Base-induced cycloreversion of nitrile oxide cycloadducts: conversion of imines into secondary and tertiary amides and aromatic aldehydes into acids without a conventional oxidising agent

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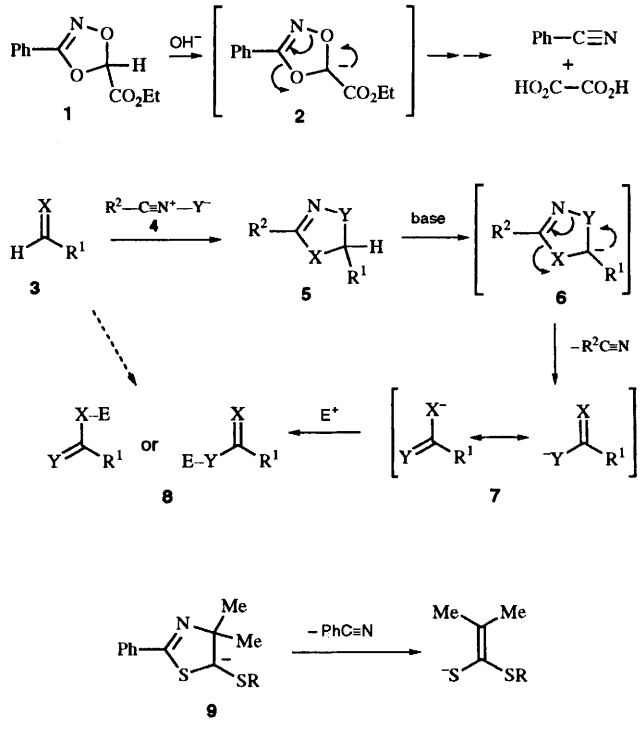
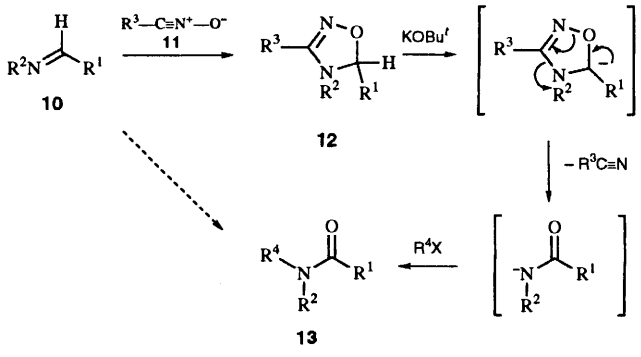
A series of substituted Δ^2-1,2,4-oxadiazolines (4,5-dihydro-1,2,4-oxadiazoles) 12 have been prepared by 1,3-dipolar cycloaddition of nitrile oxides to imines and are found, upon treatment with KOBu^t, to undergo cycloreversion to give nitriles and amide anions. These can be protonated to give secondary amides or treated *in situ* with alkyl halides to give tertiary amides in moderate to good overall yield, although the reaction is restricted to examples with an aromatic substituent at the 5-position. The 1,4,2-dioxazoles 15, formed by cycloaddition of benzonitrile oxide to aromatic aldehydes, similarly undergo cycloreversion allowing direct conversion either into substituted benzoic acids or their methyl esters.

In 1961 Huisgen and Mack reported that attempted base hydrolysis of the ester group in the 1,4,2-dioxazole **1** resulted in a cycloreversion process of the 5-anion **2** as shown to give benzonitrile and, after further hydrolysis, oxalic acid.[1,2] Since the dioxazole is readily formed by 1,3-dipolar cycloaddition of benzonitrile oxide to ethyl glyoxylate, this represents an unusual method for overall oxidation of the aldehyde function to a carboxylic acid without using a conventional oxidising agent. The great versatility of the 1,3-dipolar cycloaddition process means that a variety of heterocyclic compounds **5** with X and Y being RN, O or S are potentially accessible by cycloaddition of nitrilium betaines **4** to **3**.[3] In principle, these could undergo similar cycloreversion upon deprotonation to form the anions **6**, and the resulting delocalised anion **7** could then be alkylated on either heteroatom to give the products **8**. The overall two-step conversion of **3** into **8** in this way would seem to be of considerable synthetic value, especially in cases where the nature of the groups present in R^1 prohibit the use of strongly oxidising or acidic conditions. Apart from the reaction of **1**, one of the few previous examples of cycloreversion of such an anion with elimination of a nitrile is the decomposition of **9**, formed by addition of RLi to the corresponding thiazoline-thione, which affords benzonitrile and the dithioester anion as shown.[4] In this paper we describe the successful use of this method for the conversion of imines into secondary and tertiary amides and of aromatic aldehydes to acids and esters.[5]



Results and discussion

A range of 1,2,4-oxadiazolines **12** were readily prepared in moderate to excellent yield by cycloaddition of the appropriate nitrile oxide **11** to the imines **10** (Table 1). Benzonitrile oxide **11** (R^3 = Ph) was generated in the presence of the dipolarophile following the method of Huisgen and co-workers,[6] by reaction of benzhydroximoyl chloride with triethylamine. In most cases addition of triethylamine to a solution of the imine and the hydroximoyl chloride gave good results, but for the more sensitive aliphatic imine required for **12f** it was found to be better to add a solution of the hydroximoyl chloride to a solution of the imine and triethylamine. For the preparation of **12g** and **12h**, acetonitrile oxide **11** (R^3 = Me) was generated in the presence of the imine by reaction of nitroethane with PhNCO catalysed by Et_3N.[7] Of the eight oxadiazolines prepared only **12a,b** and **g** have previously been described. The NMR spectra of the compounds were distinctive with the ^1H signal for the 5-H generally appearing as a singlet in the range



δ_H 6.3–6.6 (**12f** quartet at 5.85) and the ^{13}C spectra forming a highly consistent pattern (Table 2) with signals for C-3 at δ_C 154–159 and for C-5 at δ_C 90–100.

Table 1 Preparation of the 4,5-dihydrooxadiazoles **12** and their reaction to form the amides **13**

	R^1	R^2	R^3	Yield of **12** (%)	Yield of **13** (%) for R^4 = H	Me	CH_2Ph
a	Ph	Ph	Ph	49	66	96	—
b	Ph	Bn	Ph	95	73	—	—
c	Ph	Bu^t	Ph	64	88	75	56*
d	4-$MeOC_6H_4$	Bu^t	Ph	50	47	24*	—
e	4-MeC_6H_4	Bu^t	Ph	93	85	—	—
f	Me	Bu^t	Ph	82	—	—	—
g	Ph	Ph	Me	72	71	—	10*
h	Ph	Bu^t	Me	25	28	—	—

* HMPA was added to assist alkylation.

Table 2 ^{13}C NMR spectra of 4,5-dihydrooxadiazoles **12**, δ_C

	R^1	R^2	R^3	C-3	C-5	R^1 signals	R^2 signals	R^3 signals
a	Ph	Ph	Ph	155.0	100.2	141.1 (4°), 129.7, 128.6 (2 C), 127.1 (2 C)	138.9 (4°), 125.5, 124.0 (2 C), 129.1 (2 C)	130.5, 128.9 (4°), 128.8 (2 C), 127.9 (2 C)
c	Ph	Bu^t	Ph	158.3	93.6	141.1 (4°), 128.6, 128.4 (2 C), 126.0 (2 C)	57.7 (4°), 29.8 (3 C)	130.2, 129.4 (4°), 128.8 (2 C), 128.3 (2 C)
d	4-$MeOC_6H_4$	Bu^t	Ph	158.2	93.6	159.9 (4°), 133.5 (4°), 127.3 (2 C), 113.8 (2 C), 55.3	57.6 (4°), 29.8 (3 C)	130.1, 129.5 (4°), 128.8 (2 C), 128.3 (2 C)
e	4-MeC_6H_4	Bu^t	Ph	158.2	93.7	138.4 (4°), 138.3 (4°), 129.1 (2 C), 126.0 (2 C), 21.2	57.6 (4°), 29.8 (3 C)	130.1, 129.5 (4°), 128.8 (2 C), 128.3 (2 C)
f	Me	Bu^t	Ph	157.8	91.0	22.8	57.2 (4°), 29.6 (3 C)	130.0, 129.9 (4°), 128.6 (2 C), 128.2 (2 C)
h	Ph	Bu^t	Me	154.1	95.0	141.4 (4°), 128.7, 128.6 (2 C), 126.6 (2 C)	54.6 (4°), 28.6 (3 C)	13.2

The original report of the cycloreversion of **1** involved aqueous NaOH,[1] but in a later study the same authors were able to achieve the cycloreversion using KOBu^t in Bu^{t}OH at 100 °C for 5 h.[2] We therefore began by examining the reaction of **12** with KOBu^t (1.2 equiv.) in tetrahydrofuran (THF) at room temperature (RT). In the case of **12a** this did lead to complete reaction in the desired sense to give, upon subsequent aqueous work-up, benzonitrile which was readily removed by evaporation and *N*-phenylbenzamide **13a** (R^4 = H). For several of the other examples reaction was incomplete under these conditions and the procedure was found to be optimised by using 3 equiv. of base and heating under reflux in THF for 2 h. This then gave the corresponding amides **13** (R^4 = H) in moderate to good yields (see Table 1). The only exception was compound **12f** where the aliphatic R^1 group means that the 5-position is not sufficiently acidic to be deprotonated and the cycloreversion cannot take place. This compound was recovered unchanged after treatment with KOBu^t and also stronger bases such as lithium diisopropylamide (LDA) and BuLi. The method described here allows direct two-step conversion of the imines **10** into the secondary amides **13** and compares favourably with one of the few other ways to accomplish this transformation: reaction with PCl_5 in xylene to give the imidoyl chloride followed by hydrolysis.[8] Our method is clearly preferable where acid-sensitive functional groups are present.

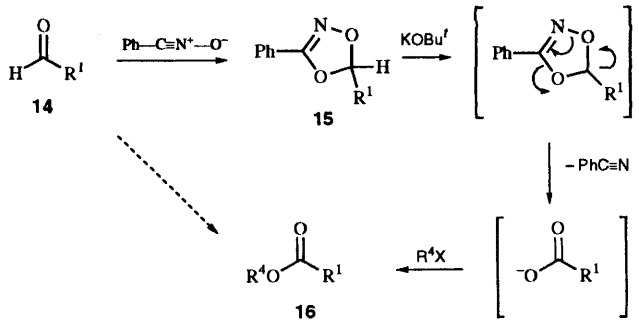
The possibility of directly obtaining tertiary amides by addition of methyl iodide or benzyl bromide to the mixture resulting from base treatment was demonstrated in selected cases (Table 1) although the anions were rather unreactive and addition of hexamethylphosphoramide (HMPA) proved to be beneficial. Use of less reactive alkyl halides such as isopropyl bromide and benzyl chloride did not result in alkylation and the secondary amides **13** (R^4 = H) were obtained in these cases.

Attention was then turned to the 1,4,2-dioxazoles **15**

Table 3 Preparation of the dioxazoles **15** and their reaction to give **16**

	R^1	Yield of **15** (%)	Yield of **16** (%) for R^4 = H	Me
a	Ph	63	97	48
b	4-ClC_6H_4	59	80	51
c	2-ClC_6H_4	26	81	—

obtained by cycloaddition of benzonitrile oxide to aromatic aldehydes. These were readily prepared by reaction of benzhydroximoyl chloride with triethylamine in the presence of an excess of the aldehyde **14** (Table 3).[2] The compounds again showed distinctive NMR signals: a singlet at $\delta_H \approx 6.8$ for the 5-H and a signal at $\delta_C \approx 105$ for C-5. Treatment with KOBu^t (3 equiv.) in THF under reflux for 2 h followed by aqueous work-up gave the corresponding acids **16** (R^4 = H) in good



to excellent yield (Table 3). The direct formation of methyl esters was similarly achieved in moderate yield in two cases by addition of methyl iodide.

Attempts to extend this method to the 1,2,4-triazolines formed by cycloaddition of diphenylnitrile imine to imines were not successful and these compounds were recovered unchanged after prolonged treatment with KOBu^t.

We have shown that the base-induced cycloreversion reported for **1** can be readily extended to the oxadiazolines **12** and the dioxazoles **15**, thus allowing two-step conversion of the imines **10** into the amides **13** and of the aldehydes **14** into the acids or esters **16**. While some limitations are clearly evident, these methods may prove valuable in cases where the presence of acid-sensitive or readily oxidisable groups rules out the use of more conventional methods.

Experimental

Melting points were recorded on a Reichert hot-stage microscope and are uncorrected. IR spectra were recorded for solids as Nujol mulls and for liquids as thin films unless otherwise indicated, on a Perkin-Elmer 1420 instrument. NMR spectra were obtained for ^{1}H at 300 MHz and for ^{13}C at 75 MHz on a Bruker AM300 instrument. All spectra were run on solutions in $CDCl_3$ unless otherwise indicated, with internal Me_4Si as reference. Chemical shifts are reported in ppm to high frequency of the reference and coupling constants J are in Hz. Mass spectra were obtained on an A. E. I. MS-902 spectrometer using electron impact at 70 eV. Ether refers to diethyl ether.

Preparation of the 4,5-dihydro-1,2,4-oxadiazoles 12

These compounds were prepared by three different methods.

Method A.[6] A solution of benzhydroximoyl chloride[9] (5 g, 32 mmol) and the appropriate imine **10** (32 mmol) in ether (50 cm^3) was stirred at 0 °C while triethylamine (3.5 g, 35 mmol) in ether (10 cm^3) was added dropwise. After the addition the mixture was stirred at 20 °C for 2 h and then filtered and evaporated to give the oxadiazoline.

Method B.[6] A solution of the imine **10** (32 mmol) and triethylamine (3.5 g, 35 mmol) in ether (25 cm^3) was stirred at 0 °C while a solution of benzhydroximoyl chloride (5 g, 32 mmol) in ether (25 cm^3) was added dropwise. After the addition the mixture was stirred at 20 °C for 2 h and then filtered and evaporated to give the oxadiazoline.

Method C.[7] A solution of nitroethane (3.75 g, 50 mmol) and triethylamine (0.2 g) in toluene (10 cm^3) was stirred at 20 °C while a solution of phenyl isocyanate (11.9 g, 100 mmol) and the appropriate imine **10** (37.5 mmol) in toluene (12.5 cm^3) was added dropwise. After the addition the mixture was heated under reflux for 1 h and then cooled to 0 °C. The resulting precipitate of diphenylurea was filtered off and the filtrate evaporated to give the crude oxadiazoline which was purified by column chromatography on silica (ether–light petroleum, 1:1). Unfortunately, it proved impossible to obtain entirely satisfactory elemental analysis data for **12c,e,f** and **h** owing to partial decomposition upon recrystallisation, but correct high resolution MS data were obtained in each case and no significant impurities were evident in the fully assigned ^{13}C NMR spectra (Table 2).

By these methods the following compounds were prepared:

3,4,5-Triphenyl-4,5-dihydro-1,2,4-oxadiazole 12a. Method A with *N*-benzylideneaniline[10] gave pale brown crystals (49%), mp 72–74 °C (from EtOAc) (lit.,[6] 74–75 °C); δ_H 7.7–7.0 (13 H, m), 6.85–6.7 (2 H, m) and 6.51 (1 H, s); δ_C see Table 2.

4-Benzyl-3,5-diphenyl-4,5-dihydro-1,2,4-oxadiazole 12b. Method A with *N*-benzylidenebenzylamine[11] gave an orange oil (72%) purified by Kugelrohr distillation, bp (oven temp.) 250 °C at 0.05 mmHg (lit.,[12] 150–160 °C at 0.2 mmHg); δ_H 7.9–7.75 (2 H, m), 7.7–7.1 (13 H, m), 6.34 (1 H, s) and 4.50 and 4.10 (2 H, AB pattern, J 16).

4-*tert*-Butyl-3,5-diphenyl-4,5-dihydro-1,2,4-oxadiazole 12c. Method A with *N*-benzylidene-*tert*-butylamine[13] gave colourless crystals (64%) (from Et_2O–CH_2Cl_2, 1:1), mp 130–131 °C (Found: C, 77.1; H, 7.8; N, 10.1; M, 280.1575. $C_{18}H_{20}N_2O$ requires C, 77.1; H, 7.2; N, 10.0%; M, 280.1576); ν_{max}/cm^{-1} 1540, 1302, 1284, 1177, 1158, 1092, 992, 848, 768, 726 and 685; δ_H 7.75–7.55 (4 H, m), 7.45–7.3 (6 H, m), 6.61 (1 H, s) and 1.20 (9 H, s); δ_C see Table 2; m/z 280 (M$^+$, 10%), 244 (6), 229 (12), 224 (96), 193 (28), 147 (98), 119 (57) and 104 (100).

4-*tert*-Butyl-5-(4-methoxyphenyl)-3-phenyl-4,5-dihydro-1,2,4-oxadiazole 12d. Method A with *N*-4-methoxybenzylidene-*tert*-butylamine[14] gave pale yellow crystals (50%), mp 105–106 °C (from light petroleum–EtOAc, 10:1) (Found: C, 73.2; H, 7.4; N, 9.1. $C_{19}H_{22}N_2O_2$ requires C, 73.5; H, 7.1; N, 9.0%); ν_{max}/cm^{-1} 1592, 1570, 1546, 1496, 1335, 1238, 1160, 1092, 1053, 1018, 852, 840, 830, 800, 750, 710 and 689; δ_H 7.75–7.55 (2 H, m), 7.55 and 6.93 (4 H, AB pattern, J 9), 7.45–7.3 (3 H, m), 6.57 (1 H, s), 3.81 (3 H, s) and 1.18 (9 H, s); δ_C see Table 2; m/z 310 (M$^+$, 11%), 254 (48), 223 (10), 208 (9), 178 (8), 151 (52) and 134 (100).

4-*tert*-Butyl-5-(4-methylphenyl)-3-phenyl-4,5-dihydro-1,2,4-oxadiazole 12e. Method A with *N*-4-methylbenzylidene-*tert*-butylamine[14] gave colourless crystals (93%), mp 137–138 °C (from hexane) (Found: C, 78.0; H, 8.1; N, 9.5; M, 294.1719. $C_{19}H_{22}N_2O$ requires C, 77.5; H, 7.5; N, 9.5%; M, 294.1732); ν_{max}/cm^{-1} 1595, 1570, 1546, 1330, 1289, 1184, 1162, 1096, 1052, 1006, 855, 805, 750, 712, 690 and 668; δ_H 7.8–7.6 (2 H, m), 7.55 and 7.22 (4 H, AB pattern, J 7), 7.5–7.35 (3 H, m), 6.60 (1 H, s), 2.35 (3 H, s) and 1.18 (9 H, s); δ_C see Table 2; m/z 294 (M$^+$, 8%), 238 (68), 207 (25), 160 (10), 147 (25), 135 (37) and 118 (100).

4-*tert*-Butyl-5-methyl-3-phenyl-4,5-dihydro-1,2,4-oxadiazole 12f. Method B with *N*-ethylidene-*tert*-butylamine[15] gave pale yellow crystals (82%), mp 169–170 °C (from hexane) (Found: M, 218.1418. $C_{13}H_{18}N_2O$ requires M, 218.1419); ν_{max}/cm^{-1} 1582, 1559, 1342, 1222, 1200, 1148, 1120, 1084, 1051, 967, 927, 903, 861, 760, 720 and 700; δ_H 7.75–7.55 (2 H, m), 7.45–7.3 (3 H, m), 5.85 (1 H, q, J 5), 1.36 (3 H, d, J 5) and 1.10 (9 H, s); δ_C see Table 2; m/z 218 (M$^+$, 10%), 203 (3), 162 (32), 147 (100), 130 (12), 119 (60) and 104 (32).

3-Methyl-4,5-diphenyl-4,5-dihydro-1,2,4-oxadiazole 12g. Method C with *N*-benzylideneaniline gave pale brown crystals (72%), mp 80–81 °C (from EtOAc) (lit.,[7] 75–76 °C); δ_H 7.55–7.15 (8 H, m), 7.05–6.85 (2 H, m), 6.48 (1 H, s) and 1.98 (3 H, s).

4-*tert*-Butyl-3-methyl-5-phenyl-4,5-dihydro-1,2,4-oxadiazole 12h. Method C with *N*-benzylidene-*tert*-butylamine gave a colourless waxy solid (25%), mp 72–73 °C (Found: M, 218.1426. $C_{13}H_{18}N_2O$ requires M, 218.1419); ν_{max}/cm^{-1}(neat) 1650, 1595, 1540, 1442, 1400, 1310, 1275, 1220, 1022, 895, 752, 718 and 695; δ_H 7.8–7.4 (5 H, m), 6.53 (1 H, s), 2.18 (3 H, s) and 1.27 (9 H, s); δ_C see Table 2; m/z 218 (M$^+$, 30%), 203 (4), 176 (5), 161 (100), 130 (28), 105 (84) and 93 (72).

Preparation of 1,4,2-dioxazoles 15[2]

A solution of benzhydroximoyl chloride (5 g, 32 mmol) and the appropriate aldehyde **14** (180 mmol) in ether (70 cm^3) was stirred at 20 °C while triethylamine (3.5 g, 35 mmol) in ether (20 cm^3) was added dropwise. The mixture was stirred for 12 h and then filtered and the filtrate evaporated. Excess of aldehyde was distilled off under reduced pressure and the residue recrystallised to give the desired dioxazole.

3,5-Diphenyl-1,4,2-dioxazole 15a. The above method with benzaldehyde gave a pale yellow solid (63%), mp 46–47 °C (from MeOH) (lit.,[16] 41–42 °C).

5-(4-Chlorophenyl)-3-phenyl-1,4,2-dioxazole 15b. The above method with 4-chlorobenzaldehyde gave a pale yellow solid (59%), mp 210–212 °C (Found: M, 259.0391. $C_{14}H_{10}{}^{35}ClNO_2$ requires M, 259.0400); δ_H 8.2–7.3 (9 H, m) and 6.82 (1 H, s); m/z 261 (^{37}Cl – M$^+$, 6%), 259 (^{35}Cl – M$^+$, 18), 243 (4), 139 (4), 121 (10), 105 (100) and 77 (32). Satisfactory elemental analysis

data could not be obtained owing to partial decomposition during recrystallisation.

5-(2-Chlorophenyl)-3-phenyl-1,4,2-dioxazole 15c. The above method with 2-chlorobenzaldehyde gave a pale yellow solid (26%), mp 59–60 °C (from light petroleum–EtOAc, 1:1) (lit.,[2] 61 °C); δ_C 105.4 (C-5).

Base-induced cycloreversion

A solution of the heterocyclic compound (15 mmol) and potassium *tert*-butoxide (1.68 g, 45 mmol) in THF (20 cm^3) was heated under reflux for 2 h. Excess of the appropriate electrophile was added to the mixture which was then stirred for 30 min before addition of saturated aqueous ammonium chloride. Extraction with CH_2Cl_2, drying and evaporation gave the product.

Compound 13a (R^4 = H). A reaction as above with 3,4,5-triphenyl-4,5-dihydro-1,2,4-oxadiazole **12a** and water gave *N*-phenylbenzamide (66%) as colourless crystals, mp 158–159 °C (lit.,[17] 162–163 °C); δ_H 7.9–7.2 (10 H, m); δ_C 165.9 (CO), 137.9 and 135.0 (both 4°), 131.8, 129.1 (2 C), 128.8 (2 C), 127.0 (2 C), 124.6 and 120.3 (2 C).

Compound 13b (R^4 = H). A reaction as above with 4-benzyl-3,5-diphenyl-4,5-dihydro-1,2,4-oxadiazole **12b** and water gave *N*-benzylbenzamide (73%) as colourless crystals, mp 102–104 °C (lit.,[18] 105–106 °C); δ_H 7.8–7.75 (2 H, m), 7.50–7.25 (8 H, m), 6.58 (1 H, br s) and 4.63 (2 H, s).

Compound 13c (R^4 = H). A reaction as above with 4-*tert*-butyl-3,5-diphenyl-4,5-dihydro-1,2,4-oxadiazole **12c** and water gave *N*-*tert*-butylbenzamide (88%) as colourless crystals, mp 129 °C (lit.,[19] 135.5 °C); δ_H 7.85–7.4 (5 H, m), 6.0–5.5 (1 H, br s) and 1.48 (9 H, s).

Compound 13d (R^4 = H). A reaction as above with 4-*tert*-butyl-5-(4-methoxyphenyl)-3-phenyl-4,5-dihydro-1,2,4-oxadiazole **12d** and water gave *N*-*tert*-butyl-4-methoxybenzamide (47%) as colourless crystals, mp 114–115 °C (lit.,[20] 115 °C); δ_H 7.69 and 6.88 (4 H, AB pattern, *J* 10), 5.90 (1 H, br s), 3.84 (3 H, s) and 1.45 (9 H, s).

Compound 13e (R^4 = H). A reaction as above with 4-*tert*-butyl-5-(4-methylphenyl)-3-phenyl-4,5-dihydro-1,2,4-oxadiazole **12e** and water gave *N*-*tert*-butyl-4-methylbenzamide (85%) as colourless crystals, mp 110–111 °C (lit.,[20] 116.5–117 °C); δ_H 7.62 and 7.21 (4 H, AB pattern, *J* 10), 5.92 (1 H, br s), 2.38 (3 H, s) and 1.48 (9 H, s).

Compound 13g (R^4 = H). A reaction as above with 3-methyl-4,5-diphenyl-4,5-dihydro-1,2,4-oxadiazole **12g** and water gave *N*-phenylbenzamide (71%) as colourless crystals, mp 164–165 °C (lit.,[17] 162–163 °C); δ_H as **13a**

Compound 13h (R^4 = H). A reaction as above with 4-*tert*-butyl-3-methyl-5-phenyl-4,5-dihydro-1,2,4-oxadiazole **12h** and water gave *N*-*tert*-butylbenzamide (28%) as colourless crystals, mp 133–134 °C (lit.,[19] 135.5 °C); δ_H as **13c**.

Compound 13a (R^4 = Me). A reaction as above with 3,4,5-triphenyl-4,5-dihydro-1,2,4-oxadiazole **12a** and iodomethane gave *N*-methyl-*N*-phenylbenzamide (96%) as colourless crystals, mp 60–61 °C (lit.,[21] 63 °C); δ_H 7.6–7.1 (10 H, m) and 3.37 (3 H, s).

Compound 13c (R^4 = Me). A reaction as above with 4-*tert*-butyl-3,5-diphenyl-4,5-dihydro-1,2,4-oxadiazole **12c** and iodomethane gave *N*-*tert*-butyl-*N*-methylbenzamide (75%) as colourless crystals, mp 74–76 °C (lit.,[22] 78.5–80 °C); δ_H 7.6–7.4 (5 H, m), 2.80 (3 H, s) and 1.40 (9 H, s).

Compound 13c (R^4 = CH_2Ph). A reaction as above with 4-*tert*-butyl-3,5-diphenyl-4,5-dihydro-1,2,4-oxadiazole **12c** and benzyl bromide but with the addition of HMPA (5 cm^3) gave a material shown spectroscopically to consist largely of *N*-benzyl-*N*-*tert*-butylbenzamide (56%) as colourless crystals, mp 98 °C; δ_H 7.7–7.2 (10 H, m), 4.48 (2 H, s) and 1.43 (9 H, s).

Compound 13d (R^4 = Me). A reaction as above with 4-*tert*-butyl-5-(4-methoxyphenyl)-3-phenyl-4,5-dihydro-1,2,4-oxadiazole **12d** and iodomethane but with the addition of HMPA (5 cm^3) gave slightly impure *N*-*tert*-butyl-4-methoxy-*N*-methylbenzamide (24%) as colourless crystals, mp 60–62 °C (Found: M, 221.1413. $C_{13}H_{19}NO_2$ requires *M*, 221.1416); ν_{max}/cm^{-1} 1645, 1605, 1508, 1300, 1250, 1167, 1060, 1032, 842, 768 and 715; δ_H 7.52 and 6.95 (4 H, AB pattern, *J* 10), 3.87 (3 H, s), 2.93 (3 H, s) and 1.47 (9 H, s); δ_C 173.2 (CO), 160.8 (ArC-4), 129.5 (2 C, ArC-2,6), 127.1 (ArC-1), 113.5 (2 C, ArC-3,5), 56.4 (CMe_3), 55.4 (OMe), 35.6 (NMe) and 27.8 (3 C); *m*/*z* 221 (M^+, 4%), 206 (15), 178 (3), 165 (3), 148 (8), 135 (100), 105 (13) and 77 (28).

Compound 13g (R^4 = CH_2Ph). A reaction as above with 3-methyl-4,5-diphenyl-4,5-dihydro-1,2,4-oxadiazole **12g** and benzyl bromide but with the addition of HMPA (5 cm^3) gave *N*-benzyl-*N*-phenylbenzamide (10%) as colourless crystals, mp 102–103 °C (lit.,[23] 104 °C); δ_H 7.55–6.95 (15 H, m) and 5.22 (2 H, s).

Compound 16a (R^4 = H). A reaction as above with 3,5-diphenyl-1,4,2-dioxazole **15a** and water gave benzoic acid (97%) as colourless crystals, mp 122–123 °C (lit.,[24] 122–123 °C).

Compound 16b (R^4 = H). A reaction as above with 5-(4-chlorophenyl)-3-phenyl-1,4,2-dioxazole **15b** and water gave 4-chlorobenzoic acid (80%) as colourless crystals, mp 230–232 °C (lit.,[24] 243 °C); δ_H 9.1 (1 H, br s) and 8.10 and 7.50 (4 H, AB pattern, *J* 8).

Compound 16c (R^4 = H). A reaction as above with 5-(2-chlorophenyl)-3-phenyl-1,4,2-dioxazole **15c** and water gave 2-chlorobenzoic acid (81%) as colourless crystals, mp 140–141 °C (lit.,[24] 142 °C).

Compound 16a (R^4 = Me). A reaction as above with 3,5-diphenyl-1,4,2-dioxazole **15a** and iodomethane gave methyl benzoate (48%) as a colourless liquid, bp 198–200 °C (lit.,[24] 199.6 °C); δ_H 8.25–8.1 (2 H, m), 7.65–7.50 (3 H, m) and 3.94 (3 H, s).

Compound 16b (R^4 = Me). A reaction as above using 5-(4-chlorophenyl)-3-phenyl-1,4,2-dioxazole **15b** and iodomethane gave methyl 4-chlorobenzoate (51%) as colourless crystals, mp 40–41 °C (lit.,[24] 44 °C); δ_H 8.12 and 7.55 (4 H, AB pattern, *J* 9) and 3.98 (3 H, s).

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