gave 7 mg and 5 mg of **11a** and **11b**. The major compound **11a** or **11b** was bulb-to-bulb distilled at 160 °C/0.25 Torr: IR (neat) ν_{max} 3020, 1690, 1620 cm^{-1}; ^1H NMR (100 MHz, $CDCl_3$) δ 5.8–5.4 (2 H, m), 3.2–1.0 (18 H, series of m); ^{13}C NMR (25.0 MHz, $CDCl_3$) δ 207.7, 184.3, 143.8, 130.7, 128.4, 45.1, 43.9, 40.2, 39.3, 35.7, 35.4, 30.6, 25.6, 24.8, 22.5. The minor compound **11a** or **11b**: IR (neat) ν_{max} 3010, 1690, cm^{-1}; ^1H NMR (100 MHz, $CDCl_3$) δ 5.64 (2 H, t), 3.0–1.0 (18 H, series of m); ^{13}C NMR (25.0 MHz, $CDCl_3$) δ 208.1, 182.8, 143.2, 130.9, 127.7, 43.6, 42.7, 42.3, 34.9, 32.4, 31.2, 26.1, 26.0, 24.8, 22.2. Anal. Calcd for $C_{15}H_{20}O$: C, 83.28; H, 9.32. Found: C, 83.32; H, 9.57. Further elution of the column with the same solvent gave the spiro enone **12**, 13 mg (which was bulb-to-bulb distilled at 170 °C/0.6 Torr): IR (neat) ν_{max} 3020, 1700, 1610 cm^{-1}; ^1H NMR (100 MHz, $CDCl_3$) δ 5.85 (1 H, br s), 5.48 (2 H, J = 6 Hz, t), 3.4–1.2 (17 H, series of m); ^{13}C NMR (25.0 MHz, $CDCl_3$) δ 208.7, 191.6, 130.9, 130.4, 126.0, 54.3 (s), 45.5, 41.7, 39.9, 35.6 (2C), 33.7, 25.7, 23.8, 23.6. Anal. Calcd for $C_{15}H_{20}O$: C, 83.28; H, 9.32. Found: C, 83.15; H, 9.34.

Preparation of 11a,b from 10. Sodium hydride (60 mg, as 50% dispersion in oil, 1.2 mmol) was placed in a 25-mL, three-necked flask equipped with dry N_2 inlet, pellet, condenser with mercury seal, and septum. The mineral oil was removed by washing twice with petroleum ether and the residue was suspended in 4 mL of dry toluene. A solution of bromo enone **10** (45 mg, 0.15 mmol) in 4 mL of dry toluene was added dropwise. The resulting solution was refluxed for 1 h, after which it was quenched with 5% HCl and extracted with ether (3 × 10 mL). The ethereal solution was washed with water and dried over Na_2SO_4. Removal of solvent gave a residue (35 mg), which was found to be identical (TLC, IR, NMR) with that obtained in the above experiments.

3,3-(Ethylenedithio)tricyclo[7.5.1.0^{4,15}]pentadeca-4-(15),11-diene (15). A solution of the tricyclic enones **11a,b** (120 mg, 0.5 mmol) and ethanedithiol (0.2 mL) in 10 mL of dry benzene in the presence of catalytic amount of *p*-toluenesulfonic acid was heated at reflux for 8 h. The organic layer was washed successively with water and 5% $NaHCO_3$ and dried over Na_2SO_4. Removal of solvent gave 150 mg of crude compound which was filtered through a silica gel (8 g) column to remove impurities. Elution with 10% benzene–petroleum ether furnished the thioacetal **15**, 143 mg (90%) (which was bulb-to-bulb distilled at 140–150 °C/0.2 Torr): IR (neat) ν_{max} 3010, 730 cm^{-1}; ^1H NMR (100 MHz, $CDCl_3$) δ 5.7–5.4 (2 H, m), 3.4–3.0 (4 H, m), 3.0–1.2 (18 H, series of m). Anal. Calcd for $C_{17}H_{24}S_2$: C, 69.80; H, 8.27. Found: C, 69.79; H, 8.2.

Tetracyclo[7.5.1.0^{4,15}.0^{12,15}]pentadecan-11-one (18). To a vigorously stirred mixture of 30 mL of liquid NH_3 and sodium (25 mg, 1.0 mmol) kept at −40 °C was carefully added thioacetal **15** (100 mg, 0.32 mmol) in 4 mL of ether. The reaction mixture was warmed and ammonia allowed to evaporate. The residue was dissolved in pentane (30 mL) and the organic layer was washed with water and dried over Na_2SO_4. The crude oily residue obtained after removal of solvent [IR (neat) ν_{max} 3020, 1460 cm^{-1}; ^1H NMR (100 MHz, $CDCl_3$) δ 5.8–5.4 (2 H, m), 3.0–1.0 (20 H, series of m)] was dissolved in 1 mL of 85% HCOOH and heated at 90 °C for 4 h. The reaction mixture was poured into ice-cold water and extracted with ether (4 × 10 mL). The ethereal layer was washed with 5% $NaHCO_3$ and dried over Na_2SO_4. Removal of solvent gave 70 mg of a crude mixture of formate esters (IR 1730 cm^{-1}) and unreacted hydrocarbon. The hydrocarbon impurity was removed by passing through a small silica gel column and the formate esters (20 mg) were dissolved in 2 mL of 10% methanolic KOH, diluted with two drops of H_2O, and refluxed for 2 h. The reaction mixture was diluted with water and extracted with ether (2 × 10 mL). The ethereal layer was washed with water and dried over Na_2SO_4. Removal of solvent gave 18 mg of a crude hydroxy compound: IR (neat) ν_{max} 3450 cm^{-1}. The hydroxy compound was dissolved in 1 mL of dry dichloromethane and was added dropwise to a solution of 35 mg PCC in 1 mL of dichloromethane at 0 °C. The reaction mixture was brought to room temperature and allowed to stir for 1 h. The resulting dark-brown residue was diluted with ether (10 mL) and filtered through a Florosil pad and repeatedly washed with dichloromethane. Removal of solvent left a dark residue that was charged on a silica gel (8 g) column. Elution of the column with 10% ethyl acetate–petroleum ether furnished the tetracyclic ketone **18** as colorless oil, 16 mg, which was shown by HPLC (Lichrosorb SI 60 (7 μm), 250 mm × 4 mm, 25 bar, 226 nm, *n*-hexane) to be a 1:3 mixture of epimers. The ketone **18**, which was bulb-to-bulb distilled at 120 °C/0.2 Torr, was characterised as follows: IR (neat) ν_{max} 1730 cm^{-1}; ^1H NMR (100 MHz, $CDCl_3$) δ 2.8–1.0 (22 H, m); ^{13}C NMR (25.0 MHz, $CDCl_3$) significant peaks observed at δ 224.6, 223.9, 64.2, 60.6, 59.1, 52.6, 51.8, 43.9, 42.6, 40.7, 39.6, 37.7, 36.7, 35.9, 35.5, 34.6, 32.6, 31.6, 30.9, 26.4; exact mass calcd (M^+) 218.1665, found 218.1691. Anal. Calcd for $C_{15}H_{22}O$: C, 82.51; H, 10.09. Found: C, 82.41; H, 10.20.

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Registry No. **1**, 72779-23-8; **7**, 110307-69-2; **8**, 111975-91-8; **9**, 111975-92-9; **10**, 111975-93-0; **11a**, 111975-94-1; **11b**, 111975-95-2; **12**, 111975-96-3; **15** (isomer 1), 111975-97-4; **15** (isomer 2), 111976-01-3; **16** (isomer 1), 111975-98-5; **16** (isomer 2), 111976-02-4; **17**, 111975-99-6; **18**, 111976-00-2.

Ritter Reactions. 3. A Simple Entry into the 3-Azatricyclo[5.3.1.0^{4,9}]undecane System[1]

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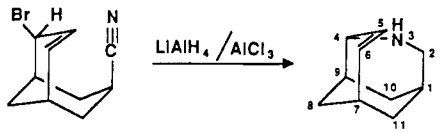
In 1979 Hassner et al.[2] reported that reduction of the bromo nitrile **1** produced a 56% yield of the tricyclic compound **2** via an intramolecular allylic halide displacement. Since this report, this reaction has remained the



sole example of the preparation of the 3-azatricyclo[5.3.1.0^{4,9}]undecane[3] skeleton. We now report a simple and effective means of synthesizing derivatives of this ring system using typical Ritter reaction[4] conditions.

Addition of 2,6-dimethylenebicyclo[3.3.1]nonane[5] (**3**) to a mixture of acetonitrile and concentrated sulfuric acid led to the isolation of a single product with mass ion m/z^+ 248 and composition $C_{15}H_{24}N_2O{\cdot}H_2O$ in 63% yield. If this monohydrate was heated above its melting point under low pressure, the material resolidified as the anhydrous compound. The latter is hygroscopic and slowly reverts to the hydrated form on exposure to the atmosphere.[6] The increase of 100 in the molecular weight of the anhydrous

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(6) Although the hydrated form gave a combustion analysis that was almost correct for a monohydrate, it is not certain at this stage whether it is a stoichiometric compound. It is clear, however, from ^1H and ^{13}C NMR data that in solution this material is a hydrated form of the imine **10** rather than having the carbinolamine structure $RC(OH)(CH_3)NHR^1$.

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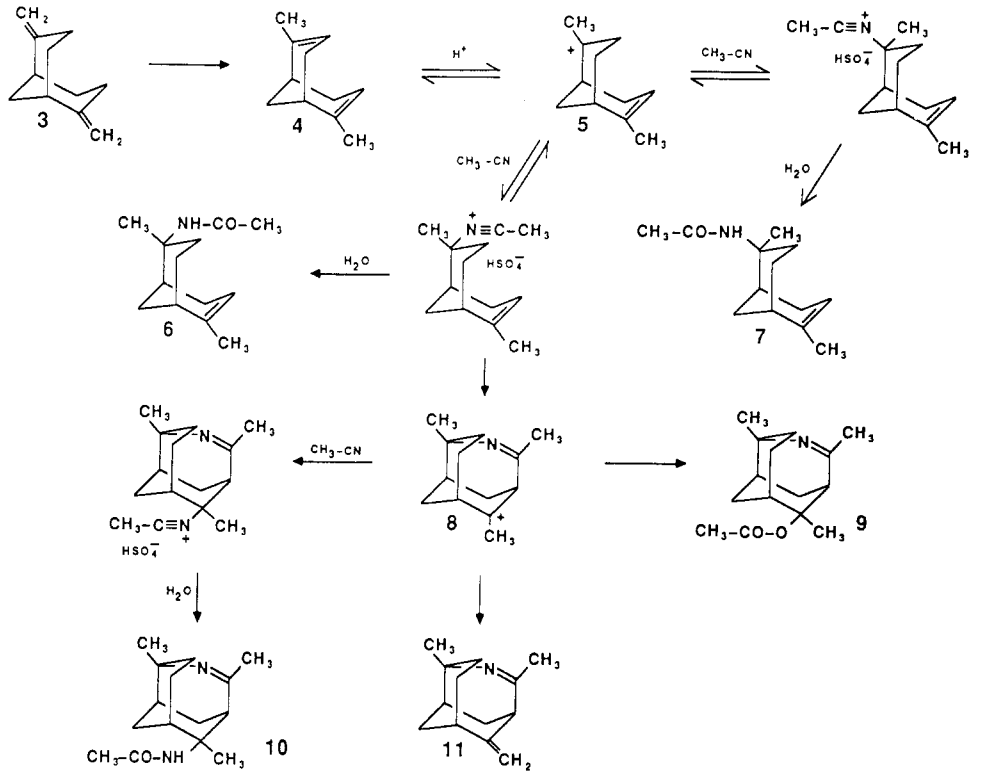
Scheme I



product over the starting material represents formal addition of two molecules of acetonitrile and one of water during the reaction. Consideration of the spectral data (see the Experimental Section) and of the likely reaction pathway led us to the conclusion that its structure was *exo*-11-acetamido-2,4,*endo*-11-trimethyl-3-azatricyclo-[5.3.1.$0^{4,9}$]undec-2-ene (**10**). Part of the reasoning used is outlined below.

One nitrogen atom was clearly present as an N-monosubstituted acetamide [IR 1640 and 1545 cm^{-1}; MS base peak m/z^+ 189 ($M - CH_3CONH_2$)$^+$; ^1H NMR δ 5.24 (br s, 1 H), 1.96 (s, 3 H)], but the involvement of the second was less obvious. A clue was the prominent MS peak (33%) with m/z^+ 148, which was considered to be (189 – CH_3CN)$^+$, but the key observation was that on D_2O exchange *both* the amide proton δ 5.24 *and* a methyl group at δ 2.13 underwent slow but complete exchange over several hours.

This methyl group, slightly further downfield than normal for an acetamide, had a chemical shift in the range anticipated for a $RC(CH_3)=NR^1$ structure.[7] It is well known that such imines[8] are in equilibrium[9] with the enamine $RC(=CH_2)NHR^1$, and that, for *N*-cycloalkylidenealkylamines, the presence of the enamine tautomer can be up to 10% in some cases.[10] This leads to a much more rapid deuterium exchange than normally encountered in the more familiar ketone–enol equilibrium and one that can be effected just by addition of D_2O or CD_3OD.[11] In this particular case, only the hydrogens of the C2-methyl group were exchanged, implying that the hydrogen(s) on the other carbon atom attached to C2 were not readily exchangeable. This is the bridgehead site C1 of the proposed structure **10**, and formation of the alternative enamine tautomer at this position would involve a bridgehead double bond, which would be expected to be formed less readily.[12]

Additional evidence supporting the imine structure **10** was available from ^{13}C NMR spectroscopy. Aliphatic imine carbons usually[13] appear in the range δ 168–175, which was also the case here. Furthermore, the imine–enamine equilibrium can be utilized to perform the unusual exchange experiment illustrated in Figure 1. If the original ^{13}C NMR spectrum is compared with that used for the D_2O-exchange experiment, the same signals are observed with only small solvent shifts (ruling out any hydrolysis reaction) except that the C2-methyl group originally at δ 29.2 has undergone deuterium exchange, leaving only a small residual signal[14] solvent-shifted to rather lower field.

Finally, it is worth commenting that while the paraffin mull IR spectrum of the compound showed a vibration at about 3080 cm^{-1}, which might be attributed to the enamine tautomer,[15] both ^1H and ^{13}C NMR solution spectra showed only the imine form (within the detection limits used in recording routine spectra). Together with the more routine data, the spectral characteristics described above require that the Ritter product have the structure **10**.

When the Ritter reaction was performed under more moderate conditions with glacial acetic acid as cosolvent, then five additional products were obtained. These were separated by preparative TLC and column chromatography. Their identities not only add support for the struc-

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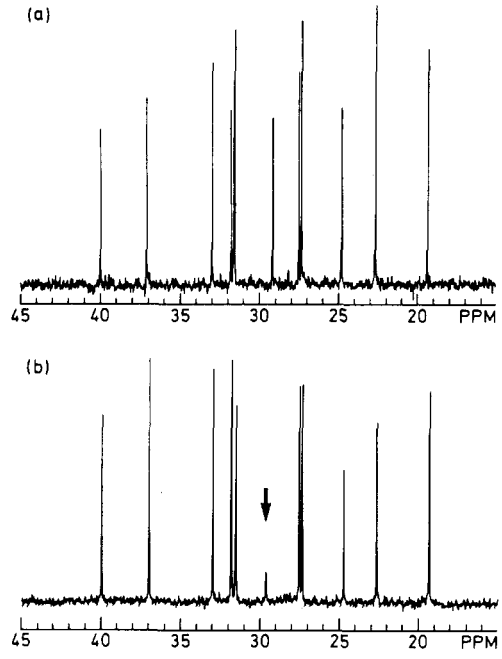

Figure 1. Partial ^{13}C NMR spectra of *exo*-11-acetamido-2,4,*endo*-11-trimethyl-3-azatricyclo[5.3.1.$0^{4,9}$]undec-2-ene **10** at 125.8 MHz over the range δ 15–45. (a) Routine spectrum in $CDCl_3$. (b) Spectrum run after several hours in $CDCl_3/D_2O$ showing the severe loss of signal from the C2-methyl group as a result of deuterium exchange.

ture **10** but help confirm its method of formation (see Scheme I). These new compounds were identified (see the Experimental Section) as 2,6-dimethylbicyclo[3.3.1]-nona-2,6-diene (**4**): an unseparated mixture of *endo*/*exo*-6-acetamido-2,6-dimethylbicyclo[3.3.1]non-2-ene (**6** and **7**), *exo*-11-acetoxy-2,4,*endo*-11-trimethyl-3-azatricyclo[5.3.1.$0^{4,9}$]undec-2-ene (**9**), and 11-methylene-2,4-dimethyl-3-azatricyclo[5.3.1.$0^{4,9}$]undec-2-ene (**11**). The relative amounts of these products depended very much on the exact conditions used.

Both the new 3-azatricyclo[5.3.1.$0^{4,9}$]undec-2-ene derivatives **9** and **11** had the same MS base peak m/z^+ 148, corresponding to the formal loss of acetic acid and acetonitrile from **9** and $(M - CH_3CN)^+$ for **11**. Fragmentation to the original diene formula is thus confirmed as being a useful analytical characteristic of these tricyclic imine structures.

It is well known[16] that diene **4** is produced readily from **3** under strongly acidic conditions, and, therefore, its isolation here is unsurprising. Protonation of **4** (see Scheme I) would produce the carbenium ion **5**, which undergoes Ritter reaction from either face to yield roughly equal amounts of the isomeric acetamides **6** and **7**. Under the moderated reaction conditions, this process competes effectively with intramolecular cyclization to the carbenium ion **8** from which the three tricyclic compounds **9**–**11** are derived. However, by use of the more strongly acidic conditions of the original reaction, formation of **8** and thence **10** dominates, assisted by the reversible nature of nitrilium ion formation from **5**.

As part of his pioneering work on the Ritter reaction, Meyers successfully added nitriles across carbenium ion sites derived from an alcohol and an alkene group.[17] These, and other related reactions,[18] proved to be effective processes for the synthesis of a variety of monocyclic and fused heterocyclic structures. Our preparation of the 3-azatricyclo[5.3.1.$0^{4,9}$]undecane skeleton represents an extension of these reactions allowing simple preparation of bridged heterocyclic systems. Developments of this process would appear to have potential in the synthesis of alkaloid-like structures.

Experimental Section

Melting points were determined on a Kofler instrument and are uncorrected. NMR spectra were recorded with a Bruker AM-500 instrument (500 MHz for ^1H, 125.8 MHz for ^{13}C) and are reported as chemical shifts (δ) relative to $(CH_3)_4Si$. Substitution of carbon atoms was determined by the DEPT procedure. Routine mass spectra were recorded on an AEI MS-12 instrument, and exact masses were recorded with a Bruker CMS47 FTICR instrument. The IR spectra were recorded on a Hitachi 260-10 spectrophotometer. Elemental analyses were carried out at The University of New South Wales by Dr. H. P. Pham.

***exo*-11-Acetamido-2,4,*endo*-11-trimethyl-3-azatricyclo-[5.3.1.$0^{4,9}$]undec-2-ene (10).** A mixture of 98% sulfuric acid (2.0 mL) and acetonitrile (10.0 mL) was stirred in a flask fitted with a reflux condenser and drying tube and cooled by an ice bath. 2,6-Dimethylenebicyclo[3.3.1]nonane[5a] (**3**; 0.52 g, 3.5 mmol) in benzene (4.0 mL) was added dropwise, but rapidly, via the condenser. Final traces of the diene were washed into the flask with more benzene (1.0 mL). The reaction was stirred for 30 min at 0 °C and then for 24 h at room temperature. Water (50 mL) was added, and after 30 min, the material was transferred to a separating funnel containing 1 M sodium hydroxide solution (100 mL). Organic material was extracted several times with chloroform. The combined chloroform extracts were washed (2 × 50 mL water) and dried (Na_2SO_4), and solvent was evaporated from the filtrate to give a clear, viscous oil, which started to crystallize after several days. Trituration with a small amount of diethyl ether followed by filtration and drying in air yielded the tricyclic amide **10** as its monohydrate (0.59 g, 63%). Recrystallization from diethyl ether gave crystalline material, which was TLC pure but which melted indistinctly over 72–75 °C: IR (paraffin mull) 3410 (s), 3320 (s), 3260 (s), 3210 (s), 3080 (s), 1655 (s), 1560 (s), 1315 (m), 1120 (m), 1030 (w), 975 (w), 890 (w) cm^{-1}; MS, m/z (>10%) 248 (M^+, 5), 190 (16), 189 ($M - CH_3CONH_2$, 100), 174 (15), 162 (10), 161 (20), 160 (79), 148 ($189 - CH_3CN$, 33), 136 (10), 133 (17), 122 (14), 120 (13), 113 (13), 112 (23), 108 (22), 107 (18), 106 (17), 105 (13), 94 (13), 93 (17), 92 (12), 91 (12), 79 (11), 71 (15), 70 (61), 60 (10), 57 (10), 55 (11), 43 (24), 42 (27), 41 (16); ^1H NMR ($CDCl_3$) δ 5.24 (s, 1 H,exchanged with D_2O), 3.23 (s, 1 H), 2.13 (s, 3 H, exchanged with D_2O), 1.96 (s, 3 H), 1.86–1.47 (m, 8 H), 1.48 (s, 3 H), 1.35–1.28 (m, 2 H), 1.27 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 171.0 (C), 169.6 (C), 59.6 (C), 58.6 (C), 40.0 (CH), 37.1 (CH), 33.0 (CH_2), 31.8 (CH), 31.6 (CH_3), 29.2 (CH_3, exchanged to CD_3 by D_2O), 27.5 (CH_2), 27.4 (CH_2), 24.8 (CH_3), 22.7 (CH_3), 19.4 (CH_2). Anal. Calcd for $C_{15}H_{24}N_2O \cdot H_2O$: C, 67.63; H, 9.84; N, 10.52. Found: C, 68.05; H, 10.14; N, 10.55.

If the monohydrate was warmed above its melting point under reduced pressure (2 mmHg), it resolidified to yield the anhydrous tricyclic amide **10**. This material had a sharp melting point (143–144 °C) and its IR spectrum was significantly different: IR (paraffin mull) 3350 (s), 3300 (s), 3070 (w), 1640 (s), 1545 (s), 1295 (m), 1115 (m), 1030 (w), 975 (w), 905 (w) cm^{-1}; MS and NMR data were the same as those for the monohydrate. Anal. Calcd for $C_{15}H_{24}N_2O$: C, 72.54; H, 9.74; N, 11.28. Found: C, 72.63; H, 9.94; N, 11.31. (This solid was hygroscopic and reverted slowly to the monohydrate on exposure to the atmosphere.)

Moderated Ritter Reactions. Dilution of the reaction using glacial acetic acid led to the formation of several new products. TLC using silica gel plates and elution with 5% ethanol + 95% chloroform separated these very effectively. The following R_f

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values were obtained: **4**, 0.96; **6/7** (mixture), 0.54; **9**, 0.41; **11**, 0.32; and **10**, 0.12. These substances were separated by preparative TLC and also by column chromatography on alumina where the order of elution was now: **4**, **11**, **9**, **6/7**, and finally **10**. The relative amounts of these products depended very much on the exact conditions chosen: (A) Diene **3** (1.04 g, 7.0 mmol) was added to a stirred mixture of 98% sulfuric acid (1.0 mL), acetonitrile (5.0 mL), and glacial acetic acid (5.0 mL) at 0 °C. The reaction was worked up as described previously after 30 min. Major products: **4**, **6/7**, **9**, and **10**. (B) Diene **3** (1.58 g, 10.7 mmol) was added to a stirred mixture of 98% sulfuric acid (1.5 mL), acetonitrile (3.0 mL), and glacial acetic acid (15.0 mL) at 0 °C. The reaction was stirred for 30 min at 0 °C and then for 3 days at room temperature. The reaction was then worked up by the usual method. Major products: **9**-**11**.

2,6-Dimethylbicyclo[3.3.1]nona-2,6-diene (4). The diene was obtained as an oil, which was identical with authentic material:[16a] IR (liquid film) 3020 (w), 2990 (s), 1670 (w), 1200 (w), 1140 (w), 1020 (m), 930 (m), 910 (m), 800 (s) cm^{-1}; ^{13}C NMR ($CDCl_3$) δ 137.2 (C), 119.2 (CH), 32.4 (CH), 30.4 (CH_2), 29.6 (CH_2), 22.4 (CH_3).

***endo*/*exo*-6-Acetamido-2,6-dimethylbicyclo[3.3.1]non-2-ene (6/7).** Roughly equal amounts of the two isomers were obtained as a mixture: mp 89-94 °C; IR (liquid film) 3320 (s), 3080 (m), 1645 (s), 1540 (s), 1305 (m), 1290 (w), 1230 (w), 1120 (w), 1030 (w) cm^{-1}; MS, m/z (>10%) 207 (M^+, 17), 149 (10), 148 (M - CH_3CONH_2, 77), 133 (18), 120 (27), 112 (49), 107 (30), 106 (12), 105 (19), 94 (13), 93 (33), 92 (21), 91 (16), 79 (10), 77 (10), 70 (100), 60 (16), 57 (11), 43 (16), 42 (10); ^1H NMR ($CDCl_3$) δ 5.40-5.34 (m, 2 H, =CH and NH), 2.18-1.80 (m, 3 H), 1.92 and 1.88 (2 s, 3 H, CH_3CONH), 1.76-1.21 (m, 7 H), 1.57 (br s, 6 H, CH_3C=), 1.47 and 1.33 (2 s, 3 H, CH_3CNHCO); ^{13}C NMR ($CDCl_3$) δ 169.5 (C), 169.1 (C), 135.7 (C), 135.6 (C), 121.9 (CH), 121.6 (CH), 57.4 (C), 57.3 (C), 33.6 (two superimposed CH, resolved if C_6D_6 was added), 33.1 (CH), 32.9 (CH), 31.2 (CH_2), 29.6 (CH_2), 28.05 (CH_2), 28.01 (CH_2), 27.25 (CH_2), 27.23 (CH_2), 25.0 (CH_3), 24.7 (CH_2), 24.5 (CH_3), 24.22 (CH_2), 24.20 (CH_3), 22.9 (CH_3), 21.94 (CH_3), 21.92 (CH_3). Anal. Calcd for $C_{13}H_{21}NO$: C, 75.32; H, 10.21; N, 6.76. Found: C, 75.04; H, 10.46; N, 6.73.

***exo*-11-Acetoxy-2,4,*endo*-11-trimethyl-3-azatricyclo[5.3.1.0^{4,9}]undec-2-ene (9).** The acetate was obtained as a solid: mp 96-97 °C after purification by sublimation; IR (paraffin mull) 1730 (s), 1680 (m), 1260 (s), 1190 (m), 1105 (m), 1080 (m), 1045 (m), 1020 (m), 885 (m), 795 (m) cm^{-1}; MS, m/z (>10%) 249 (M^+, 17), 206 (10), 164 (12), 149 (27), 148 (100), 133 (33), 121 (10), 120 (57), 108 (12), 107 (27), 106 (27), 105 (16), 95 (16), 94 (20), 93 (34), 92 (22), 91 (14), 81 (10), 79 (10), 71 (14), 70 (10), 55 (10), 43 (46), 42 (10), 41 (13); ^1H NMR ($CDCl_3$) δ 3.12 (s, 1 H), 2.26-2.22 (d, 1 H), 2.13 (s, 3 H), 2.01 (s, 3 H), 1.80-1.27 (m, 8 H), 1.60 (s, 3 H), 1.30 (s, 3 H), 1.15-1.08 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 170.4 (C), 169.2 (C), 86.9 (C), 58.8 (C), 42.0 (CH), 36.1 (CH), 32.6 (CH_2), 31.9 (CH), 31.6 (CH_3), 29.0 (CH_3), 27.3 (CH_2), 27.1 (CH_2), 22.6 (CH_3), 22.3 (CH_3), 19.8 (CH_2). Anal. Calcd for $C_{15}H_{23}NO_2$: C, 72.25; H, 9.30; N, 5.62. Found: C, 72.45; H, 9.44; N, 5.72.

11-Methylene-2,4-dimethyl-3-azatricyclo[5.3.1.0^{4,9}]undec-2-ene (11). The alkene was obtained as a mobile oil: IR (liquid film) 3075 (w), 1670 (m), 1630 (m), 1300 (w), 1195 (w), 1115 (w), 1015 (w), 890 (s) cm^{-1}; MS, m/z (>5%) 189 (M^+, 5), 149 (13), 148 (M - CH_3CN, 100), 133 (25), 120 (15), 119 (20), 107 (14), 106 (27), 105 (31), 94 (11), 93 (35), 92 (32), 91 (33), 81 (9), 80 (19), 79 (25), 78 (7), 77 (14), 68 (6), 67 (6), 65 (7), 55 (6), 53 (9), 42 (11), 41 (16), 39 (13); ^1H NMR ($CDCl_3$) δ 4.66 (d, 1 H, J = 2.2 Hz), 4.64 (d, 1 H, J = 2.2 Hz), 2.87 (s, 1 H), 2.58-2.54 (d, 2 H), 2.01 (s, 3 H), 1.97-1.46 (m, 6 H), 1.34 (s, 3 H), 1.31-1.25 (m, 1 H), 1.04-0.96 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 170.4 (C), 152.8 (C), 108.6 (CH_2), 59.2 (C), 44.9 (CH), 35.8 (CH), 33.2 (CH_2), 32.5 (CH), 32.1 (CH_2), 31.8 (CH_3), 31.4 (CH_2), 26.3 (CH_2), 25.4 (CH_3). Anal. Calcd for $[C_{13}H_{19}N]^+$ m/z 189.1512, found m/z 189.1627; calcd for $[C_{11}H_{16}]^+$ m/z 148.1247, found m/z 148.1311.

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A Kinetic Study of Reactions of Tocopherols with a Substituted Phenoxyl Radical

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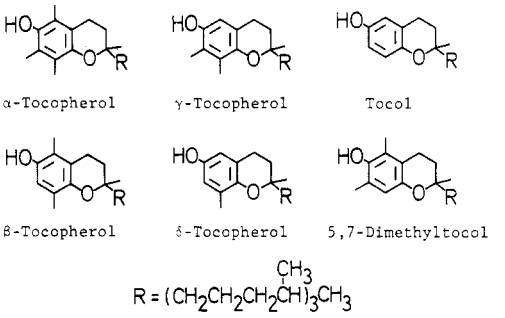
Vitamin E (α-, β-, γ-, and δ-tocopherols) is well-known to scavenge active free radicals (LOO•, LO•, and HO•) generated in biological systems. The above free radical



scavenging actions by vitamin E have been ascribed to the initial reaction of the phenolic hydroxyl group with the production of a tocopheroxyl radical.[1,2] Recently, Burton et al. have reported absolute second-order rate constants, k_1, for the reaction of α-, β-, γ-, and δ-tocopherols with poly(peroxystyryl)peroxyl radicals using the inhibited autoxidation of styrene method (reaction 1).[3-5] In a

$$\mathrm{LOO^\bullet + Toc} \xrightarrow{k_1} \mathrm{LOOH + Toc^\bullet} \qquad (1)$$

previous work, we have determined spectrophotometrically the rates of reaction of α-, β-, γ-, and δ-tocopherols with a stable substituted phenoxyl radical (2,6-di-*tert*-butyl-4-(4-methoxyphenyl)phenoxyl (ArO•)) in ethanol using stopped-flow technique as a model reaction of tocopherols with unstable free radicals (reaction 2).[6] The relative k_2

$$\mathrm{ArO^\bullet + Toc} \xrightarrow{k_2} \mathrm{ArOH + Toc^\bullet} \qquad (2)$$

values (α:β:γ:δ=100:44:47:20) obtained by the stopped-flow technique are in good agreement with the k_1 values (100:41:44:14) obtained by the inhibited autoxidation of styrene method, although the absolute values are about 600 times smaller than those for the reaction of tocopherols with the poly(peroxystyryl)peroxyl radical in chlorobenzene (see Table I).[6] The result suggests that the relative reactivities, that is, relative antioxidant activities, of tocopherols in homogeneous solution do not depend on the kinds of radicals (substituted phenoxyl and peroxyl radicals) used, while the absolute rates are considerably different from each other.

In the present work, we have measured the second-order rate constants, k_2, for the reaction of tocol and 5,7-di-

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