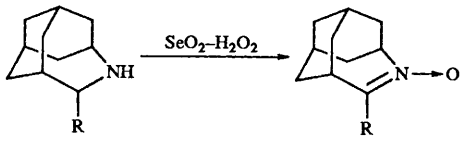
Synthesis of novel carbo- and heteropolycycles. Part 30.[1,2] 1,3-Dipolar cycloaddition of nitrile functions with some selected nitrones. Efficient synthesis of 2,3-dihydro-1,2,4-oxadiazole derivatives

Yang Yu, Naoto Watanabe, Masatomi Ohno and Shoji Eguchi *
Institute of Applied Organic Chemistry, Faculty of Engineering, Nagoya University, Furo-cho, Chikusa-ku, Nagoya 464–01, Japan

A practical reactivity of nitrile groups as dipolarophiles in 1,3-dipolar cycloadditions with 4-azahomoadamant-4-ene *N*-oxides **1** and **2**, 2,2-dimethyl-3,4-dihydro-2*H*-pyrrole *N*-oxide **8** and *N*-benzylidenephenylamine *N*-oxide **10** is reported. Benzonitriles **3c–i** reacted with these nitrones upon heating for more than 12 h to afford the corresponding 2,3-dihydro-1,2,4-oxadiazole derivatives. The reaction of acetonitrile **3b** with nitrone **1** required a prolonged reaction time (15 days). However, the reaction of an activated nitrile, methyl cyanoformate **3j**, proceeded smoothly under milder conditions (25 °C for **1**, **2** and **8**, and 80 °C for **10**).

The usefulness of nitrile functions as d^1 synthons in organic synthesis is well documented.[3] However, their use in cycloaddition chemistry is not so developed.[4] For example, nitriles react as heterodienophiles in some Diels–Alder reactions; however, an extremely high temperature is required, unless the reaction is intramolecular or the nitrile is activated by an electron-withdrawing group.[5] The use of nitriles as hetero-1,3-dipolarophiles is also quite limited; only a few reactions are known, for example, with azides, nitrile ylides and nitrile oxides.[6] The cycloaddition of nitrones with nitriles is particularly rare. To the best of our knowledge, only two cases, using aryl cyanate and tetracyanoethene, have so far been recorded.[7] In a series of synthetic studies on adamantane derivatives, we have synthesised novel homoadamantane-incorporated nitrones, 4-azahomoadamant-4-ene *N*-oxides **1** and **2**,[8] by Murahashi's oxidation procedure. Nitrones **1** and **2**



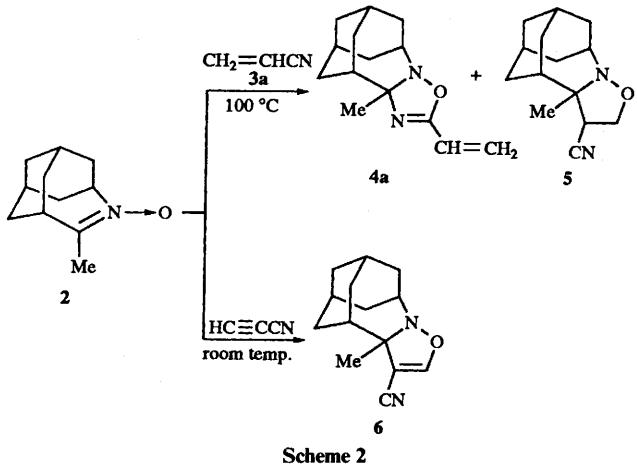
1 R = H
2 R = Me

Scheme 1

have unusual stability because they are incorporated in a rigid ring system. They were highly hygroscopic but could be stored at ambient temperature for a long time. When nitrones **1** and **2** were treated with electron-deficient alkynes, efficient and regiospecific formation of 4-substituted isoxazolines was observed. During a further survey of 1,3-dipolar cycloaddition reactivity,[8] we discovered and reported the remarkable dipolarophilicity of nitrile functions; even the ordinary C≡N triple bonds in acetonitrile and benzonitrile showed moderate reactivity toward the 1,3-dipole of the nitrones **1** and **2**. Thus, this discovery constituted a facile and direct route to 2,3-dihydro-1,2,4-oxadiazoles. With these findings in hand, we explored 1,3-dipolar cycloadditions of both activated and unactivated nitrile functions with nitrones **1** and **2**, and additionally with typical cyclic and acyclic nitrones such as 2,2-dimethyl-3,4-dihydro-2*H*-pyrrole *N*-oxide **8** and *N*-benzylidenephenylamine *N*-oxide **10**.

Results and discussion

The cycloaddition of nitrone **2** with cyanoacetylene afforded the expected 4-cyano-2,3-dihydroisoxazole **6** regiospecifically under mild conditions.[8] This cycloaddition was then attempted with acrylonitrile. In this case a higher temperature was required because of the lower reactivity of this reagent. When **2** was allowed to react with a large excess of acrylonitrile **3a** employed as a solvent at 100 °C in a sealed tube under a nitrogen atmosphere, two products in a ratio of 55:45 were obtained after chromatographic separation. Unexpectedly, the major product had no absorption due to a cyano group but absorptions at 1676 and 1602 cm^{-1} in the IR spectrum, while mass spectral and elemental analyses indicated a 1:1 cycloadduct (*m/z* 232). ^1H NMR signals showed the presence of a vinyl group at δ 5.72, 6.06 and 6.31 (ABX multiplet). These data allowed assignment of the product as 2,3-dihydro-1,2,4-oxadiazole **4a**. The structure of the minor product was consistent with the expected cycloadduct, 4-cyano-2,3,4,5-tetrahydroisoxazole **5**, based on a molecular ion peak at *m/z* 232, an IR absorption at 2247 cm^{-1} (C≡N) and ^1H NMR signals at δ 3.70, 4.05, and 4.38 (each 1 H, dd, -$CHCH_2$-) (Scheme 2).



Scheme 2

Previous work on nitrones has shown that acrylonitrile has cycloaddition reactivity exclusively at the alkene unit activated

Table 1 1,3-Dipolar cycloaddition of nitrones with nitriles

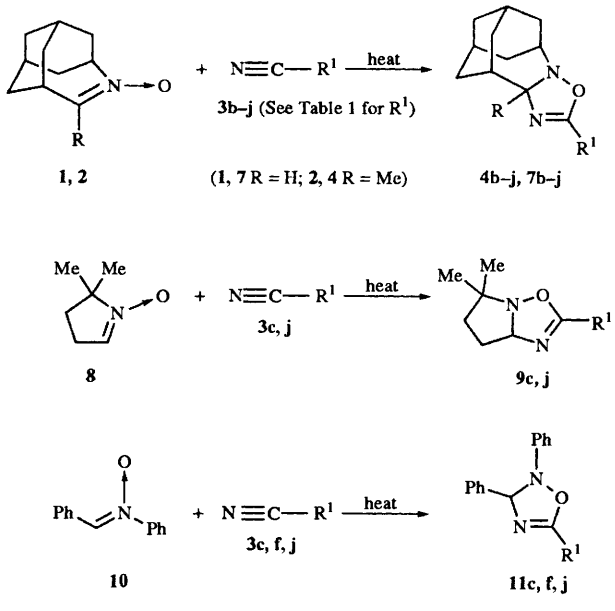
Entry	Nitrone	Nitrile (R^1)[b]	Reaction conditions[a] T/°C	t/h	Product[c]	Yield[d] (%)	Mp (°C)
1	**1**	**3b** (Me)	150	15 days	**7b**	53	94.0–97.5
2	**1**	**3c** (Ph)	150	15	**7c**	51	62.0–65.0
3	**1**	**3d** (*o*-$NO_2C_6H_4$)	100	24	**7d**	Trace	
4	**1**	**3e** (*m*-$NO_2C_6H_4$)	100	18	**7e**	64	142.0–145.5
5	**1**	**3f** (*p*-$NO_2C_6H_4$)	100	12	**7f**	58	192.0–195.0
6	**1**	**3g** (*o*-$MeOC_6H_4$)	120	48	**7g**	Trace	
7	**1**	**3h** (*m*-$MeOC_6H_4$)	120	8	**7h**	50	Oil
8	**1**	**3i** (*p*-$MeOC_6H_4$)	100	18	**7i**	58	139.5–141.5
9	**1**	**3j** (CO_2Me)	25	2	**7j**	65	101.0–103.5
10	**2**	**3b** (Me)	150	15 days	**4b**	0	
11	**2**	**3c** (Ph)	150	96	**4c**	26	118.5–121.0
12	**2**	**3d** (*o*-$NO_2C_6H_4$)	100	48	**4d**	0	
13	**2**	**3e** (*m*-$NO_2C_6H_4$)	100	60	**4e**	19	Oil
14	**2**	**3f** (*p*-$NO_2C_6H_4$)	100	36	**4f**	23	172.0–174.0
15	**2**	**3j** (CO_2Me)	25	36	**4j**	68	71.0–74.0
16	**8**	**3c** (Ph)	120	12	**9c**	54	Oil
17	**8**	**3j** (CO_2Me)	25	48	**9j**	49	Oil
18	**10**	**3c** (Ph)	120	12	**11c**	33	105.0–108.0
19	**10**	**3f** (*p*-$NO_2C_6H_4$)	120	12	**11f**	58	176.0–178.5
20	**10**	**3j** (CO_2Me)	80	24	**11j**	44	102.5–104.0

[a] Toluene was used as a solvent except for entries 1 and 10, in which acetonitrile served both as solvent and reactant. [b] 1.2 equiv. of reagent nitrile was used except for entries 1 and 10. [c] The product was chromatographed on a silica gel plate and extracted with ethyl acetate, and evaporation of the solvent left a residue as a crystal (or otherwise after being allowed to stand at room temperature). [d] Isolated yield.

with a cyano substitution,† as suggested by AM1 calculations [larger LUMO-coefficient at C=C (C_α −0.556, C_β 0.685) than at C≡N (C −0.277, N 0.382)]. Hence the present reaction is a peculiar case. Since keto nitrone **2** is stable but sterically hindered, it might react competitively at the electronically favoured but relatively congested C=C bond with the less hindered C≡N bond as the second reactive site.

The above intriguing observation prompted us to examine a similar type of reaction of nitrones **1** and **2** with ordinary aliphatic and aromatic nitriles **3b–i** as well as an activated nitrile, methyl cyanoformate **3j** (Table 1). In addition a typical monocyclic nitrone **8** and aromatic acyclic nitrone **10** were examined. The reactions of nitrones **1**, **2**, **8** and **10** were conducted in toluene with 1.2 equiv. of the nitrile at ambient temperature for **3j** (at 80 °C with **10**) and at a higher temperature, at the expense of the nitrones, for the other nitriles. Usually aromatic nitriles required prolonged heating (12–60 h), and in particular acetonitrile, which served as both a reactant and a solvent, underwent extremely slow addition to **1** (15 days). The products were separated by preparative TLC and analysed spectroscopically. The results are summarized in Scheme 3 and Table 1.

The products were shown to have a 2,3-dihydro-1,2,4-oxadiazole ring structure by the following spectral data, and hence, the nitrile groups were shown to act as hetero-1,3-dipolarophiles to all the nitrones selected in this experiment. First, the mass spectra showed the molecular ion peak exactly corresponding to a 1 : 1 cycloadduct. Typical splitting patterns of **4c**, **e**, **f**, **j** and **7b**, **c**, **e**, **f**, **h–j** were retro-1,3-dipolar cycloaddition to give a nitrone fragment ion (split *a*) for the

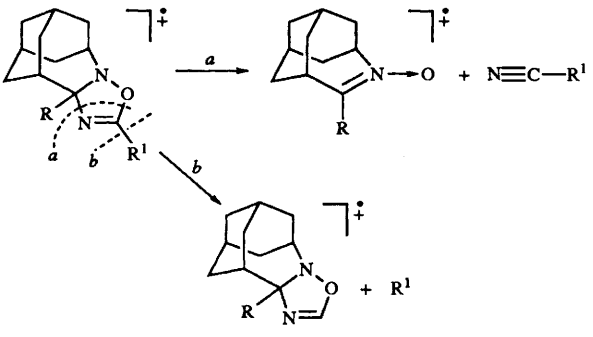


Scheme 3

cycloadducts with R^1 = Me, Ar, and decarboxylation to give a parent dihydro oxadiazole fragment (split *b*) for the cycloadducts with R^1 = CO_2Me (Scheme 4). In the IR spectra, the C=N double bond vibration of 2,3-dihydro-1,2,4-oxadiazoles appeared at 1645–1690 cm^{-1}. In the ^1H NMR spectra, resonances for 3-H (δ 5.44–5.73) and 3-Me (δ 1.53–1.57) each attached to the dihydro oxadiazole ring are observed together with resonances for the homoadamantane ring-Hs (δ 3.60–3.79) for **4c**, **e**, **f**, **j** and **7b**, **c**, **e**, **f**, **h–j**. The corresponding 3-H resonance for **11** was further shifted to a lower field by approximately 1.5 ppm and concealed in the aromatic proton range. Also observed for all the products were protons due to C-5 substituents (*e.g.*, 5-Me at δ 2.01 for **7b**).

The cycloaddition reactivity was more or less reflected in the reaction temperature, time and yield as can be seen from Table 1, and it may depend not only on the structure of the nitrones

† In fact, the cycloaddition of aldonitrone **1** to **3a** occurred only at the C=C bond to give 4-cyano and 5-cyano-2,3,4,5-tetrahydroisoxazoles (however, see ref. 6 ch. 3 for other examples in which 1,3-dipoles compete for addition to C=C and C≡N within the same molecule). The regiochemistry of **5** was determined by comparison with these products; chemical shift of isoxazole ring methylene signals at δ 4.05 and 4.38 is consistent with the 4-cyano isomer (δ 3.97 and 4.32) rather than the 5-cyano isomer (δ 2.41 and 2.66). The stereochemistry remained unsolved. Full details of 1,3-dipolar cycloadditions of nitrones **1** and **2** with electron-deficient alkenes will be reported in a separate paper.



Scheme 4

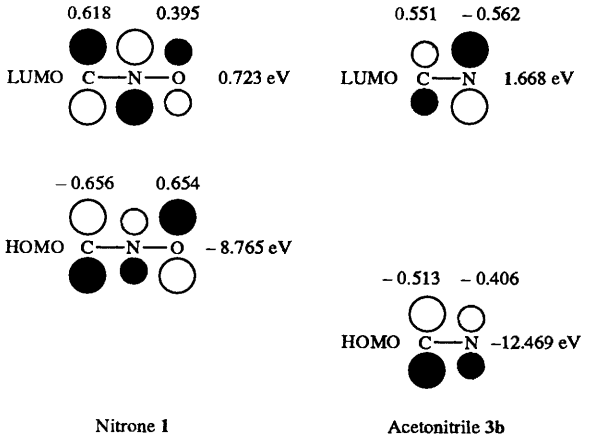


Fig. 1 Orbital interaction between nitrone 1 and acetonitrile **3b**

but also on the electronic and steric factors of the nitriles employed. From a comparison of entries 1, 2 and 9, it is clear that the reactivity increased in the order of alkyl, aryl and methoxycarbonyl nitrile; the activated nitrile, methyl cyanoformate **3j**, underwent smooth cycloaddition with nitrones **1**, **2** and **8** even at room temperature to afford 2,3-dihydro-1,2,4-oxadiazole carboxylates **7j**, **4j**, **9j**, respectively, in acceptable yields. In the case of nitrone **10** a complicated mixture was obtained with only a small amount of **11j** at room temperature, but when the reaction was carried out at 80 °C **11j** was isolated in 44% yield. The aromatic nitriles **3c**, **e**, **f**, **h**, **i** reacted with nitrone **1** at elevated temperature to give the corresponding 5-aryl-2,3-dihydro-1,2,4-oxadiazoles **7c**, **e**, **f**, **h**, **i** in moderate yields. The steric hindrance of an *ortho*-substituent on the benzene ring of aromatic nitriles and/or a methyl group at C-3 on the keto nitrone **2** decreased the reactivity, resulting in a very low yield or, at worst, no cycloadduct being formed (entries 3, 6, 10, 12 *etc.*). In contrast, *meta* and *para* substituents on the aromatic nitrile scarcely affected the yield (> 50%) regardless of their electron-donating or -withdrawing nature. The aromatic nitriles also reacted with nitrones **8** and **10** to give the corresponding cycloadducts **9c** and **11c**, **f** under similar conditions. The unactivated alkyl nitrile was much less reactive; in our hands, the highly reactive nitrone **1** was the only example to undergo cycloaddition with acetonitrile **3b** to give dihydrooxadiazole **7b** in 53% yield after heating in a sealed tube at 150 °C for 15 days (entry 1). Attempted reaction with other alkyl nitriles required too long a reaction time to obtain successful results; the cycloaddition was limited by the retro-cycloaddition and side-reactions as well as the decomposition of products.

Finally, the orbital interaction between nitrone **1** and acetonitrile **3b** was considered. AM1 calculations for these reactants are illustrated in Fig 1. If the reaction is concerted and HOMO-dipole controlled, then the HOMO-coefficient of carbon and oxygen in the nitrone **1** scarcely discriminates the regiochemistry; nevertheless, preferred overlap between nitrone–carbon and nitrile–nitrogen at the less hindered site accounts for the observed results. On the other hand interaction of the negative nitrone–oxygen and the positive nitrile–carbon should be more significant at the polar transition state.

In summary, the present work overturns the previously accepted concept that a nitrile function is not suitable for 1,3-dipolar cycloaddition with nitrones. An unactivated C≡N triple bond such as acetonitrile and benzonitrile is reactive enough to act as a hetero-dipolarophile as long as the reacting nitrones can resist decomposition under thermal conditions. With activated nitriles (*e.g.* cyanoformate) the cycloadduct is formed with ease. The results reported here demonstrate the feasibility of nitrone cycloaddition methodology for the direct and convenient synthesis of the 2,3-dihydro-1,2,4-oxadiazole ring system, which is difficult to prepare by other routes.[9,10]

Experimental

Melting points were taken on Yanagimoto micro melting point apparatus and are uncorrected. Infrared spectra were measured on a JASCO FT/IR 5300 spectrometer. ^1H and ^{13}C NMR were measured on a Varian GEMINI 200 spectrometer at 200 and at 50 MHz, respectively, for samples in $CDCl_3$ solution with Me_4Si as internal standard. *J* Values are given in Hz. Microanalyses were performed on a Perkin-Elmer 2400S elemental analyser. Mass spectra (EI, CI) were obtained using a JEOL JMS-AX 505 HA mass spectrometer at 70 eV. Thin layer chromatography was performed on Merck Kieselgel 60 F_{254} unless otherwise specified, and/or on Merck Aluminiumoxid F_{254}. All reagents were of commercial quality. Nitrones **1** and **2** were synthesized according to our previous work.[8]

Cycloaddition of nitrone 2 with acrylonitrile 3a

A solution of nitrone **2** (50 mg, 0.30 mmol) in acrylonitrile **3a** (2 cm^3) was heated in a sealed tube to 110 °C for 10 days. The excess acrylonitrile was removed under reduced pressure and purification of the crude product by preparative TLC with CH_2Cl_2–Et_2O (6:1) as eluent afforded 5-*cyano*-6-*methyl*-3-*oxa*-2-*azatetracyclo*[7.3.1.1^{7,11}.0^{2,6}]*tetradecane* **5** (R_f 0.60) in 23% yield, oil (Found: M^+, 232.1577. $C_{14}H_{20}N_2O$ requires *M*, 232.1576); ν_{max}(neat)/cm^{-1} 2924, 2247, 1261 and 1080; δ_H 4.38 (1 H, dd, *J* 8.4, 7.0), 4.05 (1 H, dd, *J* 10.6, 8.4), 3.70 (1 H, dd, *J* 10.6, 7.0), 3.55 (1 H, m), 2.30–1.25 (13 H, m) and 1.57 (3 H, s); *m/z* (EI) 232 (M^+, 20%), 179 (80), 163 (59), 122 (46) and 80 (100); *m/z* (CI) 233 (MH^+, 62%), 180 (88) and 164 (100); and 6-*methyl*-4-*vinyl*-3-*oxa*-2,5-*diazatetracyclo*[7.3.1.1^{7,11}.0^{2,6}]*tetradec*-4-*ene* **4a** (R_f 0.50) in 19% yield, oil (Found: MH^+ 233.1656, $C_{14}H_{21}N_2O$ requires *M*H, 233.1654); ν_{max}(neat)/cm^{-1} 2928, 1676, 1603 and 1047; δ_H 6.31 (1 H, dd, *J* 17.6, 10.8), 6.06 (1 H, dd, *J* 17.6, 1.6), 5.72 (1 H, dd, *J* 10.8, 1.6), 3.59 (1 H, m), 2.26 (1 H, m), 2.15–1.45 (12 H, m) and 1.48 (3 H, s); *m/z* (EI) 232 (M^+, 2%), 179 (100), 163 (23) and 162 (58); *m/z* (CI) 233 (MH^+, 100%) and 164 (38).

Cycloaddition of nitrone 1 with acetonitrile 3b

A solution of nitrone **1** (50 mg, 0.30 mmol) in acetonitrile (2 cm^3) was heated in a sealed tube at 150 °C for 15 days. The solvent was removed under reduced pressure and purification of the crude product by preparative TLC with hexane–ethyl acetate 1:1 as eluent (R_f 0.22) yielded 4-*methyl*-3-*oxa*-2,5-*diazatetracyclo* [7.3.1.1^{7,11}.0^{2,6}]*tetradec*-4-*ene* **7b** (Found: C, 70.0; H, 8.9; N, 13.4. $C_{12}H_{18}N_2O$ requires C, 69.9; H, 8.8; N, 13.6%); ν_{max}(KBr)/cm^{-1} 2922, 1686 and 1090; δ_H 5.44 (1 H, m), 3.60 (1 H, m), 2.37 (1 H, m), 2.01 (3 H, d, *J* 1.4) and 2.00–1.59 (12 H, m); δ_C 160.9, 92.6, 58.9, 35.5, 35.0, 34.5, 33.8, 31.1 (2),

26.4, 26.1 and 11.6; *m/z* (EI) 206 (M^+, 17%), 191 (12), 165 (100) and 135 (76), *m/z* (CI) 207 (MH^+, 100%) and 166 (10).

Cycloaddition of nitrones with nitriles 3c–j

General procedure. A solution of the nitrone (0.30 mmol) and the benzonitrile (0.36 mmol) in toluene (2 cm^3) was heated in a sealed tube at the temperature depicted in Table 1, while being monitored by TLC (an alumina plate was used with CH_2Cl_2–MeOH, 40:1 as eluent for nitrones **1**, **2** and **8**, and a silica gel plate with hexane–ethyl acetate, 3:1 as eluent for nitrone **10**). After the nitrone was completely consumed (see Table 1 for the reaction time), the solvent was removed under reduced pressure at room temperature. The crude residue was purified by preparative TLC (silica gel plate 20 × 20 × 0.25 mm) with the solvent specified to give the products. The reaction with **3j** was carried out similarly at ambient temperature for **1**, **2** and **8** and 80 °C for **10**. Yields and melting points are listed in Table 1.

4-Phenyl-3-oxa-2,5-diazatetracyclo[7.3.1.1^{7,11}.0^{2,6}]tetradec-4-ene 7c. (Elution: CH_2Cl_2–Et_2O, 6:1, R_f 0.54) (Found: C, 76.1; H, 7.5; N, 10.4. $C_{17}H_{20}N_2O$ requires C, 76.1; H, 7.5; N, 10.4%); ν_{max}(KBr)/cm^{-1} 2911, 1665, 1582, 1495 and 1098; δ_H 7.91 (2 H, m), 7.44 (3 H, m), 5.69 (1 H, d, *J* 4.0), 3.76 (1 H, m), 2.55 (1 H, m) and 2.10–1.50 (12 H, m); δ_C 160.5, 131.9, 128.8, 128.5, 126.0, 93.1, 59.3, 35.5, 35.2, 34.6, 33.8, 31.3, 30.9, 26.4 and 26.1; *m/z* (EI) 268 (M^+, 24%), 191 (11), 165 (100) and 135 (93); *m/z* (CI) 269 (MH^+, 100%).

4-(3-Nitrophenyl)-3-oxa-2,5-diazatetracyclo[7.3.1.1^{7,11}.0^{2,6}]-tetradec-4-ene 7e. (Elution: CH_2Cl_2–Et_2O, 6:1, R_f 0.55) (Found: C, 65.4; H, 6.2; N, 13.1. $C_{17}H_{19}N_3O_3$ requires C, 65.2; H, 6.1; N, 13.4%); ν_{max}(KBr)/cm^{-1} 2916, 1661, 1528, 1350 and 1119; δ_H 8.76 (1 H, ddd, *J* 2.4, 1.6 and 1.2), 8.37 (1 H, ddd, *J* 8.2, 2.4 and 1.2), 8.25 (1 H, ddd, *J* 7.8, 1.6 and 1.2), 7.64 (1 H, dd, *J* 8.0 and 7.8), 5.73 (1 H, d, *J* 3.8), 3.79 (1 H, m), 2.55 (1 H, s) and 2.12–1.57 (12 H, m); *m/z* (EI) 313 (M^+, 100%), 296 (81), 191 (73), 165 (87) and 135 (57); *m/z* (CI) 314 (MH^+, 100%) and 284 (12).

4-(4-Nitrophenyl)-3-oxa-2,5-diazatetracyclo[7.3.1.1^{7,11}.0^{2,6}]-tetradec-4-ene 7f. (Elution: hexane–ethyl acetate, 3:1, R_f 0.23) (Found: C, 65.4, H, 5.9, N, 13.4. $C_{17}H_{19}N_3O_3$ requires C, 65.2, H, 6.1, N, 13.4%); ν_{max}(KBr)/cm^{-1} 2911, 1663, 1522, 1346 and 1096; δ_H 8.29 (2 H, dt, *J* 9.0, 2.0), 8.09 (2 H, dt, *J* 9.0, 2.0), 5.73 (1 H, d, *J* 4.0), 3.78 (1 H, m), 2.56 (1 H, m) and 2.15–1.60 (12 H, m); *m/z* (EI) 313 (M^+, 31%), 191 (12), 165 (100) and 135 (51); *m/z* (CI) 314 (MH^+, 100%) and 150 (21).

4-(3-Methoxyphenyl)-3-oxa-2,5-diazatetracyclo-[7.3.1.1^{7,11}.0^{2,6}]tetradec-4-ene 7h. (Elution: hexane–ethyl acetate, 1:1, R_f 0.51) (Found: C, 72.3; H, 7.7; N, 9.5. $C_{18}H_{22}N_2O_2$ requires C, 72.5; H, 7.4; N, 9.4%); ν_{max}(neat)/cm^{-1} 2915, 1663, 1100 and 1042; δ_H 7.48 (1 H, dt, *J* 7.6, 1.2), 7.44 (1 H, dd, *J* 2.6, 1.2), 7.33 (1 H, dd, *J* 8.2, 7.6), 7.05 (1 H, ddd, *J* 8.2, 2.6, 1.2), 5.69 (1 H, d, *J* 4.0), 3.85 (3 H, s), 3.75 (1 H, m), 2.54 (1 H, m) and 2.10–1.55 (12 H, m); *m/z* (EI) 298 (M^+, 46%), 191 (20), 165 (95) and 135 (100); *m/z* (CI) 299 (MH^+, 100%).

4-(4-Methoxyphenyl)-3-oxa-2,5-diazatetracyclo-[7.3.1.1^{7,11}.0^{2,6}]tetradec-4-ene 7i. (Elution: hexane–ethyl acetate, 1:1, R_f 0.44), (Found: C, 72.5; H, 7.7; N, 9.1. $C_{18}H_{22}N_2O_2$ requires C, 72.5; H, 7.4; N, 9.4%); ν_{max}(KBr)/cm^{-1} 2919, 1659, 1096 and 1032; δ_H 7.86 (2 H, dt, *J* 9.0, 2.4), 6.93 (2 H, dt, *J* 9.0, 2.4), 5.66 (1 H, d, *J* 3.8), 3.85 (3 H, s), 3.74 (1 H, m), 2.52 (1 H, m) and 2.10–1.55 (12 H, m); *m/z* (EI) 298 (M^+, 27%), 165 (96) and 135 (100); *m/z* (CI) 299 (MH^+, 100%).

Methyl 3-oxa-2,5-diazatetracyclo[7.3.1.1^{7,11}.0^{2,6}]tetradec-4-ene-4-carboxylate 7j. (Elution: hexane–ethyl acetate, 1:1, R_f 0.43) (Found: C, 62.3; H, 7.3; N, 11.1. $C_{13}H_{18}N_2O_3$ requires C, 62.4; H, 7.3; N, 11.2%); ν_{max}(KBr)/cm^{-1} 2917, 1753, 1659 and 1163; δ_H 5.71 (1 H, d, *J* 3.6), 3.95 (3 H, s), 3.75 (1 H, m), 2.52 (1 H, m) and 2.07–1.61 (12 H, m); δ_C 157.1, 152.8, 93.5, 59.3, 53.8, 35.2, 34.9, 34.3, 33.8, 31.4, 31.0, 26.3 and 25.9; *m/z* (EI) 250 (M^+, 22), 191 (100), 165 (52) and 135 (56); *m/z* (CI) 251 (MH^+, 100%) and 191 (88).

6-Methyl-4-phenyl-3-oxa-2,5-diazatetracyclo[7.3.1.1^{7,11}.0^{2,6}]-tetradec-4-ene 4c. (Elution: CH_2Cl_2–Et_2O, 6:1, R_f 0.40) (Found: C, 76.6; H, 7.9; N, 9.8. $C_{18}H_{22}N_2O$ requires C, 76.6; H, 7.9; N, 9.9%); ν_{max}(KBr)/cm^{-1} 2919, 1661, 1582, 1495 and 1092; δ_H 7.94 (2 H, m), 7.47 (3 H, m), 3.69 (1 H, m), 2.39 (1 H, m), 1.56 (3 H, s) and 2.26–1.56 (12 H, m); *m/z* (EI) 282 (M^+, 2%), 267 (6), 179 (100) and 162 (38); *m/z* (CI) 283 (MH^+, 100%) and 179 (14).

6-Methyl-4-(3-nitrophenyl)-3-oxa-2,5-diazatetracyclo-[7.3.1.1^{7,11}.0^{2,6}]tetradec-4-ene 4e. (Elution: CH_2Cl_2–Et_2O, 6:1, R_f 0.68) (Found: M^+, 327.1581. $C_{18}H_{21}N_3O_3$ requires *M*, 327.1583); ν_{max}(neat)/cm^{-1} 2918, 1667, 1534, 1351 and 1138; δ_H 8.78 (1 H, ddd, *J* 2.4, 1.6 and 1.2), 8.36 (1 H, ddd, *J* 8.2, 2.4 and 1.2), 8.26 (1 H, ddd, *J* 7.8, 1.6 and 1.2), 7.64 (1 H, dd, *J* 8.2 and 7.8), 3.72 (1 H, m), 2.39 (1 H, m), 1.57 (3 H, s) and 2.20–1.57 (12 H, m); *m/z* (EI) 327 (M^+, 3%), 312 (13), 179 (100) and 162 (27); *m/z* (CI) 328 (MH^+, 100%) and 164 (30).

6-Methyl-4-(4-nitrophenyl)-3-oxa-2,5-diazatetracyclo-[7.3.1.1^{7,11}.0^{2,6}]tetradec-4-ene 4f. (Elution: hexane–ethyl acetate, 3:1, R_f 0.37) (Found: C, 66.3; H, 6.4; N, 12.5. $C_{18}H_{21}N_3O_3$ requires C, 66.0; H, 6.5; N, 12.8%); ν_{max} (KBr)/cm^{-1} 2909, 1665, 1520, 1348 and 1092; δ_H 8.30 (2 H, dt, *J* 9.0, 2.0), 8.11 (2 H, dt, *J* 9.0, 2.0), 3.71 (1 H, m), 2.40 (1 H, m), 1.57 (3 H, s) and 2.18–1.57 (12 H, m); *m/z* (EI) 327 (M^+, 5%), 312 (31), 179 (100) and 162 (65); *m/z* (CI) 328 (MH^+, 100%) and 164 (38).

Methyl 6-methyl-3-oxa-2,5-diazatetracyclo[7.3.1.1^{7,11}.0^{2,6}]-tetradec-4-ene-4-carboxylate 4j. (Elution: hexane–ethyl acetate, 1:1, R_f 0.50) (Found: C, 63.3; H, 7.6; N, 10.6. $C_{14}H_{20}N_2O_3$ requires C, 63.6; H, 7.6; N, 10.6%); ν_{max}(KBr)/cm^{-1} 2917, 1746, 1663 and 1169; δ_H 3.95 (3 H, s), 3.68 (1 H, m), 2.34 (1 H, m), 1.53 (3 H, s) and 2.08–1.59 (12 H, m); δ_C 157.3, 151.7, 96.4, 59.5, 53.7, 39.2, 35.7, 34.6, 33.0, 31.3, 30.5, 30.3, 26.5 and 26.3; *m/z* (EI) 264 (M^+, 5%), 249 (57), 205 (100), 179 (25) and 162 (17); *m/z* (CI) 265 (MH^+, 100%) and 164 (18).

8,8-Dimethyl-3-phenyl-2-oxa-1,4-diazabicyclo[3.3.0]oct-3-ene 9c. (Elution: hexane–ethyl acetate, 1:1, R_f 0.50) (Found: C, 72.3; H, 7.6; N, 12.8. $C_{13}H_{16}N_2O$ requires C, 72.2; H, 7.5; N, 13.0%); ν_{max}(neat)/cm^{-1} 2973, 1659, 1581, 1495 and 1094; δ_H 7.90 (2 H, m), 7.44 (3 H, m), 5.65 (1 H, dd, *J* 7.0, 2.8), 2.39–2.02 (2 H, m), 1.63 (2 H, m), 1.29 (3 H, s) and 1.22 (3 H, s); *m/z* (EI) 216 (M^+, 6%), 147 (3), 113 (100) and 105 (16); *m/z* (CI) 217 (MH^+, 100%).

Methyl 8,8-dimethyl-2-oxa-1,4-diazabicyclo[3.3.0]oct-3-ene-3-carboxylate 9j. (Elution: hexane–ethyl acetate, 1:1, R_f 0.33) (Found: C, 54.0; H, 7.2; N, 14.4. $C_9H_{14}N_2O_3$ requires C, 54.5; H, 7.1; N, 14.1%); ν_{max}(neat)/cm^{-1} 2975, 1755, 1657 and 1155; δ_H 5.64 (1 H, dd, *J* 7.4, 3.0), 3.93 (3 H, s), 2.40–1.95 (2 H, m), 1.64 (2 H, m), 1.28 (3 H, s) and 1.18 (3 H, s); *m/z* (EI) 198 (M^+, 4%), 139 (5), 129 (5) and 113 (100); *m/z* (CI) 199 (MH^+, 100%) and 98 (91).

2,3,5-Triphenyl-2,3-dihydro-1,2,4-oxadiazole 11c. (Elution: CH_2Cl_2, R_f 0.30) (Found: C, 80.3; H, 5.5; N, 9.1. $C_{20}H_{16}N_2O$ requires C, 80.0; H, 5.4; N, 9.3%); ν_{max}(KBr)/cm^{-1} 1655, 1601 and 1061; δ_H 8.33–7.03 (16 H, m); *m/z* (EI) 300 (M^+, 36%), 223 (3), 197 (23) and 105 (100); *m/z* (CI) 301 (MH^+, 100%).

5-(4-Nitrophenyl)-2,3-diphenyl-2,3-dihydro-1,2,4-oxadiazole 11f. (Elution: CH_2Cl_2, R_f 0.51) (Found: C, 69.6; H, 4.4; N, 12.1. $C_{20}H_{15}N_3O_3$ requires C, 69.6; H, 4.4; N, 12.2%); ν_{max} (KBr)/cm^{-1} 1616 sh, 1586, 1553, 1327 and 1065; ‡ δ_H 8.49 (2 H, dt, *J* 9.0, 2.0), 8.28 (2 H, dt, *J* 9.0, 2.0) and 7.63–7.01 (11 H, m);

‡The product was tentatively assigned to have a 2,3-dihydro structure, however, a very weak absorption at 1616 cm^{-1} is not sufficient to differentiate it from the 2,5-dihydro isomer.

m/z (EI) 345 (M^+, 24%), 242 (43), 195 (12) and 150 (100); *m/z* (CI) 346 (MH^+, 100%) and 316 (33).

Methyl 2,3-diphenyl-2,3-dihydro-1,2,4-oxadiazole-5-carboxylate 11j. (Elution: hexane–ethyl acetate, 1 : 1, R_f 0.62) (Found: C, 68.0; H, 5.1; N, 9.9. $C_{16}H_{14}N_2O_3$ requires C, 68.1; H, 5.0; N, 9.9%); ν_{max}(KBr)/cm^{-1} 1748, 1690, 1593 and 1171; δ_H 7.44 (1 H, s), 7.29–7.67 (10 H, m) and 4.03 (3 H, s); *m/z* (EI) 282 (M^+, 38%), 195 (100), 179 (80) and 120 (53); *m/z* (CI) 283 (MH^+, 100%).

AM1 calculation

Molecular orbitals of acrylonitrile and acetonitrile were calculated using MOPAC Ver 5.00 (QCPE No. 445) revised as Ver 5.01 by J. Toyoda for Apple Macintosh. See ref. 8 for the result of calculations on the nitrone **1**.

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