Photolyses of Isobornyl and Bornyl Nitrites

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Barton et al.[1] scrutinized the photolysis of alkyl nitrite[2] and demonstrated its usefulness to synthetic organic chemistry, especially in introducing functional groups into an otherwise inert, angular methyl group of steroids by means of a dramatic three-step synthesis of aldosterone acetate from corticosterone acetate.[1a]

They also pointed out that the NO group migrates to the methyl group located at the 1, 3-diaxial position. An inspection of the molecular model of isobornyl nitrite (Ia)[3] reveals that one of the gem-methyl groups and the NO group are in a quasi 1, 3-diaxial relation, fulfiling the conformational requirement of this photochemical migration; therefore, the photochemical product of Ia can be expected to be *cis*-π-oxoisoborneol oxime (IIa). In contrast to the readily-available trans-π-substituted camphor derivatives,[4] *cis*-isoketopinic acid (IIIa) and *cis*-π-hydroxycamphor (IIIb) are the only known examples of cis-π-substituted camphor derivatives. Since we have been interested in the studies of the reactivity of *cis*-π-oxocamphor (IIIc), we hoped that this expected photochemical synthesis would turn out to be the most convenient process to IIIc, as well as a general synthetic route to a cis-π-substituted camphor series of compounds which has been obtained through multistep routes.[4]

When a solution of isobornyl nitrite (Ia) in benzene was irradiated with an ultraviolet lamp for 1 hr., needles (m. p. 214~215°C, $[\alpha]_D$ −71.1° (in ethanol) were obtained. Although this compound's molecular formula was $C_{10}H_{17}O_2N$, isomeric with the starting material, and although its color reaction with ferric chloride was purple, indicating the oxime structure IIa, it soon became evident that this compound has no oxime group. The heating of the compound with acetic anhydride and sodium acetate gave only the monoacetate (m.p. 80~82°C), instead of the expected nitrile. Barton et al. observed the photochemical cleavage of the 5-membered D ring of the nitrite of a 17-ol steroid[1d] (e. g. 5α-androstane-3α, 17β-diol 3α-acetate 17β-nitrite), affording a 6-membered hydroxamic acid derivative. We suspected that the photolysis of Ia did not follow the expected schema (Fig. 1) and that the strained 5-membered ring of Ia was cleaved to the hydroxamic acid derivative, VIIIa. This was confirmed by the reduction of VIIIa with zinc powder in acetic acid to give the lactam IXa (m. p. 156~160°C, $[\alpha]_D$ −51.3° (in ethanol)), which was further converted into the imine IXb with lithium aluminum hydride. Although two alternative direction of the photochemical cleavage reaction seem possible, the one between the carbon atom carrying the nitrite group and the neighboring methylene is inconceivable by analogy with the results established by Barton et al, (*vide supra*) on the nitrite of a 17-ol steroid. This is further supported by the fact that the lactam IXa and the imine IXb were found to be not identical with α-camphidone[5] and camphidine[5] respectively. The oily reaction product freed from the hydroxamic acid VIIIa was chromatographed on an alumina column to give isoborneol (IVb) and an oil which distilled to yield a yellow liquid (b. p. 65~70°C/4 mmHg), the infrared spectrum and NMR spectrum of which showed the presence of an aldehyde group. Although the aldehyde could be converted to α-campholenic acid amide (XIIb) (m. p. 127~128°C) via α-campholenic acid (XIIa) and although its 2, 4-dinitrophenylhydrazone and semicarbazone melted rather sharply (124~126°C and 142~143°C respectively), its vapor phase chromatogram exhibited two peaks with almost equal intensities, indicating that the aldehyde is unhomogeneous. The infrared spectrum of this mixture had

1) a) D. H. R. Barton, J. M. Beaton, L. E. Geller and M. M. Pechet, *J. Am. Chem. Soc.*, **82**, 2640 (1960); **83**, 4076 (1961); b) D. H. R. Barton and J. M. Beaton, ibid., **82**, 2641 (1960); **83**, 4083 (1961); c) A. L. Nussbaum, F. E. Carlon, E. P. Oliveto, E. Townley, P. Kabasakalian and D. H. R. Barton, ibid., **82**, 2973 (1960); d) C. H. Robinson, O. Gnoj, A. Mitchell, R. Wayne, E. Townley, P. Kabasakalian, E. P. Oliveto and D. H. R. Barton, ibid., **82**, 17771 (1961); e) D. H. R. Barton and J. M. Beaton, ibid., **83**, 750 (1961); **84**, 199 (1962); f) D. H. R. Barton, R. P. Budhiraja and J. F. McGhie, *Proc. Chem. Soc.*, **1963**, 170.

2) For a relevant review, see L. Nussbaum and C. H. Robinson, *Tetrahedron*, **17**, 35 (1962).

3) For the absolute configuration of isoborneol, see A. J. Birch, *Ann. Reports*, **47**, 191 (1950).

4) E. J. Corey, M. Ohno, S. W. Chow and R. A. Scherer, *J. Am. Chem. Soc.*, **81**, 6305 (1962).

5) J. Tafel and K. Eckstein, *Ber.*, **34**, 3274 (1901).

6) R. E. Partch, *J. Org. Chem.*, **28**, 276 (1963).

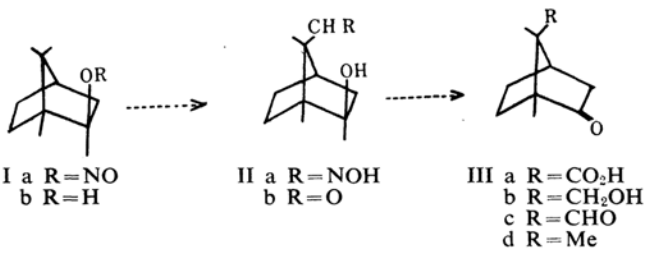

Fig. 1

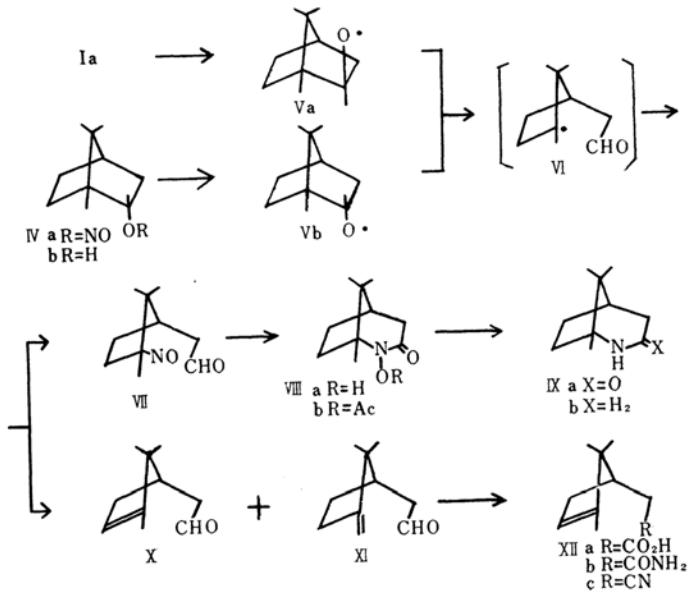

Fig. 2

TABLE I.[6] PHOTOLYSIS OF ISOBORNYL NITRITE

	5.46 mmol./100 cc. benzene			5.46 mmol./14 cc. benzene		
	Retention time min.	Yield mmol.	Molar ratio	Retention time min.	Yield mmol.	Molar ratio
VIIIa	—	1.45	2.63	—	0.16	0.22
X	54.8	0.59	1.07	54.8	0.74	1.09
XI	59.8	0.55	1	59.6	0.68	1
IIIa	—	0.00	0.00	62.6	0.07	0.11
Ib	73.8	0.21	0.38	74.6	1.33	1.95

TABLE II.[6] PHOTOLYSIS OF BORNYL NITRITE

	5.46 mmol./100 cc. benzene			5.46 mmol./14 cc. benzene		
	Retention time min.	Yield mmol.	Molar ratio	Retention time min.	Yield mmol.	Molar ratio
VIIIa	—	1.36	2.40	—	0.12	0.19
X	54.6	0.63	1.10	54.5	0.77	1.19
XI	59.5	0.57	1	59.4	0.65	1
IIId	—	0.00	0.00	62.2	0.05	0.07
IVb	79.6	0.31	0.54	82.2	1.13	1.74

peaks at 880 and 800 cm^{-1}, suggesting the presence of $>C=CH_2$ and $-CH=C<$; this was further supported by the NMR spectrum (4.80 and 5.24 τ*). These results imply that the aldehyde fraction consists of α-campholenic aldehyde (X) and iso-α-campholenic aldehyde (XI); the latter was first detected in the reaction mixture of the lead tetraacetate oxidation of isoborneol (Ib),[6] not in the photolysis of camphor (see the Experimental section). The relative molar amounts of these products together with their retention times in the vapor phase chromatograph, are summarized in Table I.[7] It is noteworthy that, in the photolysis of isobornyl nitrite (Ia) at a much higher concentration, camphor (IIId) was detected in the reaction mixture, which also contained the unsaturated aldehydes X and XI, isoborneol (Ib) and the hydroxamic acid VIIIa; however, the ratio of VIIIa to Ib, in this case, was found to be just the reverse of that observed in the low concentration experiment. The photolyses of bornyl nitrite (IVa) at low and high concentrations were carried out to give analogous results (Table II)[7] in spite of the different stereochemistry of the starting materials.

These facts suggested that these photolyses would be nonstereospecific, and that an intermediate such as VI might be common in both cases. The disproportionation of the intermediate radicals Va and Vb would be enhanced at a higher concentration, thus accounting for the relatively high yields of borneol, isoborneol and camphor in the photolyses performed in higher concentrations, but it does not seem possible to advance, without further study, a plausible mechanism to explain the rather interesting predominant formation of the hydroxamic acid (VIIIa) in the low concentration experiments.

Since Professor Barton[8] has announced that Dr. Kabasakalian of his laboratory has carried out extensive studies of the photolyses of aliphatic nitrites, including bornyl and isobornyl nitrite, we will refrain from further investigation of this problem.

Experimental*

Isobornyl Nitrite (Ia).—Into a chilled solution of 63.0 g. of isoborneol (Ib) (m. p. 211~213°C, $[\alpha]_D^{22}$ −23.5° (*c* 0.845 in ethanol)) in 450 cc. of pyridine, 38.0 g. of nitrosyl chloride[9] gas was passed in a period of 3 hr. After being stirred for 1.5 hr. at room temperature, the reaction mixture was poured into ice water and extracted with ether. The extract was washed with 2% hydrochloric acid and dried over anhydrous sodium sulfate. Removal of the solvent yielded an oil which distilled to afford 66.2 g. of yellow liquid (89% yield) (b. p. 175~176°C/9 mmHg). An infrared spectrum exhibited peaks at 1645 and 1605 cm^{-1} (-NO).

The Photolysis of Isobornyl Nitrite (Ia). — A solution of 6.0 g. of Ia in 600 cc. of benzene was cooled with running water and irradiated with a Toshiba SHL-100UV mercury lamp for 1 hr. in an atmosphere of nitrogen. The crystals which precipitated were collected and recrystallized from benzene-petroleum ether to afford 1.6 g. of the hydroxamic acid VIIIa (m. p. 214~215°C, $[\alpha]_D^{22}$ −71.1° (*c* 0.562 in ethanol)), which gave a red color with a ferric chloride solution. Infrared spectrum in Nujol mull: peaks at 3100, 1640, 1400, 1370 cm^{-1}.

Found: C, 65.70; H, 9.27; N, 7.32. Calcd. for $C_{10}H_{17}O_2N$: C, 65.54; H, 9.35; N, 7.64%.

The reaction mixture freed from the hydroxamic acid VIIIa was concentrated and chromatographed through a column of alumina to give isoborneol (Ib) (m. p. 209~210°C), identified by an infrared spectrum. The second fraction of the chromatographic separation was distilled to afford a liquid (b. p. 65~70°C/4 mmHg); an infrared spectrum in Nujol mull showed peaks at 2740, 1725, 1655, 880 and 800 cm^{-1}, and a NMR spectrum exhibited peaks at 0.26, 4.80, 5.24, 7.62 and 8.40 τ which correspond to $\underline{CHO}$, $>C=\underline{CH}-$, $>C=\underline{CH_2}$, $\underline{CH_2}CHO$, and $-HC=CH\cdot\underline{CH_3}$ respectively.

The 2, 4-dinitrophenylhydrazone was recrystallized from ethanol; m. p. 124~126°C.

Found: C, 57.91; H, 6.11; N, 16.63. Calcd. for $C_{16}H_{20}O_4N_4$: C, 57.82; H, 6.07; N, 16.86%.

The semicarbazone was recrystallized from ethanol; m. p. 142~143°C (lit.[6,10] m. p. 141~142.5°C).

Found: C, 63.12; H, 9.15; H, 20.08. Calcd. for $C_{11}H_{19}ON_3$: C, 63.07; H, 9.00; N, 19.86%.

The quantitative analyses of these products, except that of the hydroxamic acid VIIIa, were performed by means of vapor phase chromatography; they are summarized in Table I.

The Acetate VIIIb of the Hydroxamic Acid VIIIa.—A mixture of 0.5 g. of the hydroxamic acid VIIIa, 27.5 cc. of acetic anhydride and 5.5 cc. of pyridine was heated at 90~100°C for 1/2 hr. After the mixture had been concentrated at reduced pressure, the residue was recrystallized from petroleum ether to yield 0.55 g. of the acetate VIIIb.

Found: C, 64.27; H, 8.42; N, 6.51. Calcd. for $C_{12}H_{19}O_3N$: C, 63.97; H, 8.50; N, 6.22%.

The Lactam IXa.—A mixture of 0.95 g. of the hydroxamic acid VIIIa, 8.0 g. of zinc powder and 60 cc. of acetic acid was refluxed for 6 hr. After

* NMR spectra were measured at 60 Mc. in carbon tetrachloride, using tetramethylsilane as an internal reference.

7) Use was made a 5 m. column of 30% dioctyl phthalate on Cellite 545 (80~100 mesh) at 150°C, and a helium flow rate 80 cc./min. on Yanagimoto Gas Chromatograph GCG-3D type.

8) D. H. R. Barton, "On Some New Photochemical Reactions," in H. Ohtsuka, editor, "Collection of Lectures Commemorating the Inauguration of the New Shionogi Research Laboratory Building," 1963, p. 275.

* The analyses were performed in the Microanalytical Laboratory of the Institute of Polytechnics, Osaka City University.

9) J. R. Morton and H. W. Wilcok, "Inorganic Syntheses," Vol. 4, 48 (1953).

10) R. Srinivasan, *J. Am. Chem. Soc.*, **81**, 2604 (1959).

being freed from the excess zinc powder, the solution was concentrated at reduced pressure. The residue was made basic with aqueous sodium hydroxide and extracted with ether. After being washed with water and dried over anhydrous sodium sulfate, the solution was concentrated to give needles which were recrystallized from petroleum ether to afford 0.50 g. of needles (m. p. 156~160°C, $[\alpha]_D^{22}$ −51.2° (*c* 0.516 in ethanol)).

Found: C, 72.01; H, 10.39; N, 8.07. Calcd. for $C_{10}H_{17}ON$: C, 71.81; H, 10.25; N, 8.38%.

The Imine IXb.—To a stirred mixture of 0.4 g. of lithium aluminum hydride and 50 cc. of dioxane, a solution of 0.30 g. of the lactam IXa in 70 cc. of dioxane was added in a period of 15 min. The mixture was refluxed for 28 hr. and decomposed with water. After the alumina deposited had been filtered, the filtrate was concentrated and made basic with aqueous ammonia. The aqueous mixture was extracted with ether, and removal of the solvent left a residue which resisted crystallization. This was then converted directly into the picrate, yellow needles (decomp. p. 250°C).

Found: C, 49.84; H, 5.78; N, 14.73. Calcd. for $C_{16}H_{22}O_7N_4$: C, 50.26; H, 5.80; N, 14.65%.

α-Campholenic Acid Amide (XIIb).—The aldehyde fraction (1.0 g.) obtained from the photolysis of isobornyl nitrite (Ia) was added to a solution of 2.4 g. of silver nitrate in 10 cc. of water. To the stirred mixture, 1.2 g. of sodium hydroxide were added, and the stirring was continued for 30 min. After being freed from the deposit, the mixture was washed with ether. The aqueous solution was made acidic with hydrochloric acid and extracted with ether. After washing with water, the solvent was removed, yielding 0.75 g. of a viscous liquid; 0.3 g. of this was converted into the acid chloride with thionyl chloride (1.5 cc.). The acide chloride was added to concentrated aqueous ammonia, and the acid amide XIIb deposited was recrystallized from aqueous ethanol (m. p. 127~128°C (lit.[11] 130.5°C)), which was identified as α-campholenic acid amide by comparing it with an authentic specimen prepared from α-campholenic nitrile[11] (XIIc) by alkaline hydrolysis.

Found: C, 71.65; H, 10.28; N, 8.35. Calcd. for $C_{10}H_{17}ON$: C, 71.81; H, 10.25; N, 8.38%

Bornyl Nitrite (IVa).—A chilled solution of 22.3 g. of borneol (IVb) in 200 cc. of pyridine was saturated with nitrosyl chloride gas, and the solution was allowed to stand at room temperature for 30 min. After the usual work up (*vide supra*), 17.9 g. of yellow liquid (b. p. 72~74°C/6 mmHg) was obtained.

The Photolysis of Camphor (IIId).—A solution of 2.0 g. of camphor (IIId) in 200 cc. of benzene was irradiated as was isobornyl nitrite for 1 hr. The product was analyzed by vapor phase chromatography,[7] which indicated the presence of 0.31 g. of α-campholenic aldehyde (X) and 1.26 g. of camphor, but no trace of iso-α-campholenic aldehyde (XI).

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11) F. W. Tiemann, *Ber.*, **28**, 2168 (1895).