Tetrahedron. Vol. 27, pp. 2399 to 2408 Pergamon Press 1971. Printed in Great Britain

MECHANISM OF DECOMPOSITION OF A PHOSPHORYLATED TRIAZOLINE

EVIDENCE FOR A 3,2-*endo,endo* METHYL MIGRATION IN A NORBORNYL SYSTEM[1]

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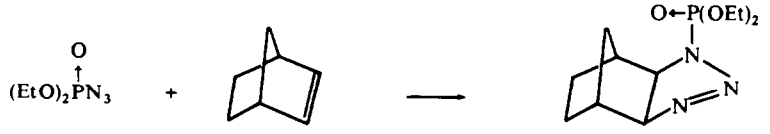
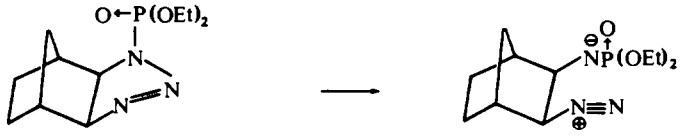
(*Received in the USA* 3 *March* 1971; *Received in the UK for publication* 16 *March* 1971)

Abstract—Diethyl phosphorazidate (**1**) and 2-methyl-2-norbornene (**7**) condense to give two isomeric phosphorylated amidates **10** and **11**. Hydrolysis of the mixture of **10** and **11** gave *endo*-3-methyl-2-norbornanone (**13**) and *exo*-3-methyl-2-norbornanone (**14**) in the ratio of 86:14. On the basis of this result it is shown that a 3,2-*endo,endo* methyl migration occurs in the decomposition of the initially formed triazoline (**8**).

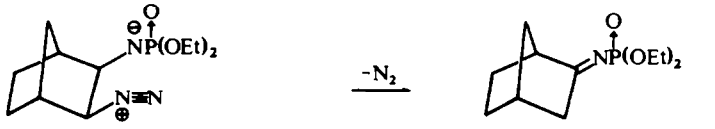
IN A previous report[3] we demonstrated that the decomposition of the triazoline **3**, formed from the 1.3-dipolar addition of diethyl phosphorazidate (**1**) and norbornene (**2**), occurs by two consecutive first-order reactions (Eqs 2 and 3), with the intermediacy of a diazonium betaine **4**. It was also shown by deuterium labelling studies that the



1 **2** **3** Eq. 1

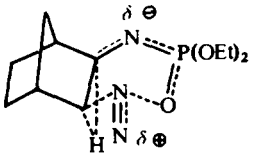


3 **4** Eq. 2



4 **5** Eq. 3

triazoline decomposition took place without any major sketal rearrangement of the norbornyl system.[4] On the basis of these studies a 6-membered transition state as shown in **6** was considered a reasonable possibility during the decomposition of **3**.



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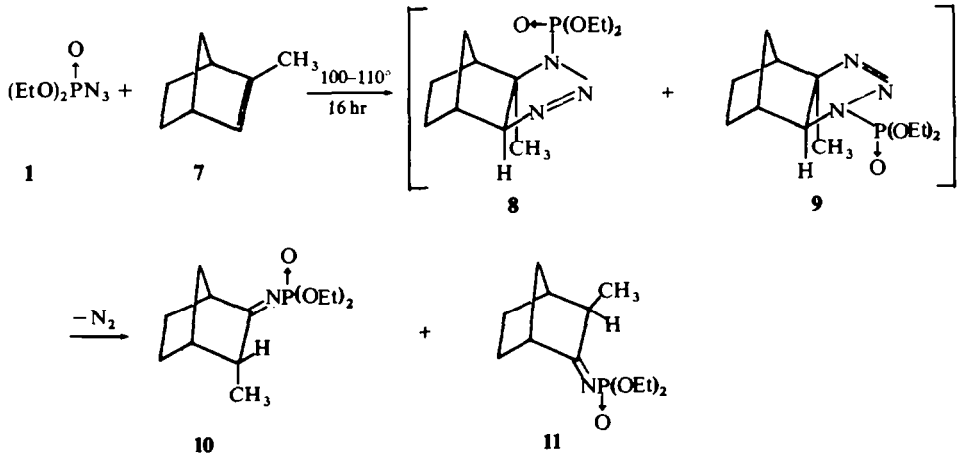
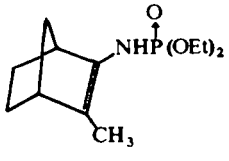
The transition state **6** implies a 3,2-*endo.endo* hydride shift, a process not known to occur in the norbornyl system.[5–7] One example of 3.2-*endo,endo* hydride shift has been reported[8] in the bornyl system during the pinacol rearrangement of 3-*endo*-phenyl-2,3-*exo,cis*-bornanediol. The purpose of the present study was to determine if Me shift *via* a 3,2-*endo,endo* migration could occur in a norbornyl system.

In the present work 1,3-dipolar addition of diethyl phosphorazidate (**1**) was carried out with 2-methyl-2-norbornene (**7**). The triazolines (**8** and **9**) were not isolated in this case as decomposition resulted under the conditions of the addition. The decomposition products were similar to the products isolated in the norbornene case,[3,4] the major components being the isomeric phosphorylated imines **10** and **11**. The IR spectrum (film) of the mixture showed small bands at 3400 and 3225 cm^{-1} which were tentatively ascribed to the possible presence of the enamine tautomer

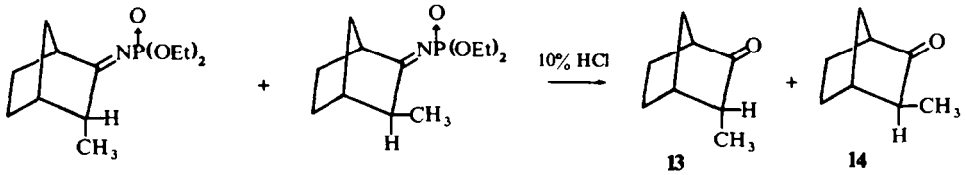


12.[4] By careful fractional distillation the enamine tautomer **12** was removed from the



12

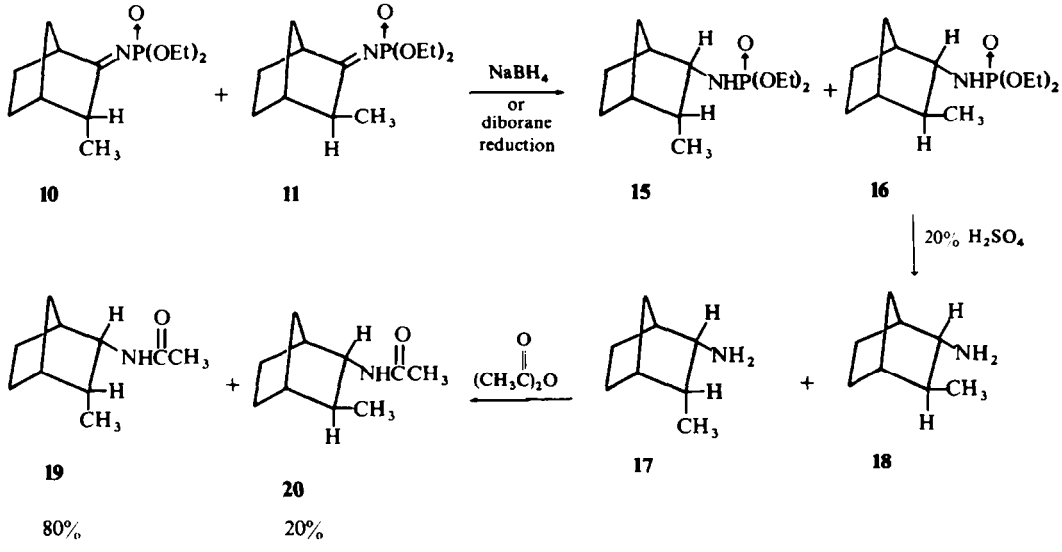
phosphorylated imines **10** and **11**. However, a separation of **10** and **11** could not be effected. The ratio of **10** to **11** was deduced from the ratio of the 3-methyl-2-norbornanones (**13** and **14**) obtained by acid hydrolysis. A mixture of **10** and **11** gave *endo*-3-methyl-2-norbornanone (**13**) and *exo*-3-methyl-2-norbornanone (**14**) in the ratio of 86:14 on treatment with 10% HCl (v/v) for 5 hr at room temperature. Under



10 **11** **13** 86% **14** 14%

these conditions there was no equilibration of the ketones **13** and **14**.

Further proof for the presence of **10** and **11** in the ratio of 86:14 was obtained by the following sequence of reactions. Sodium borohydride or diborane reduction of the mixture of phosphorylated imines **10** and **11** gave phosphorylated amines **15** and **16**. The stereochemistry of the reduction was assumed to be *exo* hydride attack on the



10 **11** **15** **16**

19 **20** **17** **18**

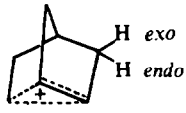
80% 20%

basis of well established *exo* hydride attack in the hydride reductions of norbornanones.[9] The mixture of phosphorylated amines **15** and **16** was then hydrolysed with 20% sulfuric acid to a mixture of amines **17** and **18** which without separation was acetylated using acetic anhydride to give a mixture of *endo*-3-methyl-*endo*-2-N-acetylaminonorbornane (**19**) and *exo*-3-methyl-*endo*-2-N-acetylaminonorbornane (**20**) in the ratio of 80:20 (by GLC). The amine acetates **19** and **20** were separated by fractional crystallization. Since the amine acetates **19** and **20** were not known in the literature, they were synthesized independently *via* the LAH reduction of the oximes

of *endo*-3-methyl-2-norbornanone and *exo*-3-methyl-2-norbornanone followed by acetylation of the resulting amines.

DISCUSSION

We have previously shown that no skeletal rearrangement occurs in the norbornyl system in the decomposition of the triazoline obtained from 2-norbornene and diethyl phosphorazidate.[4] *In the present, study formation of more than* 80% *of diethyl* endo-3-*methyl-2-norbornylidenephosphoramidate* (**10**) *from 2-methyl-2-norbornene* (**7**) *and diethyl phosphorazidate* (**1**) *shows that there has occurred an* endo,endo *migration of the* C-2 *methyl group to the* C-3 *position.* This is rather striking since 3,2-*endo,endo* migrations are stringently avoided in norbornyl systems.[5,7] In systems where there is only an *endo,endo* migration possible to the carbonium ion center, the carbonium ion undergoes rearrangement by way of Wagner–Meerwein and 6,2 hydride shifts until the migrating group becomes *exo*.[5,7] This means that the rearrangement of the carbonium ion is faster than 3,2-*endo,endo* migration. Several explanations have been offered for the stereospecificity of 3,2-migrations in norbornane systems. There are suggestions invoking nonclassical cations.[5,10–14] According to this group, because of bridging in the norbornyl cation (**20**) any attack by external nucleophile or vicinal



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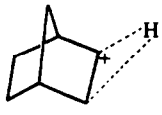
hydride shift must take place on the side of the ion opposite the bridge. Only an *exo* hydrogen is in a favorable position for such an attack. According to Brown[15] *endo*-hydride shift is hindered because of steric interactions between the migrating hydrogen and the C-5, C-6 ethylene bridge. Recently Schleyer[6] has proposed a new explanation based on relative torsional strain involved in the transition states for *exo,exo*(**21**) *vs endo,endo*-(**22**) 3,2-hydride shift. In the transition state **21** arrangements of bonds



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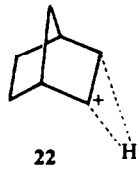

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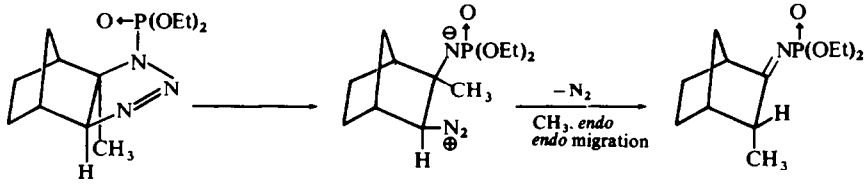
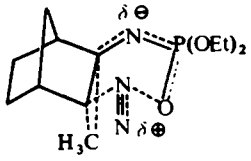
around C-1, C-2 and C-3, C-4 are of the stable skewed type, whereas they are of the less stable eclipsed type in **22**. On this basis, Schleyer has estimated that transition state **21** could be up to 6 kcal/mole more stable than transition state **22**.

In triazoline decomposition, previous studies[3,16] have indicated the intermediacy of diazonium betaines like in Eq 2. In all the 3,2-*exo,exo* migrations reported for the norbornyl system, a norbornyl cation is involved. An important factor in diazonium

ion chemistry is that the products can be formed *via* the diazonium ion bypassing a carbonium ion or *via* a carbonium ion. The partitioning between the diazonium ion and the carbonium ion may depend on structure, solvent, etc. Decomposition of the phosphorylated triazoline **8** in our work may be influenced by a subtle structural feature which could induce the decomposition to take place through the diazonium ion bypassing a carbonium ion. To illustrate, the diazonium ion can be stabilized *via* the highly polarized P → O function which could act as an *internal stabilizing group* (Transition state **24**). This could prevent any formation of carbonium ion through loss of N_2 before *endo* migration could take place. Phosphorus can be accommodated nicely in seven-membered ring systems.[17] The stabilization afforded in the intermediate **23** by the favorably situated phosphoryl function may be the contributing



8 diazonium betaine **23** **10**

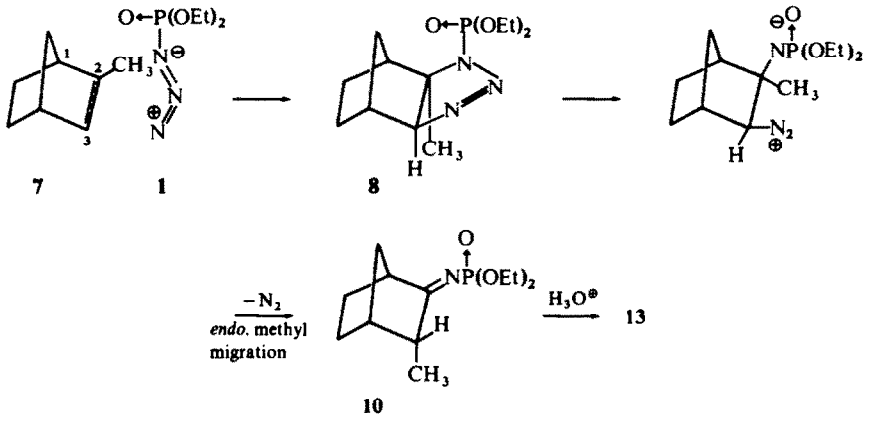


Transition state **24**

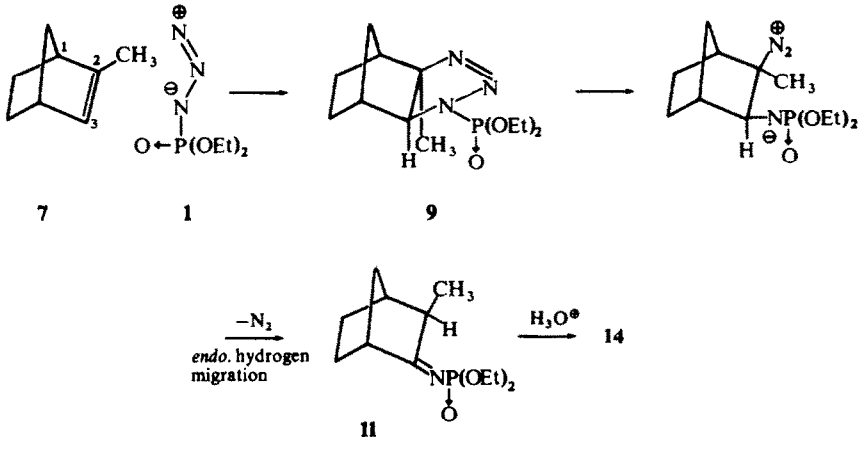
factor for the rather striking 3,2-*endo,endo* migration. Since the "locking" ability of the P → O group prevents skeletal rearrangement, the relatively unfavorable *endo* methyl migration occurs.

In the hydrolysis of the amidate mixture obtained from **1** and **7**, it was found that besides the major *endo*-3-methyl-2-norbornanone (**13**), there was also 14% of *exo*-3-methyl-2-norbornanone (**14**). The formation of the *exo* isomer **14** is rationalized on the basis of two modes of addition of the azide **1** to 2-methyl-2-norbornene (**7**). The major path can be expected to be the addition of the negative end of the azide dipole adding to the C-2 of 2-methyl-2-norbornene (**7**). Another minor path is envisioned to be the addition of the negative end of the dipole adding to the C-3 of 2-methyl-2-norborene (**7**). This could lead to the triazoline **9**, which may decompose by a 3,2-*endo,endo* migration of C-3 hydrogen giving the amidate **11**. The *exo*-3-methyl-2-norbornanone (**14**) arises from this isomeric amidate **11**. Here also the migration is *endo*, but the migration group is hydrogen instead of methyl.

Major Path



Minor Path



EXPERIMENTAL

All m.ps are uncorrected. IR spectra were recorded with a Beckman IR-5A instrument. NMR spectra were run on a Varian A-60 spectrometer.

2-Methyl-2-norbornene (7)

Dehydration of 2-*exo*-methyl-2-*endo*-hydroxynorbornane was carried out following the procedure of Sauers[18] to give a mixture of 7, 2-methylenenorbornane and a third minor component in the ratio of 4:20:1 (estimated by GLC, column: 7% SE-30, on Chrom G, 80/100, A-W, DMCS). Repeated fractional distillation of this mixture using a spinning band column gave pure 2-methyl-2-norbornene, b.p. 116° (atm. pr) n_D^{24} 1·46, [lit.[19] b.p. 119° (atm. pr), n_D^{20} 1·4621], pure 2-methylenenorbornane, b.p. 123° (atm. pr), n_D^{24} 1·471 (lit.[18] $n_D^{24/5}$ 1·4710) and intermediary fractions containing the three components.

Reaction of diethyl phosphorazidate (1) *with 2-methyl-2-norbornene* (7)

A mixture of 7* (5·4 g, 0·05 mole) and 1 (7·16 g, 0·04 mole) was heated at 100–110° under dry N_2 for 16 hr.

* The mixture of 2-methyl-2-norbornene and 2-methylenenorbornane obtained from the dehydration of 2-*exo*-methyl-2-*endo*-hydroxynorbornane could be used without separation, since it was found that the 2-methylenenorbornane did not undergo any reaction with azide 1.

The excess **7** was distilled under aspirator vacuum, to give 10·61 g of yellow oil, which upon vacuum distillation gave the mixture of *endo* isomer **10** and the *exo* ie isomer **11**, as a colorless oil (8·82 g, 83%), the mixture for 30 min., water (100 ml) was added and the mixture was extracted with ether. The extract N. 5·45. Calc. for $C_{12}H_{22}NPO_3$: P. 11·97; N. 5·40%).

Hydrolysis of the phosphoramidate mixture **10** *and* **11**

The mixture of **10** and **11** (5·18 g, 0·02 mole) obtained from the previous reaction was stirred with 10% HCl (100 ml) for 5 hr at room temp. The acidic soln was neutralized with $NaHCO_3$ aq and extracted with CH_2Cl_2 (3 × 25 ml). The organic extract was washed with water and dried ($MgSO_4$). The CH_2Cl_2 was removed using a long column and the residue distilled under reduced pressure to give the mixture of *endo*- **13** and *exo*- **14** (2·2 g, 88%), b.p. 60° (11 mm), $n_D^{23°}$ 1·4675. GLC analysis (Columns: 7%, SE-30 on Chrom G, 80/100 A-W, DMCS and 10% carbowax 20 M on Chrom W, 80/100, A-W, DMCS) showed **13** and **14** in the ratio of 86:14; IR: 1725 cm^{-1} (C=O); NMR (CCl_4) δ 0·96 (d, J = 7 Hz, C-3 *endo* Me) and 1 (d, J = 7 Hz, C-3 *exo* Me).

Sodium borohydride reduction of the phosphoramidate mixture **10** *and* **11**

a. *In methyl alcohol.* To the mixture of **10** and **11** (1·3 g, 0·005 mole) in anhyd MeOH (10 ml) was added $NaBH_4$ (190 mg; 0·005 mole) in small quantities. The mixture was stirred for 10 min after the addition and poured into water (100 ml) and extracted with ether. The ether extract was washed with water and dried ($MgSO_4$). Evaporation of the solvent and distillation of the residue (1·3 g) gave the mixture of **15** and the *exo*-methyl isomer **16** (1·22 g, 90%) b.p. 119–121° (0·25 mm) $n_D^{23°}$ 1·4695; IR (Film): 3200 (NH), 1240 (P → O) and 950–1050 cm^{-1} (broad, OMe). GLC analysis (column: 7% SE-30, on Chrom G, 80/100, A-W, DMCS) showed two peaks in the ratio of 80:20. (Found: P. 11·59; N. 5·77. Calc. for $C_{12}H_{24}NPO_3$: P. 11·88; N. 5·52%).

b. *In tetrahydrofuran.* To a suspension of $NaBH_4$ (190 mg, 0·005 mole) in THF (10 ml), the mixture of **10** and **11** (2·59 g, 0·01 mole) in THF (10 ml) was added with stirring in the course of 15 min. After stirring the mixture for 30 min., water (100 ml) was added and the mixture was extracted with ether. The extract was washed (H_2O) and dried ($MgSO_4$). Evaporation of the solvent and distillation of the residue (2·54 g) gave the same mixture of **15** and **16**, (2·45 g, 90%), b.p. 119–121° (0·25 mm), $n_D^{23°}$ 1·4695, as in the case of methanol-$NaBH_4$ reduction.

Diborane reduction of the mixture of phosphoramidates **10** *and* **11**

To a soln of the mixture of **10** and **11** (1·3 g, 0·005 mole) in dry and freshly distilled THF (20 ml) a very slow stream of diborane [generated by the slow addition of 2·5 g of BF_3-etherate in diglyme (20 ml) to 500 mg of $NaBH_4$ in diglyme (20 ml) and carried by a stream of dry N_2] was passed, and the soln was stirred for 1 hr. To the mixture 2 ml glacial AcOH was added and, after 5 min., diluted with 100 ml water and extracted with ether. The ether extract was washed with water and dried ($MgSO_4$). Evaporation of the ether and distillation of the residue gave the same reduction mixture as in the case of $NaBH_4$-THF, or $NaBH_4$-MeOH reduction. The yield of the mixture of **15** and **16** was 1·2 g (88%), b.p. 119–120° (0·25 mm).

Hydrolysis of the mixture of phosphoramides **15** *and* **16**, *and the acetylation of the resulting amines* **17** *and* **18**

The mixture of **15** and **16** (1·3 g, 0·005 mole) obtained from the previous reaction was heated with 20% sulfuric acid (v/v, 25 ml) for 5 hr on a steam bath. The mixture was cooled and neutralized with 20% $NaHCO_3$ aq. The regenerated amines **17** and **18** were extracted with ether from the aqueous soln and the ether extract was washed with water and dried ($MgSO_4$). To the ether soln, 2 ml Ac_2O was added and boiled for 3 hr. Evaporation of the solvent and excess Ac_2O gave a viscous oil, 530 mg (63%). GLC analysis (Column: 10%, Carbowax 10 M TPA, on 80/100 Chrom G.) showed two peaks in the ratio of 80:20. The mixture was separated by fractional crystallization from ether-pentane. Initially *endo*- **19** crystallized out at white plates m.p. 97·5–99·5°, which corresponded to the large peak in the GLC. Repeated crystallization gave an analytical sample of **19**, m.p. 101–102°; IR (Nujol): 3250 (NH), 1645 and 1540 cm^{-1} (amide C=O); NMR ($DCCl_3$): δ 6·7 (broad d, J = *ca* 7 Hz, N-H), 4·2 (broad m, C-2-H), 1·99 (s, $COCH_3$) and 0·8 (d, J = 7 Hz, C-3 Me). (Found: C, 72·04; H, 10·23; N, 8·24. Calc. for $C_{10}H_{17}NO$: C, 71·86; H, 10·18; N, 8·38%).

From the mother liquors *exo* **20** was obtained in small quantities, which corresponded to the smaller peak in the GLC. Repeated crystallizations gave an analytical sample of **20**, m.p. 116–117°; IR (Nujol): 3250 (NH), 1640 and 1540 cm^{-1} (amide C=O); NMR ($DCCl_3$) δ 6·8 (broad d, J = *ca* 7 Hz, NH), 1·97

(s. $COCH_3$) and 1·03 (C-3 Me). (Found: C, 71·73; H, 10·3; N, 8·19. Calc. for $C_{10}H_{17}NO$: C, 71·86; H, 10·18; N, 8·38%).

exo-3-Methyl-2-norbornanone oxime

A mixture of *exo* **14**[20] (1·24 g, 0·01 mole), hydroxylamine hydrochloride (125 g) and 1 ml pyridine in abs EtOH (10 ml) was boiled for 12 hr. The EtOH was distilled and the residue diluted with water. The mixture was extracted with ether and the extract washed with water and dried ($MgSO_4$). Evaporation of ether gave 1 g of the oxime as a viscous oil (71%). It was purified by short path distillation, b.p. 71–72° (0·25 mm); IR (Film): 3230 cm^{-1} (b, OH).

The NMR spectrum of the oxime in $DCCl_3$ showed a triplet centered at δ 1·12 for the C-3 Me protons. On closer examination it was found to be an overlap of two doublets. By adding the shift reagent[21] tris(dipivalomethanato)-europium (III) to the $DCCl_3$ soln of the oxime, the NMR spectrum was altered to show two doublets at δ 3·04 (J = 7 Hz) and δ 1·8 (J = 7 Hz) for the C-3 Me protons. The presence of two doublets was ascribed to the *syn* and *anti* isomers of the oxime. (Found: C, 69·25; H, 9·45; N, 10·2. Calc. for $C_8H_{13}NO$: C, 69·09; H, 9·35; N, 10·07%).

Lithium aluminium hydride reduction of exo-3-*methyl*-2-*norbornanone oximes and acetylation of the resulting amine* (**18**)

To a suspension of LAH (100 mg) in dry THF (10 ml), a soln of the oxime (1 g, 0·0071 mole) in THF (10 ml) was added with stirring. After the addition, the mixture was boiled for 1 hr. The mixture was cooled in ice and the complex was carefully decomposed with water. The inorganic ppts were filtered off and the filtrate extracted with ether. The extract was washed and dried ($MgSO_4$). To the ether soln, 2 ml of Ac_2O was added and boiled for 3 hr. Removal of ether and excess Ac_2O gave a colorless viscous oil which solidified from ether–pentane mixture m.p. 104–106° (598 mg, 50%). Further crystallizations gave the authentic *exo* **20** m.p. 106–107°.

Preparation of authentic endo-3-*methyl*-endo-2-N-*acetylaminonorbornane* (**19**)

An equilibrium mixture of *endo* **13** and *exo* **14** (55:45)[20] (1 g, 0·0071 mole) was oximated by treating with hydroxylamine hydrochloride (1 g), pyridine (1 ml) mixture in EtOH (10 ml) as in the previous experiment to give the mixture of oximes (1 g) of the ketones **13** and **14** as a thick oil. LAH reduction of this oxime mixture under the same conditions as in the previous experiment gave the amine mixture **17** and **18**, which without isolation was acetylated with Ac_2O (2 ml) as in the previous experiment to give a thick oil (800 mg). This was chromatographed over silica gel (45 g). Elution with chloroform initially gave the amine acetate **18**, m.p. 104–106° (106 mg). The next few fractions were mixtures of **18** and **19**. In the last two fractions amine acetate **19** was obtained in a pure state, m.p. 98–100° (100 mg). Recrystallization of these two fractions gave pure amine acetates **18**, m.p. 106–107°, and **19**, m.p. 101–102°. Mixture m. ps of these amine acetates with the corresponding amine acetates obtained from the mixture of **10** and **11** (by the reduction, hydrolysis, and acetylation sequence) was not depressed.

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