Formation of Tetracyclic Oxazolidinones from Cycloadducts of Benzylidene Ketones with 4-Phenyl-4,5-dihydro-3*H*-1,2,4-triazole-3,5-dione (PTAD) by Base-promoted Backbone Participation and Rearrangement

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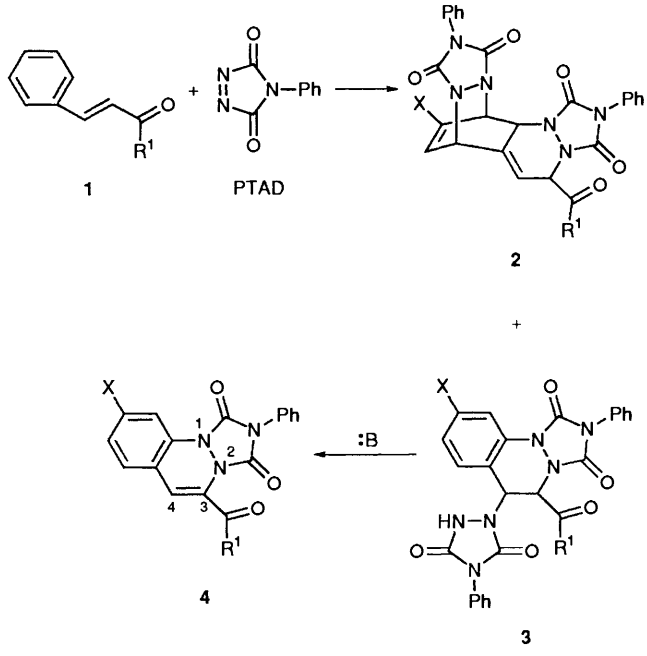
Alcoholysis and aminolysis of urazoles **4a–j** prepared by the reactions of benzylidene ketones with 4-phenyl-4,5-dihydro-3*H*-1,2,4-triazole-3,5-dione (PTAD) afforded tricyclic oxazolidinone derivatives **5a–o** in moderate yields (16–77%). The structure of compound **5b** was confirmed by a single-crystal X-ray analysis. The reaction proceeded *via* opening of the urazole ring by initial Michael addition of nucleophiles (solvents) to the enone substructure, followed by participation of the carbonyl group and final skeletal rearrangements.

The behaviour of 4-phenyl-4,5-dihydro-3*H*-1,2,4-triazole-3,5-dione (PTAD) toward alkenes shows diverse reactivities such as [4 + 2],[1] [2 + 2],[2] ene,[2] and dipolar reactions[3] to afford corresponding cycloadducts (tetrahydro-1,2,4-triazole-3,5-diones) (urazoles). However, utilization of urazoles in organic syntheses has been limited so far only to preparations of azoalkanes,[4] α-diketones,[5] and triazines.[6] This restricted use of urazoles is attributed, in part, to difficulties encountered in opening of the urazole ring, which requires relatively drastic conditions to be cleaved (*e.g.*, potassium hydroxide in refluxing alcohols).[1b,3a]

We have recently observed that benzylidene ketones **1** reacted with PTAD to afford 1:2 Diels–Alder products **2** and Diels–Alder ene products **3**, and that compounds **3** were converted easily into 1,2-dihydrocinnoline derivatives **4** in the presence of base by elimination of PTAD·H_2.[7] By inspecting the structure of the product **4**. which possesses an enone substructure in the neighbourhood of a urazole ring, one can expect that the urazole ring should be cleaved rather readily by alcoholysis and successive neighbouring-group participation. In the present paper, we describe the opening of the urazole ring and an unusual rearrangement initiated by Michael addition of nucleophiles to the enone moiety.



a; R^1 = Me, X = H
b; R^1 = Me, X = OMe
c; R^1 = Me, X = Cl
d; R^1 = Ph, X = H
e; R^1 = Ph, X = OMe
f; R^1 = 2-furyl, X = H
g; R^1 = 2-thienyl, X = H
h; R^1 = 2-pyridyl, X = OMe
i; R^1 = Bu^t, X = H
j; R^1 = Bu^t, X = OMe

Scheme 1

Results and Discussion

Addition–Elimination Reaction of PTAD.—The reaction of PTAD with a series of benzylidene ketones **1** in dichloromethane, followed by treatment with triethanolamine, gave yellow 1,2-dihydrocinnoline-1,2-dicarboximides (**4a–j**; called urazoles hereafter) through elimination of PTAD·H_2 from Diels–Alder ene adducts **3** (Scheme 1).[7] Although base-promoted preparation of urazoles **4** using isolated adducts **3** gave fairly good yields, isolation and purification of adducts **3** (silica gel chromatography and recrystallization) were troublesome because of concurrent formation of 1:2 Diels–Alder adducts **2** and the thermal instability of adducts **3**. Instead, an *in situ* reaction, in which a benzylidene ketone was allowed to react with two molar equivalents of PTAD, followed by base-catalysed elimination of a PTAD·H_2 moiety, was found to be advantageous.

Michael Addition and Rearrangement.—Treatment of an ethanolic solution of a urazole **4a** with powdered potassium hydroxide for 60 min at 25 °C resulted in loss of the characteristic yellow colour of compound **4a**. The solution was neutralized with dil. hydrochloric acid, and the resulting precipitates were collected and recrystallized from ethanol to give a tricyclic derivative **5b** possessing a 4-oxa-2,6,8-triazatricyclo[6.3.0.$0^{1,5}$]undec-9-ene-3,7-dione skeleton (called tricyclic oxazolidinone hereafter) in 77% yield. The structure of compound **5b** was assigned on the basis of spectral properties and elemental analyses. The IR spectrum of compound **5b** showed a characteristic amide band at 3320 cm^{-1}. In the mass spectrum the parent ion appeared at *m/z* 365, indicating that one molecule of ethanol had been incorporated into urazole **4a**. In the ^1H NMR spectrum a methine proton and an amide proton appeared at δ 5.35 and 6.54 as singlets, while the olefinic proton of substrate **4a** had disappeared. The ^{13}C NMR

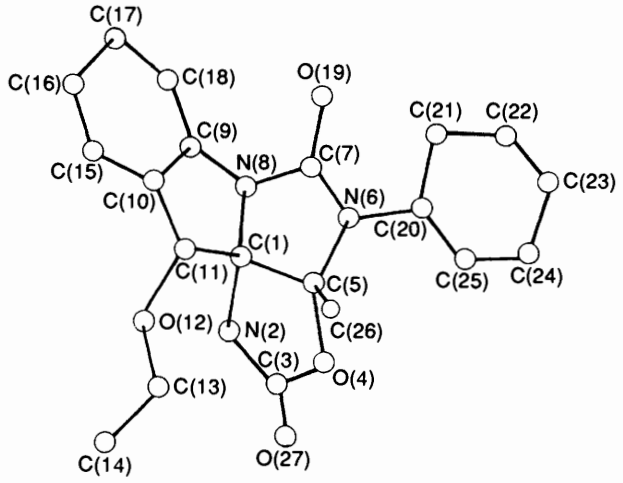
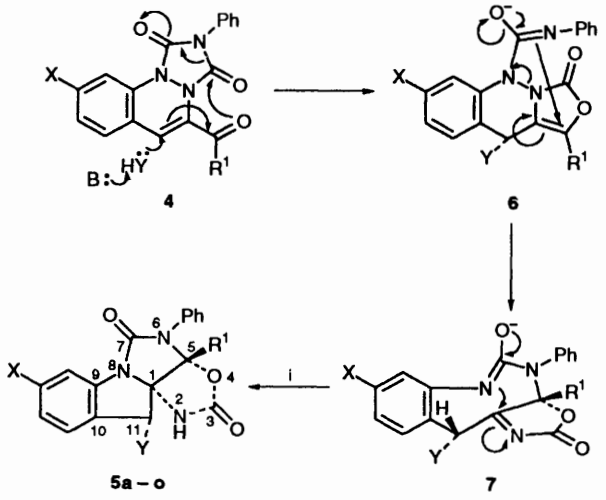


Fig. 1 ORTEP projection of the oxazolidinone **5b**, with crystallographic numbering scheme. The hydrogens and ethanol solvate were omitted for clarity.

spectrum showed two quaternary carbons and a methine carbon at δ_C 86.1 (C-1), 96.9 (C-5) and 79.7 (C-11). Elemental analyses also supported the proposed structure. Finally, X-ray crystallographic structure determination for an ethanol solvate of compound **5b** was undertaken to confirm the configuration at C-5 and C-11. An ORTEP drawing (Fig. 1) revealed that the methyl group at C-5 and the ethoxy group at C-11 have *endo* and *exo* configurations with respect to the *cis*-fused imidazolidinone–pyrroline ring, respectively. Isomer **5b** was the sole stereoisomer isolated, and attempts to detect other stereoisomers in the reaction mixture by using NMR spectroscopy were unsuccessful. The intriguing tricyclic framework of products **5** can be regarded as a heterohomologue of angular triquinane sesquiterpenes (tricyclo[6.3.0.$0^{1,5}$]undecanes; some of which display significant biological activities[8]).

Similar reaction of other urazoles also gave tricyclic oxazolidinones in moderate yields (16–77%). All alcohols tested except *tert*-butyl alcohol gave the expected products; *tert*-butyl alcohol did not react with urazole **4a**, and compound **5d** was not formed. Butylamine in ethanol also gave a tricyclic oxazolidinone **5e** with incorporation of a butylamino group in 16% yield, together with the ether compound **5b** in 23% yield. The structures of the tricyclic oxazolidinones were determined by comparison of their spectral properties with those of compound **5b**. The NMR data provide important information about the configuration of substituents at C-11. By inspecting stereochemical features of the fused imidazolidinone–pyrroline ring of compound **5b**, the proximity of 11-H with a substituent on C-5 is deduced. The observed high-field shifts (0.38–1.25 ppm) of 11-H of compounds **5h–m** clearly indicate that these compounds have the 11-*endo*-H and the 5-*endo*-phenyl (or heteroaromatic) configurations. Similarly, observed low-field shifts (0.55–0.64 ppm) of 11-H indicate the same stereochemistry for compounds **5n** and **5o**, in which the *endo* C-5 *tert*-butyl substituent makes the 11-H resonate at lower field by a steric compression effect.

A reasonable mechanism for the stereospecific formation of tricyclic oxazolidinones is depicted in Scheme 2. An initial Michael addition of a solvent molecule (nucleophile) to the enone moiety of a urazole 4 from the sterically less hindered *anti* side to the urazole ring, and subsequent opening of the urazole ring by a resulting enolate (backbone participation), affords a 3*H*-oxazolinone intermediate **6**.* A second intermediate **7** is



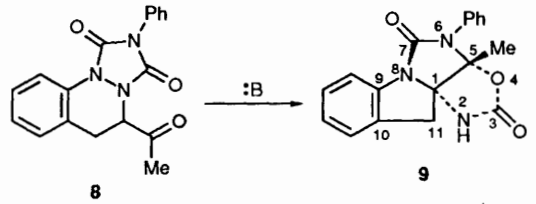
non-systematic numbering scheme (see text)

	R^1	X	Y
a;	Me	H	MeO
b;	Me	H	EtO
c;	Me	H	Pr^iO
d;	Me	H	Bu^tO
e;	Me	H	BuNH
f;	Me	OMe	EtO
g;	Me	Cl	EtO
h;	Ph	H	EtO
i;	Ph	H	Pr^iO
j;	Ph	OMe	EtO
k;	2-furyl	H	EtO
l;	2-thienyl	H	EtO
m;	2-pyridyl	OMe	EtO
n;	Bu^t	H	EtO
o;	Bu^t	OMe	EtO

Scheme 2 *Reagent:* i, H^+

formed by nucleophilic attack of the amide nitrogen atom on the enamine carbon atom, accompanied by an N–N cleavage.[10,11] Final transannular Michael addition of the amide nitrogen atom to the aza enone substructure in intermediate **7** leads to the oxazolidinones **5a–o**. A molecular model of an intermediate **7** reveals that the nucleophilic amide nitrogen atom is very close to the aza enone carbon atom.

To clarify whether the initial Michael addition of a solvent molecule is actually requisite to opening of the diazadicarboximide ring, a urazole **8** prepared by reduction of compound **4a** was allowed to react under the same conditions. The reaction of compound **8**, which possesses no enone substructure, also afforded an oxazolidinone **9**, in 75% yield [eqn. (1)]. A



(1)

non-systematic numbering scheme (see text)

deuterium-exchange reaction of **8** was followed by ^1H NMR spectroscopy in the presence of deuterium oxide and tetrabutylammonium bromide in $CDCl_3$ solution. Addition of a catalytic amount of potassium hydroxide to the solution caused immediate exchange of the methine proton before the formation of oxazolidinone **9**. This finding suggests that enolization of

* The structure of the rearranged product, previously given in ref. 9 as **6**, is now shown to be incorrect. We hope herein to revise the structure.

compound **8** occurred before the formation of compound **9**, and that the presence of an enolizable α-hydrogen atom adjacent to the diazadicarboximide ring is requisite for the present rearrangements.

Experimental

Instruments.—^{1}H and ^{13}C NMR spectra were obtained in $CDCl_3$ solutions (unless otherwise stated) on a Hitachi R-600 or a JEOL FX 200 spectrometer using tetramethylsilane as internal standard. *J*-Values are given in Hz. IR spectra were recorded on a Shimadzu R-460 spectrometer. Mass spectra were measured by a JEOL JMX DX-303 spectrometer. Elemental analyses were performed using a Yanagimoto Model MT-3 CHN analyser.

Materials.—Benzylidene ketones **1a–j** were synthesized according to the reported procedures[12] or obtained from commercial sources. PTAD was freshly prepared by Cookson's method.[13] The substrates **4a–j** were prepared by the *in situ* addition–elimination reaction described in the previous report.[7]

3-(2-*Furoyl*)-N-*phenyl*-1,2-*dihydrocinnoline*-1,2-*dicarboximide* **4f** was obtained in 72% yield, m.p. 224–225 °C (yellow powder from EtOH); δ_H 6.23 (1 H, s, 4-H), 6.40 (1 H, dd, *J* 4 and 1), 6.96–7.67 (10 H, m) and 8.10–8.33 (1 H, m); δ_C 112.9 (d), 115.1 (d), 115.3 (d), 120.0 (s), 125.8 (d), 128.1 (d), 128.6 (d), 129.2 (d), 130.7 (s), 131.0 (s), 131.3 (d), 134.8 (s), 143.2 (s), 145.8 (s), 147.6 (d), 151.4 (s) and 172.4 (s); ν_{max}(KBr)/cm^{-1} 1754, 1703, 1658 and 1624; *m/z* 371 (M^+, 100%), 196 (46), 168 (45) and 139 (9) (Found: C, 68.1; H, 3.3; N, 11.4. $C_{21}H_{13}N_3O_4$ requires C, 67.90; H, 3.53; N, 11.32%).

N-*Phenyl*-3-(2-*thenoyl*)-1,2-*dihydrocinnoline*-1,2-*dicarboximide* **4g** was obtained in 80% yield, m.p. 217 °C (yellow powder from EtOH); δ_H 6.20 (1 H, s, 4-H) and 6.97–8.30 (12 H, m); δ_C 114.5 (d), 115.4 (d), 119.9 (s), 125.7 (d), 125.8 (d), 128.0 (d), 128.4 (d), 128.6 (d), 129.1 (d), 130.7 (s), 131.1 (s), 131.3 (d), 134.6 (s), 134.7 (d), 135.8 (d), 141.8 (s), 143.0 (s), 145.7 (s) and 177.1 (s); ν_{max}(KBr)/cm^{-1} 1771, 1718, 1631 and 1488; *m/z* 387 (M^+, 100%), 240 (11), 212 (61), 184 (15), 119 (5) and 111 (49) (Found: C, 64.9; H, 3.3; N, 10.7. $C_{21}H_{13}N_3O_3S$ requires C, 65.09; H, 3.38; N, 10.85%).

7-*Methoxy*-N-*phenyl*-3-(*pyridine*-2-*carbonyl*)-1,2-*dihydrocinnoline*-1,2-*dicarboximide* **4h** was obtained in 48% yield, m.p. 210–211 °C (yellow powder from EtOH); δ_H 3.86 (3 H, s), 6.46 (1 H, s, 4-H), 7.13–7.50 (10 H, m), 7.83–8.10 (1 H, m) and 8.50–8.70 (1 H, m); δ_C 55.7 (q), 101.4 (d), 111.5 (d), 113.1 (s), 116.8 (d), 122.9 (d), 125.8 (d), 127.2 (d), 128.5 (d), 129.1 (d), 129.6 (d), 129.8 (s), 130.7 (s), 136.2 (s), 137.3 (d), 143.5 (s), 145.9 (s), 148.7 (d), 153.5 (s), 161.9 (s) and 185.6 (s); ν_{max}(KBr)/cm^{-1} 1762, 1715, 1667, 1603 and 1505; *m/z* 412 (M^+, 100%), 265 (63), 222 (26), 206 (17) and 187 (7) (Found: C, 66.8; H, 3.8; N, 13.6. $C_{23}H_{16}N_4O_4$ requires C, 66.97; H, 3.91; N, 13.59%).

N-*Phenyl*-3-*pivaloyl*-1,2-*dihydrocinnoline*-1,2-*dicarboximide* **4i** was obtained in 31% yield, m.p. 200–201 °C (yellow powder from EtOH); δ_H 1.37 (9 H, s), 5.73 (1 H, s, 4-H) and 6.95–7.90 (9 H, m); δ_C 26.8 (q), 45.2 (s), 106.7 (d), 115.3 (d), 120.1 (d), 125.8 (s), 125.9 (d), 127.0 (d), 128.7 (d), 129.3 (d), 130.1 (d), 130.5 (s), 131.7 (s), 133.4 (s), 143.0 (s), 144.9 (s) and 202.5 (s); ν_{max}(KBr)/cm^{-1} 1765, 1718, 1408 and 1356; *m/z* 361 (M^+, 100%), 157 (21) and 130 (20) (Found: M^+, 361.1429. $C_{21}H_{19}N_3O_3$ requires M, 361.1430).

7-*Methoxy*-N-*phenyl*-3-*pivaloyl*-1,2-*dihydrocinnoline*-1,2-*dicarboximide* **4j** was obtained in 78% yield, m.p. 212–214 °C (yellow powder from EtOH); δ_H 1.37 (9 H, s), 3.82 (3 H, s), 5.78 (1 H, s, 4-H), 6.62–7.13 (2 H, m) and 7.40–7.60 (6 H, m); δ_C 26.9 (q), 45.2 (s), 55.7 (q), 101.6 (d), 107.9 (d), 111.5 (d), 112.5 (s), 125.9 (d), 128.3 (d), 128.7 (d), 129.1 (s), 129.3 (d), 130.6 (s), 134.7 (s), 142.9 (s), 145.3 (s), 161.2 (s) and 202.3 (s); ν_{max}(KBr)/cm^{-1} 1767, 1723, 1608, 1408, 1280 and 1137; *m/z* 391 (M^+, 100%), 334 (17), 187 (56) and 160 (28) (Found: M^+, 391.1552. $C_{22}H_{21}N_3O_4$ requires M, 391.1530).

General Procedure of Preparation of Tetracyclic Oxazolidinones **5a–o**.—To a suspension of a compound 4 (0.50 mmol) in ethanol (20 cm^3) was added powdered potassium hydroxide (3.6 mmol), and the mixture was stirred for 60 min at 25 °C, during which time the characteristic yellow colour disappeared. The solution was neutralized by dil. hydrochloric acid to give a precipitate, which was collected by filtration and recrystallized from ethanol. NMR locants follow the non-systematic numbering scheme shown in the displayed formulae in Scheme 2.

(2R*,12R*)-2-*Methoxy*-12-*methyl*-11-*phenyl*-13-*oxa*-9,11,15-*triazatetracyclo*[7.6.0.0^{1,12}.0^{3,8}] *pentadeca*-3,5,7-*triene*-10,14-*dione* **5a** was obtained from urazole **4a** in 76% yield, m.p. 235–236 °C (powder from EtOH); δ_H 1.72 (3 H, s), 3.68 (3 H, s), 5.26 (1 H, s, 11-H), 6.51 (1 H, s, NH) and 7.30–7.52 (9 H, m); δ_C 21.0 (q), 59.9 (q), 81.4 (d, C-11), 86.1 (s, C-1), 96.9 (s, C-5), 116.3 (d), 125.2 (d), 125.4 (d), 127.8 (d), 128.2 (d), 129.2 (d), 129.6 (s), 130.8 (d), 133.9 (s), 139.3 (s), 154.1 (s) and 154.7 (s); ν_{max}(KBr)/cm^{-1} 3250, 1782, 1711, 1593 and 979; *m/z* 351 (M^+, 100%), 308 (25), 307 (22), 276 (41), 275 (25), 232 (17), 200 (22), 190 (16), 189 (42), 147 (23) and 119 (13) (Found: C, 64.9; H, 4.8; N, 11.9. $C_{19}H_{17}N_3O_4$ requires C, 64.93; H, 4.88; N, 11.97%).

(2R*,12R*)-2-*Ethoxy*-12-*methyl*-11-*phenyl*-13-*oxa*-9,11,15-*triazatetracyclo*[7.6.0.0^{1,12}.0^{3,8}]*pentadeca*-3,5,7-*triene*-10,14-*dione* **5b** was obtained from urazole **4a** in 77% yield, m.p. 109–110 °C (powder from EtOH); δ_H 1.41 (3 H, t), 1.72 (3 H, s), 3.80 (2 H, q), 5.35 (1 H, s, 11-H), 6.54 (1 H, s, NH) and 7.08–7.54 (9 H, m); δ_C 15.4 (q), 21.0 (q), 68.1 (t), 79.7 (d, C-11), 86.1 (s, C-1), 96.9 (s, C-5), 116.3 (d), 125.2 (d), 125.3 (d), 127.7 (d), 128.2 (d), 129.2 (d), 129.9 (s), 130.7 (d), 133.9 (s), 139.3 (s), 154.0 (s) and 154.5 (s); ν_{max}(KBr)/cm^{-1} 3320, 1763, 1712, 1610, 1476, 1376, 1124, 1104, 968, 764, 736 and 680; *m/z* 365 (M^+, 100%), 322 (17), 321 (30), 292 (22), 276 (36), 275 (32), 246 (13), 203 (22), 200 (24) and 158 (14) (Found: C, 65.9; H, 5.2; N, 11.6. $C_{20}H_{19}N_3O_4$ requires C, 65.72; H, 5.24; N, 11.51%).

(2R*,12R*)-2-*Isopropoxy*-12-*methyl*-11-*phenyl*-13-*oxa*-9,11,-15-*triazatetracyclo*[7.6.0.0^{1,12}.0^{3,8}]*pentadeca*-3,5,7-*triene*-10,-14-*dione* **5c** was obtained from urazole **4a** in 23% yield, m.p. 201–203 °C (needles from EtOH); δ_H 1.35 (3 H, d, *J* 6.0), 1.50 (3 H, d, *J* 6.0), 1.69 (3 H, s), 3.75 (1 H, m), 5.44 (1 H, s, 11-H), 6.29 (1 H, s, NH) and 7.27–7.58 (9 H, m); δ_C 21.1 (q), 21.8 (q), 22.9 (q), 73.3 (d), 77.1 (d, C-11), 86.1 (s, C-1), 97.1 (s, C-5), 116.2 (d), 125.1 (d), 125.2 (d), 127.7 (d), 128.2 (d), 129.2 (d), 130.2 (s), 130.6 (d), 133.9 (s), 139.5 (s), 154.0 (s) and 154.4 (s); ν_{max}(KBr) 3280, 1756, 1716, 1376, 1096, 764 and 720; *m/z* 379 (M^+, 100%), 335 (36), 292 (13), 275 (80), 217 (11), 158 (29) and 132 (75) (Found: M^+, 379.1530. $C_{21}H_{21}N_3O_4$ requires M, 379.1530).

(2R*,12R*)-2-*Butylamino*-12-*methyl*-11-*phenyl*-13-*oxa*-9,11,15-*triazatetracyclo*[7.6.0.0^{1,12}.0^{3,8}]*pentadeca*-3,5,7-*triene*-10,14-*dione* **5e**. A solution of urazole **4a** (500 mg, 1.57 mmol) and butylamine (100 mg, 1.37 mmol) in ethanol (30 cm^3) was refluxed for 60 min. The reaction mixture was then quenched with dil. hydrochloric acid. The resulting precipitates were filtered (water-pump) and chromatographed on silica gel (dichloromethane). Compound **5b** (131 mg, 23%), from the first eluent, and the title compound **5e** (98 mg, 16%), from the second eluent, were obtained; m.p. 205–206 °C (powder from EtOH); δ_H[$(CD_3)_2SO$] 0.76–1.13 (7 H, m), 1.38 (3 H, s), 1.47–1.70 (2 H, m), 5.35 (1 H, s, 11-H), 6.87–7.06 (1 H, m), 7.26–7.53 (8 H, m) and 8.16 (1 H, s); ν_{max}(KBr)/cm^{-1} 3175, 1710, 1680, 1124, 1090, 905 and 747; *m/z* 392 (M^+, 27%), 349 (57), 230 (85), 132 (39) and 131 (100) (Found: M^+, 392.1850. $C_{22}H_{24}N_4O_3$ requires M, 392.1850).

(2R*,12R*)-2-*Ethoxy*-6-*methoxy*-12-*methyl*-11-*phenyl*-13-*oxa*-9,11,15-*triazatetracyclo*[7.6.0.0^{1,12}.0^{3,8}]*pentadeca*-3,5,7-*triene*-10,14-*dione* **5f** was obtained from urazole **4b** in 50% yield, m.p. 234–235 °C (powder from EtOH); δ_H 1.35 (3 H, t), 1.70 (3 H, s), 3.75 (2 H, q), 3.80 (3 H, s), 5.32 (1 H, s, 11-H), 6.17 (1 H, s, NH), 6.95 (1 H, dd, *J* 4 and 1) and 7.30–7.47 (7 H, m); δ_C 15.4 (q), 21.0 (q), 55.7 (q), 67.9 (t), 79.4 (d, C-11), 86.6 (s, C-1), 97.0 (s, C-5), 101.6 (d), 111.8 (d), 121.3 (s), 126.0 (d), 127.8 (d), 128.2 (d), 129.2 (d), 133.9 (s), 140.8 (s), 154.0 (s), 154.7 (s) and 162.0 (s); ν_{max}(KBr)/cm^{-1} 3375, 1768, 1731, 1597, 1113, 1073 and 738; *m*/*z* 395 (M$^+$, 100%), 352 (19), 351 (67), 323 (11), 322 (46), 307 (30), 306 (100), 305 (84), 304 (46), 278 (15), 190 (18), 188 (23), 164 (34) and 118 (26) (Found: C, 63.6; H, 5.35; N, 10.7. $C_{21}H_{21}N_3O_5$ requires C, 63.77; H, 5.36; N, 10.63%).

(2R*,12R*)-6-*Chloro*-2-*ethoxy*-12-*methyl*-11-*phenyl*-13-*oxa*-9,11,15-*triazatetracyclo*[7.6.0.0^{1,12}.0^{3,8}]*pentadeca*-3,5,7-*triene*-10,14-*dione* **5g** was obtained from urazole **4c** in 64% yield, m.p. 250–251 °C (needles from EtOH); δ_H 1.42 (3 H, t), 1.54 (3 H, s), 3.83 (2 H, q), 5.33 (1 H, s, 11-H), 6.30 (1 H, s, NH) and 7.32–7.60 (8 H, m); δ_C 15.4 (q), 21.0 (q), 68.3 (t), 79.3 (d, C-11), 86.4 (s, C-1), 96.9 (s, C-5), 116.6 (d), 125.3 (d), 126.3 (d), 127.8 (d), 128.4 (d), 129.3 (d), 133.7 (s), 136.5 (s), 140.3 (s), 153.7 (s) and 154.6 (s); ν_{max}(KBr)/cm^{-1} 3315, 1784, 1728, 1599, 1137, 1110 and 964; *m*/*z* 401 (M$^+$ + 2, 18%), 399 (M$^+$, 49), 357 (18), 355 (52), 328 (36), 326 (100), 312 (13), 310 (49), 309 (47), 308 (42), 280 (9), 237 (11), 192 (14) and 118 (33) (Found: C, 60.0; H, 4.5; N, 10.4. $C_{20}H_{18}ClN_3O_4$ requires C, 60.06; H, 4.54; N, 10.52%).

(2R*,12R*)-2-*Ethoxy*-11,12-*diphenyl*-13-*oxa*-9,11,15-*triazatetracyclo*[7.6.0.0^{1,12}.0^{3,8}]*pentadeca*-3,5,7-*triene*-10,14-*dione* **5h** was obtained from urazole **4d** in 65% yield, m.p. 240–242 °C (needles from EtOH); δ_H 1.05 (3 H, t), 3.00 (2 H, q), 4.68 (1 H, s, 11-H), 6.55 (1 H, s, NH) and 7.10–7.68 (14 H, m); δ_C 14.5 (q), 67.0 (t), 79.5 (d, C-11), 87.1 (s, C-1), 98.8 (s, C-5), 115.8 (d), 124.7 (d), 124.8 (d), 124.9 (d), 126.2 (d), 126.3 (d), 128.2 (d), 128.8 (s), 129.5 (d), 129.8 (d), 130.1 (d), 132.9 (s), 134.6 (s), 138.8 (s), 154.1 (s) and 154.4 (s); ν_{max}(KBr)/cm^{-1} 3348, 1795, 1738, 1472, 1354, 1144, 773 and 754; *m*/*z* 427 (M$^+$, 100%), 383 (3), 338 (7), 337 (8), 322 (12), 308 (32), 276 (17), 262 (34), 203 (31) and 180 (9) (Found: C, 70.2; H, 4.9; N, 9.9. $C_{25}H_{21}N_3O_4$ requires C, 70.25; H, 4.95; N, 9.84%).

(2R*,12R*)-2-*Isopropoxy*-11,12-*diphenyl*-13-*oxa*-9,11,15-*triazatetracyclo*[7.6.0.0^{1,12}.0^{3,8}]*pentadeca*-3,5,7-*triene*-10,14-*dione* **5i** was obtained from urazole **4d** in 60% yield, m.p. 231–232 °C (needles from EtOH); δ_H 0.79 (3 H, d, *J* 6), 1.05 (3 H, d, *J* 6), 2.82 (1 H, m), 4.82 (1 H, s, 11-H), 6.50 (1 H, s, NH) and 7.02–7.70 (14 H, m); δ_C 20.8 (q), 22.6 (q), 72.6 (d), 77.4 (d, C-11), 87.7 (s, C-1), 99.3 (s, C-5), 116.2 (d), 125.1 (d), 125.2 (d), 125.4 (d), 126.7 (d), 128.3 (d), 128.7 (s), 129.4 (d), 129.8 (d), 130.2 (d), 130.4 (d), 133.4 (s), 134.9 (s), 139.2 (s), 154.5 (s) and 154.8 (s); ν_{max}(KBr)/cm^{-1} 3320, 1778, 1721, 1144, 1100, 764 and 746; *m*/*z* 441 (M$^+$, 66%), 397 (23), 294 (6), 280 (11), 262 (37), 217 (11), 180 (17), 132 (40) and 105 (100) (Found: C, 70.7; H, 5.2; N. 9.5. $C_{26}H_{23}N_3O_4$ requires C, 70.71; H, 5.25; N, 9.52%).

(2R*,12R*)-2-*Ethoxy*-6-*methoxy*-11,12-*diphenyl*-13-*oxa*-9,11,15-*triazatetracyclo*[7.6.0.0^{1,12}.0^{3,8}]*pentadeca*-3,5,7-*triene*-10,14-*dione* **5j** was obtained from urazole **4e** in 58% yield, m.p. 255–256 °C (powder from EtOH); δ_H 1.03 (3 H, t), 3.10 (2 H, q), 3.83 (3 H, s), 4.38 (1 H, s, 11-H), 6.42 (1 H, s, NH), 6.65 (1 H, dd, *J* 8 and 4) and 6.83–7.83 (12 H, m); δ_C 15.0 (q), 55.7 (q), 67.3 (t), 79.7 (d, C-11), 88.1 (s, C-1), 99.5 (s, C-5), 101.6 (d), 111.9 (d), 121.4 (s), 125.5 (d), 125.9 (d), 126.8 (d), 128.8 (d), 129.4 (d), 130.3 (d), 133.5 (d), 135.1 (s), 140.9 (s), 154.6 (s), 154.8 (s) and 162.1 (s); ν_{max}(KBr)/cm^{-1} 3260, 1791, 1720, 1495, 1231 and 1028; *m*/*z* 457 (M$^+$, 100%), 368 (39), 338 (16), 292 (15), 233 (12) and 162 (15) (Found: M$^+$, 457.1636. $C_{26}H_{23}N_3O_5$ requires M, 457.1640).

(2R*,12R*)-2-*Ethoxy*-12-(2-*furyl*)-11-*phenyl*-13-*oxa*-9,11,15-*triazatetracyclo*[7.6.0.0^{1,12}.0^{3,8}]*pentadeca*-3,5,7-*triene*-10,14-*dione* **5k** was obtained from urazole **4f** in 61% yield, m.p. 243–244 °C (needles from EtOH); δ_H 1.17 (3 H, t), 3.33 (2 H, q), 4.97 (1 H, s, 11-H), 6.35 (1 H, dd, *J* 4 and 2), 6.40 (1 H, s, NH), 6.60 (1 H, dd, *J* 4 and 1) and 7.20–7.53 (10 H, m); δ_C 15.1 (q), 67.5 (t), 79.8 (d, C-11), 87.6 (s, C-1), 95.7 (s, C-5), 111.5 (d), 113.1 (d), 116.5 (d), 125.2 (d), 125.4 (d), 126.6 (d), 127.7 (d), 128.9 (d), 130.1 (s), 130.6 (d), 134.5 (s), 139.4 (s), 144.7 (d) and 154.3 (s); ν_{max}(KBr)/cm^{-1} 3250, 1788, 1700, 1166, 1107 and 777; *m*/*z* 417 (M$^+$, 100%), 373 (12), 328 (15), 322 (41), 298 (56), 276 (53), 252 (37), 211 (20), 203 (43), 160 (18) and 132 (59) (Found: M$^+$, 417.1340. $C_{23}H_{19}N_3O_5$ requires M, 417.1320).

(2R*,12R*)-2-*Ethoxy*-11-*phenyl*-12-(2-*thienyl*)-13-*oxa*-9,11,-15-*triazatetracyclo*[7.6.0.0^{1,12}.0^{3,8}]*pentadeca*-3,5,7-*triene*-10,-14-*dione* **5l** was obtained from urazole **4g** in 50% yield, m.p. 255–256 °C (needles from EtOH); δ_H 1.10 (3 H, t), 3.27 (2 H, q), 4.87 (1 H, s, 11-H), 6.60 (1 H, s, NH) and 6.90–7.73 (12 H, m); δ_C 15.2 (q), 67.8 (t), 80.2 (d, C-11), 87.8 (s, C-1), 98.1 (s, C-5), 116.4 (d), 125.3 (d), 125.4 (d), 126.1 (d), 127.2 (d), 128.2 (d), 128.4 (d), 128.7 (d), 128.8 (d), 130.1 (s), 130.6 (d), 134.8 (s), 136.8 (s), 139.4 (s), 154.0 (s) and 154.2 (s); ν_{max}(KBr)/cm^{-1} 3305, 1785, 1727, 1494, 1151 and 755; *m*/*z* 433 (M$^+$, 47%), 343 (15), 322 (31), 314 (25), 276 (38), 227 (13), 203 (41), 132 (55) and 111 (100) (Found: M$^+$ 433.1103. $C_{23}H_{19}N_3O_4S$ requires M, 433.1100).

(2R*,12R*)-2-*Ethoxy*-6-*methoxy*-11-*phenyl*-12-(2-*pyridyl*)-13-*oxa*-9,11,15-*triazatetracyclo*[7.6.0.0^{1,12}.0^{3,8}]*pentadeca*-3,5,-7-*triene*-10,14-*dione* **5m** was obtained from urazole **4h** in 47% yield, m.p. 260 °C (powder from EtOH); δ_H 1.13 (3 H, t), 3.30 (2 H, q), 3.80 (3 H, s), 4.10 (1 H, s, 11-H), 6.50 (1 H, dd, *J* 8 and 3), 6.87 (1 H, s, NH), 7.00–7.33 (8 H, m), 7.53–7.86 (2 H, m) and 8.53 (1 H, d, *J* 5); δ_C 15.1 (q), 55.6 (q), 67.3 (t), 81.2 (d, C-11), 81.7 (s, C-1), 92.2 (s, C-5), 100.6 (d), 110.5 (d), 121.5 (d), 123.1 (s), 123.3 (s), 125.4 (d), 125.5 (d), 125.8 (d), 128.2 (d), 136.5 (s), 136.7 (d), 141.6 (s), 149.6 (d), 154.8 (s), 158.6 (s) and 161.6 (s); ν_{max}(KBr)/cm^{-1} 3280, 1706, 1616, 1586, 1493 and 1464; *m*/*z* 458 (M$^+$, 3%), 415 (86), 326 (42) and 296 (100) (Found: M$^+$, 458.1597. $C_{25}H_{22}N_4O_5$ requires M, 458.1590).

(2R*,12R*)-12-(tert-*Butyl*)-2-*ethoxy*-11-*phenyl*-13-*oxa*-9,11,-15-*triazatetracyclo*[7.6.0.0^{1,12}.0^{3,8}]*pentadeca*-3,5,7-*triene*-10,-14-*dione* **5n** was obtained from urazole **4i** in 29% yield, m.p. 256 °C (powder from EtOH); δ_H 1.03 (9 H, s), 1.38 (3 H, t), 4.02 (2 H, q), 5.90 (1 H, s, 11-H), 6.40 (1 H, s, NH) and 7.30–7.60 (9 H, m); δ_C 15.6 (q), 26.2 (q), 39.2 (s), 67.9 (t), 79.1 (d, C-11), 87.3 (s, C-1), 104.0 (s, C-5), 115.1 (d), 124.4 (d), 125.2 (d), 128.0 (d), 128.8 (d), 128.9 (d), 129.8 (s), 130.7 (d), 136.9 (s), 139.3 (s), 153.8 (s) and 155.0 (s); ν_{max}(KBr)/cm^{-1} 3260, 1776, 1723, 1437, 1408, 1167 and 750; *m*/*z* 407 (M$^+$, 47%), 276 (27), 242 (100), 203 (33) and 132 (35) (Found: M$^+$, 407.1851. $C_{23}H_{25}N_3O_4$ requires M, 407.1840).

(2R*,12R*)-12-(tert-*Butyl*)-2-*ethoxy*-6-*methoxy*-11-*phenyl*-13-*oxa*-9,11,15-*triazatetracyclo*[7.6.0.0^{1,12}.0^{3,8}]*pentadeca*-3,5,-7-*triene*-10,14-*dione* **5o** was obtained from urazole **4j** in 45% yield, m.p. 178–179 °C (powder from EtOH); δ_H 1.00 (9 H, s), 1.33 (3 H, t), 4.05 (3 H, s), 4.15 (2 H, q), 5.81 (1 H, s, 11-H), 6.48 (1 H, s, NH), 7.07–7.93 (7 H, m) and 8.30–8.47 (1 H, m); δ_C 15.6 (q), 27.6 (q), 39.2 (s), 56.0 (q), 67.5 (t), 78.8 (d, C-11), 88.0 (s, C-1), 100.2 (d), 104.1 (s, C-5), 105.9 (d), 111.3 (d), 123.9 (d), 125.9 (d), 128.1 (s), 128.8 (d), 128.9 (d), 129.3 (d), 136.9 (s), 141.0 (s), 150.9 (s), 152.5 (s), 154.9 (s) and 162.7 (s); ν_{max}(KBr)/cm^{-1} 3300, 1780, 1719, 1669 and 909; *m*/*z* 437 (M$^+$, 100%) 393 (40), 378 (29), 348 (30), 332 (45) and 272 (63) (Found: M$^+$, 437.1953. $C_{24}H_{27}N_3O_5$ requires M, 437.1950).

Synthesis of the Oxazolidinone **9**.—Commercially available palladium on carbon (100 mg) and an ethanolic solution of compound **4a** (300 mg, 0.94 mmol) were placed in a reaction flask connected with an atmospheric pressure hydrogenation apparatus. Hydrogenation was carried out for *ca.* 12 h at 25 °C until uptake of hydrogen had ceased. After filtration and the removal of ethanol on a rotary evaporator, the resulting solid

was recrystallized from ethanol to afford urazole **8** in 83% yield.

Oxazolidinone **9** was prepared from urazole **8** in 75% yield according to the procedure given for the preparation of compound **5b**.

3-*Acetyl*-N-*phenyl*-1,2,3,4-*tetrahydrocinnoline*-1,2-*dicarboximide* **8** had m.p. 124–125 °C (powder from EtOH); δ_H 2.24 (3 H, s), 3.46 (2 H, d, *J* 4, 4-H_2), 5.19 (1 H, t, *J* 4, 3-H) and 7.10–7.70 (9 H, m); δ_C 26.1 (q), 28.3 (t, C-4), 59.2 (d, C-3), 116.4 (d), 117.8 (s), 124.2 (d), 126.1 (d), 128.4 (d), 128.7 (d), 128.9 (d), 129.2 (s), 131.1 (d), 132.4 (s), 146.6 (s), 150.8 (s) and 201.6 (s); ν_{max}(KBr)/cm^{-1} 1756, 1700, 1160, 756 and 748; *m*/*z* 321 (M^+ 49%), 278 (100), 159 (45) and 132 (95) (Found: C, 67.2; H, 4.6; N, 13.1. $C_{18}H_{15}N_3O_3$ requires C, 67.26; H, 4.71; N, 13.09%).

(12R*)-12-*Methyl*-11-*phenyl*-13-oxa-9,11,15-*triazatetracyclo*[7.6.0.0^{1,12}.0^{3,8}]*pentadeca*-3,5,7-*triene*-10,14-*dione* **9** had m.p. 207 °C (needles from EtOH); δ_H 1.67 (3 H, s), 3.13 (1 H, d, *J* 16, *endo*-11-H), 3.96 (1 H, d, *J*, 16, *exo*-11-H), 6.33 (1 H, s, NH) and 7.30–7.63 (9 H, m); δ_C 20.7 (q), 37.6 (t, C-11), 84.7 (s, C-1), 97.2 (s, C-5), 116.9 (d), 124.8 (d), 125.3 (d), 127.7 (d), 128.2 (d), 128.9 (d), 129.2 (d), 134.1 (s), 140.7 (s), 154.7 (s) and 154.9 (s); ν_{max}(KBr)/cm^{-1} 3270, 1763, 1716, 1473, 1164, 1145, 1090, 975 and 751; *m*/*z* 321 (M^+, 100%), 278 (21), 277 (29), 260 (29), 259 (24), 159 (99), 144 (24) and 119 (25) (Found: C, 67.2; H, 4.6; N, 13.1. $C_{18}H_{15}N_3O_3$ requires C, 67.26; H, 4.71; N, 13.09%).

X-Ray Single-crystal Analysis of Compound **5b** *Ethanol Solvate*.—A single crystal was mounted on a computer-controlled Rigaku AFC-5 diffractometer. Intensity data in the range $2 < 2\theta < 130$ were measured using graphite-monochromated Cu-Kα radiation (λ = 1.5148 Å); the ω–2θ scanning mode was used for data collection.

Crystal data. $C_{22}H_{25}N_3O_5$, M = 411.46. Monoclinic, *a* = 12.294(13), *b* = 13.201(7), *c* = 13.107(5) Å and β = 97.36(7)°, *V* = 2109.6(27) Å^3, space group $P2_1/c$, *Z* = 4, D_x = 1.295 g cm^{-3}. The structure was solved by the direct methods using the MULTAN78 program.[14] Non-hydrogen atoms were refined by the block-diagonal least-squares method with anisotropic temperature factors. The positional parameters of the hydrogen atoms were all located on a difference Fourier map and were refined with an overall isotropic temperature factor. The labelling of the atoms is given in Fig. 1.*

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* *Supplementary publication*. Tables of atomic coordinates, bond lengths and angles have been deposited at the Cambridge Crystallographic Data Centre (see *Instructions for Authors*, January issue).

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