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1,4-Diazabicyclo[2.2.2]octane (DABCO) as an Efficient Reagent for the Synthesis of Isoxazole Derivatives from Primary Nitro Compounds and Dipolarophiles: The Role of the Base

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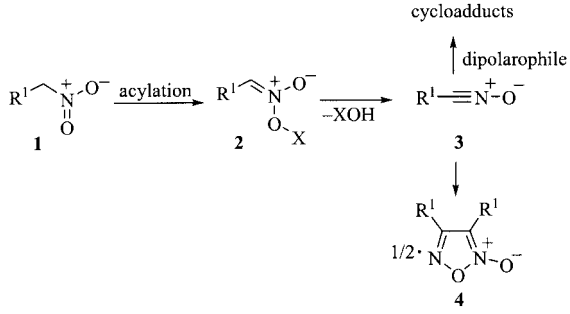
The dehydration of primary nitro compounds can be performed by bases in the presence of dipolarophiles. The reactivity of several tertiary amines or azaheteroaromatic compounds containing one or two basic centres is shown to be related to the ability of the protonated base to establish H-bonded ion pairs with the adduct that is formed from the nitronate and the dipolarophile in chloroform. Among the organic bases examined, caged tertiary diamine 1,4-diazabicyclo[2.2.2]octane (DABCO) gave the best results. The reaction is applicable to activated nitro compounds and to phenylnitromethane and affords isoxazoline derivatives in higher yields compared with those of other methods. The reaction, however, is not compatible with nitroalkanes. The proposed mechanism of the reaction is based on the collapse of the H-bonded ion pair.

Introduction

Mukaiyama and Hoshino[1] reported that phenyl isocyanate could be used as a dehydrating agent, and since then nitro compounds have become important precursors in the synthesis of heterocyclic compounds by 1,3-dipolar cycloaddition.[2] One synthetic protocol is based on the conversion of the nitro compounds into alkyl[3] or silyl nitronates,[4–6] which is then followed by cycloaddition and elimination. Other methods require the treatment of the nitro compounds with acylating agents, or the reagents must be heated in the presence of strong acids.[7–15] However, when nitro compounds are heated at reflux in mesitylene in the presence of dipolarophiles with catalytic *p*-toluenesulfonic acid (PTSA) adducts not only from the activated nitro compounds, but also from nitropropane are afforded.[16] Nonetheless, at that temperature, activated nitro compounds undergo this reaction even without an acid catalyst.[17]

Among the reports that involve the use of acylating agents for the dehydration of nitro compounds, several authors have proposed mechanisms in which an acyl derivative of nitronic acid (mixed anhydride **2**) is suggested as the intermediate which collapses to nitrile oxide **3** (Scheme 1).



X = CONHPh,[a] COMe,[b,e] COPh,[b] CO_2Et,[c] $PhSO_2$,[c] CO_2tBu [d]

Scheme 1. Dehydration of primary nitro compounds with acylating agents. [a] Ref.[1] [b] Refs.[18,11] [c] Ref.[19] [d] Ref.[20] [e] Refs.[21,22]

However, in principle, the adducts that are obtained when the reaction is performed in the presence of dipolarophiles might originate either by this route or by the addition of the acylated nitronic acid to the dipolarophile, which is then followed by elimination. This was clearly pointed out by McKillop and Kobylecki some years ago.[10] The eventual formation of nitrile oxide **3** is evidenced by the identification of furoxan **4**, its spontaneous dimerization product.

The dehydration of nitro compounds is often performed by the combination of the acylating agents (Scheme 1) with a base, but the base alone as a means for the dehydration of primary nitro compounds remained unexplored until our recent preliminary communication was published.[23] In that report, we demonstrated that the use of a dehydrating agent can be avoided, and that tertiary diamine bases, such as 1,4-diazabicyclo[2.2.2]octane (DABCO) or tetramethylethyl-

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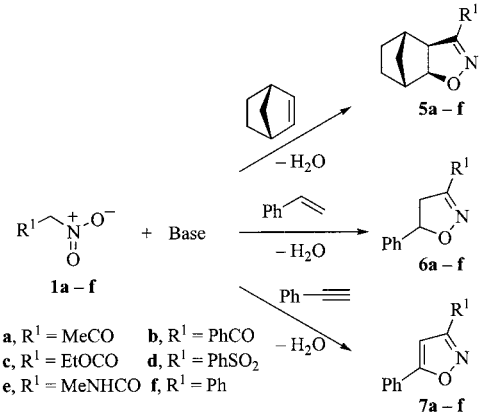
enediamine (TMEDA), promote the dehydration of the nitro compounds as a thermodynamically favoured process.

We consider here the scope and limitations of this reaction and how it is affected by the use of various bases and different solvents.

Results and Discussion

In addition to nitroacetone (**1a**), benzoylnitromethane (**1b**), ethyl nitroacetate (**1c**), phenylsulfonyl nitromethane (**1d**), already reported,[23] *N*-methylnitroacetamide (**1e**) and phenylnitromethane (**1f**) were successfully used in the title reaction (Scheme 2); primary nitroalkanes did not react under these conditions with the bases that were screened.



Scheme 2.

The results are reported in Table 1. 1-Methylimidazole is preferred over DABCO in the 1:1 reactions of benzoylnitromethane (**1b**) with norbornene, styrene and phenylacetylene because in addition to adducts **5b**, **6b** and **7b**, respectively, minor side products were obtained when DABCO was employed. These side products have been identified as furazan derivatives, which are produced from the dibenzoylfuroxan intermediate.[24] Similarly, the reaction of **1a** with the same dipolarophiles afforded some diacetylfuroxan as a side product, in addition to the expected cycloadducts.

Table 1. Isoxazole derivatives from nitro compounds in the presence of DABCO or 1-methylimidazole.[a]

Entry	R^1–NO_2	R^1	Dipolarophile	Base	Product	Conv. [%][b]	Yield [%][c]
1	**1a**	MeCO		DABCO	**5a**	100	90 (100)
2	**1a**	MeCO		DABCO	**6a**	74	60 (77)
3	**1a**	MeCO		DABCO	**7a**	–[d]	39 (37)
4	**1b**	PhCO		DABCO	**5b**	100	90 (91)
				1-methylimidazole		100	100 (99)
5	**1b**	PhCO		DABCO	**6b**	100	75 (75)
				1-methylimidazole		100	100 (100)
6	**1b**	PhCO		DABCO	**7b**	70	57 (57)
				1-methylimidazole		67	70 (68)
7	**1c**	EtOCO		DABCO	**5c**	100	100 (100)
8	**1c**	EtOCO		DABCO	**6c**	100	91 (89)
9	**1c**	EtOCO		DABCO	**7c**	100	100 (99)
10	**1d**	$PhSO_2$		DABCO	**5d**	55	50 (51)
11	**1d**	$PhSO_2$		DABCO	**6d**	100	10 (13)
12	**1d**	$PhSO_2$		DABCO	**7d**	100	20 (24)
13	**1e**	MeNHCO		DABCO	**5e**	100	96 (100)
14	**1e**	MeNHCO		DABCO	**6e**	80	70 (71)
15	**1e**	MeNHCO		DABCO	**7e**	–[d]	41 (39)
16	**1f**	Ph		DABCO	**5f**	100	95 (100)
17	**1f**	Ph		DABCO	**6f**	80	80 (79)
18	**1f**	Ph		DABCO	**7f**	–[d]	55 (52)

[a] See experimental section for details. [b] Conversion of dipolarophile determined by ^{1}H NMR spectroscopy. [c] Isolated yield determined on analytically pure product and based on dipolarophile. Yields in parenthesis are the spectroscopic yields as determined by ^{1}H NMR spectroscopy with the use of an internal standard. [d] Not determined – signals are not well-resolved in the ^{1}H NMR spectra.

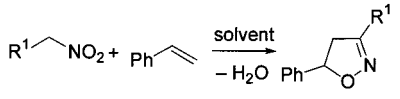
However, in this case DABCO gave the best results, as the furoxan does not react with the dipolarophiles.

All reactions have been carried out in chloroform, (see below) but those of phenylsulfonylnitromethane (**1d**, Table 1, Entries 10–12) were performed in ethanol because the reaction of **1d** with DABCO in chloroform gives rise to a (uninvestigated) precipitate. This drawback is reduced in ethanol and by the portionwise addition of DABCO to the reaction mixture; some adducts were thus prepared.

Phenylacetylene, styrene and norbornene have been considered as model dipolarophiles – their reactivity increases in the respective order, as apparent from Table 1.

The results of the reaction are largely dependent on the solvent employed. Nitro compounds **1a** and **1b** rapidly undergo cleavage with primary or secondary amines[25] as well as with hydroxylic solvents. Even the water that is produced during the course of the reaction, particularly when mixed with the solvent (THF), causes partial hydrolysis of these nitro compounds, while in chloroform this occurs to a lesser extent. Nitro compounds **1c**, **1d**, **1e** and **1f** are cleaved more slowly, thus all the listed solvents can be employed (Table 2). For this reason, the reaction of ethyl nitroacetate **1c** with styrene in the presence of DABCO was chosen as a model and carried out in different solvents.

Table 2. Effect of solvent on the reaction between styrene and nitro compounds.[a]



Entry	Reaction time [h]	R	Solvent	ε[b]	Yield [%][c]
1	40	EtOCO	EtOH	25.3	89
2	40	EtOCO	$CHCl_3$	4.84	91
3	40	EtOCO	DMSO	47.24	30
4	40	EtOCO	CH_3CN	36.64	0
5	40	EtOCO	THF	7.52	36
6[d]	40	EtOCO	CCl_4	2.24	62
7	20	PhCO	EtOH	25.3	0
8	20	PhCO	$CHCl_3$	4.84	75

[a] Reaction conditions: DABCO, 60 °C. See Experimental Section for more details. [b] CRC Handbook of Chemistry and Physics, 76th Ed., (1995–96), 6–159. [c] Spectroscopic yield as determined by the integration of the representative signals by ^{1}H NMR spectroscopy with the use of an internal standard. [d] The homogeneous medium of the reaction in tetrachloromethane separates into two layers during the course of the reaction.

The yield of product **6c** after the reaction has been heated at 60 °C for 40 h has been measured with an internal standard by ^{1}H NMR spectroscopy and is reported in Table 2 (Entries 1–6). The best results are obtained when the reaction is performed in chloroform (Entry 2) or ethanol (Entry 1). Polar aprotic solvents, such as dimethylsulfoxide and tetrahydrofuran (Entries 3 and 5, respectively), cause a reduction of the reaction rate; formation of the adduct was not detectable at all in acetonitrile. Tetrachloromethane allows the reaction to proceed, although the mixture becomes heterogeneous during the course of the reaction. Under similar conditions, norbornene and **1c** were completely converted into adduct **5c** in chloroform, as well as in tetrahydrofuran and acetonitrile. Two reactions of benzoylnitromethane (**1b**) are included in Table 1 (Entries 7 and 8). Because adduct **6b** is stable in ethanol, the lack of product in this solvent (Entry 7) indicates that starting material **1b** decomposes prior to the addition reaction. Hereinafter, chloroform will be the solvent of choice, which will allow for the comparison between the different nitro compounds.

In order to establish the role of the base, the reactions of **1b** with styrene and of **1c** with norbornene have been carried out in the presence of various tertiary amines or heteroaromatic N bases (in Table 3 the bases are arranged in decreasing order of strength, those with one basic centre first, then those with two centres).

The ability of the base to promote the reaction was monitored by the percent conversion of the dipolarophile into the products and the corresponding spectroscopic yield after a fixed interval (20 h for **5b**, 40 h for **4c**). The values obtained are, in general, very close, which indicates that the dipolarophile is completely converted into the adduct. The considerable difference between the values of the percent conversion and the spectroscopic yield that is observed in some reactions of **1b** (Table 3, Entries 1, 2, 6 and 8–10) is due to the already mentioned presence of the furazan side product.

Benzoylnitromethane (**1b**) and styrene do not react with pyridine nor with tribenzylamine (Table 3, Entries 3 and 4), but the reaction does occur with stronger bases such as quinuclidine or triethylamine (Table 3, Entries 1 and 2). A considerable amount of furazan is produced with these tertiary amines, via the dibenzoylfuroxan intermediate.[24] Nitroacetone (**1a**) behaves similarly; diacetylfuroxan is found as a byproduct (see above).

The presence of an additional basic N atom causes a sharp increase in the reaction rate. The reaction only fails when very weak bases such as 2,2′-dipyridyl, pyrazine and pyrazole (Table 3, Entries 17–19) are employed, and it also fails with urotropine and with 2-dimethylaminopyridine (Table 3, Entries 16 and 13, respectively).

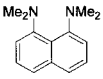
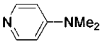
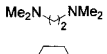
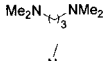
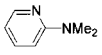
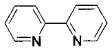
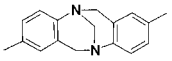
The reaction of ethyl nitroacetate (**1c**) with norbornene is more selective. The reaction occurs at an appreciable rate only with quinuclidine and with all compounds having an additional basic N atom, with the exceptions mentioned for benzoylnitromethane (**1b**). However, the reaction in this case also fails with the very strong bases such as 1,8-bis(dimethylamino)naphthalene (proton-sponge) and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) (Table 3, Entries 5 and 6).

The strength of the base (pK_{HB^+} refers to the dissociation constant of the conjugate acid in dissociating solvents like water, acetonitrile or dimethylsulfoxide) cannot be used to explain all of the results that are reported in Table 3. Nitro compound **1c** reacts with quinuclidine, but it does not react with triethylamine or with tribenzylamine; nitro com-

Table 3. Screened bases for the reactions of **1c** with norbornene and **1b** with styrene.[a]

(a) EtO_2C NO_2 + **1c** → Base, 40h → **5c**

(b) PhCO NO_2 + **1b** + Ph → Base, 20h → **6b**

Entry	Base	pK_{BH^+}[b]	pK_{HB}	**5c** Conv. [%][c]	**5c** Yield [%][d]	**6b** Conv. [%][c]	**6b** Yield [%][d]
1		10.76[e](10.87)	2.71[u]	65	63	100	63
2	Et_3N	10.68[f](10.62)	1.98[u]	0	–	74	46
3	$(PhCH_2)_3N$	5.38[g](6.90)	0.10[u]	0	–	0	–
4		5.37[h](5.23)	1.86[v]	0	–	0	–
5		12.1[i](12.40)	–0.55[w]	0	–	74	75
6		11.6[k](13.27)	3.82[x]	0	–	77	56
7		9.87[h](9.52)	2.80[v]	90	90	58	59
8		9.42[i](8.86)	2.32[u]	100	100	66	49
9		8.72[f](8.19)	2.63[u]	100	100	100	75
10		9.81[m](9.88)		59	60	73	53
11		7.64[n](7.76)		100	98	66	65
12		7.12[o](7.01)	2.72[x]	69	66	68	69
13		7.03[p](7.00)	1.61[v]	0	–	0	–
14		7.03[q](7.18)		62	61	53	55
15		5.53[q](5.77)		35	35	32	29
16		4.89[r](5.28)	1.93[u]	0	–	0	–
17		4.33[s](4.40)		0	–	0	–
18		0.5[t](1.0)	1.22[v]	0	–	0	–
19		2.53[q](2.57)		0	–	0	–
20		(7.67)		0	–	0	–
21		(4.68)	1.15[j]	0	–	0	–

[a] In a typical experiment the dipolarophile (1.0 equiv.) was added to a mixture of the base (0.5 equiv.) and the nitro compound (2.5 equiv.) in $CHCl_3$ and stirred in a sealed tube heated at 60 °C for the indicated time. [b] Refers to the dissociation constant of the protonated base in water. Values calculated with the use of Advanced Chemistry Development (ACD/Labs) Software V8.14 for Solaris (© 1994–2006 ACD/Labs) are shown in parenthesis. [c] Conversion of dipolarophile evaluated by ^{1}NMR spectroscopy. [d] Spectroscopic yield determined by ^{1}H NMR spectroscopy with the use of an internal standard. [e] Ref.[26] [f] Ref.[27] [g] Ref.[28] [h] Ref.[29] [i] Ref.[30] [j] Ref.[31] [k] Ref.[32] [l] Ref.[33] [m] Ref.[34] [n] Ref.[35] [o] Ref.[36] [p] Ref.[37] [q] Ref.[38] [r] Ref.[39] [s] Ref.[40] [t] Ref.[41] [u] Ref.[48] [v] Ref.[49] [w] Ref.[31] [x] Ref.[50]

pounds **1b** and **1c** react with 4-dimethylaminopyridine, but they do not react with 2-dimethylaminopyridine; they also react with benzimidazole, but they do not react with hexamethylenetetramine. Strong bases (proton-sponge and DBU) allow the reaction to occur with **1b** but not with **1c**. However, starting nitro compound **1b** is rapidly cleaved as water is produced during the reaction.

The above results find a better fitting with the concept of H-bonding basicity rather than with Brønsted basicity.[42]

A proton transfer process proceeds across several stages, chiefly: neutral H-bonded complex, H-bonded ion-pair, solvent separated ion pair, separated free ions. "Which particular intermediate or product species occur in detectable quantities will depend on the reacting donor–acceptor pair and the solvent".[42] Thus, the complete proton transfer occurs in dissociating solvents (water, MeCN, DMSO) and is measured by the pK_{HB^+}. The ion pair basicity refers to the equilibrium between the base and the acid with the H-bonded ion pair. This equilibrium constant is indicated as K_{ip} and has been measured in THF solutions[43] and found to be inconsistent with pK_{HB^+} values in acetonitrile.[43] A good linear correlation was reported between K_{ip} and the 2nd order interconversion constant measured for the racemization of (*S*)-profen thioesters in isooctane.[44]

The equilibrium between various N bases with 4-fluorophenol and their hydrogen-bonded complexes (Scheme 3)[45–47] is established in nondissociating solvents like CCl_4 or C_2Cl_4 (closer to our reaction conditions where chloroform is the solvent).

Base + HO–C$_6$H$_4$–F ⇌ Base ···· HO–C$_6$H$_4$–F

$$K_f = \frac{[\text{Base}\cdots\text{HO-C}_6\text{H}_4\text{-F}]}{[\text{Base}][\text{HO-C}_6\text{H}_4\text{-F}]} \qquad pK_{HB} = \log_{10} K_f$$

Scheme 3.

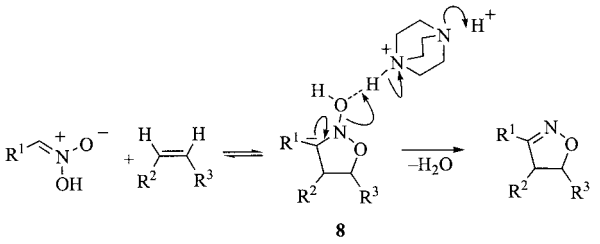
The results have been reported on a pK_{HB} scale or as the thermodynamic parameters of the equilibrium. A highly positive value of pK_{HB} corresponds to a high H-bonding basicity.

Indeed, quinuclidine (pK_{HB} = 2.71) and tribenzylamine (pK_{HB} = 0.10) have been reported as the two extremes in the aliphatic tertiary amine pK_{HB} scale.[48] The hydrogen-bond basicities of pyridine (pK_{HB} = 1.86), 4-dimethylaminopyridine (pK_{HB} = 2.80) and 2-dimethylaminopyridine (pK_{HB} = 1.61) agree with their different behaviour in the present reaction.[49]

For 1-methylimidazole, a reaction occurs with either compounds **1a** or **1c**, and a value of pK_{HB} = 2.72 has been measured.[50] The low value (pK_{HB} = 1.15) reported for Tröger base agrees with the observed lack of reactivity in either of the model reactions (Table 3, Entry 21).

Reported values of K_{ip} agree with the observed reactivity in the present work; compare quinuclidine (pK_{ip} = 0.15) with triethylamine (pK_{ip} = 2.11) and tribenzylamine (pK_{ip} = 2.41).

These remarks support the role of H-bonding, which was invoked in our preliminary account[23] to explain the dramatic improvement caused by amines having a second basic centre. The cleavage of the exocyclic N–O bond might occur in nitronate adduct intermediate **8** as illustrated in Scheme 4 or in the conjugate nitronic acid adduct.



Scheme 4.

This mechanism rules out the nitrile oxide as an intermediate in the reaction of the nitro compounds (**1c**–**1f**). In fact, the presence of the dipolarophiles is required for compounds **1c**–**1f** to react and directly give the adducts while dehydration occurs after the cycloaddition (Scheme 4). No furoxans are detected in the reaction mixture.

However, in the reactions with DABCO, the identification of 3,4-diacetylfuroxan among the reaction products of nitroacetone (**1a**) and the identification of furazans derived from 3,4-dibenzoylfuroxan among the reaction products of benzoylnitromethane (**1b**)[24] suggests that in these cases (at least in part) the nitro compound undergoes dehydration prior to cycloaddition. However, nitroacetone (**1a**) and benzoylnitromethane (**1b**) react faster in the presence of the dipolarophile than in its absence, and the cycloadducts are the main products even with no excess of dipolarophile.

Moreover, in the reaction of nitroacetone (**1a**) with styrene, by ^{1}H NMR spectroscopic analysis, the molar ratio between adduct **6a** (CH_3 at δ = 2.53 ppm) and the furoxan (**4**, R^1 = $COCH_3$, CH_3 at δ = 2.65 and δ = 2.80 ppm, respectively) was found to be 0.69 after a 2 h reaction time and 1.27 when styrene was no longer detected in the reaction mixture but still in presence of excess nitroacetone (6 h reaction time). Furoxan **4** (R^1 = PhCO) is not stable under the reaction conditions. This means that the dehydration occurs in part after the cycloaddition has occurred even with nitro compounds **1a** and **1b**.

Conclusions

Although not all of the findings can be fully understood, the following conclusions can be drawn. In summary: (1) By the treatment with tertiary amines or aromatic azaheterocycles only nitro compounds **1a** and **1b** undergo, in part, direct dehydration to the corresponding nitrile oxides, but, in general, participation of a dipolarophile is necessary. (2) The efficiency of different bases in chloroform as the solvent indicates that the process is related to their ability to establish H-bonded ion-pairs rather than to the strength of the base. (3) The best results are achieved with bases containing a second basic centre. These results are rationalized in Scheme 4, which suggests that a pre-equilibrium exists with the cycloadduct of nitronate **8**. Intermediate **8** is H-bonded to the protonated base and undergoes cleavage of the exocyclic N–O bond according to the curly arrows with dehydration. The dehydration of the nitro compounds to nitrile oxides in the absence of a dipolarophile is only observed for nitro compounds **1a** and **1b**. The enhanced reactivity of **1a** and **1b** compared to nitro compounds **1c**, **1d** and **1f** has already been noticed and is related to the ability of the carbonyl group to enolize.[51] Phenylsulfonylnitromethane (**1d**) appears particularly sluggish in this reaction.

In other solvents (Table 2), the reaction course is hard to rationalize since it can be modified by hydrogen-bonding donor or acceptor properties, by the strength of the base and by the dielectric constant of the solvent. The solvent can also affect the splitting of ion pairs into separated ions.

Experimental Section

General: Melting points were measured with a Büchi 510 apparatus and are uncorrected. Chromatographic separations were performed on silica gel; R_f values refer to TLC carried out on 25 mm silica gel plates (Merck F254) with the same eluent indicated for the column chromatography, unless otherwise stated. ^{1}H- and ^{13}C NMR spectra were recorded with a Mercuryplus 400 spectrometer. Multiplicity of the ^{13}C NMR signals and assignments were determined by means of HMQC and gHMBC experiments. Chemical shifts were determined relative to the residual solvent peak ($CHCl_3$: 7.24 ppm for ^{1}H NMR and 77.0 ppm for ^{13}C NMR). Mass spectra were obtained in EI mode with a 70 eV ionising voltage. Commercially available (Lancaster and Aldrich) benzoylnitromethane, ethyl nitroacetate, phenylsulfonylnitromethane were used as supplied. All bases are commercially available and used as supplied. $CHCl_3$ (ethanol-free) was filtered through a short pad of potassium carbonate prior to use. IR spectra were recorded with a Perkin–Elmer 881 spectrophotometer. Elemental analyses were obtained with an Elemental Analyser Perkin–Elmer 240C apparatus.

Preparation of Nitropropanone·Dicyclohexylamine Salt: Salt **1a**·dicyclohexylamine) was obtained according to a previously described procedure[52] from nitromethane (7.36 g, 120 mmol), K*t*BuO (13.4 g, 120 mmol) and phenyl acetate (8.16 g, 60 mmol) as a white solid. Yield 8.55 g, 50%. M.p. 135–139 °C (Ref.[52] 135–137 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.04–1.28 (m, 6 H, cyclohexyl-*H*), 1.32–1.48 (m, 4 H, cyclohexyl-*H*), 1.60 (d, *J* = 11.9 Hz, 4 H, cyclohexyl-*H*), 1.75 (d, *J* = 12.7 Hz, 4 H, cyclohexyl-*H*), 2.00 (s, 3 H, $COCH_3$), 3.08–3.18 (m, 2 H, 2 × CHN^+), 6.82 (s, 1 H, $CHNO_2$) ppm. ^{13}C NMR (100.58 MHz, $CDCl_3$): δ = 24.8 (t, cyclohexyl-*C*), 25.2 (t, cyclohexyl-*C*), 28.4 (t, cyclohexyl-*C*), 29.2 (q, $COCH_3$), 53.0 (d, 2 C, 2 × $CHNH_2^+$), 112.5 (d, $CHNO_2$), 187.0 (s, *C*=O) ppm.

General Method for Reaction of Nitropropanone (1a) with Dipolarophiles

Nitropropanone (**1a**) was freshly prepared from its dicyclohexylamine salt by its treatment with HCl (2 M) and extracted three times with CH_2Cl_2. The combined organic phases were dried with Na_2SO_4, filtered and the solvent removed under reduced pressure to afford **1a** as a white solid. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.31 (s, 3 H, CH_3CO), 5.25 (s, 2 H, CH_2NO_2). A solution of **1a** (175 mg, 1.06 mmol), DABCO (24 mg, 0.212 mmol) and the di-

polarophile (0.424 mmol) in anhydrous and ethanol-free chloroform (1.4 mL) was stirred for 20 h in a sealed vessel (Schlenk) heated at 60 °C. The solvent was then removed, and the residue dissolved in diethyl ether (15 mL) and washed with water (3 × 15 mL) and, for **4a**, with NaOH (1 M, 3 × 15 mL) and brine (3 × 15 mL). The organic layer was dried (sodium sulfate) and concentrated; if necessary, the residue was then column chromatographed on silica gel.

Isoxazoline 5a: Pentane/diethyl ether, 10:1, R_f = 0.3. Clear oil. Yield 69 mg, 90%. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.04–1.35 (m, 4 H, Norb-*H*), 1.47–1.57 (m, 2 H, Norb-*H*), 2.43 (s, 3 H, C*H*$_3$CO), 2.50 (m, 1 H, Norb-*H*), 2.59 (m, 1 H, Norb-*H*), 3.23 (d, J = 8.4 Hz, 1 H, C*H*C=N), 4.63 (d, J = 8.4 Hz, 1 H, C*H*ON) ppm. ^{13}C NMR (100.58 MHz, $CDCl_3$): δ = 22.5 (t, Norb-*C*), 26.9 (q, *C*H$_3$CO), 27.1 (t, Norb-*C*), 32.2 (t, Norb-*C*), 39.0 (d, Norb-*C*), 42.9 (d, Norb-*C*), 54.2 (d, *C*C=N), 90.7 (d, *C*ON), 158.7 (s, *C*=N), 193.2 (s, *C*=O) ppm. MS (EI): *m*/*z* (%) = 179 (100) $[M]^+$, 164 (2) $[M - CH_3]^+$, 136 (6) $[M - COCH_3]^+$, 108 (10), 91 (20), 67 (91). IR ($CDCl_3$): $\tilde{\nu}$ = 2968, 2879, 1687, 1569 cm^{-1}. $C_{10}H_{13}NO_2$ (179.22): calcd. C 67.02, H 7.31, N 7.82; found C 66.83, H 7.46, N 7.87.

Isoxazoline 6a: Pentane/ethyl acetate, 10:1, R_f = 0.3. Clear oil. Yield 48 mg, 60%. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.53 (s, 3 H, C*H*$_3$CO), 3.13 (dd, J = 17.8 and 8.8 Hz, 1 H, 4-H), 3.53 (dd, J = 17.8 and 11.6 Hz, 1 H, 4-H), 5.75 (dd, J = 11.6 and 8.8 Hz, 1 H, 5-H), 7.28–7.39 (m, 5 H, Ph-*H*) ppm. ^{13}C NMR (100.58 MHz, $CDCl_3$): δ = 26.7 (q, *C*H$_3$), 39.7 (t, C-4), 85.5 (d, C-5), 125.8 (d, 2 C, Ph-*C*), 128.7 (d, Ph-*C*$_{para}$), 128.9 (d, 2 C, Ph-*C*), 139.5 (s, Ph-*C*$_{ipso}$), 157.8 (s, C-3), 193.0 (s, *C*=O) ppm. MS (EI): *m*/*z* (%) = 189 (18) $[M]^+$, 172 (32), 143 (16), 115 (19), 105 (24) $[PhCO]^+$, 104 (100), 77 (43) $[Ph]^+$. IR ($CHCl_3$): $\tilde{\nu}$ = 3069, 3035, 2923, 1690, 1578 cm^{-1}. $C_{11}H_{11}NO_2$ (189.21): calcd. C 69.83, H 5.86, N 7.40; found C 69.93, H 5.93, N 7.43.

Isoxazole 7a: White solid. Yield 31 mg, 39%. M.p. 98–99 °C (Ref.[53] 98–99). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.67 (s, 3 H, C*H*$_3$CO), 6.86 (s, 1 H, 4-H), 7.44–7.48 (m, 3 H, Ph-*H*), 7.76–7.80 (m, 2 H, Ph-*H*$_{ortho}$) ppm. ^{13}C NMR (100.58 MHz, $CDCl_3$): δ = 27.3 (q, *C*H$_3$), 97.7 (d, C-4), 125.9 (d, 2 C, Ph-*C*$_{ortho}$), 126.7 (s, Ph-*C*$_{ipso}$), 129.1 (d, 2 C, Ph-*C*$_{meta}$), 130.7 (d, Ph-*C*$_{para}$), 162.6 (s, C-3), 171.6 (s, C-5), 192.1 (s, *C*=O) ppm. MS (EI): *m*/*z* (%) = 187 (79) $[M]^+$, 172 (6) $[M - CH_3]^+$, 145 (16), 115 (19), 105 (28) $[PhCO]^+$, 77 (66) $[Ph]^+$, 51 (100). IR ($CHCl_3$): $\tilde{\nu}$ = 1705, 1572, 1446, 1436 cm^{-1}. $C_{11}H_9NO_2$ (187.19): calcd. C 70.58, H 4.85, N 7.48; found C 70.55, H 5.03, N 7.49.

General Method for Reactions of Benzoylnitromethane (1b) with Dipolarophiles

A solution of benzoylnitromethane (**1b**, 175 mg, 1.06 mmol), 1-methylimidazole (17 mg, 0.21 mmol) and the dipolarophile (0.424 mmol) in anhydrous and ethanol-free chloroform (1.4 mL) was stirred for 20 h (norbornene) or 40 h (styrene and phenylacetylene) in a sealed vessel (Schlenk) heated at 60 °C. The solvent was then removed. The residue was dissolved in diethyl ether (15 mL) and washed with brine (3 × 15 mL), NaOH (1 M, 3 × 15 mL) and brine again (3 × 15 mL). The organic layer was dried (sodium sulfate), filtered and concentrated to afford the title compound. When necessary, the workup was repeated.

Isoxazolidine 5b: Clear oil. Yield 103 mg, 100%. Analytical and spectroscopic data were identical to those previously reported.[24]

Isoxazolidine 6b: Light yellow oil. Yield 106 mg, 100%. Analytical and spectroscopic data were identical to those previously reported.[24]

Isoxazole 7b: Yellow solid. Yield 76 mg, 70%. Analytical and spectroscopic data were identical to those previously reported.[24]

General Method for the Reactions of Ethyl Nitroacetate (1c) with Dipolarophiles

A solution of ethyl nitroacetate (**1c**, 141 mg, 1.06 mmol), DABCO (24 mg, 0.212 mmol) and dipolarophile (0.424 mmol) in anhydrous and ethanol-free chloroform (1.4 mL) was stirred for 40 h in a sealed vessel (Schlenk) heated at 60 °C. The solvent was then removed. The residue was dissolved in diethyl ether (15 mL) and washed with brine (3 × 15 mL), sat. Na_2CO_3 solution (3 × 15 mL), and brine again (3 × 15 mL). The organic layer was dried (sodium sulfate) and concentrated to afford the cycloadduct.

Isoxazoline 5c: Clear oil. Yield 89 mg, 100%. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.08–1.43 (m, 4 H, Norb-*H*), 1.34 (t, 3 H, J = 7.1 Hz, C*H*$_3$), 1.49–1.57 (m, 2 H, Norb-*H*), 2.56 (m, 1 H, Norb-*H*), 2.59 (m, 1 H, Norb-*H*), 3.27 (d, J = 8.4 Hz, 1 H, C*H*C=N), 4.31 (m, 2 H, OC*H*$_2$), 4.64 (d, J = 8.4 Hz, 1 H, C*H*ON) ppm. ^{13}C NMR (100.58 MHz, $CDCl_3$): δ = 14.1 (q, *C*H$_3$), 22.6 (t, Norb-*C*), 27.2 (t, Norb-*C*), 32.3 (t, Norb-*C*), 39.3 (d, Norb-*C*), 42.9 (d, Norb-*C*), 56.5 (d, *C*C=N), 61.9 (t, O*C*H$_2$), 90.3 (d, *C*ON), 152.3 (s, *C*=N), 160.9 (s, *C*=O) ppm. MS (EI): *m*/*z* (%) = 209 (49) $[M]^+$, 192 (19), 164 (20), 67 (100). IR (KBr): $\tilde{\nu}$ = 2968, 1718 (C=O), 1583 cm^{-1}. $C_{11}H_{15}NO_3$ (209.2): calcd. C 63.14, H 7.23, N 6.69; found C 63.07, H 7.36, N 6.51.

Isoxazoline 6c: Clear oil. Yield 85 mg, 91%. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.36 (t, 3 H, J = 7.2 Hz, C*H*$_3$), 3.20 (dd, J = 17.6 and 8.8 Hz, 1 H, 4-H), 3.62 (dd, J = 17.6 and 11.6 Hz, 1 H, 4-H), 4.35 (q, 2 H, J = 7.2 Hz, OC*H*$_2$), 5.75 (dd, J = 11.6 and 8.8 Hz, 1 H, 5-H), 7.30–7.37 (m, 5 H, Ph-*H*) ppm. ^{13}C NMR (100.58 MHz, $CDCl_3$): δ = 14.1 (q, *C*H$_3$), 41.5 (t, C-4), 62.1 (t, *O*C*H*$_2$), 85.0 (d, C-3), 125.7 (d, 2 C, Ph-*C*), 128.7 (d, Ph-*C*), 128.9 (d, 2 C, Ph-*C*), 139.5 (s, Ph-*C*), 151.1 (s, C-5), 160.6 (s, *C*=O) ppm. MS (EI): *m*/*z* (%) = 219 (60) $[M]^+$, 202 (10), 190(2), 146 (32), 128 (71), 104 (100), 77 (41). IR ($CHCl_3$): $\tilde{\nu}$ = 1719 (C=O), 1590 cm^{-1}. $C_{12}H_{13}NO_3$ (219.24): calcd. C 65.74, H 5.98, N 6.39; found C 65.66, H 5.95, N 6.28.

Isoxazole 7c: White solid. Yield 92 mg, 100%. M.p. 49 °C (Ref.[54] 48–50 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.42 (t, 3 H, J = 7.0 Hz, C*H*$_3$), 4.35 (q, 2 H, J = 7.0 Hz, OC*H*$_2$), 6.61 (s, 1 H, 4-H), 7.45–7.50 (m, 3 H, Ph-*H*), 7.76–7.82 (m, 2 H, Ph-*H*$_{ortho}$) ppm. ^{13}C NMR (100.58 MHz, $CDCl_3$): δ = 14.2 (q, *C*H$_3$), 62.2 (t, *O*C*H*$_2$), 99.9 (d, C-4), 125.9 (d, 2 C, Ph-*C*$_{ortho}$), 126.6 (s, Ph-*C*$_{ipso}$), 129.1 (d, 2 C, Ph-*C*$_{meta}$), 130.8 (d, Ph-*C*$_{para}$), 157.0 (s, C-3), 160.0 (s, *C*=O), 171.7 (s, C-5) ppm. MS (EI): *m*/*z* (%) = 217 (57) $[M]^+$, 172 (22), 145 (24), 105 (100), 77 (58). IR ($CHCl_3$): $\tilde{\nu}$ = 1735 (C=O), 1613, 1573, 1448 cm^{-1}. $C_{12}H_{11}NO_3$ (217.22): calcd. C 66.35, H 5.10, N 6.45; found C 66.04, H 5.09, N 6.08.

General Method for the Reactions of Phenylsulfonylnitromethane (1d) with Dipolarophiles

A solution of phenylsulfonylnitromethane (**1d**, 214 mg, 1.06 mmol), DABCO (5 mg, 0.042 mmol) and the dipolarophile (0.424 mmol) in ethanol (1.4 mL) was stirred in a sealed vessel (Schlenk) heated at 60 °C. Additional DABCO (20 mg, 0.170 mmol) was added during the reaction in four increments after 16 h, 32 h, 48 h and 64 h. After 80 h, the formed precipitate was filtered off, and the clear solution concentrated. The residue was dissolved in diethyl ether (15 mL), washed with brine (3 × 15 mL), NaOH (1 M, 3 × 15 mL), brine again (3 × 15 mL), and the organic layer dried (sodium sulfate). The solvent was evaporated, and the residual oil was purified by column chromatography with the indicated eluent to give the pure cycloadducts.

Isoxazoline 5d: Hexane/diethyl ether, 3:1, R_f = 0.23. White powder. Yield 59 mg, 50%. M.p. 85–86 °C (Ref.[55] 85–86 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.04–1.10 (m, 1 H, Norb-*H*), 1.20–1.28 (m, 2 H, Norb-*H*), 1.33–1.39 (m, 1 H, Norb-*H*),1.48–1.60 (m, 2 H, Norb-*H*), 2.57 (m, 1 H, Norb-*H*), 2.74 (m, 1 H, Norb-*H*), 3.42 (d, *J* = 8.4 Hz, 1 H, C*H*C=N), 4.68 (d, *J* = 8.4 Hz, 1 H, C*H*ON), 7.54–7.60 (m, 2 H, Ph-*H*), 7.65–7.70 (m, 1 H, Ph-H_{para}), 7.94–7.99 (m, 2 H, Ph-*H*) ppm. ^{13}C NMR (100.58 MHz, $CDCl_3$): δ = 22.4 (t, Norb-*C*), 26.8 (t, Norb-*C*), 32.4 (t, Norb-*C*), 39.5 (d, Norb-*C*), 42.7 (d, Norb-*C*), 55.6 (d, *C*C=N), 91.6 (d, *C*ON), 128.8 (d, 2 C, Ph-*C*), 129.3 (d, 2 C, Ph-*C*), 134.6 (d, Ph-*C*), 138.2 (s, Ph-*C*), 160.7 (s, *C*=N) ppm. MS (EI): *m*/*z* (%) = 277 (5) $[M]^+$, 221, (9), 210 (4), 141 (60) $[SO_2Ph]^+$, 125 (13), 108 (28), 77 (100) $[Ph]^+$, 67 (84). IR ($CHCl_3$): $\tilde{\nu}$ = 2968, 2878, 1326, 1166 cm^{-1}. $C_{14}H_{15}NO_3S$ (277.34): calcd. C 60.63, H 5.45, N 5.05; found C 60.70, H 5.66, N 4.95.

Isoxazoline 6d: Hexane/diethyl ether, 4:1, R_f = 0.1. Column chromatography monitored by TLC with different eluent (hexane/diethyl ether, 3:2, R_f = 0.37). Clear oil. Yield 11 mg, 10%. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.32 (dd, *J* = 9.0 and 17.3 Hz, 1 H, 4-H), 3.72 (dd, *J* = 11.4 and 17.3 Hz, 1 H, 4-H), 5.78 (dd, *J* = 9.0 and 11.4 Hz, 1 H, 5-H), 7.14–7.42 (m, 5 H, Ph-*H*), 7.55–7.80 (m, 3 H, Ph-*H*), 7.98–8.08 (m, 2 H, Ph-*H*) ppm. ^{13}C NMR (100.58 MHz, $CDCl_3$): δ = 40.3 (t, C-4), 86.0 (d, C-5), 125.8 (d, 2 C, Ph-*C*), 128.8 (d, 2 C, Ph-*C*), 128.9, (d, Ph-*C*), 129.0 (d, 2 C, Ph-*C*), 129.3 (d, 2 C, Ph-*C*), 134.7 (d, Ph-*C*), 137.2 (s, Ph-*C*), 138.2, (s, Ph-*C*), 159.6 (s, C-3) ppm. MS (EI): *m*/*z* (%) = 287 (11) $[M]^+$, 146 (44), 128 (72), 115 (31), 104 (39), 77 (100) $[Ph]^+$. IR ($CHCl_3$): $\tilde{\nu}$ = 1448, 1328 cm^{-1}. $C_{15}H_{13}NO_3S$ (287.34): calcd. C 62.70, H 4.56, N 4.87; found C 62.84, H 4.36, N 4.94.

Isoxazole 7d: Hexane/diethyl ether, 3:1, R_f = 0.27. Yellowish solid. Yield 24 mg, 20%. M.p. 120–121 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.89 (s, 1 H, 4-H), 7.40–7.80 (m, 8 H, Ph-*H*), 8.02–8.18 (m, 2 H, Ph-*H*) ppm. ^{13}C NMR (100.58 MHz, $CDCl_3$): δ = 97.9 (d, C-4), 126.0 (s, Ph-*C*),126.1 (d, 2 C, Ph-*C*), 128.7 (d, 2 C, Ph-*C*), 129.2 (d, 2 C, Ph-*C*), 129.5 (d, 2 C, Ph-*C*), 131.4 (d, Ph-*C*), 134.7 (d, Ph-*C*), 138.7 (s, Ph-*C*), 166.3 (s, C-3), 172.6 (s, C-5) ppm. MS (EI): *m*/*z* (%) = 285 (4) $[M]^+$, 141 (44) $[SO_2Ph]^+$, 105 (6), 77 (77) $[Ph]^+$. IR ($CHCl_3$): $\tilde{\nu}$ = 1449, 1432, 1345, 1334 cm^{-1}. $C_{15}H_{11}NO_3S$ (285.32): calcd. C 63.14, H 3.89, N 4.91; found C 62.89, H 3.89, N 4.89.

Preparation of *N*-Methylnitroacetamide (1e): Ethyl nitroacetate (**1a**, 1.33 g, 10.0 mmol) was treated with methylamine (40% water solution, 7.8 mL), and the mixture stirred at room temperature for 3 d. A stream of N_2 was bubbled through the mixture and then HCl (5%) was added (12 mL, pH = 1–2). The aqueous solution was then concentrated to dryness, and the yellow solid residue was mixed with CH_2Cl_2 (100 mL). The obtained suspension was vigorously stirred at room temperature for 2 h. After filtration, the solvent was removed under reduced pressure to afford **1e** as a white solid. Yield 1.08 g, 92%. M.p. 68–69 °C (Ref.[56] 67–69 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.90 (d, *J* = 4.8 Hz, 3 H, CH_3), 5.08 (s, 2 H, CH_2), 6.48 (br. s, 1 H, N*H*) ppm. ^{13}C NMR (100.58 MHz, $CDCl_3$): δ = 26.7 (q, *C*H_3), 77.8 (t, *C*H_2), 160.7 (s, *C*=O) ppm. MS (EI): *m*/*z* (%) = 118 (5) $[M]^+$, 88 (1), 72 (82), 58 (100) $[CH_3NCO]^+$. IR ($CDCl_3$): $\tilde{\nu}$ = 3433 (NH), 1696 (C=O), 1563, 1533, 1416, 1374 cm^{-1}. $C_3H_6N_2O_3$ (118.08): calcd. C 30.51, H 5.12, N 23.72; found C 30.47, H 5.21, N 23.56.

General Method for the Reactions of *N*-Methylnitroacetamide (1e) with Dipolarophiles

A solution of **1e** (125 mg, 1.06 mmol), DABCO (24 mg, 0.212 mmol) and the dipolarophile (0.424 mmol) in anhydrous and ethanol-free chloroform (1.4 mL) was stirred for 20 h in a sealed vessel (Schlenk) heated at 60 °C. The solvent was then removed, and the residue was dissolved in diethyl ether (15 mL), washed with water (3 × 15 mL), NaOH (1 M, 3 × 15 mL) and then brine (3 × 15 mL). The organic layer was dried (sodium sulfate) and concentrated to afford the final product.

Isoxazoline 5e: Colourless crystals. Yield 82 mg, 100%. M.p. 123–124 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.02–1.12 (m, 1 H, Norb-*H*), 1.20–1.36 (m, 1 H, Norb-*H*), 1.22–1.38 (m, 2 H, Norb-*H*), 1.44–1.59 (m, 2 H, Norb-*H*), 2.53 (m, 1 H, Norb-*H*), 2.60 (s, 1 H, Norb-*H*), 2.85 (d, *J* = 5.2 Hz, 3 H, CH_3), 3.33 (d, *J* = 8.4 Hz, 1 H, C*H*C=N), 4.58 (d, *J* = 8.4 Hz, 1 H, C*H*ON), 6.57 (br. s, N–*H*) ppm. ^{13}C NMR (100.58 MHz, $CDCl_3$): δ = 22.6 (t, Norb-*C*), 25.9 (NH*C*H_3), 27.1 (t, Norb-*C*), 32.2 (t, Norb-*C*), 39.2 (d, Norb-*C*), 42.9 (d, Norb-*C*), 55.7 (d, *C*C=N), 89.7 (d, *C*ON), 154.2 (s, C-3), 160.4 (s, *C*=O) ppm. MS (EI): *m*/*z* (%) = 194 (6) $[M]^+$, 165 (4), 127 (8), 81 (77), 58 (100) $[CH_3NCO]^+$. IR (KBr): $\tilde{\nu}$ = 3435 (NH), 2968, 1676 (C=O), 1588, 1542 cm^{-1}. $C_{10}H_{14}N_2O_2$ (194.23): calcd. C 61.84, H 7.26, N 14.42; found C 61.55, H 7.27, N 14.28.

Isoxazoline 6e: White solid. Yield 60 mg, 70%. M.p. 111 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.92 (d, *J* = 5.1 Hz, 3 H, NCH_3), 3.25 (dd, *J* = 18.0 and 8.8 Hz, 1 H, 4-H), 3.64 (dd, *J* = 18.0 and 11.3 Hz,1 H, 4-H), 5.71 (dd, *J* = 11.4 and 8.8 Hz, 1 H, 5-H), 6.64 (br. s, 1 H, N*H*), 7.28–7.40 (m, 5 H, Ph-*H*), ppm. ^{13}C NMR (100.58 MHz, $CDCl_3$): δ = 26.1 (q, N*C*H_3), 41.2 (t, C-4), 84.7 (d, C-5), 125.9 (d, 2 C, Ph-*C*), 128.6 (d, Ph-*C*), 128.8 (d, 2 C, Ph-*C*), 139.6 (s, Ph-*C*), 153.6 (s, C-3), 160.1 (s, *C*=O) ppm. MS (EI): *m*/*z* (%) = 204 (36) $[M]^+$, 203 (60),187 (33), 105 (21), 104 (61), 58 (100) $[CH_3NCO]^+$. IR ($CHCl_3$): $\tilde{\nu}$ = 3453 (NH), 1679 (C=O), 1596, 1541 cm^{-1}. $C_{11}H_{12}NO_2$ (204.23): calcd. C 64.69, H 5.92, N 13.72; found C 64.30, H 5.88, N 13.78.

Isoxazole 7e: White solid. Yield 35 mg, 41%. M.p. 198–199 °C (Ref.[57] 199–200 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.01 (d, *J* = 4.8 Hz, 3 H, NCH_3), 6.95(s, 1 H, 4-H), 7.42–7.50 (m, 3 H, Ph-*H*), 7.74–7.80 (m, 2 H, Ph-*H*) ppm. ^{13}C NMR (100.58 MHz, $CDCl_3$): δ = 26.1 (q, N*C*H_3), 99.0 (d, C-4), 125.9 (d, 2 C, Ph-C_{ortho}), 126.8 (s, Ph-C_{ipso}), 129.1 (d, 2 C, Ph-C_{meta}), 130.7 (d, Ph-C_{para}), 159.1 (s, C-3)*, 159.6 (s, *C*=O)*, 171.7 (s, C-5), ppm, *may be exchanged. MS (EI): *m*/*z* (%) = 202 (38) $[M]^+$, 172 (34) [M – NHCH]$^+$, 145 (20), 105 (56) $[PhCO]^+$, 77 (44) $[Ph]^+$, 58 (100) $[CONHMe]^+$. IR ($CHCl_3$): $\tilde{\nu}$ = 3433, 1685 (C=O), 1551, 1447 cm^{-1}. $C_{11}H_{10}N_2O_2$ (202.21): calcd. C 65.34, H 4.98, N 13.85; found C 65.59, H 5.03, N 13.81.

Preparation of Phenylnitromethane (1f): Crude compound **1f** (8 g, 97%) was obtained according to a previously described procedure from benzyl bromide (10.3 g, 60.0 mmol), sodium nitrite 6.21 g, (90.0 mmol) and urea (7.09 g), in DMF (90 mL).[58] The workup was slightly modified, diethyl ether was used as the solvent for the extraction instead of dichloromethane. Freshly pure **1f** was prepared immediately prior to use through chromatography: pentane/diethyl ether, 10:1 R_f = 0.3. ^{1}H NMR and ^{13}C NMR spectroscopic data are identical to those reported in the literature.[59,60]

General Method for the Reaction of Phenylnitromethane (1f) with Dipolarophiles

A solution of **1f** (146 mg, 1.06 mmol), DABCO (24 mg, 0.212 mmol) and the dipolarophile (0.424 mmol) in anhydrous and ethanol-free chloroform (1.4 mL) was stirred for 20 h (norbornene) or 40 h (styrene and phenylacetylene) in a sealed vessel (Schlenk) heated at 60 °C. The solvent was then removed; the residue was dissolved in diethyl ether (15 mL) and washed with water (3 × 15 mL), NaOH (1 M, 3 × 15 mL) and then brine (3 × 15 mL portions). The organic layer was dried (sodium sulfate) and concen-

trated. The crude product was triturated in ice-cold diethyl ether and then filtered to afford the final product.

Isoxazoline 5f: Colourless crystals. Yield 86 mg, 95%. M.p. 98–99 °C (Ref.[61] 99–100 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.16–1.39 (m, 4 H, Norb-*H*), 1.50–1.62 (m, 2 H, Norb-*H*), 2.51 (m, 1 H, Norb-*H*), 2.60 (s, 1 H, Norb-*H*), 3.48 (d, J = 8.4 Hz, 1 H, C*H*C=N), 4.62 (d, J = 8.4 Hz, 1 H, C*H*OH), 7.30–7.43 (m, 3 H), 7.64–7.77 (m, 2 H, Ph-H_{ortho}) ppm. ^{13}C NMR (100.58 MHz, $CDCl_3$): δ = 22.7 (t, Norb-*C*), 27.4 (t, Norb-*C*), 32.3 (t, Norb-*C*), 39.2 (d, Norb-*C*), 42.9 (d, Norb-*C*), 57.0 (d, *C*C=N), 87.8 (d, *C*ON), 126.8 (d, 2 C, Ph-C_{ortho}), 128.6 (d, 2 C Ph-C_{meta}), 129.3 (s, Ph-C_{ipso}), 129.7 (d, Ph-C_{para}), 156.9 (s, *C*=N) ppm. MS (EI): *m*/*z* (%) = 213 (100) $[M]^+$, 184 (12), 157 (40), 146 (38), 117 (38), 104 (20), 77 (46) $[Ph]^+$, 46). IR (KBr): $\tilde{\nu}$ = 2969, 1594, 1446, 1354 cm^{-1}. $C_{14}H_{15}NO$ (213.28): calcd. C 78.84, H 7.09, N 6.57; found C 78.92, H 7.25, N 6.31.

Isoxazoline 6f: White solid. Yield 76 mg, 80%. M.p. 71–72 °C (Ref.[62] 73–74 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.92 (d, J = 5.1 Hz, 3 H, NCH_3), 3.33 (dd, J = 16.6 and 8.4 Hz, 1 H, 4-H), 3.77 (dd, J = 18.0 and 10.8 Hz,1 H, 4-H), 5.73 (dd, J = 8.8 and 10.8 Hz, 1 H, 5-H), 7.35–7.43 (m, 8 H), 7.65–7.72 (m, 2 H) ppm. ^{13}C NMR (100.58 MHz, $CDCl_3$): δ = 43.2 (t, C-4), 82.6 (d, C-5), 125.9 (d, 2 C, Ph-*C*), 126.7 (d, 2 C, Ph-*C*), 128.2 (d, Ph-*C*), 128.7 (d, 2 C, Ph-*C*), 128.8 (d, 2 C, Ph-*C*), 129.5 (s, Ph-*C*), 130.1 (d, Ph-*C*), 140.9 (s, Ph-*C*), 156.1 (s, *C*=N) ppm. MS (EI): *m*/*z* (%) = 223 (76) $[M]^+$, 206 (12), 115 (45), 104 (100), 77 (64) $[Ph]^+$, 64). IR ($CHCl_3$): $\tilde{\nu}$ = 3067, 3034, 2922, 1600, 1477, 1355 cm^{-1}. $C_{15}H_{13}NO$ (223.27): calcd. C 80.69, H 5.87, N 6.27; found C 80.55, H 6.24, N 5.99.

Isoxazole 7f: Colourless crystals. Yield 52 mg, 55%. M.p. 139–140 °C (Ref.[63] 139–140 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.82 (s, 1 H, 4-H), 7.40–7.52 (m, 6 H, Ph-*H*), 7.80–7.88 (m, 4 H, Ph-*H*) ppm. ^{13}C NMR (100.58 MHz, $CDCl_3$): δ = 97.5 (d, C-4), 125.8 (d, 2 C, Ph-*C*), 126.8 (d, 2 C, Ph-*C*), 127.5 (s, Ph-*C*), 128.9 (d, 2 C, Ph-*C*), 129.0 (d, 2 C, Ph-*C*), 129.2 (s, Ph-*C*) 130.0 (d, Ph-*C*), 130.2 (d, Ph-*C*), 163.0 (s, C-3) 170.4 (s, C-5) ppm. MS (EI): *m*/*z* (%) = 221 (47) $[M]^+$, 193 (8), 144 (14), 105 (100) $[PhCO]^+$, 77 (87) $[Ph]^+$. IR ($CHCl_3$): $\tilde{\nu}$ = 3066, 1573 (C=N), 1464, 1452, 1402 cm^{-1}. $C_{15}H_{11}NO$ (221.25): calcd. C 81.43, H 5.01, N 6.33; found C 81.47, H 5.05, N 6.51.

Screening of the Solvents

The screening of different solvents (Table 2) was performed in an apparatus where six reactions were carried out simultaneously. A mixture of DABCO (0.21 mmol) and styrene (0.42 mmol) with either **1b** or **1c** (1.06 mmol) in the solvent (1.4 mL) was heated at 60 °C for 20 h and 40 h, respectively. After the allotted time, an aliquot was withdrawn from the reaction mixture, diluted with $CDCl_3$ (0.6 mL) and the ^{1}H NMR spectrum registered. Integration of one of the proton signals of cycloadduct **6c** (3.20 or 3.62 ppm) or cycloadduct **6b** (3.38 or 3.77 ppm) and the ethylene protons of styrene (d, 5.22 ppm) gave the conversion ratio. After concentration in vacuo and addition of an internal standard (2′,4′-dimethoxyacetophenone, 27–34 mg, 0.16–0.19 mmol), an aliquot was withdrawn from the reaction mixture, dissolved in $CDCl_3$ (0.6 mL) and the ^{1}H NMR spectrum registered. Integration of the signals for the 3′- and 5′ protons of the internal standard (m, 6.40–6.58 ppm) and one of signals for the 4-H protons of cycloadduct **6c** (3.20 or 3.62 ppm) or one of the signals for the 4-H protons of cycloadduct **6b** (dd, 3.38 ppm or dd, 3.77 ppm) gave the spectroscopic yield.

Screening of the Bases

The screening of different bases (Table 3) was performed in an apparatus where six reactions were carried out simultaneously. The base (0.21 mmol), the dipolarophile (0.42 mmol), the nitro compound (1.06 mmol) and chloroform (1.4 mL) were heated at 60 °C and stirred in a sealed tube. After a preliminary screening, a reaction time that ensured the complete conversion of the dipolarophile by DABCO was applied to all the bases. This procedure allows for the comparison of the efficiency of the different bases. After the allotted time, an aliquot was withdrawn from the reaction mixture, diluted with $CDCl_3$ (0.6 mL) and the ^{1}H NMR spectrum registered. The percent conversion was evaluated for **1c** by the integration of the C*H*ON proton signal (d, 4.64 ppm) of cycloadduct **5c** and the ethylene proton signal of norbornene (s, 5.90 ppm). For **1b**, the ratio was determined by the integration of one of the 4-H proton signals (dd, 3.38 ppm or dd, 3.77 ppm) of cycloadduct **6b** and the ethylene proton signal of styrene (d, 5.21 ppm). After concentration in vacuo and addition of an internal standard (2′,4′-dimethoxyacetophenone, 27–34 mg, 0.16–0.19 mmol) an aliquot was withdrawn from the reaction mixture, dissolved in $CDCl_3$ (0.6 mL) and the ^{1}H NMR spectrum registered. Integration of the signals for the 3′- and 5′ protons of the internal standard (m, 6.40–6.58 ppm) and the signal for the C*H*ON proton (d, 4.64 ppm) of cycloadduct **5c** and one of the signals for the 4-H protons (dd, 3.38 ppm or dd, 3.77 ppm) of cycloadduct **6b** gave the spectroscopic yield. In the case of an unclear result, a duplicate experiment was run.

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