Solid-Supported Nitrile Oxides as Stable and Valuable Reactive Intermediates

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1,3-Dipolar cycloadditions of Wang resin supported nitrile oxides have been performed with several dipolarophiles to afford 5-membered heterocycles in fair yields. The nitrile oxides displayed increased stability on the solid phase, allowing clean transformations into nitrosocarbonyl intermediates, which could be trapped with suitable dienes to afford hetero Diels–Alder cycloadducts in moderate yields.

Introduction

Applications of combinatorial chemistry and other high-throughput synthetic technologies promise to revolutionize the way in which new biologically active compounds are discovered and developed. Solid-Phase Organic Chemistry (SPOC) provides a rapid method for generating small-molecule libraries, and 1,3-dipolar cycloadditions in particular are one of the most efficient methods for building structurally diverse 5-membered heterocycles. These are very often the core structure of pharmaceutical agents, or they represent useful synthetic intermediates towards their synthesis.[1,2]

Until recently, SPOC literature[3] reported few examples of 1,3-dipolar cycloadditions. Reactions involving nitrile oxides were performed by two main procedures. Typically, the simpler one involved the attachment of the dipolarophile onto the solid support, and this was then treated with a 1,3-dipole generated in situ.[4] Alternatively, the resin carried a masked functionality, such as a nitro group, which was exposed to isocyanates to afford nitrile oxides, and these were then immediately trapped with olefins.[5] More recently, different authors have suggested direct methods to prepare 1,3-dipoles on resins. In situ generation of nitrile oxides, followed by immediate trapping with dipolarophiles, has been performed both on aldoximes grafted onto Wang resin[6a] and on a β-dimethylphenylsilylmethyl ester linker.[6b] Supported hydroximoyl chlorides on Wang and chlorotrityl resins have become available as stable precursors of nitrile oxides.[6c][6d] Supported nitrile oxides have also been used to obtain small isoxazole and isoxazoline libraries.[7]

The well-known tendency of nitrile oxides to undergo dimerization reactions is reduced under solid-phase (SP) conditions, as the distance between the reactive sites is increased on resins. Accordingly, the SP approach might also stabilise other 1,3-dipoles that, under classic solution conditions, have to be generated in situ and immediately trapped by reacting dipolarophiles. Their increased stability should not only allow easier handling of 1,3-dipoles, simplifying reaction conditions and increasing yields, but should also open a route to additional, useful transformations of nitrile oxides that would otherwise be prevented.

In this paper we wish to present detailed results in the field of cycloadditions with supported nitrile oxides, focusing our attention on their stability and on their multi-step SP transformations.

Results and Discussion

Synthesis of Polymer-Bound Hydroximoyl Chlorides

Wang resin (*p*-benzyloxybenzyl alcohol resin, loading 0.89−1.03 mmol/g; **W-OH**; Scheme 1) was coupled with either *m*- or *p*-carboxybenzaldehyde according to the standard DIC/DMAP coupling procedure[8] to afford the resin-bound aldehydes **1(*m*,*p*)**. These were converted into the corresponding aldoximes **2(*m*,*p*)** by addition of an excess of hydroxylamine hydrochloride in methanol in the presence of an excess of Et_3N, and then stirring for 2 d at room temp.[6b] Treatment of **2(*m*,*p*)** with an excess of *N*-chlorosuccinimide (NCS) in dichloromethane (DCM) at room temp. for 2 h yielded the hydroximoyl chloride derivatives **3(*m*,*p*)**.[6a]

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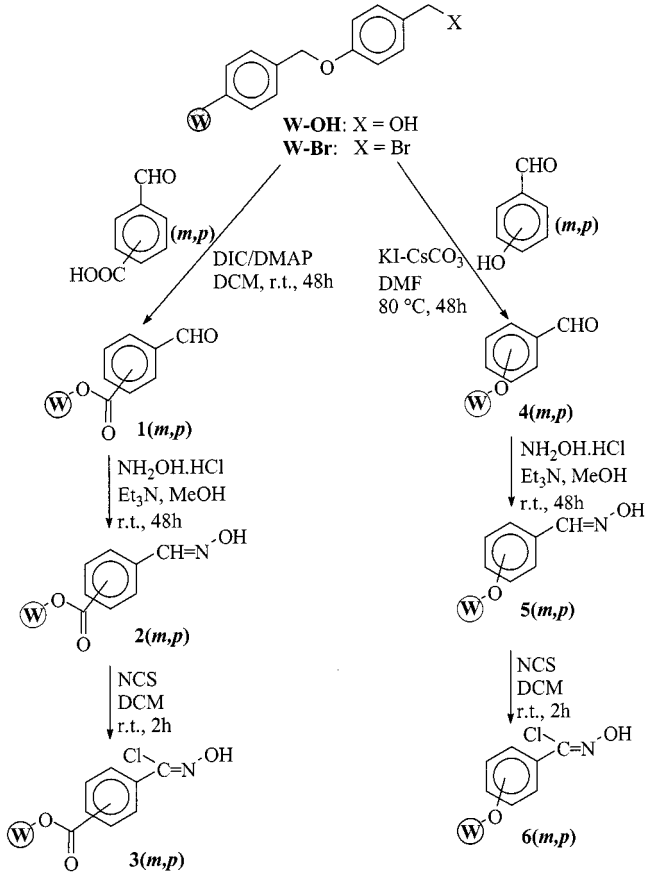


Scheme 1

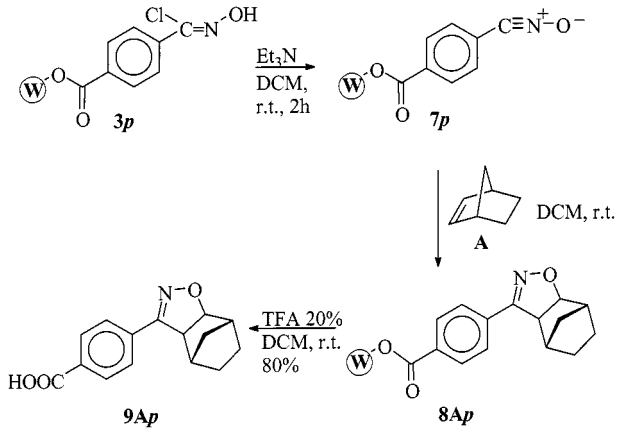
The three SP steps were monitored by gel-phase ^{13}C NMR[9] and FT IR (Diffuse Reflectance, DR) spectroscopy. Comparison of the ^{13}C NMR spectra of naked **W-OH** with those of supported aldehydes **1(*m,p*)** showed a shift from δ = 66.3 to 67.0 for the signal of the benzyl moiety (CH_2−OH), due to the neighbouring carbonyl group (δ = 191.2). Ester formation was also confirmed by FT IR, the OH stretching band at 3430 cm^{-1} disappearing and the carbonyl band of **1(*m,p*)** appearing at 1718 cm^{-1}. The aldoximes **2(*m,p*)** showed the presence of the OH FT IR stretching band at about 3398 cm^{-1} and the *CH*=N ^{13}C NMR signal at δ = 149.3. The latter signal disappeared when a chlorine atom was inserted by NCS treatment to give **3(*m,p*)**.

Alternatively, *m*- or *p*-hydroxybenzaldehyde were attached to the bromo Wang resin [4-(bromomethyl)phenoxymethyl polystyrene resin; 1.10−1.40 mmol/g; **W-Br**] under standard nucleophilic substitution conditions[10] to give the resin-bound aldehydes **4(*m,p*)**. These were converted first into the aldoximes[6b] **5(*m,p*)** and then into the corresponding hydroximoyl chlorides[6a] **6(*m,p*)** by the procedures described above. The gel-phase ^{13}C NMR and FT IR spectra were in accordance with those previously described.

Generation, Isolation, and Stability of Supported Nitrile Oxides

It is known that nitrile oxides show the propensity to undergo rapid dimerization.[11] Even though their use on solid support can circumvent this problem, providing cycloadducts in high yields and purities, the full characterization of supported nitrile oxides remained unexplored. Their stability was thus inferred by generating nitrile oxides on SP in absence of any trapping agent and monitoring the appearance of the typical nitrile oxide band by FT IR.

Excess Et_3N (2 equiv.) was added to a DCM suspension of **3*p*** at room temp., and stirring was continued for 2 h (Scheme 2). After washes with DCM and ether, a dry resin sample was analysed by FT IR (DR), revealing the presence of the typical strong nitrile oxide band[12] at 2296 cm^{-1}. The supported **7*p*** was then divided into two parts. The first aliquot was immediately converted into the supported cycloadduct by addition of an excess of norbornene (**A**) to a DCM resin suspension of **7*p*** to afford **8A*p***. The gel-phase ^{13}C NMR spectrum of **8A*p***, on comparison with that of the cycloadduct obtained by cycloaddition of benzonitrile oxide (BNO) with norbornene in solution,[13] confirmed the presence of the desired supported cycloadduct. Cleavage of **8A*p*** (TFA 20% in DCM) afforded pure carboxylic acid **9A*p*** in 80% yield (Scheme 2). The second aliquot of **7*p*** was kept in a dry-box at room temp. for 3 weeks and periodically checked for stability by FT IR. The characteristic strong nitrile oxide band did not change significantly upon standing for 2, 4, 12, or 24 hours (Table 1). The relative intensity of the nitrile oxide band showed a detectable de-



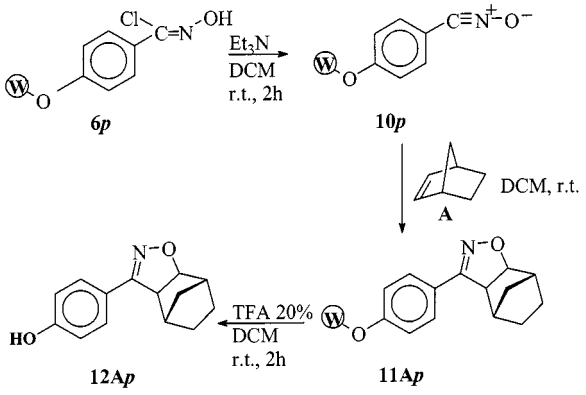
Scheme 2

Table 1. Time evolution of nitrile oxide IR band and norbornene capture yields

Run	Time	Relative intensity of the nitrile oxide band at 2296 cm^{-1}	Norbornene trapping: yield of **9A*p*** (%)
1	0	1.00	85
2	2 h	0.96	–
3	4 h	0.94	–
4	12 h	0.92	–
5	1 d	0.86	75
6	3 d	0.64	42
7	1 week	0.37	23
8	3 weeks	0.13	0

crease due to decomposition only after 3 d. After 1 week, the nitrile oxide IR band was notably weakened, and after 3 weeks only a small remnant of this band remained. A few samples of this resin were converted into the norbornene cycloadduct (runs 1, 5, 6, 7, 8; Table 1). Gel-phase ^{13}C NMR spectra showed a progressive decrease in the intensity of the characteristic norbornene adduct ^{13}C NMR signals when compared to those obtained with a freshly prepared sample. Standard cleavage gave the cycloadduct **9A*p*** with yields decreasing from 85% (run 1) to 23% (run 7). No signals attributable to the norbornene cycloadduct **8A*p*** could be detected when the resin aliquot stored for 3 weeks at room temp. was treated with norbornene and cleaved (run 8; Table 1).

In order to verify the effect of the substituent on the aromatic ring on the stability of the supported nitrile oxides, a swollen aliquot of the *p*-alkoxy-substituted derivative **6*p*** was used to generate the corresponding nitrile oxide **10*p*** by addition of an excess of Et_3N at room temp. (Scheme 3). After the usual workup, a strong FT IR band at 2296 cm^{-1} attested to the presence of the nitrile oxide moiety. No detectable changes were observed by FT IR over a couple of days. Treatment of **10p** with norbornene gave **11A*p***, which furnished cycloadduct **12A*p*** in yields similar to those obtained for **9A*p*** after TFA cleavage (Scheme 3).



Scheme 3

The increased stability of nitrile oxides on resin can presumably be attributed to site-site isolation, the near impossibility of dimerization between two molecules anchored on two resin chains. In comparison, BNO can only survive in solution for a short period (30−60 min) and undergoes rapid dimerization at room temp.[11,12,14] Even though the origin of the decomposition of nitrile oxide on resin is not clear, it could not have been due to a dimerization process since no furoxan or other dimeric products were isolated. In conclusion, supported nitrile oxides can be safely stored in a dry and cool place for at least 1 d, allowing further clean transformations of the reactive nitrile oxide functionality.

Cycloaddition Reactions to Resin-Bound Nitrile Oxides

Reactivity screening of supported nitrile oxides was performed by trapping the 1,3-dipoles generated in situ with several dipolarophiles, by applying the following standard procedure.

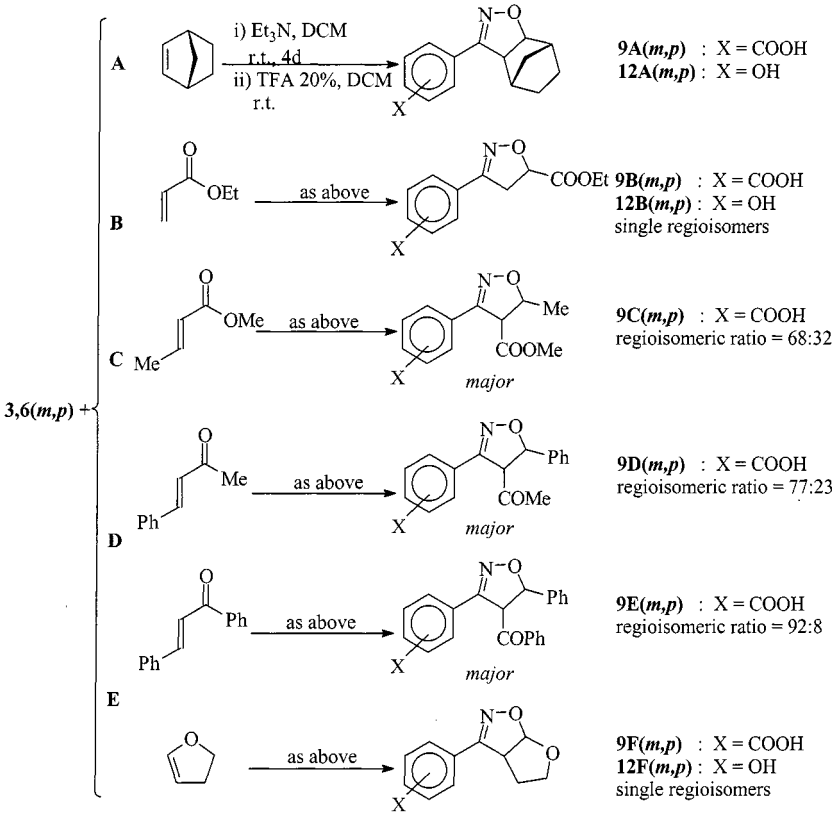
Wang resin bound hydroximoyl chlorides **3(*m,p*)** and **6(*m,p*)** (Scheme 4) were swollen in DCM, and an excess of dipolarophile (10 equiv.) was added; 2 equiv. of Et_3N was added afterwards to generate the nitrile oxides in situ, and the suspensions were stirred for 4 d at room temp. The resins were filtered and washed with DCM, MeOH, and DCM to ensure complete removal of excess reagents and finally dried under vacuum. The FT IR (DR) and gel-phase ^{13}C NMR spectra of the resins were recorded to monitor reaction completion (see Exp. Sec. for details). Cleavage of the cycloadducts with TFA (20%) in DCM at room temp. afforded the crude cycloadducts **9A−F(*m,p*)** and **12A**,**B**,**F(*m,p*)**, which were purified either by column chromatography or by simple crystallization.

Table 2 gives the yields of both crude and purified compounds **9A−F** and **12A**,**B**,**F**. The structures of the cleaved cycloadducts from the resin were confirmed by their analytical and spectroscopic data. All ^1H NMR spectra of cycloadducts **9A(*m,p*)**, **12A(*m*)**, and **12A(*p*)**[6a] were in accordance with the spectrum of the reference BNO/norbornene cycloadduct.[13] Cycloadducts **9B(*m,p*)** and **12B(*m,p*)** were obtained as single 5-substituted regioisomers, in accordance with the reported main orientations of the cycloadditions between BNO and monosubstituted α,β-unsaturated esters.[15] Cycloadducts **9C−E(*m,p*)** were isolated as mixtures of regioisomers, the structures of which were assigned by use both of spectroscopic data and of correlation with similar compounds reported in the literature.[6b,15,16] The structures of the major regioisomers, with their relative regioisomeric ratios, are shown in Scheme 4. No appreciable variations in the regioisomeric ratios could be identified on moving from solution[15,16] to SP. The cycloadducts **9F(*m,p*)** and **12F(*m,p*)** with dihydrofuran were also isolated as single regioisomers; their analytical and spectroscopic data were fully consistent with the proposed structures, in accordance with the known data of cycloadducts between BNO and dihydrofuran.[17]

The reported results clearly show the wide applicability of 1,3-dipolar cycloadditions between supported nitrile oxides generated in situ and a variety of dipolarophiles characterized by different electronic demand. The cycloadditions on SP occurred with fair to good yields (with the exception of that of dipolarophile **E**) and the purities of the products were generally acceptable.

Although *meta* or *para* substitution on the reacting 1,3-dipoles did not influence cycloaddition yields, the electronic character of the 1,3-dipole substituent, as well as the substitution pattern on the dipolarophile, did show some effects (Table 2).

As for 1,3-dipolar cycloadditions in solution, 1,2-disubstituted electron-poor alkenes displayed reactivity (and regioselectivity) lower than that of the corresponding monosubstituted olefins (Entries 3−5 vs. Entry 2). Electron-rich dipolarophiles give comparably good reaction yields (Entries 1, 6). As far as the electronic character of the aromatic substituent on the reacting nitrile oxide was concerned,



Scheme 4

Table 2. Yields after purification [yields of crude] of cycloadducts **9** and **12** from nitrile oxides generated in situ

X = COOH	Entry	Dipolarophile	**9*m***	**9*p***
	1	**A**	74 [95]	80 [94]
	2	**B**	84 [95]	80 [95]
	3	**C**	42 [79]	41 [60]
	4	**D**	47 [75]	50 [87]
	5	**E**	15 [70]	34 [75]
	6	**F**	80 [95]	90 [96]
X = OH			**12*m***	**12*p***
	7	**A**	45 [52]	43 [75]
	8	**B**	46 [59]	47 [57]
	9	**F**	54 [72]	58 [71]

lower reactivity was observed in cycloadditions involving the alkoxy-substituted nitrile oxides (Entries 7−9 vs. 1, 2, 6). These data seem to confirm the higher reactivity of electron-poor nitrile oxides with both electron-rich (Entries 1, 6) and electron-poor dipolarophiles (Entry 2).

The difference in the results obtainable by use of isolated nitrile oxide (Scheme 2) or by trapping the 1,3-dipole generated in situ was tested in cycloadditions involving dipolarophiles **A**, **B**, and **F**; the relative results are gathered in Table 3.

Table 3. Comparison between yields after purification [yields of crude] from nitrile oxides generated in situ [Method A] and isolated nitrile oxides [Method B]

Entry	Dipolarophile	Method A	Method B
1	A	80 [94]	85 [90]
2	B	80 [95]	86 [91]
3	F	90 [96]	94 [96]

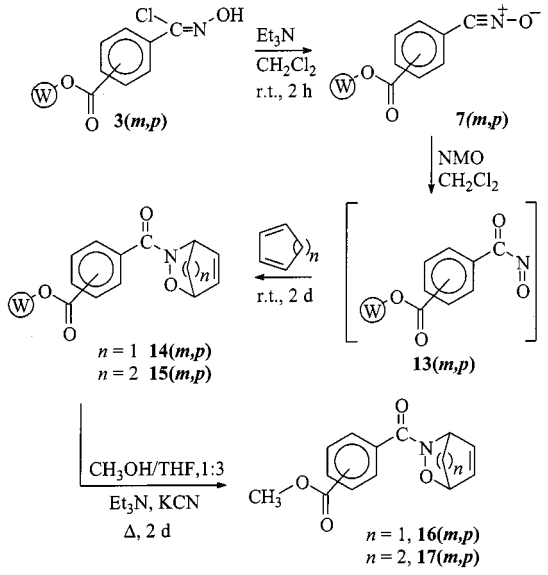
Better results were obtained by first generating the nitrile oxide on SP, since cycloaddition reactions could be run in a simpler way, affording clean cycloadducts in higher yields and allowing more flexible synthetic applications.

Mild Oxidation of Nitrile Oxides to Nitrosocarbonyl Intermediates

The stability of nitrile oxides on SP prompted us to exploit further SP transformations. Recently, it was reported that both stable nitrile oxides and also those generated in situ can be oxidized by tertiary amine *N*-oxides under mild conditions to give nitrosocarbonyl intermediates.[18] These derivatives constitute an important class of dienophiles widely used in organic syntheses and extensively studied by Kirby.[19] Nitrosocarbonyls are extremely labile and do not survive long, but must be instantly trapped in solution with suitable dienes.[18b]

Since nitrile oxides on SP could be a useful and stable source of these intermediates, we explored the possibility of generating nitrosocarbonyls on Wang resin and trapping them with typical dienes.

Wang resin-supported hydroximoyl chlorides **3(*m,p*)** (Scheme 5) were swollen in DCM and an excess of Et_3N was added at room temp. whilst stirring for 2 h. After filtration and the usual washings, the nitrile oxides **7(*m,p*)** were allowed to swell in DCM, and a solution containing an excess of *N*-methylmorpholine *N*-oxide (NMO, 3 equiv.) and an excess of either freshly distilled cyclopentadiene or 1,3-cyclohexadiene (4 equiv.) was added. The resulting suspension was vigorously stirred for 2 d at room temp. The simultaneous addition of the oxidizing and trapping agents prevented the 1,3-dipolar cycloaddition between the nitrile oxide and the diene, ensuring immediate trapping of the highly reactive nitrosocarbonyl intermediate formed by oxidation of **7(*m,p*)**. The presence of supported hetero Diels−Alder (HDA) cycloadducts **14(*m,p*)** and **15(*m,p*)** on the resins was confirmed by FT IR (DR) and gel-phase ^{13}C NMR (see Exp. Sect. for details). The cleavage procedure for HDA cycloadducts had to be optimised as the use of TFA solutions was prevented by the presence of acid-labile N−O functionalities in **14(*m,p*)** and **15(*m,p*)**.



Scheme 5

The ester-supported cycloadducts were thus cleaved under transesterification conditions: compounds **14/15(*m,p*)** were allowed to swell in a CH_3OH/THF (1:3) mixture in the presence of Et_3N (10 equiv.) and KCN (2 equiv.) under gentle reflux for 2 d.[20] The resins were washed and filtered off, and the organic phases were washed with water, dried with Na_2SO_4 and concentrated to give the crude cleaved cycloadducts **16(*m,p*)** and **17(*m,p*)** in moderate yields (20−30%). Purification by column chromatography afforded pure compounds in 10−20% yields.

Three competitive reactions − namely the desired cycloaddition of the nitrosocarbonyl intermediates, the fast decomposition of nitrosocarbonyls and the undesired cycloaddition of the nitrile oxide precursor − may account for the lower yields observed on SP with respect to the classical solution phase synthesis. As all three processes are extremely fast, it might not be easy to drive the reaction towards a single path.

On the other hand, HDA nitrosocarbonyl cycloadducts could be obtained by generating the nitrile oxide in situ in the presence of NMO. In this case the yields of HDA cycloadducts were disappointing, and sometimes the reactions did not work at all. This in our opinion constitutes the best evidence that prior isolation of the nitrile oxide and its subsequent oxidation in situ minimizes side reactions, such as degradation of the nitrosocarbonyl and/or 1,3-dipolar cycloaddition of nonoxidized nitrile oxide to the diene, and thus is essential for generation of highly reactive nitrosocarbonyl dienophiles.

These preliminary results, as related to the synthetic relevance[21] of nitrosocarbonyl intermediates, represent a "Solid" ground on which to develop nitrosocarbonyl chemistry on a polymeric "Phase".

Conclusions

The chemistry of 1,3-dipoles is widely employed in organic syntheses, and 1,3-dipoles are indeed the most powerful tool to access a variety of heterocycles. Their use in SPOC has recently received increasing attention, but difficulties in translating the solution procedures to SP are significant. For example, experimental conditions must often be properly regulated on SP since some aggressive reagents cannot be used in the presence of a polymeric support or of common SP linkers.

The results reported here refer to the preparation of various supported nitrile oxides, their isolation, and their stability after prolonged storing. Treatment with various dipolarophiles afforded good yields of cycloadducts with stereochemical outcomes similar to those of classical solution-phase chemistry. Moreover, the somewhat surprising stability of supported nitrile oxides ensured high purities in the cycloadducts and opens the way to detailed studies of supported nitrosocarbonyls. The synthesis of high-quality, diverse heterocyclic libraries should be the ultimate result of these and other ongoing investigations in our groups.

Experimental Section

All melting points are uncorrected. Elemental analyses were done with a C. Erba 1106 elemental analyser. ^1H and ^{13}C NMR spectra were recorded with a Bruker AVANCE 300 spectrometer (solvents specified). Chemical shifts are expressed in ppm from internal tetramethylsilane (δ) and coupling constants are in Hertz (Hz): br., broad; s, singlet; br. s, broad singlet; d, doublet; t, triplet; q, quadruplet; quint, quintuplet; m, multiplet. IR spectra (nujol mulls for standard compounds and DR in KBr for resins) were recorded with an FT IR Perkin−Elmer Paragon 1000 spectrophotometer, and absorptions ($\tilde{\nu}$) are in cm^{-1}. Column chromatography and TLC: H60 and GF_{254} silica gel (Merck) respectively, eluent cyclo-

hexane/ethyl acetate (9:1) to ethyl acetate. The identification of samples from different experiments was confirmed by mixed melting points and superimposable IR spectra.

Starting and Reference Materials: Wang resins were purchased from Novabiochem: *p*-benzyloxybenzyl alcohol polystyrene resin, 100−200 mesh, loading 0.89−1.03 mmol/g and 4-(bromomethyl)-phenoxymethyl polystyrene resin, 100−200 mesh, 1.10−1.40 mmol/g. Benzhydroximoyl chloride was obtained by treatment of benzaldoxime with sodium hypochlorite.[22] Addition of a slight excess of Et_3N to a DCM solution of benzhydroximoyl chloride furnished BNO, which was used to prepare (in quantitative yield) an adduct (crystallized from ethanol) by addition of norbornene (10 equiv.).[13]

Supported aldehydes[8,10] **1,4(*m,p*)**, oximes[6b] **2,5(*m,p*)**, and hydroximoyl chlorides[6a] **3,6(*m,p*)** were prepared according to the reported procedures. Diagnostic IR bands and gel phase ^{13}C NMR signals are listed in Table 4.

Table 4. Diagnostic spectroscopic data of supported of **1−6(*m,p*)**

Product	IR: $\tilde{\nu}$ [cm^{-1}]	^{13}C NMR ($CDCl_3$): δ
1(*m,p*)	1734 (C=O)	165.4 (C=O); 191.4 (CHO)
2(*m,p*)	3300 (OH)	149.2 (CH=N); 166.0 (C=O)
3(*m,p*)	3300 (OH)	165.8 (C=O)
4(*m,p*)	1701 (C=O)	191.0 (CHO)
5(*m,p*)	3260 (OH)	150.0 (CH=N)
6(*m,p*)	3260 (OH)	−

Supported Nitrile Oxide Preparation and Conversion into Norbornene Cycloadduct 9Ap: An excess of Et_3N (2 equiv.) was added at room temp. to a suspension of **3*p*** in DCM, and stirring was continued for 2 h. After washes with DCM and ether, a dry sample of the resin was analysed by FT IR (DR), revealing the presence of the typical nitrile oxide strong band at 2296 cm^{-1}. Cycloaddition of **7*p*** was performed by addition of an excess of norbornene to a DCM suspension of **7*p***. The supported cycloadduct **8*p*** gave the following characteristic signals in the gel-phase ^{13}C NMR spectrum: δ ($CDCl_3$) = 22.5, 27.2, 32.2 (CH_2); 39.1.42.3 (CH); 55.5 (CH); 88.3 (CH−O). Cleavage of **8A*p*** in TFA (20% DCM solution) afforded the carboxylic acid **9A*p***. When the complete reaction sequence was performed starting from 1.0 g of resin **3*p***, 0.20 g of cycloadduct **9A*p*** were obtained (80% yield); m.p. > 280 °C from ethanol. IR: ν_{OH} 2900, $\nu_{C=O}$ 1673 cm^{-1}. ^1H NMR: δ_H (DMSO) = 1.30 (m, 7 H, *CH*$_2$ and *CH*); 2.40 (s, 1 H, *CH*); 3.71 (d, 1 H, *CH*, *J* = 8.5); 4.65 (d, 1 H, *CH*−O, *J* = 8.5); 7.8 and 8.0 (AA′BB′ system, 4 H, arom.); 11.6 (s, 1 H, *COOH*). $C_{15}H_{15}NO_3$ (257.3): calcd. C 70.02, H 5.88, N 5.44; found C 70.0, H 5.9, N 5.4.

General Procedure for Cycloadditions between 3,6(*m,p*) and Dipolarophiles: The dipolarophile (10 equiv.) and Et_3N (2 equiv.) were added to a stirred suspension of **3,6(*m,p*)** in DCM at room temp. After the reaction mixture had been kept for 4 d at room temp., the resins were filtered off and carefully washed with DCM, MeOH, and DCM, and finally dried under vacuum. Samples of the resins were used to record FT IR (DR) and gel-phase ^{13}C NMR spectra. Characteristic spectroscopic data of supported adducts **8(*m,p*)** and **11(*m,p*)** are listed in Table 5. The cleavage of cycloadducts was performed by treatment with TFA/DCM solution (20%) for 2 h. Filtration and evaporation of the organic solvent yielded the crude products, which were purified either by column chromatography or by crystallization. When stable nitrile oxides were used, excess dipolarophile (10 equiv.) was added to the stirred suspension of the swollen resins at room temp. After 4 d, the usual workup procedure was applied.

Cycloadditions of 3(*m,p*)

Compound 9A*m*: M.p. 198−200 °C from ethanol. IR: ν_{OH} 2900, $\nu_{C=O}$ 1680 cm^{-1}. ^1H NMR: δ_H (DMSO) = 1.1−1.5 (m, 6 H, *CH*$_2$); 2.4 and 2.5 (br. s, 2 H, *CH*); 3.75 (d, *J* = 8.4, 1 H, *CH*); 4.63 (d, *J* = 8.4, 1 H, *CH*−O); 7.6−8.2 (m, 4 H, arom.); 13.0 (br. s, 1 H, *COOH*). ^{13}C NMR: δ (DMSO) = 22.4, 27.0, 32.2 (CH_2); 39.0, 43.0 (CH); 56.1 (CH); 87.8 (CH-O); 127.4, 129.7, 130.7, 131.2, 131.7 (arom.); 156.6 (C=N); 167.1 (C=O). $C_{15}H_{15}NO_3$ (257.3): calcd. C 70.02, H 5.88, N 5.44; found C 70.0, H 5.9, N 5.5.

Compound 9A*p*: M.p. > 280 °C from ethanol. IR: ν_{OH} 2900, $\nu_{C=O}$ 1670 cm^{-1}. ^1H NMR: δ_H (DMSO) = 1.1−1.5 (m, 6 H, *CH*$_2$); 2.4 and 2.5 (br. s, 2 H, *CH*); 3.75 (d, *J* = 8.4, 1 H, *CH*); 4.70 (d, *J* =

Table 5. Diagnostic spectroscopic data of supported cycloadducts **8,11(*m,p*)**

Supported cycloadducts	IR: $\nu_{C=O}$ [cm^{-1}]	^{13}C NMR ($CDCl_3$): δ
8A(*m,p*)		22.7, 27.4, 32.3 (CH_2); 39.2, 43.0 (CH); 56.7 (CH); 88.3 (CH-O); 156.3 (C=N); 166.0 (C=O)
8B(*m,p*)	1720	14.1 (CH_3); 38.5 (CH_2); 62.1 (CH_2O); 78.4 (CH-O); 155.3 (C=N); 165.7 (C=O); 169.9 (C=O)
8C(*m,p*)	1720	17.9, 20.7[a] (CH_3); 56.2, 59.4[a] (CH_3O); 82.7, 85.2[a] (CH); 154.9 (C=N); 165.3 (C=O); 169.4, 170.4[a] (C=O)
8D(*m,p*)	1718	27.5, 31.4[a] (CH_3); 65.1 (CH); 66.8 (CH); 86.4, 93.1[a] (CH-O); 153.7 (C=N); 165.3 (C=O); 202.4, 206.5[a] (C=O)
8E(*m,p*)	1730	64.2 (CH); 88.4 (CH-O); 155.0 (C=N); 164.7 (C=O); 195.1 (C=O)
8F(*m,p*)		30.3 (CH_2); 51.1 (CH); 66.4 (CH_2-O); 109.6 (O-C-O); 156.7 (C=N); 165.0 (C=O)
11A(*m,p*)		22.6, 27.3, 32.3 (CH_2); 39.2, 42.9 (CH); 57.0 (CH); 87.5 (CH-O); 156.4 (C=N)
11B(*m,p*)	1740	14.1 (CH_3); 38.8 (CH_2); 61.9 (CH_2O); 77.6 (CH-O); 156.0 (C=N); 170.1 (C=O)
11F(*m,p*)		30.5 (CH_2); 51.5 (CH); 66.3 (CH_2-O); 109.0 (O-C-O); 157.5 (C=N)

[a] Signals referred to the minor stereoisomer.

8.4, 1 H, *CH*-O); 7.7−8.0 (4 H, AA′BB′ system, arom.); 12.9 (s, 1 H, *COOH*). ^{13}C NMR: δ (DMSO) = 22.4, 27.0, 32.2 (CH_2); 39.0, 43.0 (CH); 56.0 (CH); 88.0 (CH−O); 127.1, 129.8, 130.1, 131.8, 133.3 (arom.); 156.7 (C=N); 167.1 (C=O). $C_{15}H_{15}NO_3$ (257.3): calcd. C 70.02, H 5.88, N 5.44; found C 70.0, H 5.8, N 5.4.

Compound 9B*m*: M.p. > 290 °C from ethanol. IR: ν_{OH} 3000, $\nu_{C=O}$ 1686 cm^{-1}. ^{1}H NMR: δ_H (DMSO) = 1.23 (t, 3 H, *CH*$_3$); 3.6−3.9 (2 H, AB part of ABX system, *CH*$_2$); 4.17 (q, 2 H, *CH*$_2$O); 5.30 (dd, *J* = 11.6, 6.7, 1 H, *CH*−O); 7.6−8.2 (m, 4 H, arom.); 13.0 (br. s, 1 H, *COOH*). ^{13}C NMR: δ (DMSO) = 14.3 (CH_3); 38.6 (CH_2); 61.6 (CH_2−O); 78.2 (CH−O); 127.7, 129.2, 129.7, 131.3, 131.8 (arom.); 156.0 (C=N); 167.0 (C=O); 171.8 (C=O). $C_{13}H_{13}NO_5$ (263.2): calcd. C, 59.31, H 4.98, N 5.32; found C 59.1, H 4.8, N 5.3.

Compound 9B*p*: M.p. 166−170 °C from ethanol. IR: ν_{OH} 3000, $\nu_{C=O}$ 1686 cm^{-1}. ^{1}H NMR: δ_H (DMSO) = 1.25 (t, 3 H, *CH*$_3$); 3.6−3.9 (2 H, AB part of ABX system, *CH*$_2$); 4.20 (q, 2 H, *CH*$_2$O); 5.30 (dd, *J* = 11.6, 6.7, 1 H, *CH*−O); 7.7−8.0 (4 H, AA′BB′ system, arom.); 13.0 (br. s, 1 H, *COOH*). ^{13}C NMR: δ (DMSO) = 14.3 (CH_3); 38.5 (CH_2); 61.6 (CH_2−O); 78.3 (CH-O); 127.2, 129.2, 129.7, 130.2, 132.5 (arom.); 156.0 (C=N); 167.1 (C=O); 171.8 (C=O). $C_{13}H_{13}NO_5$ (263.2): calcd. C, 59.31, H 4.98, N 5.32; found C 59.2, H 4.9, N 5.3.

Compound 9C*m*: Viscous oil (mixture of regioisomers). IR: ν_{OH} 3090, $\nu_{C=O}$ 1686 cm^{-1}. ^{1}H NMR of major isomer: δ_H (CD_3OD) = 1.44 (d, 3 H, *CH*$_3$); 3.71 (s, 3 H, *CH*$_3$O); 4.41 (d, *J* = 6.0, 1 H, *CH*); 5.10 (quint, *J* = 6.0, 6.4, 1 H, *CH*−CH_3); 7.5−8.3 (m, 4 H, arom.); 13.0 (br. s, 1 H, *COOH*). ^{13}C NMR: δ (CD_3OD) = 19.3 (CH_3); 46.4 (CH); 51.9 (CH_3−O); 58.9 (CH−O); 128.6, 130.6, 130.8, 131.2, 133.4, (arom.); 153.5 (C=N); 169.9 (C=O); 172.3 (C=O). ^{1}H NMR of minor isomer: δ_H (CD_3OD) = 1.40 (d, 3 H, *CH*$_3$); 3.80 (s, 3 H, *CH*$_3$O); 4.17 (dq, *J* = 4.3, 7.1, 1 H, *CH*−CH_3); 4.71 (d, *J* = 4.3, 1 H, *CH*−O); 7.5−8.3 (m, 4 H, arom.); 13.0 (br. s, 1 H, *COOH*). ^{13}C NMR: δ (CD_3OD) = 13.7 (CH_3); 46.4 (CH); 51.5 (CH_3−O); 82.4 (CH−O); 127.9, 130.2, 130.9, 131.0, 133.4, (arom.); 153.5 (C=N); 167.4 (C=O); 170.7 (C=O).

Compound 9C*p*: Viscous oil (mixture of regioisomers). IR: ν_{OH} 3100, $\nu_{C=O}$ 1690 cm^{-1}. ^{1}H NMR of major isomer: δ_H (CD_3OD) = 1.44 (d, 3 H, *CH*$_3$); 3.71 (s, 3 H, *CH*$_3$O); 4.42 (d, 1 H, *CH*); 5.10 (quint, 1 H, *CH*−O); 7.5−8.3 (m, 4 H, arom.); 13.0 (br. s, 1 H, *COOH*). ^{13}C NMR: δ (CD_3OD) = 19.4 (CH_3); 46.3 (CH); 51.9 (CH_3−O); 58.8 (CH−O); 126.8, 129.1, 129.6, 130.0, (arom.); 153.5 (C=N); 169.8 (C=O); 172.0 (C=O). ^{1}H NMR of minor isomer: δ_H (CD_3OD) = 1.40 (d, 3 H, *CH*$_3$); 3.79 (s, 3 H, *CH*$_3$O); 4.20 (dq, 1 H, *CH*−CH_3); 4.91 (d, 1 H, *CH*−O); 7.5−8.3 (m, 4 H, arom.); 13.0 (br. s, 1 H, *COOH*). ^{13}C NMR: δ (CD_3OD) = 13.7 (CH_3); 46.4 (CH); 51.5 (CH_3−O); 82.6 (CH-O); 126.4, 129.0, 129.4, 129.8, (arom.); 153.1 (C=N); 167.5 (C=O); 171.4 (C=O).

Compound 9D*m*: Sticky oil (mixture of regioisomers). IR: ν_{OH} 3100, $\nu_{C=O}$ 1707 cm^{-1}. ^{1}H NMR of major isomer: δ_H (CD_3OD) = 2.30 (s, 3 H, *CH*$_3$); 4.81 (d, *J* = 5.4, 1 H, *CH*); 5.87 (d, *J* = 5.4, 1 H, *CH*−O); 7.2−8.3 (m, 9 H, arom.); 13.0 (br. s, 1 H, *COOH*). ^{13}C NMR: δ (CD_3OD) = 29.9 (CH_3); 68.5 (CH); 86.1 (CH−O); 125.2, 128.0, 128.2, 128.6, 129.2, 130.8, 131.0, 131.3, 133.5 (arom.); 154.3 (C=N); 167.4 (C=O); 203.1 (C=O). ^{1}H NMR of minor isomer: δ_H (CD_3OD) = 2.00 (s, 3 H, *CH*$_3$); 4.97 (d, *J* = 4.3, 1 H, *CH*); 5.21 (d, *J* = 4.3, 1 H, *CH*−O); 7.2−8.3 (m, 9 H, arom.); 13.0 (br. s, 1 H, *COOH*). ^{13}C NMR: δ (CD_3OD) = 27.4 (CH_3); 65.9 (CH); 92.6 (CH−O); 125.2, 128.3, 128.4, 128.6, 129.3, 130.8, 131.0, 132.8, 133.4 (arom.); 154.3 (C=N); 166.1 (C=O); 206.2 (C=O).

Compound 9D*p*: Viscous oil (mixture of regioisomers). IR: ν_{OH} 3100, $\nu_{C=O}$ 1700 cm^{-1}. ^{1}H NMR of major isomer: δ_H (CD_3OD) = 2.31 (s, 3 H, *CH*$_3$); 4.81 (d, *J* = 5.4, 1 H, *CH*); 5.85 (d, *J* = 5.4, 1 H, *CH*−O); 6.9−8.2 (m, 9 H, arom.); 13.0 (br. s, 1 H, *COOH*). ^{13}C NMR: δ (CD_3OD) = 29.8 (CH_3); 68.1 (CH); 86.2 (CH−O); 125.1, 126.6, 128.2, 128.3, 128.6, 129.4, 129.7, 132.7, (arom.); 154.0 (C=N); 167.5 (C=O); 200.7 (C=O). ^{1}H NMR of minor isomer: δ_H (CD_3OD) = 2.00 (s, 3 H, *CH*$_3$); 4.99 (d, *J* = 4.1, 1 H, *CH*); 5.21 (d, *J* = 4.1, 1 H, *CH*−O); 6.9−8.2 (m, 9 H, arom.); 13.0 (br. s, 1 H, *COOH*). ^{13}C NMR: δ (CD_3OD) = 31.7 (CH_3); 63.9 (CH); 93.0 (CH−O); 126.3, 126.6, 128.2, 128.5, 128.6, 129.4, 129.7, 132.1, (arom.); 154.0 (C=N); 165.0 (C=O); 203.7 (C=O).

Compound 9E*m*: Viscous oil (mixture of regioisomers). IR: ν_{OH} 3097, $\nu_{C=O}$ 1708 cm^{-1}. ^{1}H NMR of major isomer: δ_H (CD_3OD) = 5.70 (d, *J* = 6.8, 1 H, *CH*); 5.90 (d, *J* = 6.8, 1 H, *CH*−O); 7.0−8.3 (m, 14 H, arom.); 13.0 (br. s, 1 H, *COOH*). ^{13}C NMR: δ (CD_3OD)= 63.2 (CH); 88.2 (CH−O); 126.0−139.1 (arom.); 155.4 (C=N); 166.0 (C=O); 196.1 (C=O). ^{1}H NMR of minor isomer: δ_H (CD_3OD) = 5.43 (d, *J* = 5.2, 1 H, *CH*); 5.94 (d, *J* = 5.2, 1 H, *CH*-O); 7.0−8.3 (m, 14 H, arom.); 13.0 (br. s, 1 H, *COOH*). ^{13}C NMR: δ (CD_3OD) = 55.2 (CH); 89.4 (CH−O); 126.0−139.1 (arom.); 155.4 (C=N); 167.6 (C=O); 189.0 (C=O).

Compound 9E*p*: Viscous oil (mixture of regioisomers). IR: ν_{OH} 3100, $\nu_{C=O}$ 1700 cm^{-1}. ^{1}H NMR of major isomer: δ_H (CD_3OD) = 5.40 (d, *J* = 4.5, 1 H, *CH*); 5.90 (d, *J* = 4.5, 1 H, *CH*−O); 6.9−8.3 (m, 14 H, arom.); 13.0 (br. s, 1 H, *COOH*). ^{13}C NMR: δ (CD_3OD) = 63.1 (CH); 70.6 (CH−O); 125.9−139.2, (arom.); 155.4 (C=N); 167.3 (C=O); 196.0 (C=O). ^{1}H NMR of minor isomer: δ_H (CD_3OD) = 5.55 (d, *J* = 6.1, 1 H, *CH*); 5.60 (d, *J* = 6.1, 1 H, *CH*-O); 7.0−8.3 (m, 14 H, arom.); 13.0 (br. s, 1 H, *COOH*). ^{13}C NMR: δ (CD_3OD) = 29.3 (CH); 88.3 (CH−O); 126.0−139.1 (arom.); 155.4 (C=N); 166.4 (C=O); 192.0 (C=O).

Compound 9F*m*: Viscous oil. IR: ν_{OH} 3000, $\nu_{C=O}$ 1700 cm^{-1}. ^{1}H NMR: δ_H (CD_3OD) = 2.2−2.4 (m, 2 H, *CH*$_2$); 3.52 and 4.03 (m, 2 H, *CH*$_2$−O); 4.40 (m, 1 H, *CH*); 6.30 (d, 1 H, O−*CH*−O); 7.5−8.3 (m, 4 H, arom.); 13.0 (br. s, 1 H, *COOH*). ^{13}C NMR δ (DMSO) = 30.0 (CH_2); 50.9 (CH); 66.0 (CH_2−O); 109.2 (O−CH−O); 127.4, 128.9, 129.6, 130.3, 131.0, 131.5 (arom.); 157.4 (C=N); 166.7 (C=O). $C_{12}H_{11}NO_4$ (233.2): calcd. C, 61.80, H 4.75, N 6.01; found C 61.7, H 4.7, N 6.0.

Compound 9F*p*: M.p. 225−228 °C from ethanol. IR: ν_{OH} 3150, $\nu_{C=O}$ 1681 cm^{-1}. ^{1}H NMR: δ_H (CD_3OD) = 2.00 and 2.23 (m, 2 H, *CH*$_2$); 3.40 and 4.00 (m, 2 H, *CH*$_2$−O); 4.47 (m, 1 H, *CH*); 6.32 (d, 1 H, O−*CH*−O); 7.8−8.1 (m, 4 H, arom.); 13.0 (br. s, 1 H, *COOH*). ^{13}C NMR: δ (DMSO) = 29.2 (CH_2); 49.9 (CH); 65.2 (CH_2−O); 108.4 (O−CH−O); 125.8, 126.1, 126.3, 128.5, 129.0, 131.0 (arom.); 156.3 (C=N); 165.8 (C=O). $C_{12}H_{11}NO_4$ (233.2): calcd. C, 61.80, H 4.75, N 6.01; found C 61.8, H 4.8, N 6.1.

Cycloadditions of 6(*m*,*p*)

Compound 12A*m*: Dark brown oil. IR: ν_{OH} 3304, $\tilde{\nu}_{C=N}$ 1600 cm^{-1}. ^{1}H NMR: δ_H (CD_3COCD_3) = 1.1−1.6 (m, 6 H, *CH*$_2$); 2.50 (m, 2 H, *CH*); 3.80 (d, *J* = 8.6, 1 H, *CH*); 4.60 (d, *J* = 8.6, 1 H, *CH*−O); 6.8−7.5 (m, 4 H, arom.). ^{13}C NMR: δ (CD_3COCD_3) = 23.7, 28.0, 33.1 (CH_2); 39.8, 44.0 (CH); 60.0 (CH); 88.4 (CH−O); 116.1, 118.7, 119.0, 131.0, 132.4, 159.0 (arom.); 157.7 (C=N). $C_{14}H_{15}NO_2$ (229.3): calcd. C, 73.34, H 6.59, N 6.11; found C 73.1, H 6.5, N 6.0.

Compound 12A*p*: M.p. 169−171 °C from ethanol. IR: ν_{OH} 3304, $\nu_{C=N}$ 1600 cm^{-1}. ^{1}H NMR: δ_H (CD_3COCD_3) = 1.1−1.7 (m, 6 H, *CH*$_2$); 2.52 (br. s, 2 H, *CH*); 3.60 (d, *J* = 8.2, 1 H, *CH*); 4.60 (d, *J* = 8.2, 1 H, *CH*−O); 6.8−7.5 (4 H, AA′BB′ system, arom.). ^{13}C NMR: δ (CD_3COCD_3) = 23.6, 28.2, 33.0 (CH_2); 40.5, 44.3 (CH);

58.1 (CH); 88.2 (CH−O); 116.7, 122.4, 129.6, 159.9 (arom.); 157.3 (C=N). $C_{14}H_{15}NO_2$ (229.3): calcd. C, 73.34, H 6.59, N 6.11; found C 73.2, H 6.5, N 6.1.

Compound 12B*m*: Brown-orange oil. IR: ν_{OH} 3380, $\nu_{C=O}$ 1718, $\nu_{C=N}$ 1607 cm^{-1}. ^1H NMR: δ_H (CD_3COCD_3) = 1.29 (t, 3 H, *CH*$_3$); 3.7−3.9 (2 H, AB part of ABX system, *CH*$_2$); 4.24 (q, 2 H, *CH*$_2$O); 5.25 (dd, *J* = 11.2, 6.9, 1 H, *CH*−O); 6.9−7.3 (m, 4 H, arom.); 8.9 (br. s, 1 H, *OH*). ^{13}C NMR: δ (CD_3COCD_3) = 14.8 (CH_3); 39.7 (CH_2); 62.4 (CH_2−O); 79.7 (CH−O); 114.4, 118.3, 119.6, 131.1, 132.7, 158.8 (arom.); 157.5 (C=N); 171.0 (C=O). $C_{12}H_{13}NO_4$ (235.2): calcd. C, 61.27, H 5.57, N 5.96; found C 61.2, H 5.5, N 5.9.

Compound 12B*p*: M.p. 122−125 °C from ethanol. IR: ν_{OH} 3385, $\nu_{C=O}$ 1720, $\nu_{C=N}$ 1607 cm^{-1}. 1H NMR: δ_H (CD_3COCD_3) = 1.31 (t, 3 H, *CH*$_3$); 3.6−3.8 (2 H, AB part of ABX system, *CH*$_2$); 4.25 (q, 2 H, *CH*$_2$O); 5.17 (dd, *J* = 11.2, 6.9, 1 H, *CH*−O); 6.8−7.6 (4 H, AA′BB′ system, arom.). ^{13}C NMR: δ (CD_3COCD_3) = 14.8 (CH_3); 39.9 (CH_2); 62.3 (CH_2−O); 79.0 (CH−O); 116.8, 121.8, 129.8, 160.6 (arom.); 156.7 (C=N); 171.3 (C=O). $C_{12}H_{13}NO_4$ (235.2): calcd. C, 61.27, H 5.57, N 5.96; found C 61.2, H 5.6, N 5.9.

Compound 12F*m*: M.p. 114−116 °C from *i*Pr_2O. IR: ν_{OH} 3350, $\nu_{C=N}$ 1599 cm^{-1}. ^1H NMR: δ_H (CD_3COCD_3) = 2.13 and 2.30 (m, 2 H, *CH*$_2$); 3.49 and 4.01 (m, 2 H, *CH*$_2$−O); 4.35 (m, 1 H, *CH*); 6.25 (d, *J* = 6.3, 1 H, O−*CH*−O); 6.9−7.3 (m, 4 H, arom.); 8.6 (br. s, 1 H, *OH*). ^{13}C NMR: δ (CD_3COCD_3) = 33.0 (CH_2); 52.7 (CH); 67.2 (CH_2−O); 110.6 (O−CH−O); 114.7, 118.4, 119.6, 131.2, 131.7, 158.9 (arom.); 158.9 (C=N). $C_{11}H_{11}NO_3$ (205.2): calcd. C, 64.38, H 5.40, N 6.83; found C 64.3, H 5.4, N 6.8.

Compound 12F*p*: M.p. 146−150 °C from *i*Pr_2O. IR: ν_{OH} 3285, $\nu_{C=N}$ 1607 cm^{-1}. ^1H NMR: δ_H (CD_3COCD_3) = 2.12 and 2.30 (m, 2 H, *CH*$_2$); 3.48 and 3.98 (m, 2 H, *CH*$_2$−O); 4.35 (m, 1 H, *CH*); 6.21 (d, *J* = 6.2, 1 H, O−*CH*−O); 6.9−7.6 (m, 4 H, arom.); 8.8 (br. s, 1 H, *OH*). ^{13}C NMR: δ (CD_3COCD_3) = 33.0 (CH_2); 52.9 (CH); 67.1 (CH_2−O); 110.2 (O−CH−O); 116.9, 119.6, 129.9, 160.4 (arom.); 157.5 (C=N). $C_{11}H_{11}NO_3$ (205.2) C, 64.38, H 5.40, N 6.83); found C 64.4, H 5.4, N 6.8.

General Procedure for the Cycloadditions between Nitrosocarbonyl and Dienes: The Wang resin supported hydroximoyl chlorides **3(*m,p*)** were swollen in DCM and an excess of Et_3N was added at room temp. Stirring was continued for 2 h. After filtration and the usual washings, the nitrile oxides **7(*m,p*)** were allowed to swell in DCM, and a solution containing an excess of *N*-methylmorpholine *N*-oxide (NMO, 3 equiv.) and an excess of freshly distilled cyclopentadiene or 1,3-cyclohexadiene (4 equiv.) was then added with vigorous stirring, which was continued for 2 d at room temp. Diagnostic spectroscopic data of supported hetero Diels−Alder (HDA) cycloadducts **14(*m,p*)** and **15(*m,p*)** are listed in Table 6.

Table 6. Diagnostic spectroscopic data of supported cycloadducts **14,15(*m,p*)**

	IR: $\nu_{C=O}$ [cm^{-1}]	^{13}C NMR ($CDCl_3$): δ
14*m*	1733	48.2, 84.8, 165.5 and 171.0 (C=O)
14*p*	1718	48.2, 84.8, 165.0 and 171.0 (C=O)
15*m*	1734	21.0, 23.5, 72.1, 165.8 and 167.6 (C=O)
15*p*	1724	20.8, 23.4, 72.0, 166.0 and 167.0 (C=O)

Cleavage by Transesterification: The ester-supported cycloadducts **14,15(*m,p*)** were allowed to swell in a CH_3OH/THF (1:3) mixture in the presence of Et_3N (10 equiv.) and KCN (2 equiv.) and gently refluxed for 2 d. The resins were filtered off and the organic phases were washed with water, dried with Na_2SO_4, and concentrated to give the crude cleaved cycloadducts **16(*m,p*)** and **17(*m,p*)** in moderate yields after purification by column chromatography.

Compound 16*m*: Orange oil. IR: $\nu_{C=O}$ 1717, 1648 cm^{-1}. ^1H NMR: δ_H ($CDCl_3$) = 1.90 and 2.19 (1 H + 1 H, AB system, *CH*$_2$); 3.95 (s, 3 H, *CH*$_3$*O*); 5.39 (br. s, 2 H, *CH*); 6.40 and 6.59 (br., 2 H, *CH*=); 7.4−8.5 (m, 4 H, arom.). ^{13}C NMR: δ ($CDCl_3$) = 29.6 (CH_2); 48.2 (CH_3−O); 52.2 (CH−N); 84.8 (CH−O); 128.2, 130.1, 132.3, 133.3, 134.5 (arom.); 129.9 (CH=); 166.2, 171.1 (C=O). $C_{14}H_{13}NO_4$ (259.3): calcd. C, 64.86, H 5.05, N 5.40; found C 64.9, H 5.0, N 5.3.

Compound 16*p*: Orange oil. IR: $\nu_{C=O}$ 1724, 1642 cm^{-1}. ^1H NMR: δ_H ($CDCl_3$) = 1.89 and 2.18 (1 H + 1 H, AB system, *CH*$_2$); 3.95 (s, 3 H, *CH*$_3$*O*); 5.38 (br. s, 2 H, *CH*); 6.41 and 6.58 (br., 2 H, *CH*=); 7.83 and 8.08 (AA′BB′ system, 4 H, arom.). ^{13}C NMR: δ ($CDCl_3$) = 29.6 (CH_2); 48.2 (CH_3−O); 52.2 (CH-N); 84.8 (CH−O); 128.7, 129.2, 129.7, 133.0 (arom.); 129.9 (CH=); 166.2, 171.1 (C=O). $C_{14}H_{13}NO_4$ (259.3): calcd. C, 64.86, H 5.05, N 5.40; found C 64.8, H 5.0, N 5.4.

Compound 17*m*: Yellowish crystals. M.p. 70−72 °C from ethyl acetate. IR: $\nu_{C=O}$ 1726, $\nu_{C=C}$ 1626 cm^{-1}. ^1H NMR: δ_H ($CDCl_3$) = 1.58 and 2.25 (m, 2 H + 2 H, *CH*$_2$); 3.95 (s, 3 H, *CH*$_3$*O*); 4.78 and 5.40 (br., 1 H + 1 H, *CH*); 6.52 and 6.69 (br., 1 H + 1 H, *CH*=); 7.4−8.4 (m, 4 H, arom.). ^{13}C NMR: δ ($CDCl_3$) = 22.7 (CH_2); 29.5 (CH_2); 47.2 (CH_3−O); 52.0 (CH−N); 72.0 (CH−O); 127.9, 128.7, 129.7, 131.6, 132.9, 134.5 (arom.); 131.5 (CH=); 166.3, 167.5 (C=O). $C_{15}H_{15}NO_4$ (273.3): calcd. C, 65.92, H 5.53, N 5.13; found C 65.7, H 5.4, N 5.0.

Compound 17*p*: White crystals. M.p. 93−96 °C from ethyl acetate. IR: $\nu_{C=O}$ 1729, $\nu_{C=C}$ 1619 cm^{-1}. ^1H NMR: δ_H ($CDCl_3$) = 1.58 and 2.28 (m, 2 H + 2 H, *CH*$_2$); 3.95 (s, 3 H, *CH*$_3$*O*); 4.80 and 5.45 (br., 1 H + 1 H, *CH*); 6.52 and 6.71 (br., 1 H + 1 H, *CH*=); 7.72 and 8.06 (AA′BB′ system, 4 H, arom.). ^{13}C NMR: δ ($CDCl_3$) = 23.4 (CH_2); 29.6 (CH_2); 52.2 (CH_3−O); 52.4 (CH−N); 72.1 (CH−O); 127.4, 128.1, 131.7, 133.8 (arom.); 129.5 (CH=); 166.2, 167.5 (C=O). $C_{15}H_{15}NO_4$ (273.3): calcd. C, 65.92, H 5.53, N 5.13; found C 65.7, H 5.5, N 5.1.

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