g, 74%) as a white solid: mp 136–137 °C ($CHCl_3$/hexane); ^1H NMR ($CDCl_3$) δ 7.3 (m, 6 H, NH and aromatic), 3.3 (m, 2 H, NCH_2), 2.4 (m, 2 H, CH_2), 1.8 (m, 4 H, CH_2CH_2); ^{13}C NMR ($CDCl_3$) δ 170.7, 135.0, 128.9, 128.5, 127.1, 119.0, 54.1, 41.9, 34.5, 28.3, 25.2; IR (KBr) 2210 (CN), 1660 (C=O) cm^{-1}; MS *m/e* 214 (M^+, 22). Anal. Calcd for $C_{13}H_{14}N_2O$: C, 72.87; H, 6.58; N, 13.07. Found: C, 72.99; H, 6.63; N, 13.10.

1-(*tert*-Butyloxycarbonyl)-3-(methoxycarbonyl)hexahydro-2*H*-azepin-2-one (19). DMAP (12 mg, 0.10 mmol) was added to a stirred solution of **16** (150 mg, 0.87 mmol) in anhydrous CH_3CN (5 mL) under N_2. After 5 min, di-*tert*-butyl dicarbonate (440 mg, 2.0 mmol) was added, and the resulting mixture was stirred at room temperature for 15 h. EtOAc (25 mL) was added, and the solution was washed with 1 M $KHSO_4$ (10 mL) followed by saturated aqueous NaCl (2 × 10 mL). The organic layer was dried (Na_2SO_4) and concentrated to yield an oily residue (290 mg). This was placed on a silica preparative TLC plate and eluted with ether. The band at R_f 0.68 was removed by washing with $CHCl_3$, and the washings were concentrated to give **19** (260 mg, 63%) as a colorless oil: ^1H NMR ($CDCl_3$) δ 3.7 (s, 3 H, CO_2CH_3), 3.5 (m, 3 H, CH, NCH_2), 2.4 (m, 2 H, $CHCH_2$), 1.5 (m, 13 H, *tert*-butyl, CH_2CH_2); IR (liquid film) 1750, 1710, 1690 (C=O) cm^{-1}.

3-(Aminocarbonyl)-3-phenylhexahydro-2*H*-azepin-2-one (20). In a pear-shaped pressure bottle was placed a suspension of **18** (1.5 g, 7.0 mmol) in concentrated HCl (1.5 mL), and gaseous HCl was bubbled through the mixture at 0 °C for 20 min. The bottle was sealed, and the mixture stirred at room temperature for 48 h. The solution was adjusted to pH 7 by adding saturated aqueous $NaHCO_3$, and the resulting mixture was extracted with $CHCl_3$ (2 × 50 mL). The combined organic layers were dried (Na_2SO_4) and concentrated in vacuo to provide crude **20** (1.4 g, 86%): mp 192–193 °C ($CHCl_3$/hexane); ^1H NMR ($CDCl_3$) δ 7.3 (m, 5 H, aromatic), 6.8 (br s, 1 H, NH), 5.9 (br s, 2 H, NH_2), 2.8 (m, 2 H, NCH_2), 2.6 (m, 2 H, CCH_2), 1.6 (m, 4 H, CH_2CH_2); ^{13}C NMR (1:1 $CDCl_3$/DMSO-d_6) δ 176.7, 175.3, 136.1, 129.0, 127.8, 127.6, 63.7, 41.6, 30.8, 27.9, 24.1; IR (KBr) 1680, 1655 (C=O) cm^{-1}; MS *m/e* 232 (M^+, 61). Anal. Calcd for $C_{13}H_{16}N_2O_2$: C, 67.22; H, 6.93; N, 12.06. Found: C, 67.16; H, 6.97; N, 12.10.

3-[*N*-(Methoxycarbonyl)amino]-3-phenylhexahydro-2*H*-azepin-2-one (21). To a stirred solution of **20** (1.0 g, 4.3 mmol) in anhydrous CH_3OH (50 mL) under N_2 was added $Pb(OAc)_4$ (7.62 g, 17.2 mmol). The mixture was warmed to 55–58 °C while stirring for 19 h. The solvent was removed on a rotary evaporator, 10% aqueous $NaHCO_3$ (20 mL) added to the residue, and the resulting mixture extracted with $CHCl_3$ (2 × 60 mL). The combined organic extracts were washed with water (2 × 30 mL) and dried (Na_2SO_4), and the solvent was removed. The residual oil was triturated with 25% ether/hexane to provide **21** (0.80 g, 71%) as a white solid: mp 149–150 °C; ^1H NMR ($CDCl_3$) δ 7.3 (m, 5 H, aromatic), 6.8 (m, 2 H, 2 NH), 3.5 (s, 3 H, $NHCO_2CH_3$), 2.7 (m, 2 H, NCH_2), 1.2 (m, 6 H, $CH_2CH_2CH_2$); IR (KBr) 1710, 1650 (C=O) cm^{-1}; MS *m/e* 262 (M^+, 30). Anal. Calcd for $C_{14}H_{18}N_2O_3$: C, 64.10; H, 6.91; N, 10.68. Found: C, 64.18; H, 6.94; N, 10.63.

3-Phenyl-1,5,6,7-tetrahydro-2*H*-azepin-2-one (22). A solution of **21** (40 mg, 0.15 mmol) and pTsOH (1 mg) in dry toluene (20 mL) was heated at reflux for 36 h using a Dean–Stark trap. TLC indicated no reaction. Additional pTsOH (30 mg, 0.15 mmol) was added, and heating was continued for an additional 12 h. TLC revealed starting material and several new products. A third portion of pTsOH (30 mg, 0.15 mmol) was added, and heating was continued for an additional 12 h. The solvent was removed on a rotary evaporator, and the residual oil was placed on a preparative silica TLC plate (EtOAc). Two bands were removed by washing with $CHCl_3$. The minor one (R_f 0.61) was **5** (2 mg, 5%), which was identical with that produced from **20** (described above). The major band (R_f 0.42) provided **22** (18 mg, 63%) as a white solid: mp 138–139 °C; ^1H NMR ($CDCl_3$) δ 7.3 (m, 5 H, aromatic), 7.1 (br s, 1 H, NH), 6.6 (t, 1 H, vinyl CH), 3.3 (m, 2 H, NCH_2), 2.4 (m, 2 H, allylic CH_2), 1.9 (m, 2 H, NCH_2CH_2); ^{13}C NMR ($CDCl_3$) δ 173.0, 139.1, 137.0, 131.6, 128.4, 127.7, 127.0, 39.6, 29.6, 23.9; IR (KBr) 1640 (C=O, C=C) cm^{-1}; MS *m/e* 187 (M^+). Anal. Calcd for $C_{12}H_{13}NO$: C, 76.98; H, 6.99; N, 7.47. Found: C, 76.81; H, 6.86; N, 7.40.

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Nitrile Additions to *C,N*-Diacylimines. Formation of 4-Amidooxazoles[1]

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Nitriles are shown to react with *C,N*-diacylimines **2**, generated in situ from **1** or **4** in the presence of Lewis acids, to produce 4-amidooxazoles **5** and **6** in good to excellent yield. Diamides are sometimes also produced. The reaction was followed by NMR spectroscopy, and mechanistic pathways are discussed.

Introduction

The ability of the imine function to add to other multiple bond compounds has been used extensively for the construction of heterocyclic molecules.[2] Among imines, the *N*-acylimine moiety has been shown to readily undergo amidoalkylations with olefins, acetylenes, and aromatic compounds,[3] as well as to act as dienophiles[4a–d] or as diene components[4e] in hetero-Diels–Alder reactions. It was of interest to compare the behavior of a rare series of imines,[4f] namely *C,N*-diacylimines **2**, to that of their simpler analogues.

As a possible entry to **2** we chose the *N*-(α-methoxy-β,β-dimethoxyalkyl)benzamides **1**, or the *N*-(α-methoxy-β-ketoalkyl)amides **4**, which in turn are readily obtained

(1) Synthetic Methods 35. For part 34, see: Rai, L. K. M.; Hassner, A. *Heterocycles* **1990**, *31*, 817.

(2) (a) Govindachari, T. R.; Chinnasamy, P.; Rajeswari, S.; Chandrasekaran, S.; Premila, M. S.; Natarajan, S.; Nagarajan, K.; Pai, B. R. *Heterocycles* **1984**, *22*, 585. (b) Maryanoff, B. E.; McComsey, D. F.; Almond, H. R., Jr.; Mutter, M. S.; Bemis, G. W.; Whittle, R. R.; Olofson, R. A. *J. Org. Chem.* **1986**, *51*, 1341. (c) Ben-Ishai, D.; Peled, N.; Sataty, I. *Tetrahedron Lett.* **1980**, *21*, 569.

(3) Zaugg, H. E. *Synthesis* **1984**, 85 and references cited.

(4) (a) Weinreb, S. M.; Staib, R. R. *Tetrahedron* **1982**, *38*, 3087. (b) Weinreb, S. M. *Acc. Chem. Res.* **1985**, *18*, 16. (c) Ben-Ishai, D.; Goldstein, E. *Tetrahedron* **1971**, *27*, 3119. (d) Jung, M. E.; Shishido, K.; Light, L.; Davis, L. *Tetrahedron Lett.* **1981**, *22*, 4611. (e) Scola, P. M.; Weinreb, S. M. *J. Org. Chem.* **1986**, *51*, 248. (f) Boger, D. L.; Weinreb, D. N. *Hetero Diels–Alder Methodology in Organic Synthesis*; Academic Press: San Diego, 1987; p 39.

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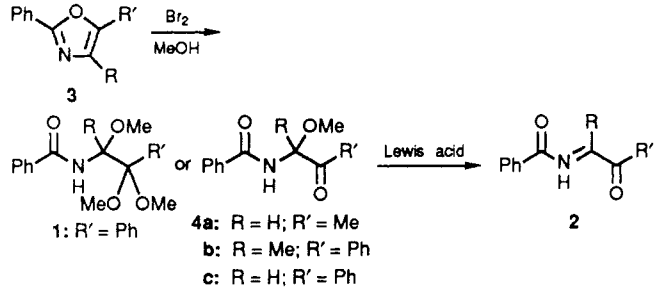
from 2-aryloxazoles **3** on treatment with bromine in methanol.[5] We expected the *N*-(methoxyalkyl)amides **1**



3

1: R′ = Ph

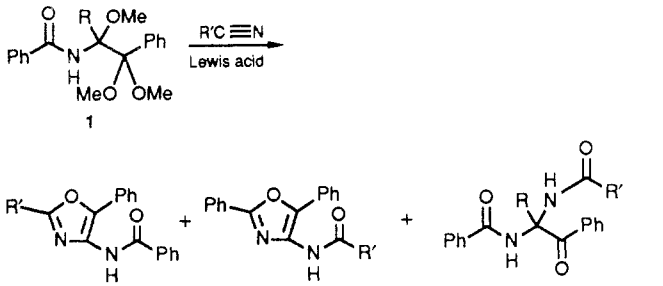
4a: R = H; R′ = Me
b: R = Me; R′ = Ph
c: R = H; R′ = Ph

2

or **4** to be convertible into a diacylimine of type **2** under Lewis acid catalysis. In this paper we report the addition of the relatively inert nitrile function[6] to *C,N*-diacylimines, leading to the virtually unknown[7] 4-amidooxazoles **5** and **6** and/or to diamides **7**.

Results

When trimethoxy amide **1** was heated with acetonitrile as the solvent under reflux for 1 h in the presence of a catalytic amount of boron trifluoride etherate, followed by aqueous workup and flash chromatography, amidooxazoles **5** and **6** were isolated in quantitative yield. Similar results were obtained when methoxy keto amide **4c** was used instead of **1**. Other Lewis acids can be used as catalysts; for instance, $POCl_3$ gave the same results as BF_3 etherate; $TiCl_4$ gave poorer yields. The reaction was checked for various nitriles (aliphatic, aromatic, and unsaturated) and was found to be general (see Table I), producing 4-amidooxazoles and sometimes diamide **7**.



1

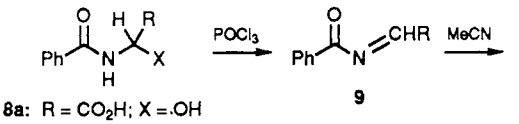
5 (R = H)

6 (R = H)

7a: R = H; R′ = Me
b: R = Me; R′ = Me
c: R = H; R′ = hexyl
d: R = H; R′ = CH=CHMe
e: R = H; R′ = Et

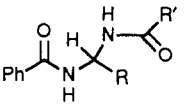
The isomer ratio of 4-benzamidooxazole:4-(alkylamido)oxazoles (**5**:**6**) formed in the reaction of **1** with nitriles is ca. 1.5:1. With propanenitrile, hexanenitrile, and crotononitrile the amount of diamide **7** was significant (entries C, D, E).

When amide **4b**, in which R = Me rather than H, was used as a substrate, only diamide **7** was isolated (see F). The reaction of other *N*-acylimines **9** (see G, H) with nitriles in the presence of $POCl_3$ was examined and found to lead to diamides **10**.



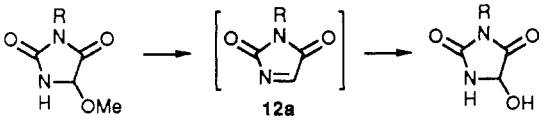
8a: R = CO_2H; X = OH
b: R = H; X = OMe

9



10a: R = CO_2H; R′ = Me
b: R = H; R′ = Me
c: R = H; R′ = Ph
d: R = COMe; R′ = Me

The *N*-acylimines **9** were formed in situ from *N*-(α-hydroxyalkyl)- or *N*-(α-methoxyalkyl)amides **8**.[8,9] Benzamidoglyoxalic acid **8a** was particularly reactive and added acetonitrile quantitatively within minutes. Reaction of **8b** yielded the expected diamide **10b** (61%) and **10c** as a byproduct (13%). The latter apparently resulted from reaction of **9** with benzamide (released from **8b**). No nitrile addition products were observed when the cyclic *N*-acylimine precursor **11** was heated with acetonitrile; the hydroxyhydantoin **12** that was isolated was presumably formed on aqueous workup from diacylimine **12a**.



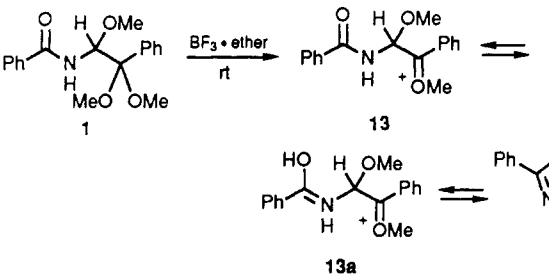
11

12a

12

R = 4-Cl-C_6H_4

Under milder conditions, i.e. at room temperature, but still using BF_3·etherate as a catalyst and the nitrile in excess, no addition of acetonitrile to the diacylimine was observed; instead only cyclization to dimethoxyoxazoline **14** took place. Heating of **14** under the reaction conditions led to amidooxazoles, implying the existence of an equilibrium between **14** and **13a**.



1

13

13a

14

When **1** was treated with 2 equiv of acetonitrile in chloroform in the presence of BF_3·etherate at room temperature, only starting material and **14** were detected; on reflux only small amounts of amidooxazoles **5** and **6** were formed. Apparently formation of **5** and **6** from **13** requires heating and an excess of nitrile.

(5) Hassner, A.; Fischer, B. *Tetrahedron* **1989**, *45*, 6249.
(6) (a) Reference 4a, p 3097. (b) Padwa, A. *1,3-Dipolar Cycloaddition Chemistry*; John Wiley & Sons: New York, 1984; Vol. 1, p 640. (c) Though the reaction of acylimines with nitriles in organic solvents has not been reported, there is precedence for this type of reaction in aqueous acidic medium. Magat, E. E.; Salisbury, L. F. *J. Am. Chem. Soc.* **1951**, *73*, 1035.
(7) (a) Turchi, I. J. *Oxazoles*; John Wiley & Sons: New York, 1986; p 88. (b) The only 4-aminooxazoles reported are those described by Lakhan R.; Singh, R. L. *J. Heterocycl. Chem.* **1988**, *25*, 1413; *Org. Prepar. Proced. Internat.* **1989**, *21*, 141. These reports include the isolation of 2-methyl-4-benzamido-5-phenyloxazole, mp 138–139 °C (compare our identical compound **5a**, mp 185 °C). We tried to repeat Lakhan's synthesis of 4-aminooxazoles (2-methyl-5-phenyl; 2-ethyl-5-phenyl; and 2,5-diphenyl) by heating benzoyl cyanide with acetaldehyde, propanal, or benzaldehyde, respectively, with ammonium acetate (dried or nondried) in acetic acid at 100–120 °C using distilled and nondistilled reagents, and the only solid product isolated in these reactions was benzamide in ca. 5% yield.
(8) Zoller, U.; Ben-Ishai, D. *Tetrahedron* **1975**, *31*, 863.
(9) (a) Zaugg, H. E. Org. *React.* **1965**, *14*, 52. (b) Hellmann, H. *Angew. Chem.* **1957**, *69*, 463.

Table I. Lewis Acid Catalyzed Nitrile Addition to *C,N*-Diacylimines (2)

entry	nitrile	*C,N*-diacyl-imine precursor	temp, °C	time, h	% yield of products 5	6	7 or 10
A	CH_3CN	1	80	1	95[a] (1.3:1)		–
B	PhCN	1	90–100	3	58[b]		–
C	$CH_3(CH_2)_4CN$	1	90	1.5	41[c] (1.2:1)		21 (**7c**)
D	$CH_3CH{=}CHCN$	1	80–90	1.5	43	30	20 (**7d**)[d]
E	CH_3CH_2CN	1	80–90	1.5	22	35	31 (**7e**)
F	CH_3CN	**4b**	70	0.5	–	–	42 (**7b**)[e]
G	CH_3CN	**8a**	80	0.08	–	–	100 (**10a**)
H	CH_3CN	**8b**	80	1.5	–	–	61 (**10b**)[f]
I	CH_3CN	**4a**	80	1.5	traces		85 (**10d**)

[a] Total yield before chromatographic separation. [b] Followed by starting material. [c] **5c** and **6c** could not be separated. [d] Cis + trans isomers. [e] Followed by a minor unidentified product. [f] Methylene bisbenzamide was obtained as a side product (13% yield).

Structure Proof and Spectra

The structure assignment to the 4-amidooxazoles **5** and **6** is based on mass spectra and IR, ^1H NMR, ^{13}C NMR, MS, and elemental analyses.[10] Though ^1H NMR spectra were not very revealing, ^{13}C NMR data were helpful and in good accordance with literature data on oxazoles.[11] By examining the spectra of a number of 4-amidooxazoles, we found that typical ranges for the chemical shift of the skeletal carbons in our oxazole products are as follows: C-2, 158.5–162.4; C-4, 126.2–127.9; C-5, 141.5–142.7 ppm. Another typical feature in the ^1H NMR spectra is the shape of the aromatic peaks. When a benzamide moiety is present at C-4, the aromatic hydrogen peaks are badly resolved due to the dynamic process of the amide segment. The presence of an acetamide group at C-4 causes the appearance of two peaks for the amide methyl group. These peaks coalesce when the spectrum was taken in DMSO at 90 °C. The chemical shifts of the aromatic protons also supply important information regarding the position of the phenyl group. Ortho protons of a phenyl group at C-2 appear at 8.04–8.07 ppm, while those attached to C-5 are found at 7.58–7.72 ppm. Ortho protons of the benzamide aromatic ring attached to C-4 appear at 7.92–7.96 ppm.

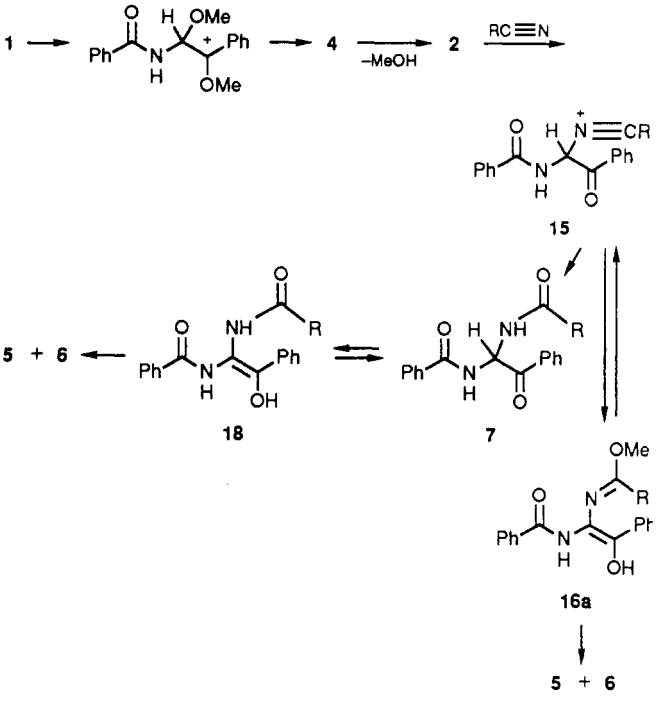
Discussion of Mechanism and NMR Experiments

The main products from the reaction of **1** or **4** with nitriles RCN were 4-amidooxazoles containing the RCN moiety either as the 4-amido group (see **6**) or incorporated into the heterocyclic ring with R as the 2-substituent (see **5**). In some cases open chain diamides **7** were also or exclusively formed.

In order to learn more about possible intermediates in the reaction we monitored by NMR the reaction of **1** in CD_3CN in the presence of $POCl_3$ at 77 °C. The first step in the reaction appears to be deketalization of **1** to **4** which proceeds within a few minutes in the presence of a small amount of water (present in the acetonitrile and detectable by NMR) so that, 7 min after addition of $POCl_3$, two of the three methoxy peaks from **1** disappeared and a broad peak for methanol at 3.03 ppm appeared. At the same time the methine doublet shifted from 5.58 to 6.47 ppm (as in authentic **4c**) and new ortho protons became visible at lower field (8.05 ppm).

Next a *C,N*-diacylimine **2** (*o*-benzoyl protons at 8.06 and 7.77 ppm) was formed, which reacted rapidly with a nitrile[6c] to form a nitrilium ion **15** and then a diamide **7**.

When the ketoamide **4c** was dissolved in CD_3CN and $POCl_3$ was added, three compounds were discernible by NMR within 2 min: starting material **4c**, diacylimine **2**, and keto diamide **7c** in a ratio of 1.1:1:0.17. After 11 min this ratio was 1:0.8:1.75, and after 2 h no starting material or imine could be detected. The products were keto diamide **7c** (methine singlet at 6.76 ppm at 77 °C, but at 20 °C a methine triplet and a broad NH doublet is noticed) and 4-acetamidooxazole **6** in a ratio of 1:1. The mechanism shown below is consistent with these findings.



Finally, when pure keto diamide **7c** was treated under reaction conditions, oxazoles **5** and **6** formed within 2 h (NMR), indicating that ring closure of **16**, the enol form of keto diamide **7**, can take place either in the direction of the acetamide or the benzamide grouping.

The fact that the keto diamide **7b** (see entry F) or amides **10a,b** (entries G, H), which are incapable of enolization to **16**, did not yield oxazoles but only the diamide product is consistent with this interpretation. Keto diamide **10d** is also the sole product (entry I) in the case of the acetyl system **4a**.

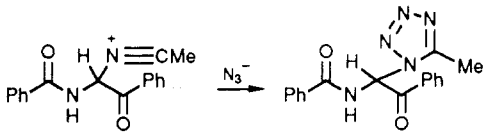
Under scrupulously anhydrous conditions, in an attempt to convert **15** exclusively to oxazole **5**, the same ratio of oxazoles **5** and **6** was obtained as before. Hence, it seems likely that two paths are available to **15**: (a) direct closure to oxazole **5** or (b) trapping by methoxide released from **1** (or **4**) or by water. Either intermediate **16a** or **7** can lead to oxazoles **5** and **6**.

Evidence for the existence of a nitrilium ion intermediate **15** was obtained by carrying out the reaction of **4c**

(10) Elemental analyses of some of the amidooxazoles also support the structure.

(11) (a) Hiemstra, H. A.; Houwing, H. A.; Possel, O.; van Leusen, A. M. *Can. J. Chem.* **1979**, *57*, 3168. (b) Reference 78, p 348.

in acetonitrile with a catalytic amount of BF_3·etherate under argon and strict exclusion of moisture in the presence of a polymeric azide.[12] The product was tetrazole



15 17

17, detected in 10% conversion after 15 min of reflux. There was no increase in yield of **17** at longer reaction times.

In conclusion, *C,N*-diacylimines **2** can be generated in situ from **1** or **4** in the presence of Lewis acids, and they react with nitriles (in excess) to produce diamides which can ring close to 4-amidooxazoles **5** and **6**. Formation of 4-amidooxazoles occurs only when the keto diamide **7** is enolizable. This method provides a convenient entry to oxazoles bearing nitrogen functions of C-4 (which are virtually unknown)[7] via the corresponding C-4 unsubstituted oxazoles (providing the substituent on C-2 is aromatic).

Experimental Section

General. NMR spectra were recorded on a Bruker AM 300 FT NMR instrument, ^1H spectra at 300 MHz and ^{13}C spectra at 75.5 MHz, in $CDCl_3$ using TMS as an internal standard (unless otherwise indicated). Mass spectra were obtained on a Finnigan 4021 instrument. IR spectra were recorded on a Perkin-Elmer Model 457 instrument. Nitriles were distilled before use, acetonitrile was distilled over phosphorus pentoxide. Starting materials **8a**,[8] **8b**,[9] **11**[2c] were prepared according to literature procedures. In the ^{13}C spectra superscripts a and b refer to uncertainty in peak assignment to specific carbons.

Reaction of *C,N*-Diacylimines with Nitriles: General Procedure. To a hot solution of the diacylimine precursor **1**, **4**, **8b**, **8a**, **11** (0.5 mmol) in nitrile (4 mL) was added a catalytic amount (0.05 mmol) of Lewis acid (phosphorus oxychloride or BF_3·etherate) at 80–90 °C. The mixture was heated for 1–3 h and then poured into ice-cold water, basified (K_2CO_3) to pH 9–10, and extracted with $CHCl_3$. The solvent was evaporated under reduced pressure, and the residue was chromatographed over silica gel. The products were eluted with EtOAc–hexane.

Reaction of *N*-(1,2,2-Trimethoxy-2-phenylethyl)benzamide (1) with Acetonitrile. A mixture of **1** (0.16 g, 0.5 mmol) and $POCl_3$ (0.018 mL, 0.2 mmol) in acetonitrile was heated under reflux for 1 h to afford 4-amidooxazoles **5a** and **6a** (0.132 g, 95% total yield, 1.3:1). After chromatography (EtOAc–hexane, 1:2) the mixture was separated to give **5a** as a white solid (mp 185 °C) and **6a** as a white solid (mp 218 °C).

2-Methyl-4-benzamido-5-phenyloxazole (5a): ^1H NMR δ 8.08 (NH, 1 H, br s), 7.92 (Ph-*o*, 2 H), 7.58 (5-Ph-*o*, 2 H), 7.57 (Ph-*p*, 1 H), 7.47 (Ph-*m*, 2 H), 7.37 (5-Ph-*m*, 2 H), 7.28 (5-Ph-*p*, 1 H), 2.48 (CH_3, 3 H, s); ^{13}C NMR δ 166.1 (NHC=O), 158.8 (C-2), 142.4 (C-5), 133.5 (Ph-*i*), 132.1 (Ph-*p*), 129.1[a] (5-Ph-*i*), 128.7 (Ph-*m*), 128.5 (5-Ph-*m*), 128.1 (5-Ph-*p*), 127.8[a] (C-4), 127.4 (Ph-*o*), 125.0 (5-Ph-*o*), 14.2 (Me); IR (KBr pellet) ν max 3260 (NH), 1660 (NHCO), 1615 (C=N) cm^{-1}; MS *m/e* 279 (MH^+). **2,5-Diphenyl-4-acetamidooxazole (6a)**: ^1H NMR δ (DMSO, 90 °C) 8.04 (2-Ph-*o*, 2 H), 7.72 (5-Ph-*o*, 2 H), 7.6 (2-Ph-*m*+*p*), 7.50 (5-Ph-*m*, 2 H), 7.38 (5-Ph-*p*, 1 H), 2.08 (CH_3, 3 H, s); ^{13}C NMR δ 168.98 (HNC=O), 156.9 (C-2), 141.5 (C-5), 131.6[b] (2-Ph-*i*), 131.4[b] (5-Ph-*i*), 130.1 (2-Ph-*p*), 128.5[a] (5-Ph-*m*), 128.2[a] (2-Ph-*m*), 127.6 (5-Ph-*p*), 126.2 (C-4), 125.4 (2-Ph-*o*), 124.3 (5-Ph-*o*), 22.0 (CH_3); IR (KBr pellet) ν max 3450 (NH), 1650 (NHCO), 1530 (C=N) cm^{-1}; MS *m/e* 279 (MH^+). Anal. Calcd for $C_{17}H_{14}N_2O_2$: C, 73.76; H, 5.07; N, 10.07. Found: C, 73.63; H, 5.28; N, 10.23.

Reaction of 1 with Benzonitrile. A mixture of **1** (0.16 g, 0.5 mmol) and $POCl_3$ (0.01 mL, 0.05 mmol) in benzonitrile (3 mL) heated at 90–100 °C for 3 h afforded 4-amidooxazole **5b** as a yellowish solid (0.1 g, 58%, after chromatography EtOAc–hexane, 1:2 and then 1:1). **2,5-Diphenyl-4-benzamidooxazole (5b)**: ^1H NMR δ 8.07 (2-Ph-*o*, 2 H), 8.02 (NH, 1 H, br s), 7.96 (4-Ph-*o*, 2 H), 7.69 (5-Ph-*o*, 2 H), 7.58 (4-Ph-*p*, 1 H), 7.5 (2-Ph-*m*+*p*, 4-Ph-*m*, 5 H), 7.41 (5-Ph-*m*, 2 H), 7.32 (5-Ph-*p*, 1 H); ^{13}C NMR δ 166 (NHC=O), 158.5 (C-2), 142.6 (C-5), 133.4 (4-Ph-*i*), 132.3 (4-Ph-*p*), 130.6 (2-Ph-*p*), 128.8[a] (5-Ph-*m* + 4-Ph-*m*), 128.6[a] (2-Ph-*m*), 128.3 (5-Ph-*p*), 127.9[b] (C-4), 127.8[b] (2-Ph-*i*), 127.5 (4-Ph-*o*), 127.0[b] (5-Ph-*i*), 126.3 (2-Ph-*o*), 125.3 (5-Ph-*o*); MS *m/e* 341 (MH^+).

Reaction of 1 with Hexanenitrile. A mixture of **1** (0.15 g, 0.48 mmol) and BF_3·etherate (0.03 mL, 0.24 mmol) and hexanenitrile (2 mL) heated at 90 °C for 1.5 h afforded **5c**, **6c** and **7c**. Separation by chromatography (EtOAc–hexane, 1:5, 1:3.5, 1:2, 1:1) gave **5c** and **6c** as a yellow oil (0.065 g, 41%) and **7c** as a white solid (mp 164 °C) (0.034 g, 21%). **2-Hexyl-4-benzamido-5-phenyloxazole (5c)**: ^1H NMR δ 8.04 (NH, 1 H, br s), 7.92 (4-Ph-*o*, 2 H), 7.59 (5-Ph-*o*, 2 H), 7.5–7.4 (4-Ph-*m*+*p*, 3 H), 7.37 (5-Ph-*m*, 2 H), 7.28 (5-Ph-*p*, 1 H), 2.79 (CH_2-oxazole, 2 H, t, *J* = 8.5 Hz), 1.71 (CH_2, 2 H, m), 1.39–1.33 (CH_2CH_2, 4 H, m), 0.91 (CH_3, 3 H, t, *J* = 7 Hz); ^{13}C NMR δ 165.9 (NHC=O), 162.4 (C-2), 141.5 (C-5), 133.5 (4-Ph-*i*), 132.1 (4-Ph-*p*), 128.7 (4-Ph-*m*), 128.5 (5-Ph-*m*), 127.9 (5-Ph-*p*), 127.4 (4-Ph-*o*), 125.0 (5-Ph-*o*), 31.2, 28.3, 26.5, 22.2 (CH_2), 13.8 (CH_3); IR (KBr pellet) ν max: 3280 (NH), 1660 (NHC=O), 1620 (C=N) cm^{-1}; MS *m/e* 335 (MH^+), 238 ($MH^+ - CH_3(CH_2)_4CN$). **2,5-Diphenyl-4-heptanamidooxazole (6c)**: ^1H NMR δ 8.10 (2-Ph-*o*, 2 H), 7.66 (5-Ph-*o*, 2 H), 7.60–7.40 (other Ar-H), 2.47 (CH_2-oxazole, 2 H, br t, *J* = 8.5 Hz), 1.71 (CH_2, 2 H, m), 1.39–1.33 (CH_2CH_2, 4 H, m), 0.91 (CH_3, 3 H, t, *J* = 7 Hz); ^{13}C NMR δ 170.0 (NHC=O), 142.6 (C-5), 130.5 (2-Ph-*p*), 128.7 (2-Ph-*m* + 5-Ph-*m*), 126.2 (2-Ph-*o*), 125.2 (5-Ph-*o*), 36.7, 31.4, 25.1, 22.3 (CH_2), 13.8 (CH_3); MS *m/e* 335 (MH^+). **2-Benzamido-2-heptanamido-1-phenylethanone (7c)**: ^1H NMR δ 8.42 (NH, 1 H, d, *J* = 7 Hz), 8.07 (Ph-*o*, 2 H), 7.81 (PhCON-*o*, 2 H), 7.63 (NH, 1 H, d, *J* = 7 Hz), 7.55 (Ph-*p*, 1 H), 7.50 (PhCON-*p*), 7.4 (PhCON-*m* + Ph-*m*), 6.43 (CH, 1 H, t, *J* = 7 Hz), 2.20 (CH_2, 2 H, t, *J* = 7.5 Hz), 1.53 (CH_2, 2 H, quintet), 1.25–1.11 (CH_2CH_2, 4 H, m), 0.78 (CH_3, t, *J* = 7.5 Hz); ^{13}C NMR δ 192.8 (C=O), 173.7 (NHC=O), 167.3 (NHC=O), 134.0 (Ph-*i*), 133.5[a] (Ph-*p*), 132.9[a] (PhCON-*i*), 132.1 (Ph-*p*), 128.7, 128.6, 128.5 (PhCON + *m* + *o* + Ph-*m*), 127.3 (Ph-*o*), 60.0 (CH), 36.0, 24.9, 31.1, 22.2 (CH_2), 13.8 (CH_3); IR (KBr pellet) ν max 3280 (NH), 1700 (C=O), 1670 (NHC=O) cm^{-1}; MS *m/e* 353 (MH^+), 238 ($MH^+ - H_2N(CH_2)_4CH_3$); HRMS 353.1846 (MH^+), calcd for $C_{21}H_{25}N_2O_3$ 353.1865.

Reaction of 1 with 2-Butenenitrile. A mixture of **1** (0.17 g, 0.54 mmol) and $POCl_3$ (0.02 mL, 0.1 mmol) in 2-butenenitrile (3 mL) was heated at 80–90 °C for 1.5 h. 2-Butenenitrile was distilled out under reduced pressure, and the residue was dissolved in $CHCl_3$ and worked up as usual. Chromatography (EtOAc–hexane, 1:2, and then MeOH) provided **5d** as a yellow oil (cis + trans) (0.07 g, 43%), **6d** as a white solid (0.06 g, 30%) (trans, mp 255 °C), and **7d** as a white solid (cis + trans) (0.035 g, 20%). **2-Propenyl-4-benzamido-5-phenyloxazole (5d)**: ^1H NMR δ 8.09 (NH, 1 H, br s), 7.92 (4-Ph-*o*, 2 H), 7.61 (5-Ph-*o*, 2 H), 7.56 (4-Ph-*p*, 1 H), 7.47 (4-Ph-*m*, 2 H), 7.36 (5-Ph-*m*, 2 H), 7.27 (5-Ph-*p*, 1 H), 6.80 (CH=C*H*CH_3, 1 H, dq, *J* = 16.5, 7 Hz), 6.26 (C*H*=$CHCH_3$, 1 H, dm, *J* = 16.5 Hz), 1.95 (CH_3, 3 H, dd, *J* = 7, 1.6 Hz); ^{13}C NMR δ 166.1 (NHC=O), 158.0 (C-2), 141.6 (C-4), 135.9 (C=C), 133.4 (4-Ph-*i*), 132.0 (4-Ph-*p*), 130.1 (5-Ph-*i*), 128.8, 128.6 (4-Ph-*m*, 5-Ph-*m*), 128.0 (5-Ph-*p*), 127.5 (4-Ph-*o*), 125.1 (5-Ph-*o*), 117.4 (C=C), 18.4 (CH_3); MS *m/e* 305 (MH^+), 238 ($MH^+ - CH_3CH$=CHCN). **2,5-Diphenyl-4-(2-butenamido)oxazole (6d)**: ^1H NMR (CD_3OD) δ 8.08 (2-Ph-*o*, 2 H), 7.73 (5-Ph-*o*, 2 H), 7.5 (2-Ph-*m*+*p*, 3 H), 7.46 (5-Ph-*m*, 2 H), 7.36 (5-Ph-*p*, 1 H), 7.02 (CH=C*H*CH_3, 1 H, dq, *J* = 16.5, 7 Hz), 6.22 (C*H*=$CHCH_3$, 1 H, dm, *J* = 16.5 Hz), 1.96 (CH_3, 3 H, d, *J* = 7 Hz); ^{13}C NMR (CD_3OD) δ 160.0 (C-2), 143.9 (C=C), 137.9 (C-5), 134.7 (2-Ph-*i*), 133.1 (5-Ph-*i*), 132.0 (2-Ph-*p*), 130.1, 129.8 (2-Ph-*m*, 5-Ph-*m*), 129.6 (5-Ph-*p*), 128.1 (C-4), 127.3 (2-Ph-*o*), 126.1 (5-Ph-*o*), 125.3 (C=C), 18.0 (CH_3); MS *m/e* 305 (MH^+). Anal. Calcd for $C_{19}H_{16}N_2O_2$: C, 74.98; H, 5.30. Found: C, 74.56; H, 5.46. **2-Benzamido-2-(2-butenamido)-1-phenylethanone (7d)**: ^1H NMR δ 8.80 (NH, 1 H, br d, *J* = 6.25 Hz), 8.19 (NH, 1 H, br d, *J* = 6.25 Hz), 8.04 (Ph-*o*, 2 H), 7.73 (PhCON-*o*, 2 H), 7.45–7.20 (PhCON-*m*+*p*, Ph-*m*+*p*, 6 H), 6.75 (C*H*=CHCH$_3$, 1 H, dq, *J* = 15, 6.5 Hz), 6.60

(12) Hassner, A.; Stern, M. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 478; *J. Org. Chem.* **1990**, *55*, 2304.

(CH, 1 H, t, J = 6.25 Hz), 5.88 (CH=C*H*CH_3, 1 H, dq, J = 15, 1.25 Hz), 1.68 (CH_3, 3 H, dd, J = 6.5, 1.25 Hz); ^{13}C NMR δ 193.1 (C=O), 167.4, 166.2 (NHC=O), 141.9 (C=C), 134.0 (Ph-*i*), 133.5 (Ph-*p*), 132.9 (PhCON-*i*), 132.0 (PhCON-*p*), 128.8 (Ph-*o*), 128.5 (PhCON-*m* + Ph-*m*), 127.4 (PhCON-*o*), 124.2 (C=C), 59.9 (CH), 17.7 (CH_3); MS CI (NH_3) m/e 323 (MH^+).

Reaction of 1 with Propanenitrile. A mixture of 1 (0.15 g, 0.48 mmol) and $POCl_3$ (0.02 mL, 0.1 mmol) in propanenitrile (3 mL) was heated at 80–90 °C for 1.5 h, the nitrile was evaporated under reduced pressure, and the residue was dissolved in $CHCl_3$ and worked up as usual. Chromatography (EtOAc–hexane, 1:1) gave **5e** (0.03 g, 22%), **6e** (0.048 g, 35%), and **7e**, mp 218 °C (0.045 g, 31%). **2-Ethyl-4-benzamido-5-phenyloxazole (5e)**: ^1H NMR δ 8.00 (NH, 1 H, br s), 7.93 (4-Ph-*o*, 2 H), 7.59 (5-Ph-*o*, 2 H), 7.57 (4-Ph-*p*, 1 H), 7.48 (4-Ph-*m*, 2 H), 7.38 (5-Ph-*o*, 2 H), 7.29 (5-Ph-*p*, 1 H), 2.48 (CH_2, 2 H, q, J = 7.5 Hz), 1.38 (CH_3, 3 H, t, J = 7.5 Hz); ^{13}C NMR δ 166.1 (NHC=O), 163.1 (C-2), 142.2 (C-5), 133.5 (4-Ph-*i*), 132.1 (4-Ph-*p*), 129.2[a] (5-Ph-*i*), 128.7[a] (C-4), 128.6[b] (4-Ph-*m*), 128.5[b] (5-Ph-*m*), 128.0 (5-Ph-*o*), 127.9 (5-Ph-*o*), 125.0 (5-Ph-*o*), 21.8 (CH_2), 10.9 (CH_3); MS m/e 293 (MH^+), 238 ($MH^+ - CH_3CH_2CN$). Anal. Calcd for $C_{18}H_{16}N_2O_2$: C, 73.95; H, 5.52. Found: C, 74.24; H, 5.76. **2,5-Diphenyl-4-propionamidooxazole (6e)**: ^1H NMR (CD_3OD) δ 8.08 (2-Ph-*o*, 2 H), 7.75 (5-Ph-*o*, 2 H), 7.65–7.35 (other Ar-H), 7.32 (5-Ph-*p*), 2.89 (CH_2, 2 H, q, J = 7.5 Hz), 1.41 (CH_3, 3 H, t, J = 7.5 Hz); MS m/e 293 (MH^+). **2-Benzamido-2-propionamido-1-phenylethanone (7e)**: ^1H NMR δ 8.50 (NH, 1 H, br d, J = 7 Hz), 8.10 (3-Ph-*o*, 2 H), 7.79 (PhCON-*o*, 2 H), 7.55 (Ph-*p*, 1 H), 7.38 (PhCON-*p*), 7.45–7.35 (Ph-*m* + PhCON-*m*), 6.52 (CH, 1 H, t, J = 7 Hz), 2.28 (CH_2, 2 H, q, J = 7 Hz), 1.10 (CH_3, 3 H, t, J = 7 Hz); ^{13}C NMR δ 192.5 (C=O), 174.5 (NHC=O), 167.3 (NHC=O), 133.9[a] (PhCON-*i*), 133.7[b] (PhCON-*p*), 133.5[a] (Ph-*i*) 132.2[b] (Ph-*p*), 128.6 (Ph-*m* + PhCON-*m*), 128.5 (PhCON-*o*), 127.2 (Ph-*o*), 59.9 (CH), 29.2 (CH_2), 9.2 (CH_3); MS m/e 311 (MH^+), 238 ($MH^+ - CH_3CH_2C(O)NH_2$); HRMS 311.1400 (MH^+), calcd for $C_{18}H_{18}N_2O_3$ 311.1395.

Reaction of 2-Benzamido-2-methoxy-1-phenyl-1-propanone with Acetonitrile. From **4b** (0.024 g, 0.085 mmol) and $POCl_3$ (0.003 mL, 0.042 mmol) in acetonitrile (1.5 mL) at 70 °C for 0.5 h **7b** was obtained, after chromatography (EtOAc–hexane, 1:1), as a yellow oil. (0.011 g, 42%). **2-Benzamido-2-methyl-2-acetamido-1-phenylethanone (7b)**: ^1H NMR δ 8.54 (NH, 1 H, br s), 8.23 (Ph-*o*, 2 H), 8.06 (NH, 1 H, br s), 7.82 (PhCON-*o*, 2 H), 7.55–7.40 (other Ar-H, 6 H), 2.08 (CH_3, 3 H, s), 1.98 (CH_3, 3 H, s); IR (neat) ν max 3400 (NH), 1690 (CO), 1660, 1650 (NHC=O) cm^{-1}; MS m/e 311 (MH^+), 252 ($MH^+ - CH_3C(O)NH_2$).

Reaction of 2-Benzamido-2-hydroxyacetic Acid (8a) with Acetonitrile. A mixture of **8a** (0.156 g, 0.8 mmol) and $POCl_3$ (0.016 mL, 0.08 mmol) heated under reflux in acetonitrile (3 mL) for 5 min afforded **10a** as a white solid which precipitated on the walls of the flask. The product **10a** (mp 204 °C) (0.189 g, 100%) needed no further purification. **1-Benzamido-1-acetamidoacetic acid (10a)**: ^1H NMR (DMSO) δ 9.28 (NH, 1 H, d, J = 7.3 Hz), 8.63 (NH, 1 H, d, J = 7.3 Hz), 7.88 (Ph-*o*, 2 H), 7.58 (Ph-*p*, 1 H), 7.50 (Ph-*m*, 2 H), 5.77 (CH, 1 H, "ddd", J = 7.3 Hz), 1.90, 1.85 (CH_3, 3 H, s, two rotamers); ^{13}C NMR δ 169.9 (NHC=O), 169.3 (CO_2H), 165.9 (NHC=O), 133.2 (Ph-*i*), 131.6 (Ph-*p*), 128.3 (Ph-*m*), 127.3 (Ph-*o*), 56.5 (CH), 22.3 (CH_3); IR (KBr pellet) ν max 3350 (NH), 3280 (OH), 1715 (CO_2H), 1665 (NHC=O), 1630 (NHC=O) cm^{-1}; MS m/e 237 (MH^+), 219 ($MH^+ - H_2O$), 191 ($MH^+ - CO_2H$); HRMS 237.0876 (MH^+), calcd for $C_{11}H_{13}N_2O_4$ 237.0875.

Reaction of 1-Benzamido-1-methoxymethane (8b) with Acetonitrile. Amide **8b** (0.1 g, 0.6 mmol) and $POCl_3$ (0.01 mL, 0.05 mmol) heated in acetonitrile (3 mL) under reflux for 1.5 h afforded **10b** (0.07 g, 61%, mp 181 °C) and methylene bisbenzamide (0.02 g, 13%) after chromatography (EtOAc–hexane, 1:1). **1-Benzamido-1-acetamidomethane (10b)**: ^1H NMR δ 7.79 (Ph-*p*, 2 H), 7.53 (Ph-*p*, 1 H), 7.44 (Ph-*m*, 2 H), 6.90 (NH, 1 H, br s), 4.81 (CH_2, 2 H, "t", J = 6 Hz), 2.00 (CH_3, 3 H, s); ^{13}C NMR δ 171.4 (PhNHC=O), 168.4 (MeNHC=O), 133.4 (Ph-*i*), 131.9 (Ph-*p*), 128.5 (Ph-*m*), 127.1 (Ph-*o*), 45.1 (CH_2), 23.0 (CH_3); MS m/e 193 (MH^+), 122 ($PhC(O)NH_2$); HRMS 192.0891 (M^+) calcd for $C_{10}H_{12}N_2O_2$ 192.0899.

Reaction of 1-Benzamido-1-methoxy-2-propanone (4a) with Acetonitrile. A mixture of **4a** (0.034 g, 0.16 mmol) and BF_3·etherate (0.02 mL, 0.16 mmol) in acetonitrile (2 mL) heated under reflux for 1.5 h afforded after chromatography **10d** as a white solid mp 198–199 °C (0.032 g, 85%) followed by traces of **5i** and **6i**. **1-Benzamido-1-acetamido-2-propanone (10d)**: ^1H NMR δ 8.22 (NH, 1 H, br d), 7.84 (Ph-*o*, 2 H), 7.64 (NH, 1 H, br d), 7.53 (Ph-*p*, 1 H), 7.43 (Ph-*m*, 2 H), 5.43 (CH, 1 H, t, J = 7 Hz), 2.30 (CH_3, 3 H, s), 2.05 (CH_3, 3 H, s); ^{13}C NMR δ 199.9 (C=O), 171.0 (PhNHC=O), 167.7 (MeNHC=O), 132.4 (Ph-*p*), 128.7 (Ph-*m*), 127.3 (Ph-*o*), 63.6 (CH), 25.3 (CH_3), 22.8 (CH_3); MS m/e 235 (MH^+), 176 ($MH^+ - CH_3C(O)NH_2$); HRMS 235.1080 (MH^+), calcd for $C_{12}H_{15}N_2O_3$ 235.1082.

4,5-Dimethoxy-2,5-diphenyl-2-oxazoline (14). A solution of 1 (0.14 g, 0.45 mmol) and BF_3·etherate (0.027 mL, 0.22 mmol) in dry $CHCl_3$ (3 mL) was stirred at room temperature for 1.5 h. The solvent was evaporated, and the residue was chromatographed on basic alumina (EtOAc–hexane, 1:3). **14** was obtained as a colorless oil (0.053 g, 42%) followed by starting material. **14**: ^1H NMR δ 8.13 (2-Ph-*o*, 2 H), 7.6–7.4 (other Ar-H, 8 H), 5.23 (4-H, 1 H, s), 3.30, 3.26 (OMe, 3 H, s); ^{13}C NMR δ 165.6 (C=N), 133.9 (5-Ph-*i*), 132.1 (2-Ph-*p*), 128.7[a] (5-Ph-*m* + 5-Ph-*p*), 128.4[a] (2-Ph-*m*), 128.0[b] (5-Ph-*o*), 127.5 (2-Ph-*i*), 127.4 (2-Ph-*o*), 112.1 (C-5), 103.8 (C-4), 56.5, 51.3 (OMe); MS m/e 284 (MH^+), 252 (MH^+ – MeOH).

1-(1′-Benzamido-2′-oxo-2′-phenylethyl)-5-methyltetrazole (17). To a solution of **4** (0.1 g, 0.37 mmol) in dry acetonitrile (3 mL) in a flame-dried system under Ar was added polymeric azide reagent[12] (0.3 g, 0.74 mmol) and freshly distilled BF_3·etherate (0.01 mL, 0.08 mmol). After 10 min of reflux, the solvent was removed, and NMR and MS analyses of the crude product indicated the presence of **17** (10% yield according to NMR) together with starting **4**. **17**: ^1H NMR δ 8.17 (3-Ph-*o*, 2 H), 7.82 (1-Ph-*o*, 2 H), 7.6–7.4 (other Ar-H), 6.75 (CH, 1 H, d, J = 6 Hz), 2.00 (CH_3, 3 H, s); MS m/e 321 (MH^+), 238 (MH^+ – tetrazole), 84 (tetrazole).

Supplementary Material Available: NMR spectra for **5a,b,d,e**, **5c + 6c**, **7b–e**, and **10a,b,d** (25 pages). Ordering information is given on any current masthead page.