

BECKMANN REARRANGEMENT OF CAMPHOR AND FENCHONE OXIMES OVER PHOSPHORUS PENTOXIDE IN TOLUENE AND AUTOXIDATION OF RESULTING NITRILES

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Camphor oxime, when subjected to the Beckmann rearrangement under the action of phosphorus pentoxide in toluene, yields *dl*- α -campholene nitrile, while fenchone oxime gives a rearranged lactam in addition to *dl*- α -fencholene nitrile. Autoxidation of the two nitriles gives hydroperoxide at the tertiary carbon atom.

Introduction

The Beckmann rearrangement of camphor and fenchone oximes has already been studied under the action of a variety of acidic reagents. The rearrangement of camphor oxime with thionyl chloride,¹ hydrochloric acid^{2,3} and sulphuric acid⁴ has been investigated earlier. In most of the cases the products obtained are the unsaturated nitriles with the exception that in the case of concentrated hydrochloric acid 2,3,3-trimethylcyclopentene-4-acetic acid is the main product. Nageli⁵ has obtained *dl*- α -campholene nitrile as a result of the action of acetyl chloride on camphor oxime. Tiemann,⁶ working on the constitution of camphor, has obtained the same nitrile (as that of Nageli) while using concentrated sulphuric acid and camphor oxime.

The rearrangement of fenchone oxime with mineral acids⁷ has resulted in the formation of fencholene nitrile. Further, the oxime, when treated with *p*-toluenesulphonyl chloride, phosphorus pentachloride or sulphuric acid at low temperatures⁸ has given the unsaturated nitrile and a solid lactam.

Although phosphorus pentoxide as such⁹ or in combination with various solvents¹⁰⁻¹² or supports¹³ has been applied to a number of cyclisation rearrangements, it has been used very rarely as a reagent for the Beckmann rearrangement. No reference has been found in literature where this reagent might have been used in the Beckmann rearrangement of camphor and fenchone oximes. The studies presented in this paper have therefore, been carried out in order to investigate the rearrangement products from camphor and fenchone oximes under the conditions of this reagent. The present work shows that this reagent is identical in its effects on camphor oxime to the reagents already tried. The reagent, however, in the case of fenchone oxime resembles *p*-toluenesulphonyl chloride, phosphorus pentachloride and sulphuric

acid as it brings about rearrangement and dehydration simultaneously.

During these investigations, the liquid nitriles resulting from the rearrangement of the oximes were found to undergo a change in that campholene nitrile started crystallising while fencholene nitrile became viscous in about a month's time. The suspicion that the products were suffering autoxidation was substantiated; the measurement of peroxide formation as well as the structural studies of the autoxidised products have confirmed this view held by the authors.

It may be pointed out that the phenomenon of the autoxidation of such nitriles has not so far been recorded in literature. The authors appear to be the first to make such an observation and provide its explanation in this paper.

Experimental

All melting and boiling points are uncorrected. Infrared spectra were recorded with the Beckmann IR-5A and Perkin Elmer model 227 spectrophotometers. NMR was run on a Varians A-60 spectrophotometer in deuterated chloroform with tetramethyl silane as the internal reference. Rotations were determined in chloroform with Bellingham and Stanley Ltd. No. 450602 polarimeter. Microanalyses were carried out by A. Bernhardt Microanalytisches Laboratorium, W. Germany.

CAMPHOR OXIME

Hydroxylamine hydrochloride, 0.45 mole (31 g) and sodium acetate (60 g) were dissolved in water (150 ml) and camphor 0.3 mole (50 g) was added. Ethanol (300 ml) was added to the mixture which was then refluxed for 30 minutes on a water-bath. The alcohol-water mixture was distilled to (250 ml) under reduced pressure and then chilled in an ice bath. The precipitated

oxime was filtered under suction, dried on a filter paper and recrystallised from hexane (42 g), m.p. 118-119°.

FENCHONE OXIME

Fenchone oxime was prepared as above. However, the mixture containing fenchone and hydroxylamine hydrochloride was refluxed for 3 hours to obtain maximum yield of the oxime. Recrystallisation of the oxime was carried out from benzene-hexane, m.p. 161-162°.

BECKMANN REARRANGEMENT OF CAMPHOR OXIME OVER PHOSPHORUS PENTOXIDE

The oxime (15 g) was dissolved in hot toluene (150 ml) in a 250-ml round bottom flask and phosphorus pentoxide (30 g) was added. The flask was fitted with a reflux condenser and heated on a steam bath. After specified intervals of time the reaction mixture was thrown on crushed ice. The organic layer was separated and the aqueous solution after having been saturated with sodium chloride was extracted with ether (3 times, 50 ml each). The combined extracts were washed with saturated sodium carbonate solution until neutral and finally with water. Ether was removed on a water bath and toluene under suction in an oil bath at 120°. The residual liquid was fractionated by distillation and the fraction between 222-224° was collected. This fraction was *dl*- α -campholene nitrile (C, 80.79; H, 9.61; N, 9.33; mol. wt., 148; C₁₀H₁₅N requires C, 80.48; H, 10.13; N, 9.39; mol. wt., 149).

BECKMANN REARRANGEMENT OF FENCHONE OXIME OVER PHOSPHORUS PENTOXIDE

This reaction was carried out under conditions similar to camphor oxime. However, after the removal of toluene the residue was chilled in an ice bath whence it separated into a crystalline solid (needles) and mother liquor. The liquid was fractionated by distillation and the fraction between 217-219° was collected. This fraction was *dl*- α -fencholene nitrile. The solid, m.p. 158-159°, was found to be a rearranged product C₁₀H₁₇NO (C, 72.80; H, 10.34; N, 7.92; C₁₀H₁₇NO requires C, 71.81; H, 10.25; N, 8.38).

Reduction of the Nitriles.—The liquid nitrile (2 g) was dissolved in dry ether and lithium aluminium hydride (5 g) was added. The mixture was allowed to stand for half an hour. The excess lithium aluminium hydride was decomposed with hydrous ether and then with water. The ethereal layer was dried over anhydrous sodium sulphate

and evaporated. The residue gave the amine (1.9 g). *dl*- α -Camphylamine, b.p. 194-196°, in the case of campholene nitrile while *dl*- α -fencholene amine, b.p. 205°, in the case of fencholene nitrile.

Hydrolysis of the Nitriles.—Campholene nitrile was hydrolysed¹⁴ to *dl*- α -campholenic acid amide m.p. 122°, which was converted by further hydrolysis¹⁵ to a liquid acid *dl*- α -campholenic acid, b.p. 169/40. Fencholene nitrile on hydrolysis gave *dl*- α -fencholenic acid amide m.p. 98-99° and *dl*- α -fencholenic acid, b.p. 254-6°/dec.

DEHYDRATION OF THE CRYSTALLINE SOLID AS OBTAINED FROM THE REARRANGEMENT OF FENCHONE OXIME OVER PHOSPHORUS PENTOXIDE¹⁶

The solid (2.1 g) was taken in petroleum ether (62-82°) (20 ml); phosphorus pentachloride (2.1 g) was added and the mixture was first allowed to stand for 24 hours with occasional shaking and then heated for 1 hour on a steam bath. It was finally thrown on ice. The aqueous mixture was repeatedly extracted with ether. The combined extracts were washed first with sodium bicarbonate saturated solution and then with water. The extract was dried over anhydrous sodium sulphate and evaporated. A liquid was obtained which on standing deposited white needles. The two phases were separated by filtration. The solid (0.22 g) was found to be the unreacted original crystalline solid from its m.p. and mixed m.p. The liquid (0.8 g) was found to be *dl*- α -fencholene nitrile. It was confirmed by its IR spectrum which was identical in all respects with the nitrile obtained from fenchone oxime and phosphorus pentoxide.

Results

The results are tabulated below:

TABLE I.—THE EFFECT OF REACTION TIME ON THE YIELD OF REARRANGED PRODUCTS FROM 15 G EACH OF CAMPHOR AND FENCHONE OXIMES.

Reaction time in minutes	The yield and nature of products from					
	Camphor oxime			Fenchone oxime		
	Liquid in g	Solid in g	Unreacted in g	Liquid in g	Solid in g	Unreacted in g
10	2.5	—	9.8	8.7	—	3.5
30	11.62	—	—	9.39	2.69	—
60	11.42	—	—	7.5	2.12	—
120	10.9	—	—	7.0	1.5	—

Discussion

Camphor and fenchone employed in the reactions were racemic mixtures as they showed no rotation. Their racemic nature was further confirmed by their melting and boiling points. The oximes obtained from them also proved to be the racemic mixtures from their melting points and their lack of rotation.

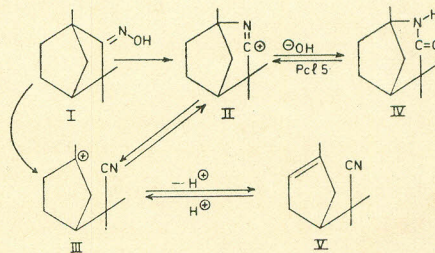
The oximes were observed to undergo the Beckmann fission¹⁷ rather than the Beckmann rearrangement. The action of phosphorus pentoxide in toluene on camphor oxime is similar to that of strong acids such as the sulphuric and hydrochloric acid and acid-generating reagents such as acetyl chloride. The oxime gets dehydrated to a liquid nitrile with other minor products such as β -campholene nitrile. The resultant nitrile is *dl*- α -campholene nitrile as shown by IR ($-\text{C}\equiv\text{N}$ stretching 4.5μ ; $\text{C}=\text{C}$, 12.5μ ; Vinyl 3.4μ) specific rotation and reduction to *dl*- α -campholene amine, hydrolysis to an amide and to *dl*- α -campholenic acid. The dehydration of the oxime was complete in about half an hour (Table 1). Prolonged reaction time was immaterial for obtaining any further rearranged product. It may be argued that the rearrangement interval of 30 minutes was rather too long and, therefore, the resulting product was the nitrile only and no other intermediate product. The possibility of having such an intermediate product was eliminated; when the time of reaction was reduced to 10 minutes, the reaction mixture was found to contain the unreacted oxime (9.8 g) and the nitrile (2.3 g) only (Table 1). It is, hence, inferred that the reaction is the direct dehydration of the oxime to the nitrile.

The reaction with fenchone oxime, however, followed a different course. It yielded a solid product in addition to the products which have already been obtained by the action of dilute mineral acids on fenchone oxime. The main product in this case too was *dl*- α -fencholene nitrile as confirmed by its IR ($-\text{C}\equiv\text{N}$ stretching 4.5μ ; $\text{C}=\text{C}$, 6.03μ & 12.5μ ; Vinyl stretching 3.32μ), specific rotation, $[\alpha]_D = \pm 0$ reduction to *dl*- α -fencholene amine and hydrolysis to *dl*- α -fencholenic acid amide and finally to *dl*- α -fencholenic acid. The additional solid product was found to be the rearranged product isomeric with fenchone oxime previously obtained by Wallach¹⁸ by mixing the two optical isomers in equal amounts and by Cottingham in his studies on the Beckmann rearrangement of fenchone oxime over various reagents other than phosphorus pentoxide at room temperature. The melting point and IR spectrum (in KBr), CO stretching 6.1μ ;

NH stretching 3.15μ , show that it is a rearranged product. The identity of this solid was established as 1,4,4-trimethyl-2-azabicyclo(3.2.1)octan-3-one (IV) which is a lactam, a fact which has been established as follows. Treatment of this lactam with phosphorus pentachloride produced *dl*- α -fencholene nitrile as confirmed by IR which was identical in all details with the IR of the nitrile obtained from the direct reaction of fenchone oxime and phosphorus pentoxide.

The amount of the rearranged products in this case was dependent on the time of reaction. Maximum yields were obtainable with 30 minutes reaction time. If the reaction period was reduced to 10 minutes, the unreacted oxime (3.5 g, Table 1) was found to be still present in the reaction mixture. With prolonged reaction time the quantity of the lactam and the nitrile decreases and it is assumed that both are converted to low boiling products.

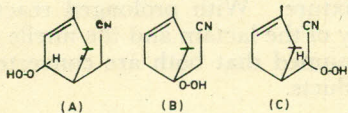
There seems no obvious reason for this difference of behaviour of the two oximes. Cottingham⁸ proposes two possible reaction paths which are: (1) the oxime I forms a carbonium ion (II) which gets dehydrated to the nitrile (V) and (2) the oxime (I) first gets dehydrated to (III) which then hydrolyses as in the Ritters reaction¹⁹ and finally rearranges to the lactam (IV). Cottingham favours the former reaction path. The possibility of the hydrolysis of the nitrile to an amide is ruled out due to the fact that a large excess of phosphorus pentoxide is always present at the end of the reaction. Phosphorus pentoxide has been used by Wallach²⁰ to dehydrate fencholenic acid amide to fencholene nitrile. That the quantity of the rearranged product decreases and does not increase with the prolonged reaction time shows that the lactam is dehydrated to the corresponding nitrile and not *vice versa* supplements the former reaction path. The proposition that the production of the nitrile might be through the lactam formation is also ruled out as in that case the quantity of the lactam at certain intervals of time should be approaching the theoretical yield but this was contrary to the authors experimental observation.



The oxygen absorption by the two nitriles when placed at room temperature* is a clear case of autoxidation. The product in the case of campholene nitrile is white needles, m.p. 122-123°, and corresponds to $C_{10}H_{15}NO_2$ (Found: C, 66.25; H, 8.29; N, 7.67; mol. wt., 187; $C_{10}H_{15}NO_2$ requires: C, 66.27; H, 8.34; N, 7.77; mol. wt., 181).

Although no crystalline product could be isolated from fencholene nitrile, it became increasingly viscous due to autoxidation as evidenced by the liberation of iodine from potassium iodide.

The oxidised product of campholene nitrile could be either A or B as the allylic positions or



methine hydrogens are known to suffer the attack. The IR of the solid (in KBr) shows $-C\equiv N$ stretching 4.56μ , $>C=C-$ stretching 6.2μ and 12.65μ and $-O-O-H$ stretching 11.6μ . We assign structure B to the product on the basis of its NMR characteristics which are: sharp singlet at 1.99τ , hydroperoxide hydrogen (area 1); a triplet at 4.58τ , olefinic hydrogen (area 1) four closely spaced lines at $7.2-7.5\tau$, methylene α -to the hydroperoxide (area 2). The methylene of the cyanomethyl appeared as a diffused multiplet between 7.8 and 8.6τ (area 2). The three methyl groups appeared as separate singlets at 8.7τ , 9.07τ and 9.17τ each having an area equal to three protons. Total area from the integral curve is 15 protons. The third structure (C) is ruled out as the $-O-O-H$ is likely to cause considerable downfield shift of the methine hydrogen.

*A room temperature of 20° is most favourable.

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