Photoinduced Molecular Transformations. Part 119.[1] Photochemical Nitrogen Insertion into Bicyclo[2.2.1]heptanones; the Photochemistry of Oximes of (+)-Fenchone and (+)-Camphor[2]

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The photolysis of the oxime of (+)-fenchone in methanol gave a 1:1 ratio of two isomeric lactams, 1,4,4-trimethyl-2-azabicyclo[3.2.1]octan-3-one (13%) and its previously undescribed isomer, 1,4,4-trimethyl-3-azabicyclo[3.2.1]octan-2-one (13%), with the accompanying formation of alkenoic acid amides (10%). Photolysis of the oxime of (+)-camphor in methanol similarly gave two isomeric lactams, 1,8,8-trimethyl-2-azabicyclo[3.2.1]octan-3-one (α-camphidone) (12%) and 1,8,8-trimethyl-3-azabicyclo[3.2.1]octan-2-one (12%), in a 1:1 ratio, as well as an alkenoic acid amide (α-campholenic amide) (32%). Nitriles arising from photochemical α-fission were obtained, in 11 and 6% yield, through photolysis of the respective oximes. Therefore, methyl groups attached to the α-carbons had little affect on the direction of the photoreaction of bicyclo[2.2.1]heptanone oxime. 2- and 3-Azabicyclo[3.2.1]octanones can thus be synthesized by the photoreaction of bicyclo[2.2.1]heptanone oximes, which can be carried out without the use of any other reagent.

Our previous studies[3,4] concerning the photochemistry of several steroidal cyclic ketone oximes have shown that two structurally isomeric lactams are always produced in moderate to good yield, and that the yield of the lactam, which results from migration of the carbon centres substituted more with the alkyl groups, does not differ appreciably from those which result from a migration of less substituted carbon centres when these oximes are photolysed in methanol. Research carried out by Just and colleagues has shown similar results concerning unsymmetrically α-substituted cyclohexanone oximes.[5,6]

Our previous study concerning the photolysis of chiral cyclic ketone oximes also disclosed that the configurations of the migrating carbon leading to the formation of lactams are retained.[3a–c]

Another feature of the photoreaction of oximes in methanol is its reluctance to produce nitriles arising from α-fission. We have found that the oximes of cyclic ketones that lead to a second-order Beckmann rearrangement by treatment with Lewis acids seldom give products that result from photochemical α-fission, but rather afford two isomeric lactams in fair yields.[3,7,8] Exceptions are substrates such as a highly substituted 6-methyl-2,4,6-tri-t-butylcyclohexadienone oxime[9] and highly strained oximes,[10,11] which give nitriles from ionic α-fission.

We have therefore pointed out that this property of excited oximes is of considerable utility in the synthesis of lactams which are not accessible by ordinary ground-state reactions of oximes.[3c,4]

It has been reported that a mixture of nitriles resulting from α-fission is virtually an exclusive product when resulting from the photolysis of camphor oximes in methanol.[12] Since the major products of the photolysis of the parent norcamphor oxime 1 are subsequently reported to be two lactams, 2 and 3, accompanied by small amounts of the corresponding ring-opened amides 4 and 5,[13] (Scheme 1) the exclusive formation of the nitriles from camphor oxime cannot be taken as a general property of the photoreaction of bicyclo[2.2.1]heptanone oximes, but must be considered as being anomalous; the observed α-fission, if correct, should be attributed to the effects of the methyl groups attached to C-1 and C-7.

We were therefore interested in the above mentioned anomalous behaviour of excited oximes of substituted bicyclo-[2.2.1]heptanones and have investigated the photochemistry of
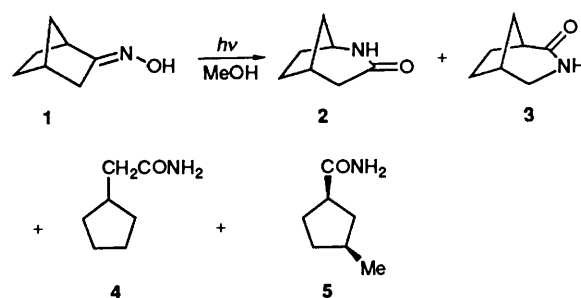

Scheme 1

fenchone oximes 6 in which all of the hydrogens attached to the carbon adjacent to the hydroxyimino group are substituted by methyl groups. We also reinvestigated the products of the photoreaction of camphor oxime 13 in which the α-carbon of the hydroxyimino group is less substituted by methyl groups than is the α-carbon of fenchone oxime 6, in order to gain more insight into the structure–photoproduct relationship which we believe is important for applications of the reactions of excited oximes to synthetic problems.

Results

Photochemistry of Oxime 6 of (+)-Fenchone (Scheme 2).—Irradiation of oxime 6[14] of (+)-fenchone in methanol under nitrogen with a low-pressure Hg arc generated in a Rayonet photochemical reactor for 15 h resulted in 96% conversion of the oxime and afforded a product mixture from which two pure products (B and C) as well as two mixtures of isomeric products (A and D) were isolated by preparative TLC (PLC) with silica gel followed by PLC with alumina and by HPLC (see Experimental section). The least polar product (A) was identified as being a mixture of isomers of nitriles 7 and 8 (11%), by its IR, ^{1}H NMR, and mass spectra (see Experimental section). The next less polar products, B and C, which were separated from a 1:1 mixture by HPLC, were two isomeric lactams: 11 (13%) and 12 (13%). The crystalline lactam 11 was identical with an authentic sample prepared by Beckmann rearrangement of (+)-fenchone oxime according to a procedure reported by Cottingham.[15]

Scheme 2
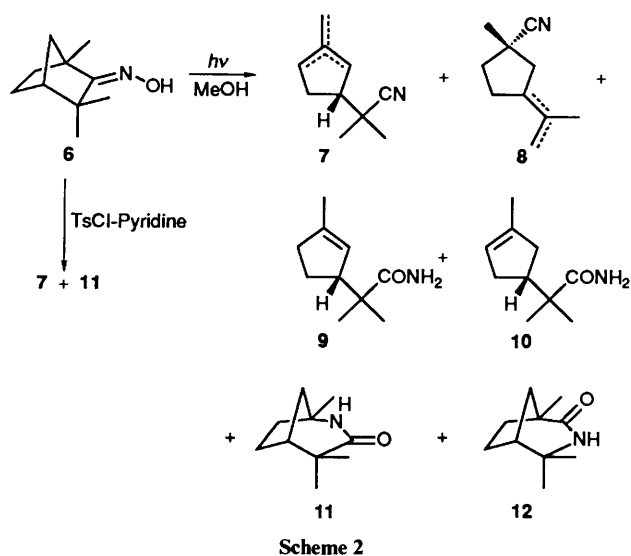
The IR spectrum of the previously unreported isomeric crystalline lactam 12 exhibited a series of bands, at 3280, 1660 and 1625 cm^{-1}, which were assignable to the lactam function. The NMR spectrum (400 MHz) included three singlets, at δ 1.20, 1.25 and 1.26 (each 3 H), assignable to one of the three methyl groups. The effects on the chemical shifts of the three singlets due to the tertiary Me group in lactam isomers 11 and 12 in CDCl$_3$ upon addition of a paramagnefic shift reagent,[16] Eu(dpm)$_3$, [0.5 mol dm^{-3} Eu(dpm)$_3$ in CDCl$_3$], established the structure of the two lactams 11 and 12; although *two* singlets out of the three which were assignable to the methyl groups of lactam 11 shifted to lower field, only *one* singlet out of the three assignable to the methyl group of lactam 12 shifted to lower field (δ 5.08, 5.35 and 5.33) on the addition of Eu(dpm)$_3$. The methyl signals which shifted upon the addition of a paramagnetic shift reagent are assignable to the methyl groups attached to the carbon α to their carbonyl group. These results thus confirm that lactams 11 and 12 are 1,4,4-trimethyl-2-azabicyclo[3.2.1]octan-3-one and 1,4,4-trimethyl-3-azabicyclo[3.2.1]octan-2-one.

The most polar crystalline product (D), which was purified by HPLC, was found to be a 1:1 mixture of the isomeric amides 9 and 10 (10%). The IR spectrum included a series of bands assignable to the CONH$_2$ group (see Experimental section); the ^{1}H NMR spectrum (400 MHz) exhibited a pair of signals assignable (each) to the Me group attached to the trigonal carbon of amides 9 and 10 as well as signals due to a pair of olefinic protons in the cyclopentene structure of amides 9 and 10; the EI mass spectrum exhibited the base peak at m/z 87, assignable to the (M − Me$_2$CHCONH$_2$)$^+$ ion. A 1:1.8 mixture of amides 9 and 10 was then prepared by alkaline hydrolysis of a mixture of nitriles 7 obtained by Beckmann rearrangement of (+)-fenchone oxime 6. The IR and the ^{1}H NMR spectra were qualitatively in agreement with those of the aforementioned mixture of amides obtained by photolysis of oxime 6.

Beckmann Rearrangement of (+)-*Fenchone Oxime* **6** (*Scheme* 2).—Beckmann rearrangement of the oxime of racemic fenchone has already been reported by Cottingham.[15] He reported that treatment of fenchone oxime with toluene-*p*-sulphonyl chloride–pyridine, phosphorus pentachloride, or sulphuric acid led to the formation of a single lactam (compound 11) and a mixture of nitriles 7. We repeated his work in order to obtain lactam 11 and nitriles 7 for direct comparison with those products obtained by photolysis, and for the preparation of amides 7 and 8, as well as for direct comparison. Oximation of (+)-fenchone according to Cottingham's

procedure gave a single oxime **6**. A nitrile mixture, compounds 7, and lactam 11 were thus obtained in 87 and 9% yield, respectively. Hydrolysis of the nitrile mixture in 95% ethanol with potassium hydroxide afforded a crystalline product, which was purified by HPLC to give a 1:1.8 mixture of the two isomeric amides 9 and 10. As mentioned previously, the IR and ^{1}H NMR spectra of these amide mixtures were qualitatively identical with those of the amide mixture from the photolysis of oxime **6**.

Photochemistry of (+)-*Camphor Oxime* **13** (*Scheme* 3).— Irradiation of the oxime 13[17] of (+)-camphor in methanol at 20–30 °C under nitrogen with a low-pressure Hg arc generated

Scheme 3
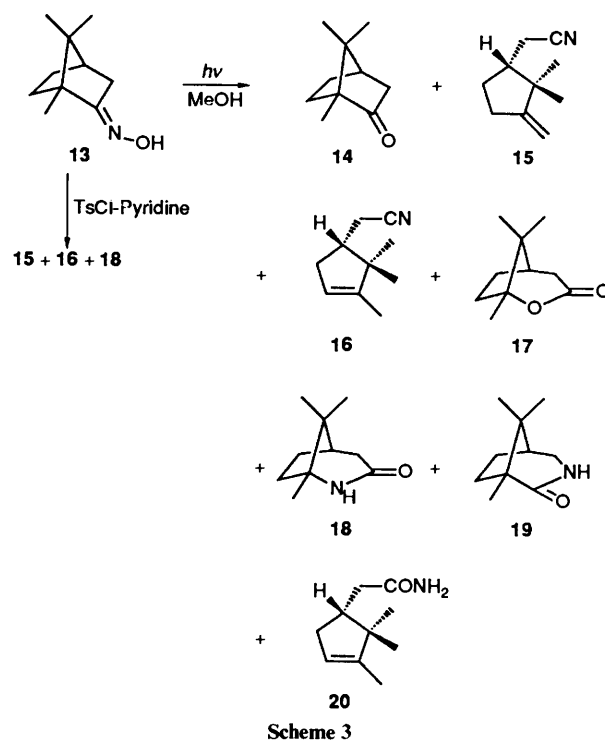
in a Rayonet photochemical reactor for 15 h resulted in 85% conversion of the oxime, and afforded an oily mixture of products. Separation by extensive PLC, in order of polarity, gave (+)-camphor 14 (4%), a mixture of isomeric nitriles 15 (4%) and 16 (2%), 1,8,8-trimethyl-2-oxabicyclo[3.2.1]oxtan-3-one 17[18] (6%), 1,8,8-trimethyl-2-azabicyclo[3.2.1]octan-3-one 18[12,19] (12%), an isomeric lactam, 1,8,8-trimethyl-3-azabicyclo[3.2.1]octan-2-one 19 (α-camphidone)[20,21] (12%) and the amide 20[21,22] (α-campholenic amide) (32%). Details of the product analysis are given in the Experimental section.

Beckmann Rearrangement of (+)-*Camphor Oxime* **13** (*Scheme* 3).—Treatment of the oxime 13 of (+)-camphor under the conditions of a Beckmann rearrangement has been reported to result exclusively in the formation of products arising from cleavage.[20,23] Treatment of (+)-camphor oxime 13 with toluene-*p*-sulphonyl chloride–pyridine under the same conditions as mentioned for the Beckmann rearrangement of (+)-fenchone oxime 6 gave a product mixture from which a 4:3 mixture of nitriles 15 and 16 (86%) was obtained. In addition to this product, arising from cleavage, lactam 18 was isolated, for the first time, by PLC (silica gel) in 0.75% yield. It is interesting to note that a lactam (compound 18) is formed in a yield poorer than in the case of fenchone oxime, in which the carbons α to the hydroxyimino group are more substituted by methyl groups than is the α-carbon of camphor oxime.

Discussion

The foregoing experiments have disclosed that the major products of the photolysis of (+)-fenchone oxime 6 in methanol are nearly equal amounts of two isomeric lactams, compounds 11 and 12, in a combined yield of 26%, with accompanying formation of isomeric unsaturated amides, compounds 9 and 10 (10%).

The results of the photolysis of (+)-camphor oxime 13 in methanol give nearly equal amounts of two isomeric lactams, compounds 18 and 19 (a combined yield of 24%), as well as a ring-opened amide, compound 20 (32%), as the major products. In contrast to the report on the photolysis of camphor oxime,[12] nitriles 15 and 16 arising from α-fission are only minor products in our experiments. These results for the oximes of two natural bicyclo[2.2.1]heptanones are in line with those for bicyclo-[2.2.1]heptanone oxime.[13] The results are also nearly parallel to those obtained in the photolysis of steroidal 5- and 6-membered cyclic ketone oximes[3,4,7,8] and unsymmetrically α-substituted cyclohexanone oximes,[5,6] as far as the formation of lactams is concerned. Two structurally isomeric lactams are produced, and the difference in the yields of the lactams (which results from the migration of the carbon centres which are more substituted with alkyl groups and those from the migration of the less substituted carbon centres) is not appreciable. The present results again validate our proposed pathway regarding the photochemical formation of lactams from alicyclic ketone oximes;[3a,3c] the lactams are formed from excited alicyclic ketone oximes via reorganization of singlet excited oxaziridine intermediates in a fully concerted manner.* Moreover, the photochemical formation of lactams 11, 12, 18 and 19 from oximes of fenchone and camphor indicates that the photo-reaction of oximes carried out without any other reagent is useful in synthesis, since an ordinary Beckmann rearrangement of fenchone oxime[15] gives no lactam 12, and camphor oxime has given neither lactam 18 nor lactam 19 (α-camphidone) with use of a Beckmann rearrangement catalyst.[20,23] Our foregoing experiment, however, gave for the first time the formation of lactam 18 in very poor yield (0.17%) by treatment of camphor oxime with a Beckmann rearrangement catalyst. The formation of α-camphidone 19 in <1% yield by Schmidt reaction of camphor with azide–sulphuric acid–chloroform has been reported.[25] It was only in 1980 that Krow and Szczepanski reported that a reflux of camphor with hydroxylamine-O-sulphonic acid in formic acid for 20 h gave α-camphidone 19 in 46% yield.[21]

Thus, photoreactions carried out under neutral conditions at room temperature may be useful for nitrogen insertion into bicyclo[2.2.1]heptanones, which process has been extensively reviewed by Krow,[26] to give lactams such as 12, 18 and 19.

On the Pathways of Formation of Unsaturated Amides 9, 10 and 20 and Lactone 17.

—Results of the photolysis of oximes 6 and 12 of two natural bicyclo[2.2.1]heptanones in methanol, however, differ from those concerning the photolysis of monocyclic or fused 5- and 6-membered-ring cyclic ketone oximes in one respect: the photolysis of oximes 6 and 12 gave substantial amounts of unsaturated acid amides 9, 10 and 20. We have found[3] that no [or at most only a minor amount (7%) of] unsaturated acid amides are obtained in photoreactions of most steroidal ketone oximes.

It is interesting to note here that saturated acid amides, in contrast to unsaturated acid amides, are formed when mono-

cyclic 6-membered-ring cyclic ketone oximes are photolysed in isopropyl alcohol[27] instead of methanol.

We have already proposed[3c] that such unsaturated amides such as 9, 10 and 20 are likely to be formed from oxaziridine intermediates. Scheme 4 outlines one of the pathways from
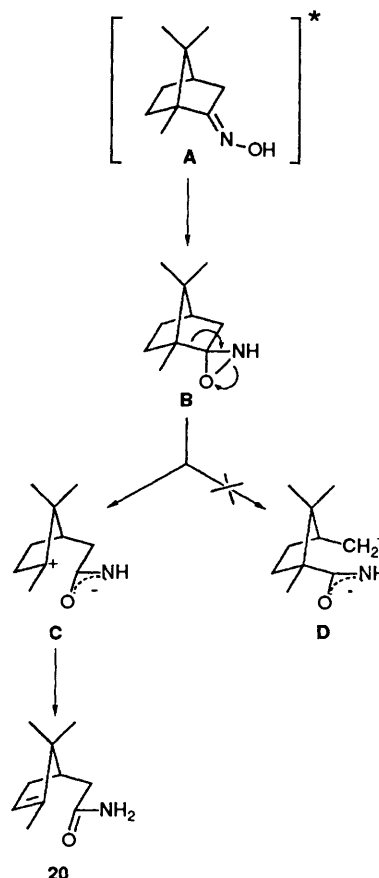
Scheme 4

excited camphor oxime A to amide 20. As outlined above, these amides are most likely formed via ionic thermal rearrangements of oxaziridine B. This rearrangement may involve a regiospecific ionic cleavage of the oxaziridine to give a more stabilized tertiary carbocation C, from which a proton is lost, giving alkenoic acid amide 20. In agreement with this pathway, no isomeric amide which can arise from a primary radical D, for example, was found in the product of the photoreaction of camphor oxime 13. An alternative mechanism whereby C–C cleavage takes place through a radical process is less likely since the preferred reaction of a tertiary radical which corresponds to the tertiary carbocation C would be abstraction of a hydrogen from the solvent to give an alkanoic amide.

There are, naturally, other possible, but less likely, pathways: the amides are formed from excited oxaziridine intermediates, as in the formation of lactams, but from an excited state of the oxaziridines which differs from the excited state leading to lactams.

Though the formation of lactone 17 seems to be anomalous, it is most likely a secondary photoproduct; it is probably formed from the reaction of an intermediate generated from an excited camphor (formed from the oxime 13) with a trace of con-taminating oxygen in the solvent.

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* We would like to note here that our conclusion[3c] concerning the pathway of the formation of lactams from excited alicyclic ketone oximes has been incorrectly quoted in ref. 24. Our results exclude the intervention of any radical intermediates (in most cases) in the formation of lactams from excited oximes.

Experimental

M.p.s were determined with either a Yanagimoto m.p.

apparatus or with a Laboratory Devices Mel-Temp., IR spectra were determined for Nujol mulls with a Hitachi-Perkin Elmer Model 125 spectrophotometer, unless stated otherwise. ^{1}H NMR spectra were determined with a Hitachi R-22 (90 MHz), JEOL FT-NMR FX 100 (100 MHz) or FX 400 (400 MHz) spectrometer (solvent CDCl$_3$; SiMe$_4$ as internal reference). J-Values are given in Hz. Mass spectra were determined with a JEOL JMS-D 300 spectrometer (70 eV), either by the Faculty of Pharmaceutical Sciences of this University or the Faculty of Agriculture. Elemental analyses were performed by the Faculty of Pharmaceutical Sciences. PLC was carried out on Merck silica gel 60 PF$_{254}$, No. 7749 or Merck precoated aluminium oxide 60 PF$_{254}$, No. 5713. HPLC was performed with a Waters Model 45 pump equipped with a Model 48 UV detector at 230 nm, or with a Model R401 differential refractometer, Model U6K injector and a Nippon Denshikagaku dual-channel recorder (Model Unicorder U-228). Waters Radical Pack Cartridge Silica (10 μm; 8 mm ID × 10 cm) and hexane containing 5% isopropyl alcohol (2 cm^3 min^{-1}) as a mobile phase were used.

Oxime 6 of (+)-Fenchone.—(+)-Fenchone (9 g, Wako, Pr. Grade), hydroxylamine hydrochloride (7.7 g), water (11 cm^3) and 95% ethanol (38 cm^3) containing 30% aq. NaOH (14 cm^3) were stirred and heated under reflux for 20 h under nitrogen atmosphere (according to Cottingham's procedure[15]). Water (50 cm^3) was added to this mixture and precipitated oxime was collected by filtration. The crude oxime was dissolved in dichloromethane (50 cm^3), and the solution was washed with water and dried over anhydrous sodium sulphate. Evaporation gave a crude oxime, which was recrystallized from 99% ethanol to give fenchone oxime 6 (8.2 g, 83%), m.p. 169–170 °C (sealed tube, MEL-TEMP) (lit.,[14a] 164–165 °C); δ(270 MHz) 1.22, 1.30 and 1.33 (each 3 H, each s, 3 × Me).

Photoreaction of (+)-Fenchone Oxime 6.—A solution of (+)-fenchone oxime 6 (400 mg) in methanol (240 cm^3) was irradiated with a low-pressure Hg arc, generated by a Rayonet photochemical reactor, at 20–30 °C under nitrogen for 15 h. The solvent was evaporated off on a rotary evaporator under reduced pressure at room temperature to give an oily mixture of products. The products were subjected to PLC (silica gel; solvent: dichloromethane containing 2% of methanol) to give 6 fractions A–F in order of mobility. Each fraction was dissolved in diethyl ether, and the solutions were washed with water and dried over anhydrous sodium sulphate. Removal of the solvent from each fraction gave a gummy product.

Fraction A (43 mg, R_f 0.9) was an oily mixture of seco nitriles 7 and 8; ν$_{max}$(neat)/cm^{-1} 2230 (C≡N); δ(100 MHz) 1.32 (3 H, s, Me), 1.36 (3 H, s, Me), 1.73 (3 H, s, C=CMe), and 4.75, 4.87 and 5.28 (C=CH); m/z 149 (M$^+$ of 7 and 8, 30%), 123 [(M − C≡N)$^+$, 34] and 81 ([(M − Me$_2$CCN)$^+$ of 7, 100].

Fractions B (17 mg, R_f 0.75), D (38 mg, R_f 0.55) and F (7 mg, R_f 0.25) were intractable mixtures. Fraction C (16 mg, R_f 0.6) was the starting oxime 6. Fraction E (161 mg, R_f 0.4) was again subjected to PLC (alumina) with dichloromethane containing 2% methanol to give three fractions: E^1, E^2 and E^3. Each fraction was extracted with 2:1 dichloromethane–methanol; the residues obtained upon removal of the solvent were dissolved in dichloromethane, and the solutions were washed with water and dried over anhydrous sodium sulphate. The most mobile fraction was E^1 (4 mg, R_f 0.9), which gave an intractable mixture. The next mobile, crystalline fraction, E^2 (101 mg, m.p. 100–104 °C, R_f 0.5), was a 1:1 mixture of two lactams, 11 and 12. The two lactams were separated by repeat HPLC to give 1,4,4-trimethyl-2-azabicyclo[3.2.1]octan-3-one 11 (retention volume 16.4 cm^3) and 1,4,4-trimethyl-3-azabicyclo-[3.2.1]octan-2-one 12 (retention volume 15.6 cm^3). The lactam

11 recrystallized from light petroleum (boiling range 30–60 °C), was identical with an authentic specimen prepared by a Beckmann rearrangement of (+)-fenchone oxime, according to a procedure reported by Cottingham[15] (*vide infra*).

The new *lactam* 12 was recrystallized from light petroleum to give a sample for analysis. M.p. 129.5–130.0 °C (Found: C, 71.6; H, 10.2; N, 8.1. C$_{10}$H$_{17}$NO requires C, 71.81; H, 10.25; N, 8.38%); ν$_{max}$/cm^{-1} 3280 (NH), 1660 and 1625 (lactam C=O); δ(400 MHz) 1.20, 1.25 and 1.26 (each 3 H, s, 1,4,4-trimethyl), 1.49–2.08 (7 H, m) and 5.05 (NH); m/z 167 (M$^+$, 6.6%) and 152 [(M − CH$_3$)$^+$, 100].

The most polar, crystalline fraction, E^3 (39 mg, R_f 0.3), m.p. 106–107.5 °C, was a mixture of amides 9 and 10, which was subjected to HPLC in the same manner as that described above. The residue from the main peak with its retention value (retention volume 22.2 cm^3) was recrystallized from diethyl ether–light petroleum to give a mixture of amides, 9 and 10, m.p. 111–114 °C; ν$_{max}$/cm^{-1} 3400 (NH), 3210 (NH), 1650 (amide C=O) and 1615 (amide C=O); δ(400 Hz) 1.11 (3 H, s, α-Me of 10), 1.13 (3 H, s, α-Me of 10), 1.74 (3 H, br s, 3-Me of 10), 5.28 (1 H, septet, J 1.8, 4-H) and 5.66 (2 H, br, NH$_2$); 1.127 (3 H, s, α-Me of 9), 1.132 (3 H, s, α-Me of 9), 1.68 (3 H, br s, 3-Me of 9), 5.23 (1 H, sextet, J 1.8, 2-H of 9) and 5.48 (2 H, br, NH$_2$). Ratio 10:9 from the ratio of the integrals of 3-Me and 4-H groups was 1.7:1; m/z 167 (M$^+$, 2%), 123 [(M − CONH$_2$)$^+$, 8], 87 [(M − Me$_2$CHCONH$_2$)$^+$, 100] and 81 [(M − Me$_2$CHCONH$_2$)$^+$, 27].

Beckmann Rearrangement of (+)-Fenchone Oxime 6.—The reaction was carried out essentially according to a procedure reported by Cottingham[15] for a Beckmann rearrangement of (±)-fenchone oxime. To a stirred, ice-cooled solution of oxime 6 (1.0 g) in dry pyridine (4 cm^3) was added a solution of toluene-p-sulphonyl chloride (1.7 g) in dry pyridine (6 cm^3) dropwise. The solution was kept in a refrigerator for 24 h, and then poured into ice–water (150 cm^3). The aq. solution was extracted with diethyl ether. The organic layers were combined, washed successively with dil. aq. hydrochloric acid and brine, and finally dried over anhydrous sodium sulphate. Work-up by the usual method gave an oily product (856 mg), which was subjected to PLC (silica gel; dichloromethane containing 2% of methanol) to afford two fractions. The more mobile fraction (R_f 0.95–0.9) (726 mg, 87%) was a mixture of nitriles 7, ν$_{max}$(neat)/cm^{-1} 2230 (C≡N); δ(100 MHz) 1.27, 1.29 and 1.32 (each s, Me), 1.72 (CH=C*Me*) and 4.86 and 5.27 (CH=C). A more polar, crystalline fraction (R_f 0.2; extracted with 1:2 methanol–dichloromethane) (91 mg, 9%) was recrystallized twice from light petroleum to afford lactam 11, m.p. 140–141 °C, which was identical in every respect with the sample obtained by the photoreaction.

Hydrolysis of a Mixture of Nitriles 7 obtained by the Beckmann Rearrangement of Oxime 6.—The mixture of nitriles 7 (334 mg) was dissolved in 95% ethanol (7 cm^3) containing 30% potassium hydroxide and the solution was heated under reflux for 2 h. After evaporation of the solvent, the residue was extracted with water–dichloromethane. The organic layer was dried over anhydrous sodium sulphate. The solution was worked up in the usual manner to give an oily product (228 mg), which was shown by TLC and its ^{1}H NMR spectrum to be a mixture of an unchanged starting material (major) and amides. The oily product was treated with light petroleum to afford a crystalline material (40 mg), m.p. 114–115.5 °C. A portion of the crystalline product (20 mg) was subjected to HPLC in the manner as described for the purification of photoamides 9 and 10. The main fraction (15 mg) with its retention value (22.2 cm^3) was collected and recrystallized from diethyl ether–light petroleum to give a 1:1.8 mixture of isomeric of amides 9 and 10. The IR and ^{1}H NMR spectra were qualitatively in accord

with those of a mixture of amides 9 and 10 obtained from photoreaction of compound 6.

Photoreaction of (+)-Camphor Oxime 13.—A solution of oxime 13 (400 mg), m.p. 119–120 °C (sealed tube, Yanagimoto m.p. apparatus) (lit.,[17] 115 °C; lit.,[25] 118–119 °C): δ(270 MHz) 1.22, 1.30 and 1.33 (each 3 H, each s, 3 × Me), of (+)-camphor in methanol (special grade; 240 cm³) was irradiated for 15 h under nitrogen at 20–30 °C, as described for the oxime 6 of (+)-fenchone. Removal of solvent under reduced pressure at room temperature gave an oily product mixture (390 mg), which was subjected to PLC (silica gel) with dichloromethane containing 2% methanol to give five fractions (A–E) in order of decreasing mobility. Fraction A (extracted with Et₂O) and fractions B–E (extracted with 2:1 CH₂Cl₂–MeOH), obtained by removal of the solvents, were again dissolved in diethyl ether, and the solutions were washed with brine, dried over anhydrous sodium sulphate and worked up by the usual method.

The most mobile fraction, A (45 mg) show bands at 2240 (CN) and 1740 cm⁻¹ (camphor) in the IR spectrum (neat). This mixture was found to be a 2:2:1 mixture of camphor 14, α-campholenonitrile 16, and its isomer 15 by comparison of the ¹H NMR spectra with those of camphor and the two nitriles[12] prepared according to the reported procedure.[28,29]

Fraction B (20 mg, 6%), m.p. 168 °C (from light petroleum), was identified as 1,8,8-trimethyl-2-oxabicyclo[3.2.1]octan-3-one 17 by direct comparison with an authentic specimen[18] prepared by Baeyer–Villiger oxidation of (+)-camphor. Fraction C (59 mg) was the starting oxime. The crystalline fraction D (40 mg, 12%) was lactam 19 (α-camphidone), which was recrystallized from light petroleum, gave a sample for analysis, m.p. 234–236 °C (sealed tube, MEL-TEMP) (lit.,[20a] 228–230 °C; lit.,[20b] 230–231 °C; lit.,[20c] 230 °C; lit.,[21] 234–236 °C; δ(400 MHz) 0.95, 1.05 and 1.10 (each 3 H, s, Me), 3.01 (1 H, dt, J 11.2 and 2.1, 4α-H), 3.47 (1 H, dd, J 3.4 and 11.2, 4β-H) and 5.70 (1 H, br s, NH); m/z 167 (M⁺, 56%) and 152 [(M − Me)⁺, 100].

Fraction E (179 mg) was a mixture and was again subjected to PLC (alumina) with dichloromethane containing 2% methanol to give three fractions (E¹, E² and E³ in order of decreasing mobility). Fraction E¹ (7 mg) was an intractable mixture. Fraction E² (40 mg, 12%) was recrystallized from light petroleum to give pure isomeric lactam 18, m.p. 197–198 °C (sealed tube, MEL-TEMP) (lit.,[19] 156–160 °C; lit.,[12] 133–136 °C); ν_{max}/cm^{-1} 3500, 3470, 3180 and 3060 (NH) and 1655 (C=O); δ(400 MHz) 0.97, 1.02 and 1.12 (each 3 H, s, Me), 1.87–2.08 (5 H, m), 2.18 (1 H, dd, J 18.1 and 1.5, 4α-H), 2.66 (1 H, ddd, J 2.7, 4.6 and 18.1, 4β-H) and 6.07 (1 H, br s, NH); δ[90 MHz; Eu(dpm)₃] 1.54, 1.98 and 3.02 (each 3 H, s, Me); m/z 167 (M⁺, 30%), 152 [(M − Me)⁺, 3.7], 139 [(M − CO)⁺, 32], 124 [(M − NHCO)⁺, 99] and 110 [(M − CH₂NHCO)⁺, 100].

The crystalline fraction E³ (108 mg, 32%) was α-campholenic amide 20, which was recrystallized from methanol–light petroleum to afford an analytical sample, m.p. 130.5–131 °C (lit.,[21] 127–128 °C; lit.,[22a] 124 °C; lit.,[22b] 130 °C); ν_{max}/cm^{-1} 3375 and 3200 (NH), 1660 and 1625 (amide); δ(100 MHz) 0.78 and 1.09 (each 3 H, s, Me), 1.63 (3 H, d, J 1.5, =CMe), 1.6–2.3 (5 H, m), 5.23 (1 H, br s, CH=C), 5.83 and 6.30 (each 1 H, each br s, NH₂); m/z 167 (M⁺, 12.5%), 109 [(M − CH₂CONH₂)⁺, 46], 108 [(M − CH₃CONH₂)⁺, 100] and 93 [(M − CH₂CONH₂ − H − Me₃)⁺, 82]. This amide was identical with a sample prepared by alkaline hydrolysis[22b,23] of nitrile 16 (α-campholenic nitrile).[23]

Beckmann Rearrangement of (+)-Camphor Oxime 13.—Camphor oxime 13 (1.0 g) in dry pyridine (8 cm³) was subjected to Beckmann rearrangement with tosyl chloride (1.74 g) in the

same manner as described for the Beckmann rearrangement of (+)-fenchone oxime. The product mixture was subjected to PLC (silica gel) with dichloromethane containing 2% methanol to give two fractions. The more mobile fraction (R_f 0.95–0.9) (760 mg, 86%) was a 3:4 mixture of nitriles 15 and 16, ν_{max}/cm^{-1} 2240 (CN); δ(100 MHz) 0.58 and 1.03 (each 3 H, each s, Me of 15), 1.68 (3 H, d, J 1.7, C=CMe of 16), 5.23 (1 H, br s, CH= of 16); 0.89 and 1.13 (each 3 H, each s, 16) and 4.80 and 4.84 (each 1 H, each d, J 2.3, *exo*-methylene protons of 15). A more polar fraction (R_f 0.2) (7.5 mg, 0.75%) was the crystalline lactam 18, m.p. 197–198 °C (from light petroleum), identical with the sample from the photoreaction mentioned above.

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