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SYNTHESIS OF ADAMANTANE DERIVATIVES—43[1]

1,3-DIPOLAR CYCLOADDITION REACTIVITY OF METHYLENEADAMANTANE DERIVATIVES WITH SUBSTITUTED BENZONITRILE OXIDES

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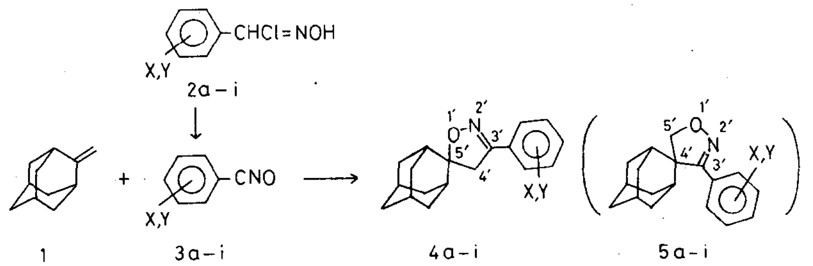
Abstract—The 1,3-dipolar cycloaddition reactivity and regioselectivity of methyleneadamantane **1**, ethyl adamantylideneacetate **7a**, adamantylideneacetonitrile **7b** and ω-methoxymethyleneadamantane **7c** with substituted benzonitrile oxides **3a-i** were calculated by CNDO/2 method using the perturbation equation derived by Klopman and Salem. The calculation predicted an exclusive formation of adamantan - 2 - spiro - 5′ - 3′ - aryl - $\Delta^{2'}$ - isooxazoline **4a-i** in the reactions of **1**, **7a** and **7b** with **3a-i**, and a formation of 67–69:33–31 mixture of **4a-i** and isomeric **5a-i** in the reaction of **7c** with **3a-i**. The predicted exclusive formation of **4a-i** were experimentally observed in the reactions of **1**, **7a** and **7b** with **3a-i** generated from **2a-i** with Et_3N or thermally, but the reaction of **7c** with **3a** did not afford the corresponding adducts. A considerably higher reactivity of C≡N triple bond than C=C double bond was observed in the reaction of **7b** with **3a** and 1,2,4-oxadiazole derivative **11** was obtained as the major product.

The 1,3-dipolar cycloaddition reaction is well known as one of the most useful methods for synthesis of 5-membered heterocycles and it is also theoretically attractive. Recently Houk *et al.*[2] and Bastide *et al.*[3] investigated the reactivity, regioselectivity and periselectivity of various 1,3-dipolar cycloadditions on the basis of the frontier orbital perturbation theory[4] assuming a concerted 4-centered mechanism,[5] which led to a satisfactory understanding of reactivity, regiochemistry and periselectivity phenomena.[6] As part of our continuing investigations on adamantane spiro heterocycles[7] and in conjunction with our interest in biological properties of these compounds,[8,9] synthesis of various substituted adamantane - 2 - spiro - 5′ - 3′ - aryl - $\Delta^{2'}$ - isooxazolines became necessary. We investigated 1,3-dipolar cycloaddition reactivity of methyleneadamantane derivatives with substituted benzonitrile oxides as a facile route to the desired compounds.[10] This paper describes the calculated reactivity and regioselectivity based on the perturbation equation of chemical reactivity derived by Klopman[11] and Salem[12] as well as the experimental results of the 1,3-dipolar cycloadditions.

RESULTS AND DISCUSSION

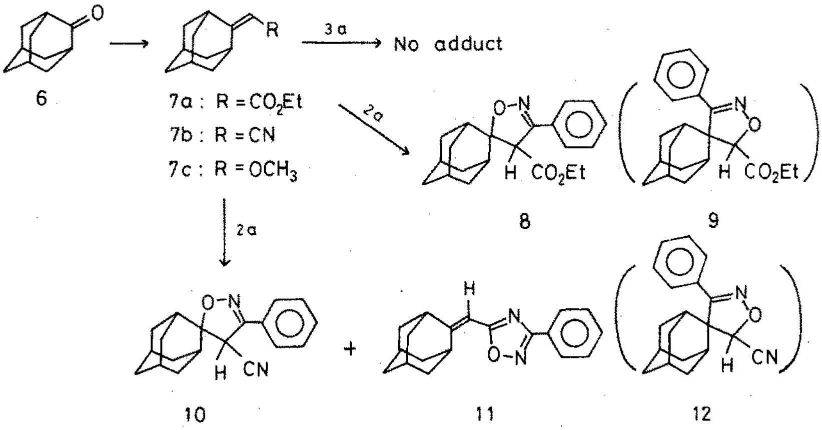
Theoretical treatment of the reactivity and regioselectivity of the 1,3-*dipolar cycloadditions of methyleneadamantane derivatives with substituted benzonitrile oxides.* In view of recent satisfactory predictions of the reactivity and regioselectivity of 1,3-dipolar cycloadditions of nitrile oxides by Houk *et al.*[2] and Bastide *et al.*[3] the reactivity and regioselectivity of the 1,3-dipolar cycloadditions of methyleneadamantane **1** and its derivatives **7a**, **7b** and **7c** (Schemes 1 and 2) with nine benzonitrile oxides **3a-3i** were calculated on the basis of the perturbation equation derived by Klopman[11] and Salem.[12] According to the perturbation theory, the energy change which accompanies the interaction of two molecules involved in a cycloaddition reaction can be expressed by eqn (1)

$$\Delta E = \underbrace{-\sum_{a,b}(q_a+q_b)\beta_{ab}S_{ab}}_{\text{I}} + \underbrace{\sum_{k,l}\frac{Q_kQ_l}{K_eR_{kl}}}_{\text{II}} + \underbrace{\sum_{r}^{\text{occ}}\sum_{s}^{\text{vac}} - \sum_{s}^{\text{occ}}\sum_{r}^{\text{vac}}\frac{2(\Sigma_{ab}C_{ra}C_{sb}\beta_{ab})^2}{E_r-E_s}}_{\text{III}}. \quad (1)$$



2–5					
	a :	X = H	Y = H	f : X = 4-Cl	Y = H
	b :	X = 2-NO$_2$	Y = H	g : X = 2-Cl	Y = 4-Cl
	c :	X = 3-NO$_2$	Y = H	h : X = 4-CH$_3$	Y = H
	d :	X = 4-NO$_2$	Y = H	i : X = 4-OCH$_3$	Y = H
	e :	X = 2-Cl	Y = H		

Scheme 1.



Scheme 2.

Here, the first term I of the right side of eqn (1) is the closed shell repulsion term, the second term II is the Coulombic repulsion or attraction term, and the third term III represents the interaction of all the occupied orbitals of the one molecule with all the unoccupied orbitals of the other. In this equation, q_a and q_b are electron densities at interacting atomic orbitals a and b respectively, β_{ab} and S_{ab} are the resonance integral and the overlap integral for the atomic orbitals a and b respectively. Q_k and Q_l are the charges at the interacting atoms k and l, R_{kl} is the distance between the atoms k and l. In this study, 1.75 Å was employed as R_{kl} because this value corresponds to the distance of maximum σ-type overlap of the carbon p-atomic orbitals, and the corresponding values were used as β_{ab} and S_{ab}, i.e. $\beta_{CC} = 6.22$, $\beta_{CO} = 5.38$, and $S_{CC} = 0.2974$, $S_{CO} = 0.2075$. As the local dielectric constant K_e, the value of ether at 25° ($K_e = 4.244$) was employed. C_{ra} and C_{sb} in III mean the coefficients of the atomic orbital a in the molecular orbital r and the atomic orbital b in the molecular orbital s respectively, and E_r and E_s mean the energies of the molecular orbitals r and s, respectively.

It is generally accepted that the third term III of eqn (1), especially the frontier orbital term, is adequate for the purpose of brief discussion[6] but in this study the complete calculations of eqn (1) were performed for the reactions of methyleneadamantane **1** and benzonitrile oxides **3a-i** using CNDO/2 method[13] and the results are summarized in Table 1.

According to the values in Table 1, I contributes to unstability of the state, II to stability for spiro - 5′ - isooxazolines **4a-i** (orientation A) but to unstability for the regioisomer spiro - 4′ - isooxazolines **5a-i** (orientation B) and III to stability. In I, the formation of 4′ - isooxazoline (orientation B) is less unfavorable than 5′ - isooxazoline. On the contrary, in II and III, the formation of 5′ - isooxazoline is favorable than 4′-isomer. Clearly, the contribution of III (orbital control term) is large. Furthermore, the energy difference between two orientations A and B is largest in III, though the absolute energy value of I is largest of the three terms. The calculated isomer ratio using the Boltzmann distribution law shows that the desired 5′-isooxazolines (orientation A) should be formed exclusively (100:0). It is also not-

Table 1. Calculated energy changes for two orientations in the reactions of **1** with **3a-i** using eqn (1)

No.	X,Y	Orientation[a]	(I)/eV	(II)/eV	(III)/eV	ΔE^b/eV	Isomer ratio[c] A:B
a	H	A	7.157	−0.032	−4.836	2.289	100:0
		B	7.025	0.069	−4.547	2.547	
b	2-NO_2	A	7.169	−0.041	−4.783	2.344	100:0
		B	7.037	0.073	−4.512	2.598	
c	3-NO_2	A	7.160	−0.032	−4.797	2.332	100:0
		B	7.029	0.067	−4.507	2.589	
d	4-NO_2	A	7.146	−0.040	−4.761	2.346	100:0
		B	7.015	0.073	−4.473	2.614	
e	2-Cl	A	7.138	−0.041	−4.787	2.310	100:0
		B	7.007	0.075	−4.496	2.586	
f	4-Cl	A	7.160	−0.032	−4.814	2.314	100:0
		B	7.028	0.068	−4.527	2.569	
g	2,4-Cl_2	A	7.145	−0.040	−4.775	2.330	100:0
		B	7.013	0.073	−4.487	2.599	
h	4-CH_3	A	7.151	−0.032	−4.840	2.280	100:0
		B	7.020	0.069	−4.548	2.542	
i	4-OCH_3	A	7.127	−0.041	−4.802	2.284	100:0
		B	6.995	0.076	−4.502	2.569	

[a] A is the direction toward forming **4**, and B toward **5**, respectively. [b] More favorable orientation is underscored. [c] Calculated value, using the Boltzmann distribution law.

able that a very excellent correlation is found between ΔE and the Hammett's σ constants ($r = 0.978$, $n = 6$: $\Delta E = 2.295 + 0.060\sigma$; X = H, 3-$NO_2$, 4-$NO_2$, 4-Cl, 4-$CH_3$, 4-$OCH_3$).

In order to see the substituent effect on methyleneadamantane, the orbital control term III in eqn (1) was calculated similarly for the reactions of ethyl adamantylidenacatate **7a**, adamantylidenacetonitrile **7b**, and ω-methoxymethyleneadamantane **7c** with benzonitrile oxides **3a-i**. The results are shown in Table 2, in which the calculated isomer ratio and relative reactivity are also shown.

In the reactions of **7a** and **7b** with **3a-i**, the calculation predicts the exclusive formation of spiro - 5' - $\Delta^{2'}$ - isooxazoline derivatives (orientation A) but in the reaction of **7c**, the formation of a mixture of spiro - 5' - isooxazoline and spiro - 4' - isooxazoline in 67–69:33–31 ratio. As for relative reactivity of substituted benzonitrile oxides, p-methylbenzonitrile oxide **3h** and unsubstituted benzonitrile oxide **3a** are predicted to be the most reactive.

The observed results of the 1,3-*dipolar cycloadditions of methyleneadamantane derivatives with substituted benzonitrile oxides.* Although several methods of generation of nitrile oxide are known,[10] dehydrochlorination of the corresponding hydroximic acid chlorides with triethylamine or by heating in toluene was employed in this study. The generated nitrile oxides **3a-i** from the corresponding hydroximic acid chlorides **2a-i** with triethylamine in ether were allowed to react with **1** and **7a-c** in 1.5:1.0 molar ratio at room temp. (20–25°) for 24 hr. The products were isolated after chromatography. As shown in Table 3, **1** afforded the corresponding adducts **4a-i** in low to moderate yields, but **7a-c** did not afford the corresponding adducts with **3a** under the same conditions and only diphenylfuroxan, a dimer of **3a** was produced.

The adducts **4a-i** were characterized as adamantane - 2 - spiro - 5' - 3' - aryl - $\Delta^{2'}$ - isooxazolines respectively on the basis of analytical and spectral data (Table 4). In the ^1H NMR spectra, all the adducts **4a-i** revealed characteristic two protons singlet at δ 3.0–3.3 due to 4'-methylene protons, supporting the assigned structures **4a-i**. 5' - Methyleneprotons signals of regioisomeric **5a-i** should appear around δ 4.0[14] but no such signals appeared in the adducts, therefore, it was concluded that adamantane - 2 - spiro - 5' - $\Delta^{2'}$ - isooxazolines **4a-i** were formed exclusively in the reactions of **1** with **3a-i** in accord with the theoretical prediction. Although no kinetic measurements were carried out, comparison of the yields of **4a-i** indicated also p-methylbenzonitrile oxide **3h** to be the most reactive as expected.

Since no adducts were obtained in the reactions of **7a-c** with **3a** generated from **2a** and triethylamine in ether at room temp., the reactions of **7a-c** with **3a** generated thermally[15] in refluxing toluene were examined. The reaction of **7a** with 1.1-fold excess amount of **2a** in refluxing toluene for 15.5 hr gave an adduct **8** in 8.2% yield (90.1% for reacted **7a**), which was characterized as adamantane - 2 - spiro - 5', 4' - ethoxycarbonyl - 3' - phenyl - $\Delta^{2'}$ - isooxazoline based on analysis and spectral data. In ^1H NMR spectrum, **8** revealed characteristic singlet at δ 4.15 for one proton. This chemical shift is very similar to 4-methine proton's signal (δ 4.07) of 5,5 - dimethyl - 4 - methoxycarbonyl - 3 - phenyl - Δ^2 - isooxazoline reported by Huisgen *et al.*[14a,c,f] but is considerably higher than that (δ 5.15) reported for 5 - methoxycarbonyl - 3 - phenyl - Δ^2 - isooxazoline,[14a,c,f] and hence, the possibility of **9** for this adduct **8** was excluded. The observed regiochemistry is the expected one and also the same reported for the reactions of methyl β,β-dimethylacrylate with **3a**.[14c]

The reaction of adamantylideneacetonitrile **7b** with **2a** in refluxing toluene for 30 hr gave two adducts **10** and **11** in 2.7 and 50% yields, respectively. The adduct **10** revealed characteristic ^1H NMR singlet at δ 4.24 for one proton and was characterized as adamantane - 2 - spiro - 5' - 4' - cyano - 3' - phenyl - $\Delta^{2'}$ - isooxazoline, a cycloadduct of **3a** to C=C double bond of **7b**. The major

Table 2. Calculated energy changes for two orientations in the reactions of **7a-c** with **3a-i** using the orbital control term (III)

		7a		7b		7c	
Compd	Orientation[a]	ΔE^b_{III} / eV	Reactivity[d]	ΔE_{III} / eV	Reactivity	ΔE_{III} / eV	Reactivity
3a	A	$\underline{-4.743}$(100)[c]	1	$\underline{-4.871}$ (100)	1	$\underline{-4.643}$(67)	1
	B	−4.301 (0)		−4.537(0)		−4.626(33)	
3b	A	$\underline{-4.673}$(100)	0.06	$\underline{-4.804}$(100)	0.07	$\underline{-4.603}$(67)	0.21
	B	−4.268(0)		−4.497(0)		−4.585(33)	
3c	A	$\underline{-4.690}$(100)	0.13	$\underline{-4.818}$(100)	0.12	$\underline{-4.609}$(68)	0.26
	B	−4.256(0)		−4.489(0)		−4.590(32)	
3d	A	$\underline{-4.649}$(100)	0.02	$\underline{-4.776}$(100)	0.02	$\underline{-4.577}$(69)	0.07
	B	−4.224(0)		−4.453(0)		−4.557(31)	
3e	A	$\underline{-4.686}$(100)	0.11	$\underline{-4.813}$(100)	0.10	$\underline{-4.596}$(68)	0.16
	B	−4.249(0)		−4.482(0)		−4.577(32)	
3f	A	$\underline{-4.714}$(100)	0.32	$\underline{-4.842}$(100)	0.31	$\underline{-4.625}$(67)	0.49
	B	−4.279(0)		−4.513(0)		−4.607(33)	
3g	A	$\underline{-4.669}$(100)	0.05	$\underline{-4.796}$(100)	0.05	$\underline{-4.588}$(68)	0.11
	B	−4.239(0)		−4.470(0)		−4.569(32)	
3h	A	$\underline{-4.749}$(100)	1.29	$\underline{-4.877}$(100)	1.26	$\underline{-4.645}$(67)	1.06
	B	−4.302(0)		−4.538(0)		−4.627(33)	
3i	A	$\underline{-4.711}$(100)	0.29	$\underline{-4.836}$(100)	0.25	$\underline{-4.605}$(68)	0.22
	B	−4.257(0)		−4.492(0)		−4.586(32)	

[a] A is the direction toward forming 5'-isomer, and B toward 4'-isomer, respectively. [b] More favorable orientation is underscored. [c] Calculated isomer ratio, using the Boltzmann distribution law. (%) [d] Relative values, compared with a unsubstituted compound. Calculated values, using the Boltzmann distribution law.

Table 3. Physical properties of adamantane - 2 - spiro - 5′ - $\Delta^{2'}$ - isooxazolines

Compd	m.p. (°C)	Yield (%)	Formula	Found C	(Calcd) H	(%) N
4a	84–86	30.0[a]	$C_{18}H_{21}NO$	80.84	7.95	5.19
				(80.86	7.92	5.24)
4b	170–171	23.8[a]	$C_{18}H_{20}N_2O_3$	69.07	6.36	9.20
				(69.21	6.45	8.97)
4c	189–190	31.6[a]	$C_{18}H_{20}N_2O_3$	69.32	6.38	8.90
				(69.21	6.45	8.97)
4d	292–294	22.0[a]	$C_{18}H_{20}N_2O_3$	69.27	6.47	8.90
				(69.21	6.45	8.97)
4e	92–94	36.7[a]	$C_{18}H_{20}NOCl$	71.52	6.76	4.79
				(71.63	6.68	4.64)
4f	173–174	38.7[a]	$C_{18}H_{20}NOCl$	71.73	6.72	4.50
				(71.63	6.68	4.64)
4g	89–91	29.0[a]	$C_{18}H_{19}NOCl_2$	64.17	5.86	4.31
				(64.29	5.70	4.17)
4h	131–132	50.8[a]	$C_{19}H_{23}NO$	81.37	8.20	4.75
				(81.10	8.24	4.98)
4i	164–166	15.8[a]	$C_{19}H_{23}NO_2$	76.85	7.62	4.61
				(76.74	7.80	4.71)
8	101–102	8.2	$C_{21}H_{25}NO_3$	74.20	7.31	3.88
				(74.31	7.42	4.13)
10	182–183	2.7	$C_{19}H_{20}N_2O$	78.24	6.94	9.36
				(78.05	6.89	9.58)

[a]The values were calculated on the basis of reacted methyleneadamantane.

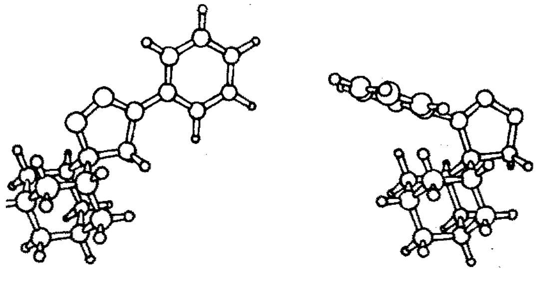
Table 4. Spectral data of adamantane - 2 - spiro - 5′ - $\Delta^{2'}$ - isooxazolines

Compd	IR, cm^{-1} (KBr)	NMR chemical shift, δ ($CDCl_3$, 60 MHz)
4a	1600, 1570, 1500, 770, 690	1.5–2.5(m, 14H), 3.14(s, 2H), 7.3–7.5(m, 5H)
4b	2920, 2880, 1620, 1580, 1540, 1360, 920	1.5–2.5(m, 14H), 3.04(s, 2H), 7.5–8.1(m, 4H)
4c	2920, 2880, 1600, 1580, 1540, 1360, 950	1.3–2.5(m, 14H), 3.20(s, 2H), 7.4–8.5(m, 4H)
4d	2920, 2870, 1600, 1580, 1510, 1350, 920	1.1–2.6(m, 14H), 3.17(s, 2H), 7.82(d, J = 9.0 Hz, 2H), 8.27(d, J = 9.0 Hz, 2H)
4e	2920, 2880, 1600, 1580, 1530, 1360, 920, 760	1.4–2.6(m, 14H), 3.30(s, 2H), 7.1–8.5(m, 4H)
4f	2920, 2880, 1600, 1500, 1360, 1100, 930	1.4–2.6(m, 14H), 3.12(s, 2H), 7.33(d, J = 9.0 Hz, 2H), 7.61(d, J = 9.0 Hz, 2H)
4g	2920, 2880, 1600, 1500, 1110, 760	1.4–2.6(m, 14H), 3.20(s, 2H), 7.1–7.7(m, 3H)
4h	2920, 2900, 2880, 1600, 1460, 1360, 920	1.4–2.3(m, 14H), 2.33(s, 3H), 3.10(s, 2H), 7.13(d, J = 9.0 Hz, 2H), 7.51(d, J = 9.0 Hz, 2H),
4i	2920, 2870, 1610, 1600, 1520, 1450,	1.4–2.5(m, 14H), 3.10(s, 2H), 3.80(s, 3H), 6.7–7.7(m, 4H)
8	3080, 2920, 2880, 1720, 1610	1.13(t, J = 7.5 Hz, 3H), 1.4–2.5(m, 14H), 4.12(q, J = 7.5 Hz, 2H), 4.15(s, 1H), 7.25–7.80(m, 5H)
10	2920, 2860, 2210,	1.40–2.70(m, 14H), 4.24(s, 1H), 7.30–7.90(m, 5H)

adduct **11** revealed ^1H NMR signals at δ 6.15 (s, 1H) as well as signals due to phenyl protons and adamantylidene protons, and ^{13}C NMR signals at δ 170.2(s), 101.2(d), 175.4(s) and 168.1(s) due to two vinylic and two imino carbons as well as signals due to phenyl and adamantylidene carbons. **11** had a absorption maximum at 244 nm (ϵ = 30,700) in MeOH which is very similar to that reported for 3,5-diphenyl-1,2,4-oxadiazole.[16] Therefore **11** was characterized as 5 - adamantylidenemethyl - 3 - phenyl - 1,2,4 - oxadiazole. It is notable that **11** was produced as the major adduct since considerably higher reactivity of C=C double bond than C≡N triple bond is well known in the reactions of conjugated nitriles with nitrile oxides.[17] The present novel results may be due to steric hindrance of the adamantylidene group for attacking **3a** to the C=C double bond in **7b**.

The reaction of **7c** with **2a** was carried out similarly but only intractable tar was produced because **7c** was not stable under the reaction conditions. All of these results are summarized in Scheme 2.

Finally it should be mentioned that in all of the above 1,3-dipolar cycloadditions, the regiochemistry observed is also favorable by the steric reason. The molecular figures of two regioisomers **4a** and **5a** are depicted in the most stable conformations in Fig. 1.



4a 5b

Fig. 1. Molecular figures of two isomers, 4a and 5a, in the most stable conformations.

The van der Waals non-bonded interaction energies are 19.3 kcal/mol for **4a** and 51.3 kcal/mol for **5a** respectively,[18] supporting **4a** as sterically more stable isomer.

EXPERIMENTAL

General. All m.p. were measured on Yanaco micro m.p. apparatus, and were uncorrected. IR spectra were taken on a Jasco IRA-1 spectrometer. ^1H NMR spectra were recorded on a Jeol C-60HL (60 MHz) spectrometer and ^{13}C NMR spectra on a Jeol JNM-FX60 (15.04 MHz) spectrometer respectively using TMS as an internal standard. Elemental analyses were carried out on Perkin–Elmer 240 elemental analyzer.

Calculations. Calculations were carried out using FACOM 230-75 computer at Nagoya University Data Processing Center. The geometries of the molecules necessary for CNDO/2 calculations were constructed using standard bond lengths and angles[13] or the results of X-ray analyses in the literature.[10]

General procedure of the 1,3-dipolar cycloadditions of methyleneadamantane **1** *with substituted benzonitrile oxides* **3a-i**. To a stirred and ice-cooled soln of substituted **2a-i** (1.4 mmol) prepared by the methods of Werner or Rheinboldt *et al.*[19,20] in ether (10 ml), triethylamine (1.4 mmol) was added. The stirring was continued for 3 min, and then the mixture was washed with ice-water and dried (Na_2SO_4). To this nitrile oxide soln **1**[21] (1.0 mmol) was added and the mixture was stirred for 24 hr at room temp. (20-25°) and refluxed for 0.5 hr. After removal of the solvent, the residue was purified on a silica gel column eluting with n-hexane-CH_2Cl_2 (for results, see Tables 3 and 4).

The reaction of ethyl adamantylideneacetate **7a** *with* **3a** *generated thermally from* **2a**. A mixture of **2a** (171 mg, 1.10 mmol) and **7a**[22] (220 mg, 1.00 mmol) in toluene (3 ml) was heated under reflux for 15.5 hr. After removal of the solvent at 40° (20 mm) and unreacted **7a** at 90-95° (0.2 mm), the residue was purified on a silica gel column eluting with CH_2Cl_2–$CHCl_3$ to afford *adamantane - 2 - spiro - 5' - 4' - ethoxycarbonyl - 3' - phenyl -* $\Delta^{2'}$ *- isooxazoline* **8** as colorless crystals (25 mg, 8.2%, 90.1% for reacted **7a**) after one recrystallization from n-hexane. See Tables 3 and 4 for physical and analytical data.

Adamantylideneacetonitrile **7b**. This nitrile was previously prepared by Mariani[23] by hydrolysis and decarboxylation of ethyl adamantylidenecyanoacetate but we prepared **7b** by direct condensation of adamantanone **6** with acetonitrile.[24] To a refluxing mixture of powdered KOH (66 mg, 1.1 mmol) and 18 - crown - 6 - ether (10 mg, 0.018 mmol) in anhyd acetonitrile (4 ml) and benzene (4 ml), a soln of **6** (150 mg, 1.0 mmol) in acetonitrile (2 ml) and benzene (2 ml) was added dropwise in an argon atmosphere during 0.5 hr, and the mixture was refluxed for 6 hr. The cooled mixture was poured onto ice-water and extracted with CH_2Cl_2 (25 ml × 3). The combined extracts were washed with water and dried (Na_2SO_4). Removal of the solvent gave a crude product which was purified on a silica gel column eluting with CH_2Cl_2 to afford unreacted **6** (10 mg) and adamantylideneacetonitrile **7b** as colorless crystals after sublimation (114 mg, 65.8%, 70.6% for reacted **6**): m.p. 72–73°; IR (KBr) 3060, 2940, 2870, 2210, 1630 and 1460 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.98(s, 1H), 3.15(m, 1H), 2.58(m, 1H) and 2.30–1.50(m, 12H). (Found: C, 82.22; H, 8.71; N, 8.07. $C_{12}H_{15}N$ requires: C, 83.19; H, 8.73; N, 8.08%).

The reaction of **7b** *with* **3a** *generated thermally from* **2a**. A mixture of **7b** (173 mg, 1.00 mmol) and **2a** (160 mg, 1.03 mmol) in toluene (3 ml) was heated under reflux for 35 hr. After removal of the solvent, the residue was purified on a silica gel column eluting with CH_2Cl_2–$CHCl_3$. The first fraction gave unreacted **7b** (60 mg, 34.7% recovery) and the second fraction gave 5 - *adamantylidenemethyl* - 3 - *phenyl* - 1,2,4 - *oxadiazole* **11** as crystals (CH_2Cl_2-n-hexane) (145 mg, 50%): m.p. 85–86°; IR (KBr) 2920, 2860 and 1650 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.3–7.3(m, 5H), 6.15(s, 1H), 4.15(broad s, 1H), 2.12(broad s, 1H) and 2.2–1.7(m, 12H); ^{13}C NMR ($CDCl_3$) δ 175.4(s, 1C), 170.2(s, 1C), 168.1(s, 1C), 130.9(d, 1C), 128.7(d, 2C), 127.5(d, 2C), 127.3(s, 1C), 101.2(d, 1C), 41.7(d, 1C), 40.2(t, 2C), 39.2(t, 2C), 36.8(t, 1C), 34.0(d, 1C), 27.8(d, 2C).

The third fraction gave *adamantane* - 2 - *spiro* - 5' - 4' - *cyano* - 3' - *phenyl* - $\Delta^{2'}$ - *isooxazoline* **10** as crystals (8 mg, 2.7%). (For physical data see Tables 3 and 4).

ω-Methoxymethyleneadamantane **7c**. This compound was previously prepared as an intermediate for synthesis of 2 - adamantanecarboxaldehyde but it was not characterized.[25] To a stirred and ice-cooled mixture of triphenylmethoxy - methylphosphonium chloride (1.40 g, 4.08 mmol) and anhyd ether (10 ml) was added n-BuLi (15% n-hexane soln, 5.0 ml). After stirring for 45 min at room temp., **6** (525 mg, 3.50 mmol) was added to the stirred mixture. The stirring was continued for 2 hr at the same temp. and for 0.5 hr at 40–45°. The mixture was treated with anhyd $ZuCl_2$ (5 g) and the resulting ppt was removed by decantation and washed with ether (5 ml × 2). The combined washings and ethereal soln was dried (Na_2SO_4). Removal of the solvent gave a crude product which was purified on alumina (Wako, Basic Grade I) eluting with n-hexane to afford **7c** as a colorless oil (115 mg, 20%): n_D^{15} 1.5254; IR (film) 1680, 1450 and 1130 cm^{-1}; ^1H NMR (CCl_4) δ 5.56(s, 1H), 3.40(s, 3H), 2.88(broad s, 1H), 2.16(broad s, 1H) and 2.05–1.60(m, 12H). (Found: C, 81.08; H, 9.93. $C_{12}H_{18}O$ requires: C, 80.90; H, 10.11%).

The reaction of **7c** *with phenylhydroximic acid chloride* **7a**. A mixture of **7c** (60 mg, 0.36 mmol) and **2a** (112 mg, 0.72 mmol) in toluene (3 ml) was heated under reflux for 33 hr. Removal of the solvent gave a dark brownish oil, from which no pure products could be isolated after chromatography (silica gel) but a fraction revealed an IR spectrum very similar to adamantanecarboxaldehyde.

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