphene with dilute nitric acid at 100° is reported to give a 1% yield of compound,mp 228-9.5°,which on basis of further conversion to tricyclene acid is presumed to have structure VI(Nametkin,Chem.Abstr.,48,154(1954);for earlier claims by Konovlov see (2)).

mp 205-206°(dec.,sealed capillary);analysis(3),IR(λmaxKBr 2.88(-OH),4.5(-C≡N)μ), NMR(δ$CDCl_3$ 4.08(m,non-bridgehead t-proton)).

Reaction of anhydrobromonitrocamphane with excess of MeMgI is reported to yield compound mp 117°,having an unusual bromoiminocarbinol structure(4). Surprisingly this compound obtained according to procedure described(4) has been found to be nitrogen-free and is assigned structure VII;analysis(3),IR(λmax KBr 2.92(-OH), 5.92(C=O)μ),NMR(δ$CCl_4$ 4.7(octet, due to small long range coupling, non-bridgehead t-proton),2.12(s,-C(=O)-$CH_3$),1.09,1.00(bridgehead Me)). The cyano hydroxy compound VI on treatment with excess of MeMgI gave the bromine-free compound VIII corresponding to the ketone VII, as a low melting crystalline solid;analysis(3),IR(λmax film 2.97(-OH),6.00(C=O)μ; both indicative of hydrogen bonding), NMR(δ $CDCl_3$ 4.85 (octet,non-bridgehead t-proton),2.16(s,-C(=O)-$CH_3$),1.13,1.03(bridgehead Me));further the acetyl derivative formed in quantitative yields on treatment with $Ac_2O$/pyridine had the predicted behaviour;analysis(3),IR(λmax film 5.77(-O-C(=O)-$CH_3$),5.92(C=O)μ) ,NMR(δ$CCl_4$ 5.5(octet,nonbridgehead t-proton),2.05,2.00(s,s,-O-C(=O)-$CH_3$,-C(=O)-$CH_3$),1.11, 1.02(bridgehead Me)).These transformations could be explained as follows:




VII (X=Br)

VIII (X=H)

The tricyclic isoxazoline system V, formed under mild conditions from camphene, could be expected to be of use in the synthesis of diversely substituted bicyclic systems.

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REFERENCES

1. J.Meinwald,and J.T.Ouderkirk,J.Am.Chem.Soc.,82,480(1960);J.Meinwald, H.C.Hwang,D.Christman and A.P.Wolf,J.Am.Chem.Soc.,82,483(1960).
2. E.E. van Tamelen and J.E.Brenner, J.Am.Chem.Soc.,79,3839(1957).
3. Elemental analytical data in excellent accord with theory has been obtained for this substance.
4. P.M. Ginning and W.A. Noyes, J.Am.Chem.Soc.,44,2567(1922).