Ritter reactions. Part 14.[1] Rearrangement of 3,3,7,7-tetramethyl-6-methylidenebicyclo[3.3.1]nonan-2-one

Djamal Djaidi, Ivy S. H. Leung, Roger Bishop,* Donald C. Craig and Marcia L. Scudder

School of Chemistry, The University of New South Wales, UNSW SYDNEY, NSW 2052, Australia

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When the bicyclic ketone **1** is reacted with concentrated sulfuric acid and acetonitrile a complex sequence of reactions ensues. The compounds **2**–**6** are formed, with several of these being obtainable in good yields through careful control of the reaction conditions. X-Ray crystallography was used to determine unambiguously the structures of **4**–**6**. These molecular conversions involve both rearrangement and Ritter reactions, and mechanistic explanations are proposed.

Introduction

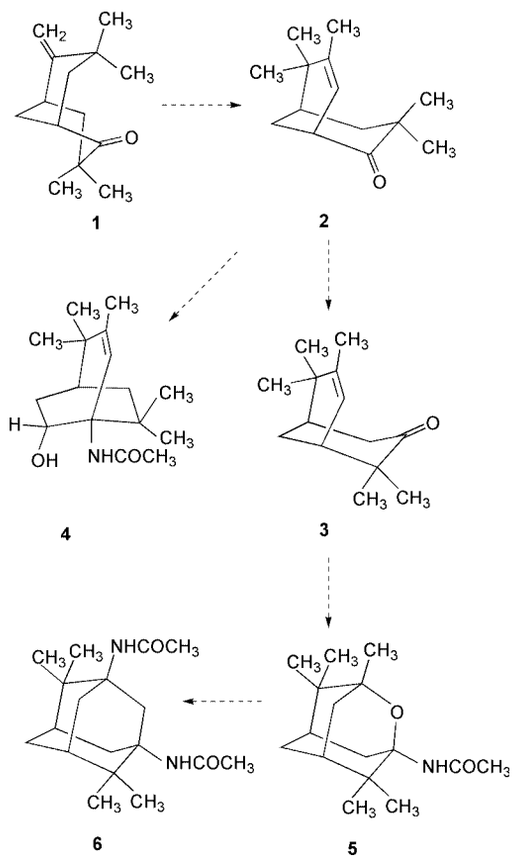
The Ritter reaction describes the addition of carbenium ion and nitrile reagents, together with associated events. In its most familiar form, a substrate such as an alcohol or alkene is treated with strong acid to generate the carbenium ion. The nitrile then reacts with it to produce a nitrilium ion whose hydrolysis affords an amide product. However, since carbenium ions can be produced from many different functional groups, and by a wide range of different techniques, the Ritter reaction provides a particularly versatile synthetic method.[2,3]

One particularly interesting situation is to deliberately combine Ritter reaction with Wagner–Meerwein rearrangement which can result in complex, and sometimes unpredictable, reaction sequences. In this paper we describe the unusual rearrangement processes which occur when 3,3,7,7-tetramethyl-6-methylidenebicyclo[3.3.1]nonan-2-one **1** is subjected to Ritter reaction conditions.

Results and discussion

The unsaturated ketone **1** was prepared in 68% yield by reaction of the corresponding diketone[4] with 1.25 equivalents of methylenetriphenylphosphorane, followed by chromatographic purification. Compound **1** was then subjected to Ritter reaction conditions using acetonitrile and 98% sulfuric acid and found to afford the products **2**–**6**. Through careful variation of the concentrations, reaction temperatures, and reaction times, each of these materials (except **3**) could be isolated in a pure state. In addition, compounds **2**, **5** and **6** were obtained in moderate to high yields.

Since all five products were produced through rearrangement reactions, considerable care must be taken in their identification. Hence the structures of the three solid compounds **4**–**6** were determined by single crystal X-ray analysis. Not only does application of Ritter reaction conditions to **1** provide simple and clean one-step syntheses of these compounds, but their identification also reveals the reaction pathways involved. Scheme 1 shows the sequential relationship of the five products, which are now discussed in turn.



Scheme 1 *Reagents*: i. 98% H_2SO_4, CH_3CN; ii. H_2O.

3,3,6,6,7-Pentamethylbicyclo[3.3.1]non-7-en-2-one 2

Reaction of the unsaturated ketone **1** (Expt. A) gave a 76% yield of an isomeric compound $C_{14}H_{22}O$ as an oil. This material still contained a non-conjugated carbonyl group (ν_{max} 1715 cm^{-1} and δ_C 216.2) but its alkene group was now trisubstituted [ν_{max} 850 cm^{-1}, δ_C 145.0 (C) and 120.4 (CH)]. The NMR data, δ_H 5.27 (1H) and 1.65 (3H), clearly revealed the partial structure –CH=C(CH_3)– thereby indicating that this rearranged product has the structure **2**.

This structural assignment is supported by our earlier work on diene **7** which was rearranged simply and cleanly (75% yield) into the new diene **8**. The latter then could be converted further into the adamantyl amide **9** (Scheme 2).[4]

Mechanistically these alkene rearrangement processes involve protonation, 1,2-methyl migration, and deprotonation steps. The bicyclo[3.3.1]nonane ring system prefers, when possible, to adopt the twin chair conformation.[5,6] This is prevented in both **1** and **7** by the presence of the *endo*-C3 and *endo*-C7 methyl groups. Hence the driving force for these rearrangements is relief of transannular steric crowding, concomitant with conversion of the alkene group from di- to tri-substitution. The ultimate formation of product **9** reflects the thermo-

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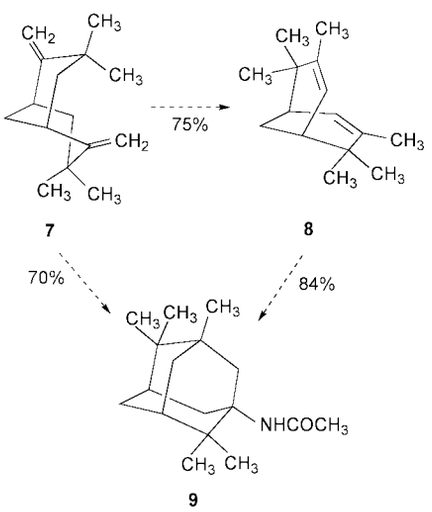
Table 1 Numerical details of the solution and refinement of the three structures

Compound	(**4**)·(H_2O)	**5**	**6**
Formula	$C_{16}H_{27}NO_2 \cdot H_2O$	$C_{16}H_{27}NO_2$	$C_{18}H_{30}N_2O_2$
M	283.4	265.4	306.5
Space group	$P2_1/c$	$P2_1/c$	$C2/c$
a/Å	17.444(6)	13.730(5)	16.222(7)
b/Å	7.241(1)	11.477(4)	11.361(3)
c/Å	13.329(5)	9.621(4)	9.661(4)
β/°	111.55(1)	96.43(2)	113.08(2)
V/Å^3	1565.9(8)	1507(1)	1638(1)
T/°C	21(1)	21(1)	21(1)
Z	4	4	4
μ/mm^{-1}	0.616	0.562	0.599
No. of intensity measurements	2962	2227	1548
R_{merge}	0.023	0.013	0.022
No. of independent observed reflections	1935	1083	1154
No. of reflections (*m*) and variables (*n*) in final refinement	1935 182	1083 174	1154 101
$R = \Sigma^m\|\Delta F\|/\Sigma^m\|F_o\|$	0.042	0.065	0.042
$R_w = [\Sigma^m w\|\Delta F\|^2/\Sigma^m w\|F_o\|^2]^{1/2}$	0.061	0.104	0.061
$s = [\Sigma^m w\|\Delta F\|^2/(m - n)]^{1/2}$	1.50	1.81	2.04



Scheme 2 *Reagents*: i. 98% H_2SO_4, CH_3CN; ii. H_2O.

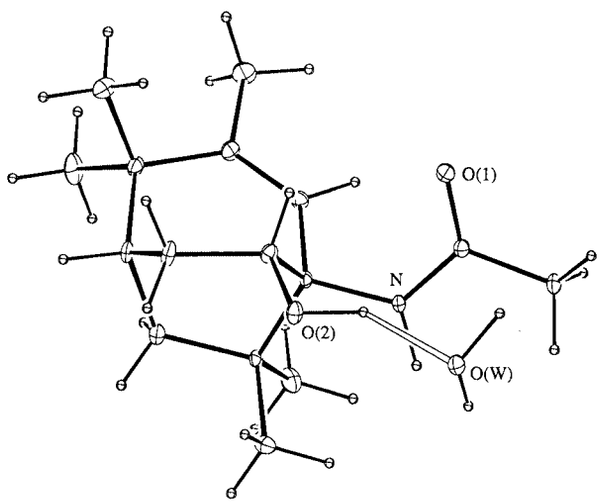


Fig. 1 Molecular structure of the product (**4**)·(H_2O) determined by X-ray crystallography. Only the oxygen and nitrogen atoms are labelled, and the one hydrogen bond shown is indicated by a hollow bond.

dynamic stability of the 1-adamantyl cation relative to the other carbenium ions involved in the rearrangement processes.[7,8]

When **1** was reacted under slightly more severe conditions (Expt. B) small amounts of Ritter amide products were observed. While the major product was still **2**, it was now contaminated by small amounts of a second unsaturated non-conjugated ketone (δ_C 218.3). This material is believed to be 4,4,7,8,8-pentamethylbicyclo[3.3.1]non-6-en-3-one **3** but unfortunately it could not be separated from the mixture. In light of the unambiguous identity of products **5** and **6**, however, the structure **3** is the most reasonable one on mechanistic grounds.

1-Acetamido-3,4,4,8,8-pentamethylbicyclo[3.2.2]non-2-en-7-ol 4

Reaction of ketone **1** under the conditions of Expt. C gave rise to a 12% yield of a solid product. Mass spectrometry revealed a molecular weight of 265, corresponding to the formal addition of acetamide. The presence of an acetamido group CH_3-CONH– was clearly indicated by the spectral data: ν_{max} 1640 cm^{-1}, δ_H 5.68 (NH) and 2.03 (CH_3CO), δ_C 170.9 (CONH); and a –CH=C(CH_3)– unit could also be identified: δ_H 5.34 (1H, q) and δ_C 141.3 (C) and 131.2 (CH); together with four further methyls attached to quaternary sp^3 carbons.

The exact structure of this material was problematic, however, until it was recrystallised from aqueous ethanol and X-ray structure determination showed it to be 1-acetamido-3,4,4,8,8-pentamethylbicyclo[3.2.2]non-2-en-7-ol **4** monohydrate (Fig. 1). Numerical details of the solution and refinement of this and the subsequent X-ray structures are shown in Table 1.

Formation of this Ritter reaction product was unexpected and is surprising on a number of grounds. Bicyclo[3.3.1]nonane derivatives (whose skeleton comprises two conjoined cyclohexane rings) are normally lower in energy than their bicyclo-[3.2.2]nonane isomers. The product found here also contains alkene and secondary alcohol groups, both of which are potentially active in Ritter reactions. In addition, only one alcohol isomer (that with the hydroxy group *anti*- to the largest ring bridge) was isolated. Furthermore, the Ritter product was always obtained as the monohydrate compound.

The structure of (**4**)·(H_2O) comprises a stack of sandwich-like layers. Each layer comprises two sheets of **4** molecules with their hydrocarbon groups creating the two outer layer faces. Hence only weak hydrophobic dispersion forces operate between adjacent layers.

The amide and hydroxy groups of both sheets of **4** molecules face inwards in the sandwich-like layer, hydrogen bonding to water molecules, and creating a hydrophilic filling in the middle of the sandwich (Fig. 2).

In the structure (**4**)·(H_2O) each water molecule participates in two donor and two acceptor hydrogen bonds. Water hydrogens are donated to the amide carbonyl oxygen of one, and the hydroxy group oxygen of a second, **4** molecule. Hydrogens are

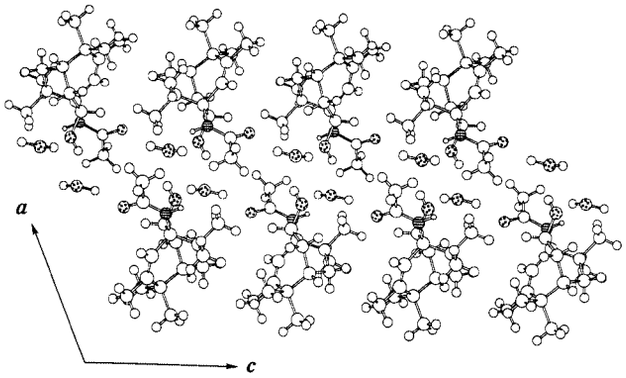


Fig. 2 Section through one sandwich-like layer present in the structure of (**4**)·(H_2O), showing the hydrophobic outer surfaces and its polar, hydrogen bonded interior. Oxygen atoms are stippled and nitrogen atoms are hatched. All hydrogen atoms are included in this figure.

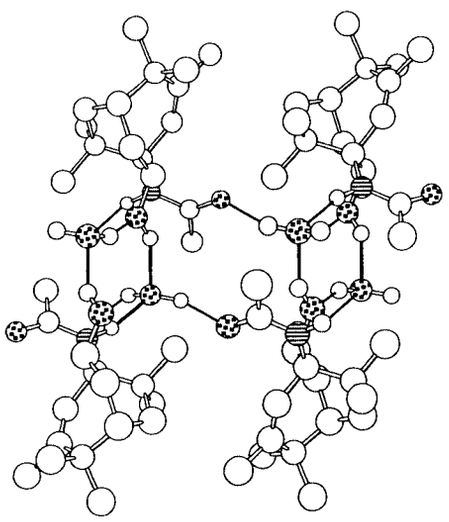


Fig. 3 The intermolecular hydrogen bonding arrangement present in solid **4** monohydrate. Each water molecule is hydrogen bonded to four different molecules of the hydroxy acetamide **4** thus giving rise to the two-dimensional hydrogen bonded arrangement. Oxygen atoms are stippled and nitrogen atoms are hatched. The O–H and N–H hydrogens are the only hydrogen atoms included in this figure. Hydrogen bonds are indicated using solid atomic connectors.

accepted from the amide N–H of a third (translationally related to the second), and the hydroxy O–H of a fourth, molecule of **4**. These arrangements are illustrated in Fig. 3. A two-dimensional sheet of intermolecular hydrogen bonding is thereby established in the centre of each layer.

A possible reaction route to **4** could involve protonation of the carbonyl group of **2**, a 1,2-propeno ring shift producing the secondary carbenium ion **10**, formation of the protonated epoxide **11**, and then finally Ritter reaction through the tertiary carbenium ion **12** (Scheme 3). Compound **4** itself is not an intermediate on the way to products **5** and **6** (as demonstrated by Expt. D), but all reactions prior to amide formation should be reversible thus allowing **12** to potentially re-access the main reaction pathway in Scheme 1.

1-Acetamido-3,4,4,8,8-pentamethyl-2-oxatricyclo[3.3.1.$1^{3,7}$]-decane 5

Reaction of **1** (Expt. E) gave 38% of a product **5** whose NMR and IR data showed an absence of alkene and ketone carbonyl groups. The formula $C_{16}H_{27}NO_2$, indicated by its MS and combustion analysis data, corresponds with formal addition of acetamide to the starting material. The presence of an acetamido group CH_3CONH– was again indicated by the IR and NMR data, the latter also revealing the presence of a further

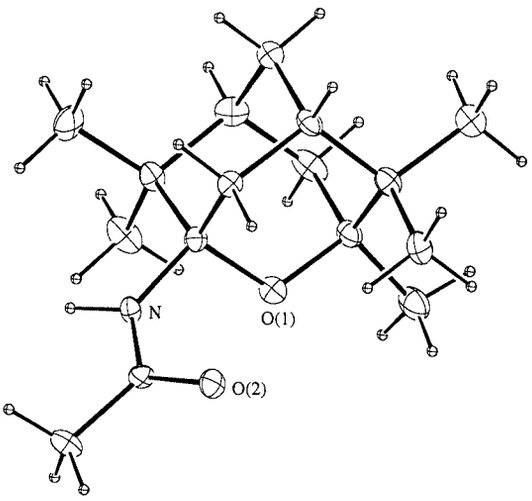
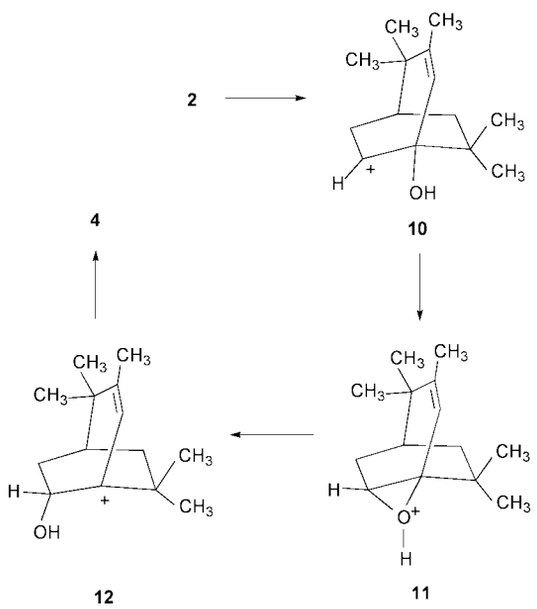


Fig. 4 Molecular structure of the rearrangement product **5** determined by X-ray crystallography. Only the oxygen and nitrogen atoms are labelled.



Scheme 3 Schematic reaction pathway for the formation of **4**.

five methyls on sp^3 quaternary carbons. The ^{13}C NMR spectrum contained two quaternary carbons at 87.7 and 78.2 ppm which suggested an adjacent oxygen atom but, once again, the definitive structure **5** was provided by X-ray determination (Table 1 and Fig. 4).

Formation of the acetylated hemi-aminal **5** is easily understood if the unsaturated ketone **3** (discussed earlier) is an intermediate. Protonation of its alkene group, followed by internal trapping of the tertiary carbenium ion by the carbonyl group oxygen, would produce a 2-oxa-1-adamantyl ion. Ritter reaction with acetonitrile then would lead directly to **5**.

Reaction of **5** under Ritter conditions (Expt. F) resulted in formation of the product **6**, thus demonstrating that the hemi-aminal derivative is a genuine intermediate on the reaction pathway shown in Scheme 1.

1,3-Bis(acetamido)-4,4,8,8-tetramethyltricyclo[3.3.1.$1^{3,7}$]decane 6

Reaction of **1** (Expt. G) gave a bis(acetamide) product (77% yield) with molecular weight of 306 and formula $C_{18}H_{30}N_2O_2$, which corresponded to formal addition of two acetamide and loss of one water molecules. Its proton decoupled ^{13}C NMR spectrum showed only ten signals which indicated C_2 symmetry.

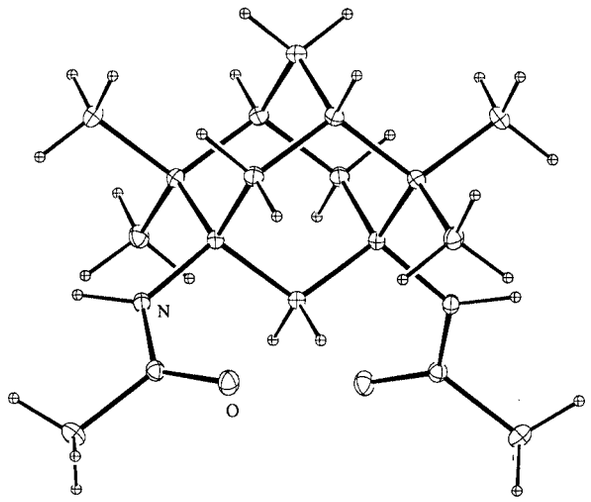


Fig. 5 Molecular structure of the rearrangement product **6** determined by X-ray crystallography. Only the oxygen and nitrogen atoms are labelled.

The most probable structure was the 1,3-bis(acetamido)-adamantane derivative **6** and this was confirmed by X-ray determination (Table 1 and Fig. 5).

Formation of **6** can be envisaged by protonation of the ether oxygen of **5**, followed by ring opening of either C–O bond to produce alternative bicyclo[3.3.1]nonane structures with a carbenium ion and hydroxy group at C3 and C7, or the reverse. Loss of water from either intermediate would result in a tertiary carbenium ion at C3 (stabilised by the acetamido group) and a methylidene group at C7. Internal cyclisation to the adamantyl ion derivative, followed by Ritter reaction, then finally yields **6**. The product **6** can also be produced from **1** (Expt. H) under rather different reaction conditions, albeit in lower yield (39%).

Conclusions

The unsaturated ketone **1** has been shown to undergo a complex sequence of rearrangement and Ritter reactions. Mechanistic explanations for these processes have been proposed. Since these molecular conversions are one-pot reactions they provide extremely simple synthetic routes to a number of alicyclic products difficult to access by other means.

Experimental

^{1}H (300 MHz) and ^{13}C (75.3 MHz) NMR spectra were recorded as $CDCl_3$ solutions on a Bruker ACF300 instrument and are reported as chemical shifts (δ) relative to $SiMe_4$. The substitution of carbon atoms was determined by the DEPT procedure and coupling constants (J) measured in hertz (Hz). Melting points were determined with a Kofler instrument and are uncorrected. Mass spectra were recorded using a VG Quattro triple quadrupole instrument employing electron impact. The IR spectra were recorded on a Perkin-Elmer 298 infrared spectrophotometer.

3,3,7,7-Tetramethyl-6-methylidenebicyclo[3.3.1]nonan-2-one 1

Methylenetriphenylphosphorane (0.05 mol) in dry DMSO (50 cm^3), prepared following the Corey procedure,[9] was stirred under an atmosphere of dry nitrogen. A solution of 3,3,7,7-tetramethylbicyclo[3.3.1]nonane-2,6-dione[4] (8.32 g, 0.04 mol) in dry DMSO (20 cm^3) was added, resulting in warming and darkening of the mixture. This was stirred and heated at 75 °C for 2 h, cooled to room temperature (rt), then water (300 cm^3) added. The mixture was extracted several times using diethyl ether, the combined extracts washed with water, and then dried (Na_2SO_4). Evaporation of solvent from the filtrate gave an oil containing some white solid (Ph_3PO). This mixture was chromatographed on alumina eluting first with 60–80 °C petroleum, followed by petroleum containing increasing amounts of diethyl ether. Some diene **7** was eluted first, followed by the ketone **1** (petroleum–ether 1 : 1) as an oil (5.60 g, 68%), lit.[4] 30%. ν_{max}(film)/cm^{-1} 3070w, 1700s, 1625m, 1455m, 1380m, 1360m, 890s, 675m; δ_C ($CDCl_3$) 220.7 (C), 160.2 (C), 108.1 (CH_2), 45.0 (CH_2), 43.1 (C), 42.5 (CH_2), 42.2 (CH), 37.2 (CH), 35.2 (C), 32.7 (CH_3), 32.2 (CH_3), 31.3 (CH_3), 29.4 (CH_2), 28.0 (CH_3).

3,3,6,6,7-Pentamethylbicyclo[3.3.1]non-7-en-2-one 2

Expt. A: Unsaturated ketone **1** (1.03 g, 0.005 mol) and acetonitrile (8 cm^3) were stirred at rt in a flask fitted with a reflux condenser and drying tube. Concentrated sulfuric acid (98%, 0.5 cm^3) was added dropwise, causing warming and producing a pale yellow solution. After 15 min, water (30 cm^3) was added causing a yellowish oil to separate. The reaction was extracted using diethyl ether, and the combined ether extracts washed (satd. aq. $NaHCO_3$, then H_2O) and dried (Na_2SO_4). After evaporation of solvent from the filtrate, the oil was eluted through a short plug of alumina using 40–60 °C petroleum. Evaporation of solvent gave the rearranged ketone **2** as a colourless liquid (0.78 g, 76%) bp 281 °C (Found: C, 81.35; H, 10.6. $C_{14}H_{22}O$ requires C, 81.5; H, 10.75%); ν_{max} (film)/cm^{-1} 2980s, 2940s, 1715s, 1455m, 1270w, 1155w, 1120w, 1100w, 1030m, 1010w, 850m; δ_H 5.27 (1H, d, J 6.3, =CH), 2.86 (1H, br m, C1 bridgehead H-C), 2.25–1.70 (5H, m), 1.65 (3H, br s, =C–CH_3), 1.15 (6H, s, CH_3), 1.10 (3H, s, CH_3), 1.07 (3H, s, CH_3); δ_C 216.2 (C), 145.0 (C), 120.4 (CH), 48.2 (CH), 42.5 (C), 40.8 (CH_2), 39.9 (CH), 37.7 (C), 32.7 (CH_3), 30.3 (CH_3), 29.7 (CH_3), 27.1 (CH_2), 24.7 (CH_3), 19.0 (CH_3); m/z (EI, >10%) 206 (M^+, 11%), 191 (12), 135 (29), 134 (100), 122 (11), 121 (69), 119 (34), 107 (51), 105 (17), 96 (11), 93 (14), 91 (26), 79 (11), 77 (11), 57 (14), 43 (11), 41 (29), 39 (11), 32 (11), 29 (11), 28 (51).

Expt. B: As for A, but using concd. sulfuric acid (1.5 cm^3) which caused considerable warming and generation of a dark orange solution. After the same isolation procedure a yellowish oil was obtained. ^{13}C NMR spectroscopy indicated this to be a 3 : 1 mixture of **2** plus a second unsaturated, non-conjugated ketone believed to be 4,4,7,8,8-pentamethylbicyclo[3.3.1]non-6-en-3-one **3**: δ_C 218.3 (C), 123.6 (C), 121.0 (CH) (and other peaks).

1-Acetamido-3,4,4,8,8-pentamethylbicyclo[3.2.2]non-2-en-*anti*-7-ol (4) monohydrate

Expt. C: Unsaturated ketone **1** (1.30 g, 6.3 mmol) and acetonitrile (10 cm^3) were stirred at 0 °C in a flask fitted with a reflux condenser and drying tube. Concentrated sulfuric acid (3 cm^3) was added slowly and dropwise *via* the condenser. Acetonitrile (10 cm^3) was used to wash in the final traces of acid. The mixture was stirred at 0 °C for 30 min, then at rt for 6 days. Water (50 cm^3) was added, and after 30 min the pH was raised to 11 using aq. NaOH (2 M). Organic material was extracted using chloroform. The combined extracts were washed with water (4 × 100 cm^3) and dried (Na_2SO_4). Evaporation of solvent from the filtrate gave the crude products (0.90 g). Trituration with a little diethyl ether, followed by filtration, removed a small amount of the bis(amide) **6**. Evaporation of solvent from the filtrate gave a waxy yellowish–orange solid. Recrystallisation from aq. ethanol (1 : 1) gave the acetamide **4** as its monohydrate (0.20 g, 12%) mp 176–178 °C (water loss at 167 °C) (Found: C, 68.0; H, 10.4; N, 4.6. $C_{16}H_{27}NO_2{\cdot}H_2O$ requires: C, 67.8; H, 10.3; N, 4.9%); ν_{max}(paraffin mull)/cm^{-1} 3430m, 3300s, 3200m, 1640s, 1500s, 1280m, 1170w, 1065m, 995w, 845m, 710m; δ_H 5.68 (1H, br s), 5.34 (1H, q, J 1.6), 4.68 (1H, t, J 9.2), 2.75 (1H, br s), 2.50–2.40 (1H, m), 2.03 (3H, s), 1.78–1.49 (4H, m), 1.63 (3H, d, J 1.6), 1.16 (3H, s), 1.07 (3H, s), 1.00 (3H, s), 0.96 (3H, s); δ_C 170.9 (C), 141.3 (C), 131.2 (CH),

69.8 (CH), 65.1 (C), 42.0 (C), 39.8 (CH), 38.9 (CH_2), 37.2 (C), 31.3 (CH_2), 29.1 (CH_3), 27.8 (CH_3), 27.7 (CH_3), 26.5 (CH_3), 24.4 (CH_3), 20.8 (CH_3); *m/z* (M^+ and >15%) 265 (M^+, 6%), 108 (15), 91 (18), 79 (15), 77 (15), 67 (16), 57 (18), 55 (27), 53 (18), 44 (41), 43 (100), 42 (78).

Expt. D: Acetamide **4** hydrate (0.10 g, 0.35 mmol) and acetonitrile (2 cm^3) were stirred at 0 °C in a flask fitted with a reflux condenser and drying tube. Concentrated sulfuric acid (0.4 cm^3) was added dropwise. The mixture was allowed to warm to rt and was stirred for 6 days. Water (5 cm^3) was added, and after 30 min the pH was raised to 11 using 2 M aq. NaOH. Organic material was extracted using chloroform (3 × 10 cm^3), the combined extracts were washed with water (4 × 50 cm^3), and dried (Na_2SO_4). Evaporation of solvent from the filtrate gave no bis(acetamide) product **6**. Only a trace of oily material was recovered.

1-Acetamido-3,4,4,8,8-pentamethyl-2-oxatricyclo[3.3.1.$1^{3,7}$]-decane 5

Expt. E: Unsaturated ketone **1** (1.30 g, 6.3 mmol) and acetonitrile (10 cm^3) were stirred at 0 °C in a flask fitted with a reflux condenser and drying tube. Concentrated sulfuric acid (5 cm^3) was added slowly and dropwise *via* the condenser, with the final traces being washed in with more acetonitrile (10 cm^3). The mixture was stirred at 0 °C for 30 min, then overnight at rt. Water (50 cm^3) was added, the mixture stirred for 30 min, then the pH raised to 11 by addition of aq. NaOH (2 M). Organic material was extracted using chloroform. The combined organic extracts were washed (4 × 100 cm^3 water) and dried (Na_2SO_4). Evaporation of solvent from the filtrate gave the crude products (1.33 g). Trituration with a little acetone, followed by filtration, removed a small amount of the solid bis-(acetamide) **6**. Solvent was removed from the filtrate and the residue dissolved in the minimum volume of chloroform. This was chromatographed on silica, eluting first with 60–80 °C petrol, and then petrol containing increasing proportions of chloroform. The hemi-aminal **5** was obtained using 1 : 1 petrol–chloroform and recrystallised from hot water (0.64 g, 38%) mp 159–161 °C (Found: C, 72.2, H, 10.1; N, 5.0. $C_{16}H_{27}NO_2$ requires: C, 72.4, H, 10.25; N, 5.3%); ν_{max}(paraffin mull)/cm^{-1} 3320s, 1650s, 1525s, 1370s, 1350s, 1335m, 1285m, 1245w, 1150w, 1080m, 1030m, 930w; δ_H ($CDCl_3$) 5.53 (1H, br s), 2.67 and 2.58 (1H, d, J_{AB} 13.9), 2.51 and 2.47 (1H, dd, J_{AB} 13.9 and 2.6), 1.95 (3H, s), 1.89–1.56 (6H, m), 1.11 (3H, s), 1.09 (3H, s), 1.04 (3H, s), 1.01 (3H, s), 0.97 (3H, s); δ_C ($CDCl_3$) 168.8 (C), 87.7 (C), 78.2 (C), 40.3 (CH), 40.0 (CH), 39.3 (C), 36.8 (C), 32.8 (CH_2), 29.7 (CH_2), 27.3 (CH_2), 24.9 (CH_3), 24.14 (CH_3), 24.06 (CH_3), 23.8 (CH_3), 22.7 (CH_3), 22.5 (CH_3); *m/z* (EI, >20%) 265 (M^+, 41%), 164 (21), 127 (30), 55 (30), 43 (100), 42 (72).

Expt. F: Concentrated sulfuric acid (5 cm^3) was placed in a flask fitted with a reflux condenser and drying tube and cooled to 0 °C. Acetonitrile (5 cm^3) was added dropwise with stirring. A solution of compound **5** (1.00 g, 3.77 mmol) in benzene (5 cm^3) was added dropwise. The reaction was allowed to warm to rt and was stirred for a further 6 days. Water (20 cm^3) was added and then the pH raised to 11 (2 M aq. NaOH). Organic material was extracted using chloroform (3 × 50 cm^3), the combined extracts washed with water (4 × 100 cm^3) and dried (Na_2SO_4). Evaporation of solvent from the filtrate gave a light yellow solid. This was dissolved in hot toluene, filtered, and allowed to stand. Fluffy white crystals of the bis(acetamide) **6** (0.55 g, 48%) were obtained. This material was identical in all respects to that obtained from the reactions of ketone **1** described below.

1,3-Bis(acetamido)-4,4,8,8-tetramethyltricyclo[3.3.1.$1^{3,7}$]decane 6

Expt. G: Ketone **1** (1.30 g, 6.3 mmol) and acetonitrile (20 cm^3) were stirred at 0 °C in a flask fitted with a reflux condenser and drying tube. Concentrated sulfuric acid (5 cm^3) was added slowly and dropwise. The reaction mixture was stirred at 0 °C for a further 30 min, then at rt for 6 days. Water (50 cm^3) was added, then after stirring for 30 min, the mixture was adjusted to pH 11 by addition of aq. NaOH (2 M). Organic material was extracted several times using chloroform. The combined extracts were washed (4 × 100 cm^3) and dried (Na_2SO_4). Evaporation of solvent from the filtrate gave the bis(acetamide) **6** (1.48 g, 77%) mp 285–287 °C (from toluene) (Found: C, 70.9; H, 10.1; N, 8.9. $C_{18}H_{30}N_2O_2$ requires C, 70.6; H, 9.9; N, 9.1%); ν_{max}(paraffin mull)/cm^{-1} 3360s, 3300m, 1635s, 1510s, 1340w, 1285w, 1260w, 1165w, 715w; δ_H ($CDCl_3$) 5.12 (2H, br s, NH), 2.81–2.67 (4H, m, CH_2), 1.90 (6H, s, CH_3CO-), 1.94–1.54 (6H, m), 1.14 (6H, s), 1.07 (6H, s); δ_C ($CDCl_3$) 169.8 (C), 58.1 (C), 41.3 (CH), 38.6 (C), 34.1 (CH_2), 30.2 (CH_2), 27.3 (CH_2), 24.9 (CH_3), 23.3 (CH_3), 22.7 (CH_3); *m/z* (EI, >20%) 307 (21%), 306 (M^+, 100), 291 (73), 263 (67), 232 (72), 222 (21), 221 (73), 122 (27), 121 (27), 120 (27), 109 (23), 108 (23), 107 (35), 105 (29), 95 (22), 94 (27), 93 (24), 91 (31), 86 (24), 84 (36), 79 (20), 69 (20), 60 (21), 43 (50).

Expt. H: Ketone **1** (1.03 g, 0.005 mol) and acetonitrile (5 cm^3) were stirred at rt in a flask fitted with a reflux condenser and drying tube. Concentrated sulfuric acid (3 cm^3) was added dropwise. Addition of the final 0.5 cm^3 was strongly exothermic resulting in vigorous refluxing and generation of a light red–brown colour. Water (40 cm^3) was added after 1 h producing a pale yellow solution and precipitation of a white solid. Extraction using chloroform, was followed by washing (satd. aq. $NaHCO_3$, then H_2O), drying (Na_2SO_4), filtration, and evaporation to give the bis(acetamide) **6** as a white solid (0.59 g, 39%) with identical spectral data to material prepared by Expt. G.

Determination of the three crystal structures †

Reflection data were measured with an Enraf-Nonius CAD-4 diffractometer in $\theta/2\theta$ scan mode using graphite monochromated copper radiation (λ 1.5418 Å). Data were corrected for absorption.[10] Reflections with $I > \sigma(I)$ were considered observed. The structures of (**4**)·(H_2O) and **6** were determined by direct phasing (SIR92[11]) and Fourier methods. The structure of **5** was twinned about *c*, giving perfect overlap for *hk0* data, and partial overlap for *hkl* with $l = 3n$. A partial data set comprising the resolved data for one component was used to solve the structure. Refinement[12] was carried out using full data, allowing the relative proportions of the two twin components to vary. Refinement of non-hydrogen atoms in all three structures was anisotropic with hydrogen atoms included in calculated positions.[12] Reflection weights used were $1/\sigma^2(F_o)$, with $\sigma(F_o)$ being derived from $\sigma(I_o) = [\sigma^2(I_o) + (0.04I_o)^2]^{1/2}$. Atomic scattering factors and anomalous dispersion parameters were from International Tables for X-Ray Crystallography.[13] ORTEP-II[14] running on a Power Macintosh 7200/120 was used for the structural diagrams, and a DEC Alpha AXP workstation was used for calculations.

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† CCDC reference number 207/434. See http://www.rsc.org/suppdata/p1/b0/b002544p/ for crystallographic files in .cif format.

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