IR ($CHCl_3$) 3500 (br), 1700 cm^{-1}.

5-Hydroxy-2-[(trimethylsilyl)oxy]-2-methyl-3-nonanone (5b): ^1H NMR ($CDCl_3$) δ 3.98 (1 H, m), 3.05 (1 H, br s), 2.76 (2 H, m), 1.31 (6 H, s), 1.6–1.1 (6 H, m), 0.90 (3 H, br t), 0.14 (9 H, s); IR ($CHCl_3$) 3500 (br), 1700 cm^{-1}.

5-Hydroxy-2-[(trimethylsilyl)oxy]-2,5-dimethyl-3-octanone (5c): ^1H NMR ($CDCl_3$) δ 2.80 (2 H, m), 1.6–1.3 (10 H, m), 1.21 (3 H, s), 0.91 (3 H, br t), 0.17 (9 H, s); IR ($CHCl_3$) 3450 (br), 1700 cm^{-1}.

5-Hydroxy-2-[(trimethylsilyl)oxy]-4-*n*-propyl-2-methyl-3-octanone (5d): ^1H NMR ($CDCl_3$) δ 4.25 (1 H, m), 3.94 (1 H, m), 1.9–1.2 (14 H, m), 0.90 (3 H, br t), 0.17 (9 H, s); IR ($CHCl_3$) 3450 (br), 1705 cm^{-1}.

Hydroxy ketone 5e: ^1H NMR ($CDCl_3$, 300 MHz) δ 4.43 (1 H, q), 3.40 (1 H, dt), 2.0–1.5 (6 H, m), 1.37 (3 H, s), 1.34 (3 H, s), 0.18 (9 H, s); IR ($CHCl_3$) 3450 (br), 1700 cm^{-1}.

Hydroxy ketone 5f: ^1H NMR ($CDCl_3$) δ 4.05 (1 H, m), 3.03 (1 H, m), 2.0–1.4 (14 H, m), 0.19 (9 H, s); IR ($CHCl_3$) 3500 (br), 1700 cm^{-1}.

3-Hydroxy-3-methylhexanoic Acid, Methyl Ester. General Oxidative Cleavage Procedure. Aqueous 0.5 M periodic acid (8.4 mL, 4.2 mmol) was added to a solution of crude **5c** (156 mg, partially desilylated) in methanol (5 mL). After stirring 90 min at 25 °C, the reaction was diluted with water, extracted with EtOAc, dried ($MgSO_4$), and concentrated. The crude acid was directly esterified with diazomethane. The resultant methyl ester was purified by flash chromatography (20% EtOAc/hexane) to give 40 mg of **6c** (42% from **4c**): ^1H NMR ($CDCl_3$, 300 MHz) δ 3.72 (3 H, s), 2.53 (1 H, d), 2.45 (1 H, d), 1.7–1.3 (5 H, m), 1.24 (3 H, s), 0.92 (3 H, t); IR ($CHCl_3$) 3520 (br) 1720 cm^{-1}.

3-Hydroxy-2-*n*-propylhexanoic acid, methyl ester: purified by flash chromatography (20% EtOAc/hexane); ^1H NMR ($CDCl_3$, 300 MHz) δ 3.71 (3 H, s), 3.67 (1 H, m), 2.47 (1 H, m), 1.9–1.2 (9 H, m), 0.92 (6 H, two overlapping t); IR ($CHCl_3$) 3500 (br), 1715 cm^{-1}; MS (of derived trimethylsilyl ether), *m/e* calcd for $C_{10}H_{21}O_3Si$ (M - CH_3) 217.1260, found 217.1260.

Generation and Reduction of Methoxy-Substituted Isoxazolines 10. Addition of benzenesulfonylcarbonitrile oxide and displacement with methoxide were both conducted according to the procedure of Wade.[17] Reduction to **11a,b** was carried out by following the standard reduction procedure (method 2).[3a]

Acknowledgment. The National Institutes of Health (GM-31678) is thanked for partial support of this project. Support from the Health, Research, and Services Foundation is also gratefully acknowledged. We thank Dr. A. Marcus for the high-resolution mass spectra.

Registry No. **1a**, 91157-51-6; **1b**, 91157-52-7; **1c**, 91157-53-8; **1d**, 91157-54-9; **1e**, 91157-73-2; **1f**, 91157-55-0; **1g**, 91157-56-1; **2a**, 42052-52-8; **2b**, 91157-57-2; **2c**, 59671-45-3; **2d**, 91157-58-3; *cis*-**2e**, 91157-59-4; *trans*-**2e**, 91157-74-3; **2f**, 91157-60-7; **3a**, 5397-27-3; **3b**, 91157-61-8; **3c**, 5292-13-7; **3e**, 91157-62-9; **4a**, 91157-63-0; **4b**, 91157-64-1; **4c**, 91157-65-2; **4d**, 91157-66-3; **4e**, 91157-67-4; **4f**, 91157-68-5; **5a**, 76777-60-1; **5b**, 76777-62-3; **5c**, 91157-69-6; **5d**, 91157-70-9; **5e**, 91157-71-0; **5f**, 91157-72-1; **6a**, 3480-87-3; **6b**, 17587-29-0; **6c** (methyl ester), 91178-20-0; **6d** (methyl ester), 91157-75-4; **6e**, 17502-28-2; **6f** (methyl ester), 936-03-8; **7**, 55816-65-4; **7** (alcohol), 5447-98-3; Ia, 27143-81-3; Ia (oxime chloride), 3273-26-5; $PhCH{=}CH_2$, 100-42-5; $C_4H_9CH{=}CH_2$, 592-41-6; *trans*-*n*-proCH=CHpro-*n*, 14850-23-8; *cis*-PhCH=CHPh, 645-49-8; $C_3H_7C(CH_3){=}CH_2$, 763-29-1; Me_3SiCl, 75-77-4; PhNCO, 103-71-9; methylenecyclohexane, 1192-37-6; cyclopentene, 142-29-0; cyclohexene, 110-83-8.

Selective Carbon–Carbon Bond Formation at the Oxazole Ring. Cycloadditions and Michael-Type Additions of Ketenes to 1,3-Oxazoles

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1,3-Oxazole (**1a**) and 4-methyl-1,3-oxazole (**1b**) react with dichloroketene (DCK) affording the 2-(dichloroacetyl)oxazoles **3a** and **3b**, respectively, very likely via the corresponding *N*-acyloxazolium ylides as intermediates. 2-(*N*-Benzyl-*N*-methylamino)-1,3-oxazole (**1c**) and *tert*-butylcyanoketene (TBCK) give the 5-acyl derivative **4c** and a mixture of the diastereomeric 2:1 cycloadducts **5** and **6** constituted by a δ-lactone ring condensed across the former C_4–C_5 bond of **1c**. The 4-methyl derivative **1d** affords the ketone **4d** and the enol ester **7**, whereas the 4,5-dimethyl derivative **1e** undergoes the addition of 2 mol of TBCK and ring fission producing a 2,5-dihydrofuran derivative **8**. Other ketenes, namely diphenyl- (DPK), chlorocyano- (CCK), and dichloroketene (DCK), react with **1c** and **1d** to give the corresponding 5-acyl derivatives **4**, and in the case of DCK only, also the enol ester **11**. Plausible schemes accounting for the formation of products **4**–**11** involve as a common step, the initial attack of the ketene at C_5 of the oxazole ring to give a zwitterion which undergoes different reactions depending on the substitution at C_4 and C_5 of the heterocycle.

The chemistry of 1,3-oxazoles[1] continues to attract interest because of the presence of the oxazole ring in numerous biologically active compounds both natural and synthetic.[2] Oxazole derivatives can be prepared by various cyclization reactions, whereas effective methods for the direct introduction of a functional group in the oxazole ring are rare. In fact, electrophilic substitutions are often accompanied by the same reaction on an aromatic substituent and many nucleophilic substitutions are precluded because of ring scission.[1a] The most synthetically useful reactions of oxazoles are [4 + 2] cycloadditions with olefinic and acetylenic dienophiles.[1a] These reactions give unstable bicyclic systems which undergo fragmentation and rearrangement to pyridine or furan derivatives.[1] The reaction with dimethyl acetylenedicarboxylate is the only one reported[3] to give isolable bicyclic products, however these

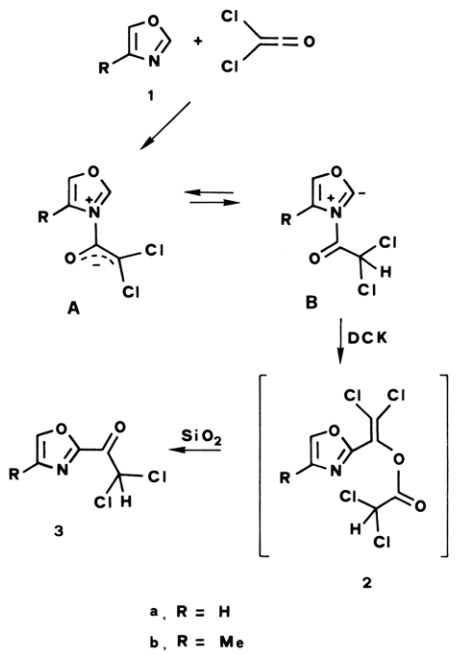
(1) (a) Lakhan, R; Ternai, B. *Adv. Heterocycl. Chem.* **1974**, *17*, 99. (b) Turchi, I. J.; Dewar, M. J. S. *Chem. Rev.* **1975**, 389. (c) Turchi, I. J. *Ind. Eng. Chem. Prod. Res. Dev.* **1981**, *20*, 32.

(2) Cooper, R. D. G. In "Topics in Antibiotic Chemistry"; Sammes, P. G., Ed.; Ellis Horwood Ltd.: Chichester, 1980; Vol. 3, p 39. Bentley, P. H.; Berry, P. D.; Brooks, G.; Gilpin, M. L.; Hunt, E.; Zomay, I. I. In "Recent Advances in the Chemistry of β-Lactam Antibiotics"; Gregory, G. I., Ed.; Royal Society of Chemistry: London, 1981; Special Publication no. 38. Westley, J. W.; Evans, R. H.; Blount, J. F. *J. Antibiot.* **1979**, *32*, 874. Liesch, J. M.; Rinehart, K. L. *J. Am. Chem. Soc.* **1977**, *99*, 1645. Evans, D. A.; Sacks, C. E.; Kleschick, W. A.; Taber, T. R. *Ibid.* **1979**, *101*, 6789. Grieco, P. A.; Kanai, K.; Williams, E. *Heterocycles* **1979**, *12*, 1623. Meyers, A. I.; Amos, R. A. *J. Am. Chem. Soc.* **1980**, *102*, 870. Nagao, Y.; Yamada, S.; Fugita, E. *Tetrahedron Lett.* **1983**, *24*, 2287.

(3) Medveskaya, L. B.; Kondrat'eva, G. Ya.; Bykonova, N. V. *Izv. Akad. Nauk. SSSR, Ser. Khim.* **1979**, *7*, 1613; *Chem. Abstr.* **1979**, *91*, 175251.

0022-3263/84/1949-3478$01.50/0

Scheme I



have been shown to be 2:1 cycloadducts accross the C=N bond. On the other hand, there are no examples of [2 + 2] cycloadditions although this would constitute a direct entry to condensed bicyclic systems among which those with the clavam[4] or isoclavam skeleton[5] are important for their potential antibiotic activity.

In relation to our studies on the reactivity of 1,3-thiazoles with activated unsaturated electrophiles,[6] we are investigating the behavior of 1,3-oxazoles with the same reactants. In this paper we describe the reactions of some 1,3-oxazoles **1** with ketenes, a class of highly reactive heterocumulenes which are well known for their tendency to take part in thermally induced [2 + 2] cycloadditions with both isolated and conjugated carbon–carbon[7] and carbon–nitrogen[8] double bonds. Fused four-membered rings were not obtained; instead the reactions afforded 2:1 cycloadducts across the C_4–C_5 bond and Michael-type adducts at C_2 or C_5, depending on the oxazole substituents. This constitutes a new approach for carbon–carbon bond formation at the oxazole ring.

Results and Discussion

1,3-Oxazole (**1a**) and its 4-methyl derivative **1b** on treatment with 1 equiv of dichloroketene (DCK) (generated in situ by dehydrohalogenation of the corresponding acyl chloride by Et_3N[9]) gave low yields[10] of the corresponding 2-acyloxazoles **3a** (7%) and **3b** (25%). The yield of **3b** was not improved using a 2:1 molar ratio of ketene:oxazole. In both cases the NMR spectra of the crude reaction mixture revealed the formation of a primary product, very likely the enol ester **2**, which fragments to **3** on standing or when subjected to isolation procedures.[11]

The formation of substitution products at C_2 from oxazoles **1a** and **1b** with DCK shows the same reactivity as the analogous thiazoles[12] with the same ketene. Direct electrophilic attack by DCK at C_2 of the oxazole ring is incompatible with the lowest charge density on this atom as indicated by molecular orbital calculations[13] and the common chemical behavior of oxazoles toward electrophiles.[14] Therefore, it is conceivable that as for thiazoles,[12] the reaction occurs via the ylide B (Scheme I), which constitutes an activated species suitable for the electrophilic attack at C_2 by DCK. The presence of Et_3N employed for the ketene generation may contribute to ylide formation as does the proton migration in the zwitterion A. Although differing in rate of formation and stability, oxazolium and thiazolium 2-ylides are well-known intermediates which have been postulated in the base-catalyzed proton exchange and decarboxylation of oxazolium and thiazolium cations.[15]

Since ketenes are electrophilic at the central carbon of the cumulative system,[16] the donor character of the oxazole ring was enhanced by a 2-dialkylamino substituent.[17] The required 2-(*N*-benzyl-*N*-methylamino)-1,3-oxazoles **1c–e** were readily prepared by *N*-methylation of the corresponding 2-(*N*-benzylamino) derivatives which in turn were obtained by the alkylcyanamide–hydroxy ketone condensation method.[18]

The reaction of 2-(*N*-benzyl-*N*-methylamino)-1,3-oxazole (**1c**) with 1 equiv of *tert*-butylcyanoketene (TBCK) in benzene at room temperature afforded the 1:1 Michael-type adduct **4c** (25%) as the main product together with a mixture of the diastereomeric 2:1 cycloadducts **5** (8%) and **6** (7%). Since the excess of **1c** was recovered unchanged, other products besides those isolated were not formed in relevant amounts. The overall yield and product distribution did not change by a reversed order of mixing

(4) Brown, D.; Evans, J. R.; Fletton, R. A. *J. Chem. Soc., Chem. Commun.* **1979**, 282.

(5) Brennan, J.; Richardson, G.; Stoodley, R. J. *J. Chem Soc., Perkin Trans. 1* **1983**, 649.

(6) (a) Dondoni, A.; Medici, A.; Venturoli, C.; Forlani, L.; Bertolasi, V. *J. Org. Chem.* **1980**, *45*, 621. (b), Medici, A.; Pedrini, P.; Venturoli, C.; Dondoni, A. *Ibid.* **1981**, *46*, 2790. (c) Medici, A.; Fogagnolo, M.; Pedrini P.; Dondoni, A. *Ibid.* **1982**, *47*, 3844. (d) Medici, A.; Pedrini, P.; Dondoni, A. *J. Chem. Soc., Chem. Commun.* **1981**, 655.

(7) Brady, W. T. *Synthesis* **1971**, 415. Bartlett, P. D. *Q. Rev. Chem. Soc.* **1971**, *25*, 473. Brady, W. T. In "The Chemistry of Ketenes, Allenes and Related Compounds"; Patai, S., Ed.; Wiley: New York, 1980; Part I, Chapter 8. Moore, H. W. *Chem. Soc. Rev.* **1973**, *2*, 415. Vogel, E.; Muller, K. *Liebigs Ann. Chem.* **1958**, 615, 31.

(8) Reinhoudt, D. N. *Adv. Heterocycl. Chem.* **1977**, *21*, 253. Schaumann, E.; Mrotzek, H. *Chem. Ber.* **1978**, *111*, 661. Schaumann, E.; Assman, F.; Mrotzek, H. *Leibigs Ann. Chem.* **1979**, 334. Moore, H. W.; Hughes, G. *Tetrahedron Lett.* **1982**, *23*, 4003. Alcaide, B.; Leon-Santiago, M. A.; Perez-Ossorio, R.; Plumet, J.; Sierra, M. A.; De la Torre, M. C. *Synthesis* **1982**, 989.

(9) Stevens, H. C.; Reich, D. A.; Brandt, D. R.; Fountain, K. R.; Gaughan, E., Jr. *J. Am. Chem. Soc.* **1965**, *87*, 5257.

(10) Generation of the ketene from trichloroacetyl chloride and zinc (Bak, D. A.; Brady, W. T. *J. Org. Chem.* **1979**, *44*, 107) did not produce any appreciable amount of products.

(11) The NMR spectra of **2** showed similar features as the relatively more stable enol ester **7** and **11** (vide infra).

(12) Medici, A.; Fantin, G.; Fogagnolo, M.; Pedrini, P.; Dondoni, A. *J. Org. Chem.* **1984**, *49*, 590.

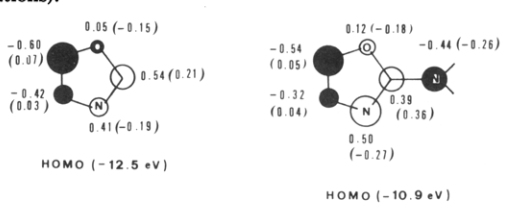
(13) Reference 1:, Sect. IIIB and ref 17.

(14) Reference 1b, Sect. IVA and IVC.

(15) Haake, P.; Bausher, L. P.; Miller, W. B. *J. Am. Chem. Soc.* **1969**, *91*, 1113. Haake, P.; Bausher, L. P.; McNeal, J. P. *Ibid.* **1971**, *93*, 7045.

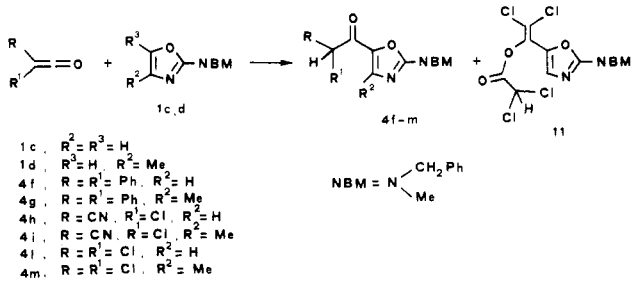
(16) Ghosez, L.; O'Donnel, M. J. In "Pericyclic Reactions"; Marchand, A. P., Lehr, R. E., Eds.; Academic Press: New York, 1977; Vol. 2, p 79.

(17) The first ionization potentials (IE) were obtained from the EPS spectra: 1,3-oxazole (**1a**) (IE = 9.75 eV); 2-(*N*-benzyl-*N*-methylamino)-1,3-oxazole (**1c**) (IE = 7.75 eV); 2-(*N*-benzyl-*N*-methylamino)-4-methyl-1,3-oxazole (**1d**) (IE = 7.60 eV) (Distefano, G., private communication). See also: Palmer, H. M.; Findlay, R. M.; Egdell, R. G. *J. Mol. Struct.* **1977**, *40*, 191. The calculated (CNDO/2) HOMO energies, coefficients and charges densities (in parentheses) (Guerra, M., private communications):



(18) Cockerill, A. F.; Deacon, A.; Harrison, R. G.; Osborne, D. J.; Prime, M.; Ross, W. G.; Todd, A.; Verge, J. P. *Synthesis* **1976**, 591.

Scheme II

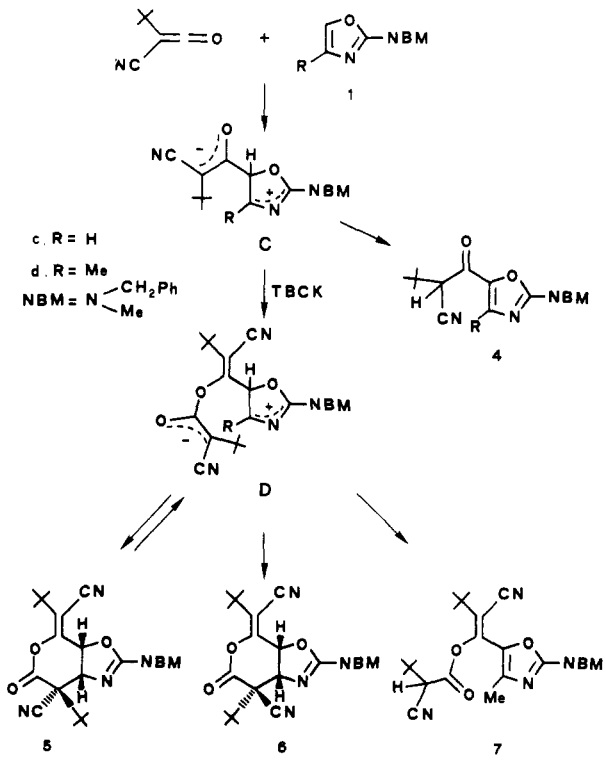


the reactants (see Experimental Section), while a virtually quantitative overall yield of cycloadducts **5** and **6** was obtained when a 3-fold molar excess of TBCK was used with respect to **1c**. The 1:1 adduct **4c** was readily characterized from its spectral characteristics. Similarly, the presence of the δ-lactone system and cis-annelation across the C_4–C_5 bond of the oxazoline ring in the 2:1 adducts **5** and **6** stemmed directly from their IR and NMR spectra (**5**, IR 1780 cm^{-1}, ^1H NMR δ 4.74 and 5.67 (J = 8.35 Hz); **6**, IR 1810 cm^{-1}, ^1H NMR δ 5.02 and 5.9 (J = 8.35 Hz)), whereas the stereochemistry of the sp^3 carbon of the lactone ring was assigned by the comparison of the above spectroscopic data with those of similar cycloadducts obtained from the reaction of TBCK with 2-(dimethylamino)-1,3-thiazole.[6a] This led us to assign to **5** the configuration having the *tert*-butyl group on the same side as the adjacent hydrogen on the bridgehead carbon, while the opposite configuration was assigned to the diastereomer **6**. With the above mentioned thiazole–TBCK cycloadducts,[6a] an identical stereochemistry at the ethylenic carbon was assumed in both compounds **5** and **6**, viz., the CN syn and the bulkier *tert*-butyl anti to the oxazole ring.

The product distribution appeared to be under kinetic control because the adducts isolated were stable under the reaction conditions and workup of the reaction mixture. However, in refluxing benzene, the cycloadduct **5** isomerized into the diastereomer **6**, which on the other hand, was recovered unaltered under the same conditions. This proves that the kinetically favored adduct **5** is less stable than **6**. Heating **5** in methanol did not produce any adduct between the assumed intermediate D and the solvent but gave mainly retrocyclization to **4c** and little isomerization to **6**. Evidence for the occurrence of the zwitterion D came from the reaction of TBCK with 1 equiv of 4-methyl-1,3-oxazole (**1d**), since this gave the corresponding Michael-type adduct **4d** (52%) and the open-chain 2:1 adduct **7** (10%) (IR 1785 cm^{-1}, ^1H NMR δ 3.33 (CH aliphatic)). A reversed ratio of these products was obtained by increasing the initial concentration of TBCK with respect to **1d** (see Experimental Section). This suggests that C_4-methyl hinders the ring closure of the zwitterion D while the proton migration from C_5 to the negatively charged carbon of the side chain takes place at a faster rate to give compound **7**.

Scheme II provides an interpretation of the above observations. As in the case of the aminothiazole–TBCK system,[6a] initial regioselective electrophilic attack by the cumulative central carbon of TBCK at C_5 of **1** constitutes a common step for the formation of all products. This is consistent with both the well-known electron-acceptor properties and charge distribution of ketenes[6a,7,19] and with the results of MO calculations on 2-amino-1,3-oxazole,[17] which indicate that the largest coefficient in the HOMO

Scheme III



is at C_5. In the present system, however, the formation of comparable amounts of the diastereomers **5** and **6** suggests that the stereochemistry of the ring closure of D is much less affected by the conformation at the enolate moiety than observed in the case of thiazoles.[6a]

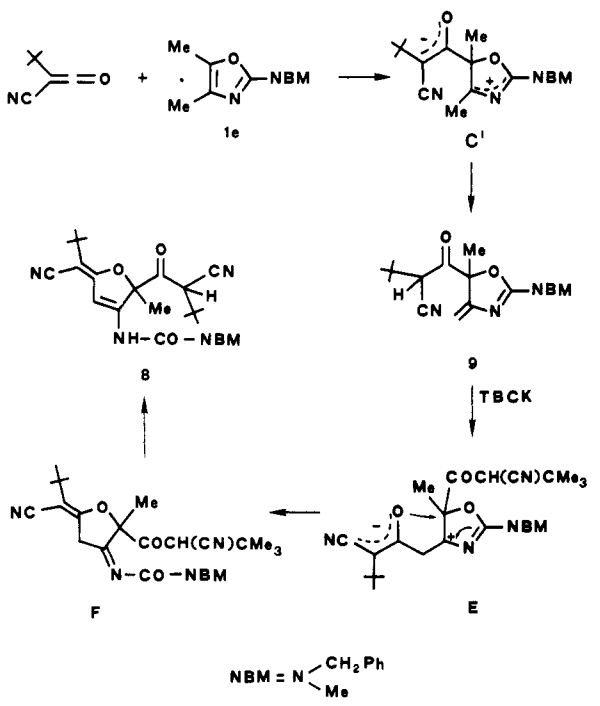
Since the mobility of the C_5 hydrogen in **1d** could in principle prevent isolation of cycloadducts across the C_4–C_5 bond, the reactivity of 4,5-dimethyl-2-(dialkylamino)-1,3-oxazole **1e** with TBCK was examined. Products were not observed after four days at room temperature from equimolar amounts of **1e** and TBCK, but a 3-fold molar excess of the ketene produced two 2:1 adducts in a 2:1 ratio. The main product **8** was characterized by X-ray crystallography as a substituted 2,5-dihydrofuran derivative (Scheme III), whereas the other compound **10** could not be characterized because it showed inconclusive spectral data (see Experimental Section) and gave crystals unadapted for X-ray analysis. This reaction should also occur via the initial formation of a zwitterion similar to C, viz., C′ which, however, cannot evolve into substitution products nor undergo cyclization reactions because of the methyl groups at C_4 and C_5. Therefore, hydrogen migration from the C_4-methyl to the enolate group at C_5 may be envisaged, this giving an intermediate **9** which adds a second molecule of TBCK and subsequently rearranges by ring transposition and tautomerism (see intermediates E and F) to give the final product **8**. Alternatively, the adduct **9**, which appears as a reasonable intermediate in this as well as in another ketene–oxazoline system,[20] may be formed by a single-step ene-type reaction involving the cumulative C=C bond of TBCK and C=CMe group of **1e**.

Other ketenes, which reacted with the oxazole **1c** and **1d**, but were inert with **1e**, were diphenyl-(DPK), chlorocyano- (CCK), and dichloroketene (DCK). In all cases, the exclusive or main product was the corresponding Michael-type 1:1 adduct **4** (Scheme IV) which formed up to

(19) Sustmann, R.; Ansmann, A.; Vahrenholt, F. *J. Am. Chem. Soc.* **1972**, *94*, 8099. Houk, K. N.; Strozier, R. W.; Hall, J. A. *Tetrahedron Lett.* **1974**, 897.

(20) Johnson, P. Y.; Caldwell, J. W. *J. Org. Chem.* **1975**, *40*, 2408.

Scheme IV



a 85% yield when a 3-fold molar excess of the ketene with respect to 1 was used. Only from the reaction of 1c with DCK was an open-chain 2:1 adduct 11 also isolated in low yield. No products other than 4l and 11 were observed in solvents of different characteristics (see Experimental Section). The formation of 11 suggests the occurrence of a 2:1 open-chain zwitterion D (Scheme II) which however does not cyclize although the steric hindrance by the C_4-methyl group is absent.

Experimental Section

General Comments. All melting points are uncorrected. ^1H NMR and ^{13}C NMR spectra (in $CDCl_3$) were obtained on a 80-MHz WP80 Bruker spectrometer. Chemical shifts are given in parts per million from Me_4Si. Mass spectra were recorded at 70 eV on a Varian MAT 112 high-resolution mass spectrometer. Infrared spectra were obtained on a Perkin Elmer Model 297 grating spectrometer. All experiments were carried out under N_2 and with freshly distilled and dried solvents.

Starting Materials. Diphenylketene (DPK) [bp 118–120 °C (1 mmHg)] was prepared from diphenylacetyl chloride and triethylamine[21] and redistilled prior to its use; *tert*-butylcyanoketene (TBCK) was generated in situ by thermolysis of the proper azidobenzoquinone;[22] chlorocyanoketene (CCK) was similarly obtained from the proper azido-2(5*H*)-furanone;[23] dichloroketene (DCK) was prepared in situ from dichloroacetyl chloride and triethylamine.[9] 1,3-oxazole (**1a**, bp 69–70 °C) was prepared as described.[24] 4-Methyl-1,3-oxazole (**1b**) was commercially available.

2-(*N*-Benzylamino)-1,3-oxazole (mp 53–54 °C) and its 4-methyl derivative (mp 112 °C) were prepared by condensation of benzylcyanamide[25] and the required hydroxy ketone, in aqueous sodium hydroxide as described.[18] The same method was employed for the preparation of **2-(*N*-benzylamino)-4,5-dimethyl-1,3-oxazole**: mp 62–63 °C (from ethyl acetate:petroleum ether); IR (CCl_4) 3460 (NH) cm^{-1}; ^1H NMR δ 1.94 (q, 3, =CMe, J_{Me-Me} = 0.97 Hz), 2.09 (q, 3, =CMe, J_{Me-Me} = 0.97 Hz), 4.46 (s, 2, NCH_2), 4.9 (br, 1, NH), 7.32 (s, 5, ArH).

Anal. Calcd for $C_{12}H_{14}N_2O$: C, 71.26; H, 6.98; N, 13.85. Found: C, 71.20; H, 6.95; N, 13.91.

Preparation of 2-(*N*-Benzyl-*N*-methylamino)-1,3-oxazoles 1. To an ice-cooled and stirred solution of the proper 2-(*N*-benzylamino)oxazole (80 mmol) in dry THF (150 mL) were added in one portion 80 mmol of sodium hydride. After the hydrogen evolution has ceased, a solution of methyl iodide (80 mmol) in THF (20 mL) was added dropwise. After 2 h at room temperature the mixture was poured into ice and extracted with ethyl ether. The organic layer was dried over anhydrous Na_2SO_4 and the solvent removed under vacuum. The crude mixture was distilled to give the 2-(*N*-benzyl-*N*-methylamino)-1,3-oxazole 1 in 60–70% yield. **2-(*N*-Benzyl-*N*-methylamino)-1,3-oxazole (1c)**: bp 97–100 °C (0.3 mmHg); IR (film) 1610 cm^{-1}; ^1H NMR δ 2.97 (s, 3, NMe), 4.6 (s, 2, NCH_2), 6.8 (d, 1, =CH, J = 1.1 Hz), 7.18 (d, 1, =CH, J = 1.1 Hz), 7.27 (s, 5, ArH).

Anal. Calcd for $C_{11}H_{12}N_2O$: C, 70.19; H, 6.43; N, 14.88. Found: C, 70.23; H, 6.40; N, 14.85.

2-(*N*-Benzyl-*N*-methylamino)-4-methyl-1,3-oxazole (1d): bp 68 °C (0.3 mmHg); IR (film) 1595 cm^{-1}; H NMR δ 2.07 (d, 3, =CMe, J_{Me-H} = 1.4 Hz), 2.95 (s, 3, NMe), 4.56 (s, 2, NCH_2), 6.92 (q, 1, =CH, J_{H-Me} = 1.4 Hz), 7.27 (s, 5, ArH).

Anal. Calcd for $C_{12}H_{14}N_2O$: C, 71.26; H, 6.98; N, 13.85. Found: C, 71.21; H, 6.94; N, 13.89.

2-(*N*-Benzyl-*N*-methylamino)-4,5-dimethyl-1,3-oxazole (1e): bp 107–108 °C (0.07 mmHg); IR (film) 1615 cm^{-1}; ^1H NMR δ 1.99 (q, 3, =CMe, J_{Me-Me} = 0.97 Hz), 2.1 (q, 3, =CMe, J_{Me-Me} = 0.97 Hz), 2.9 (s, 3, NMe), 4.53 (s, 2, NCH_2), 7.26 (s, 5, ArH).

Anal. Calcd for $C_{13}H_{16}N_2O$: C, 72.19; H, 7.46; N, 12.95. Found: C, 72.23; H, 7.41; N, 12.92.

Reaction of 1,3-Oxazole (1a) with DCK. To a stirred solution of 200 mg (2.89 mmol) of **1a** and 290 mg (2.89 mmol) of Et_3N in *n*-hexane (85 mL) was added dropwise a solution of 424 mg (2.89 mmol) of dichloroacetyl chloride in the same solvent (150 mL) in about 7 h. After 72 h, the reaction mixture was washed with water, the organic layer was dried over anhydrous Na_2SO_4, and the solvent was evaporated under vacuum. An NMR spectrum of the crude mixture showed the signals of the 2:1 open-chain adduct **2a** [δ 6.84 (s, 1, >CH), 7.44 (d, 1, =CH), 7.82 (d, 1, =CH)]. Chromatography of the reaction mixture (silica, 9:1 dichloromethane:ethyl acetate) gave 36 mg (7%) of the ketone **3a**: oil; IR (film) 1720 (C=O) cm^{-1}; ^1H NMR δ 7.06 (s, 1, >CH), 7.47 (d, 1, =CH), 7.99 (d, 1, =CH).

Anal. Calcd for $C_5H_3Cl_2NO_2$: C, 33.36; H, 1.68; N, 7.78. Found: C, 33.39; H, 1.65; N, 7.74.

Reaction of 4-Methyl-1,3-oxazole (1b) with DCK. To a stirred solution of 500 mg (6 mmol) of **1b** and 610 mg (6 mmol) of Et_3N in *n*-hexane (140 mL) was added dropwise a solution of 880 mg (6 mmol) of dichloroacetyl chloride in the same solvent (280 mL) in about 10 h. After 96 h, the reaction mixture was washed with water, the organic layer was dried over anhydrous Na_2SO_4, and the solvent was evaporated under vacuum. An NMR spectrum of the crude mixture showed the signals of the 2:1 open-chain adduct **2b** [δ 2.24 (d, 3, =CMe), 6.29 (s, 1, >CH), 7.5 (q, 1, =CH)]. Chromatography of the reaction mixture (silica, dichloromethane) gave 250 mg (21%) of the ketone **3b**: oil; IR (film) 1725 (C=O) cm^{-1}; ^1H NMR δ 2.32 (d, 3, =CMe, J_{Me-H} = 1.1 Hz), 7.09 (s, 1, >CH), 7.77 (q, 1, =CH, J_{H-Me} = 1.1 Hz); mass spectrum, *m/e* (relative intensity) 193 (M^+, 9), 109 (100).

Anal. Calcd for $C_6H_5Cl_2NO_2$: C, 37.14; H, 2.60; N, 7.22. Found: C, 37.18; H, 2.57; N, 7.24.

Reaction of 2-(*N*-Benzyl-*N*-methylamino)-1,3-oxazole (1c) with TBCK. A solution of 500 mg (2.66 mmol) of the oxazole **1c** in benzene (50 mL) was added while stirring to an equivalent solution of TBCK in benzene (ca. 35 mL). After 1 h at room temperature, the solvent was removed under vacuum and the crude mixture was chromatographed (silica, 7:3 benzene:ethyl acetate) to give in order: 78 mg (7%) of the 2:1 cycloadduct **6**, 91 mg (8%) of the diastereomer **5**, 198 mg (25%) of the 5-acyloxazole **4c**, and 287 mg (47%) of unaltered **1c**.

The δ-lactone **6**: mp 88–90 °C (from methanol); IR (KBr) 2210 (C≡N), 1810 (C=O) cm^{-1}; ^1H NMR δ 1.34 (s, 9, CMe_3), 1.41 (s, 9, CMe_3), 2.83 (s, 3, NMe), 4.41 (s, 2, NCH_2), 5.02 (d, 1, >CH, J = 8.35 Hz), 5.9 (d, 1, >CH, J = 8.35 Hz), 7.26–7.37 (m, 5, ArH);

(21) Taylor, E. C.; McKillop, A.; Hawks, G. H. *Org. Synth.* **1973**, *52*, 36.
(22) Weyiler, W.; Duncan, W. G.; Siewen, M. B.; Moore, H. W. *Org. Synth.* **1976**, *55*, 32.
(23) Moore, H. W.; Hernández, L.; Sing, A. *J. Am. Chem. Soc.* **1976**, *98*, 3728.
(24) Bredereck, H.; Bangert, R. *Chem. Ber.* **1964**, *97*, 1414.
(25) Nagy, H. K.; Tomson, A. J.; Horwitz, J. P. *J. Am. Chem. Soc.* **1960**, *82*, 1609.

^{13}C NMR δ 27.28 (q), 29.03 (q), 34.69 (s), 35.16 (q), 37.92 (s), 53.96 (t), 54.56 (s), 68.64 (d), 77.53 (d), 114.5 (s), 115.52 (s), 116.27 (s), 127.65 (d), 127.79 (d), 128.79 (d), 136.61 (s), 154.87 (s), 158.57 (s), 162.28 (s); mass spectrum, *m/e* (relative intensity) 434 (M^+, 3.5), 4.19 (4.2), 393 (3.2), 377 (2.6), 362 (4.5), 322 (5.6), 296 (4.8), 188 (48), 173 (9), 159 (47), 108 (21), 91 (100).

Anal. Calcd for $C_{25}H_{30}N_4O_3$: C, 69.10; H, 6.96; N, 12.89. Found: C, 69.22; H, 6.90; N, 12.91.

The δ-lactone **5**: mp 160–162 °C (from ethyl ether); IR (KBr) 2210 (C≡N), 1780 (C=O) cm^{-1}; ^1H NMR δ 1.24 (s, 9, CMe_3), 1.31 (s, 9, CMe_3), 2.9 (s, 3, NMe), 4.47 (s, 2, NCH_2), 4.74 (d, 1, >CH, J = 8.35 Hz), 5.67 (d, 1, >CH, J = 8.35 Hz), 7.26–7.32 (m, 5, ArH); ^{13}C NMR δ 27.47 (q), 29.3 (q), 34.61 (s), 35.49 (q), 38.77 (s), 54.18 (t), 60.5 (s), 64.54 (d), 74.58 (d), 112.78 (s), 116.82 (s), 117.4 (s), 127.82 (d), 127.83 (d), 128.83 (d), 136.6 (s), 157.22 (s), 162.19 (s), 162.8 (s); mass spectrum, *m/e* (relative intensity) 434 (M^+, 10), 419 (16), 393 (1), 37 (2), 362 (4), 296 (5), 188 (100), 173 (11), 159 (5), 108 (16), 91 (92).

Anal. Calcd for $C_{25}H_{30}N_4O_3$: C, 69.10; H, 6.96; N, 12.89. Found: C, 69.15; H, 6.89; N, 12.81.

The ketone **4c** showed the following: oil; IR (CCl_4) 2240 (C≡N), 1615 (C=O) cm^{-1}; ^1H NMR δ 1.18 (s, 9, CMe_3), 3.13 (s, 3, NMe), 3.67 (s, 1, >CH), 4.73 (s, 2, NCH_2), 7.26–7.35 (m, 5, ArH), 7.81 (s, 1, =CH); mass spectrum, *m/e* (relatively intensity) 311 (M^+, 25), 255 (39), 215 (20), 91 (100).

Anal. Calcd for $C_{18}H_{21}N_3O_2$: C, 69.43; H, 6.80; N, 13.49. Found: C, 69.51; H, 6.85; N, 13.40.

Reactions between **1c** and TBCK took place due to the following variations of the above conditions.

(a) The benzene solution of TBCK was added dropwise to the solution of **1c** (molar ratio TBCK:**1c** 1:1) and the mixture was stirred for 3 h at room temperature. Chromatography of the reaction mixture gave 89 mg (7.5%) of **6**, 140 mg (12%) of **5**, 240 mg (30%) of **4c** and 163 mg (33%) of **1c**.

(b) A benzene solution (ca. 85 mL) of **1c** (500 mg, 2.66 mmol) and TBCK (7.98 mmol), obtained by addition of the latter to the former as detailed, was stirred for 1 h at room temperature. Chromatography of the reaction mixture gave 346 mg (33%) of **6** and 760 mg (66%) of **5**.

Thermolysis of Oxazolo[4,5-*d*]2-tetrahydropyranone 5. Method A. A benzene solution (20 mL) containing 54 mg (0.124 mmol) of **5** was refluxed for 48 h. The solvent was removed under vacuum and the crude mixture was chromatographed (silica, 7:3 benzene:ethyl acetate) to give 29 mg (54%) of the diastereomer **6**, 21 mg (39%) of unaltered **5**, and 1.2 mg (3%) of **4c**.

Method B. A methanol solution (35 mL) containing 100 mg (0.23 mmol) of **5** was refluxed for 5 h. The workup as detailed above gave 1 mg (1%) of **6** and 57 mg (83%) of **4c**.

Thermolysis of Oxazolo[4,5-*d*]2-tetrahydropyranone 6. Method A. A benzene solution (20 mL) containing 54 mg (0.124 mmol) of **6** was refluxed for 48 h. The solvent was removed under vacuum and the adduct **6** was recovered unaltered.

Method B. A methanol solution (35 mL) containing 100 mg (0.23 mmol) of **6** was refluxed for 5 h. The solvent was removed under vacuum and the adduct **6** was recovered unaltered.

Reaction of 2-(*N*-Benzyl-*N*-methylamino)-4-methyl-1,3-oxazole (1d) with TBCK. A solution of 800 mg (3.96 mmol) of the oxazole **1d** in benzene (40 mL) was added while stirring to an equivalent solution of TBCK in the same solvent (ca. 40 mL). After 48 h at room temperature the solvent was removed under vacuum and the crude mixture was chromatographed (silica, 9:1 dichloromethane:ethyl acetate) to give 184 mg (10%) of the 2:1 adduct **7**, 674 mg (52%) of the 5-acyloxazole **4d** and 98 mg (12.5%) of unaltered **1d**.

The adduct **7**: mp 97–98 °C (from ethyl ether:*n*-hexane); IR (CCl_4) 2245 (C≡N), 2205 (C≡N), 1785 (C=O) cm^{-1}; ^1H NMR δ 1.15 (s, 9, CMe_3), 1.34 (s, 9, CMe_3), 2.23 (s, 3, =CMe), 2.98 (s, 3, N-Me), 3.33 (s, 1, >CH), 4.62 (s, 2, NCH_2), 7.29 (s, 5, ArH); ^{13}C NMR δ 14.92 (q), 27.67 (q), 30.03 (q), 35.02 (q), 35.46 (s), 49.24 (d), 53.86 (t), 113.97 (s), 114.92 (s), 117.13 (s), 127.76 (d), 128.01 (d), 129.02 (d), 132.87 (s), 136.48 (s), 144.88 (s), 147.04 (s), 161.95 (s), 162.27 (s); mass spectrum, *m/e* (relative intensity) 448 (M^+, 27), 325 (62), 310 (48), 282 (23), 269 (19), 229 (27), 202 (13), 123 (16), 108 (36), 91 (100).

Anal. Calcd for $C_{26}H_{32}N_4O_3$: C, 69.62; H, 7.19; N, 12.49. Found: C, 69.70; H, 7.15; N, 12.45.

The ketone **4d**: mp 136–137 °C (from carbon tetrachloride:*n*-hexane); IR (KBr) 2240 (C≡N), 1610 (C=O) cm^{-1}; ^1H NMR δ 1.13 (s, 9, CMe_3), 2.47 (s, 3, =CMe), 3.13 (s, 3, NMe), 3.83 (s, 1, >CH), 4.70 (s, 2, NCH_2), 7.33 (s, 5, ArH); mass spectrum, *m/e* (relative intensity) 325 (M^+, 30), 269 (65), 229 (54), 202 (29), 91 (100).

Anal. Calcd for $C_{19}H_{23}N_3O_2$: C, 70.13; H, 7.12; N, 12.91. Found: C, 70.10; H, 7.15; N, 12.93.

The reaction was also carried out with a molar ratio between TBCK and **1d** of 3:1. After stirring for 72 h at room temperature, the usual workup gave 750 mg (67%) of **7** and 122 mg (15%) of **4d**.

Reaction of 2-(*N*-Benzyl-*N*-methylamino)-4,5-dimethyl-1,3-oxazole (1e) with TBCK. A solution of 1 g (4.6 mmol) of **1e** in benzene (100 mL) was added while stirring to a solution of TBCK (13.8 mmol) in the same solvent (100 mL). After 2 h at room temperature, the solvent was removed under vacuum and the residue was chromatographed (silica, 9:1 dichloromethane:ethyl acetate) to give 574 mg (27%) of the 2:1 adduct **10** and 1.27 g (60%) of the 2:1 adduct **8**.

The product **10**: mp 132–133 °C (from ethyl ether:*n*-hexane); IR (KBr) 2240 (C≡N), 2195 (C≡N), 1770 (C=O), 1665 (C=O) cm^{-1}; ^1H NMR δ 1.17 (s, 9), 1.26 (s, 9), 1.27 (s, 3), 1.68 (s, 3), 3.18 (s, 3), 4.45 (d, 1), 5.37 (s, 1), 7.33 (m, 5); mass spectrum, *m/e* (relative intensity) 462 (M^+, 18), 447 (23), 366 (50), 338 (60), 282 (68), 267 (5), 242 (30), 217 (12), 120 (15), 108 (29), 91 (100).

Anal. Calcd for $C_{27}H_{34}N_4O_3$: C, 70.10; H, 7.41; N, 12.11. Found: C, 70.21; H, 7.42; N, 12.04.

The 2:1 adduct **8**: mp 176–177 °C (from chloroform:ethyl ether); IR (KBr) 3340 (NH), 2230 (C≡N), 2190 (C≡N), 1755 (C=O), 1680 (C=O) cm^{-1}; ^1H NMR δ 1.04 (s, 9, CMe_3), 1.32 (s, 9, CMe_3), 1.52 (s, 3, Me), 3.08 (s, 3, NMe), 4.0 (s, 1, >CH), 4.54 (s, 2, NCH_2), 6.81 (s, 1, =CH), 7.12 (br, 1, NH), 7.2–7.4 (m, 5, ArH); ^{13}C NMR δ 24.74 (q), 27.37 (q), 30.21 (q), 32.71 (s), 35.43 (q), 35.71 (s), 47.60 (d), 52.94 (t), 92.45 (s), 94.92 (s), 102.94 (d), 115.18 (s), 119.85 (s), 127.38 (d), 128.33 (d), 129.30 (d), 136.45 (s), 143.46 (s), 153.42 (s), 168.59 (s), 202.92 (s); mass spectrum, *m/e* (relative intensity) 462 (M^+, 33), 338 (32), 324 (12), 283 (30), 217 (31), 162 (25), 120 (25), 91 (100).

Anal. Calcd for $C_{27}H_{34}N_4O_3$: C, 70.10; H, 7.41; N, 12.11. Found: C, 70.02; H, 7.44; N, 12.15.

Reaction of Oxazole 1c with DPK. To a stirred solution of 200 mg (1.06 mmol) of **1c** in benzene (50 mL) was added a solution of 205 mg (1.06 mmol) of DPK in the same solvent (20 mL). After 2 h the solvent was removed under vacuum and the crude mixture was chromatographed (silica, 9:1 benzene:ethyl acetate) to give 150 mg (37%) of the 5-acyloxazole **4f** and 106 mg (53%) of unaltered **1c**. The ketone **4f**: mp 103–105 °C (from benzene:petroleum ether); IR (KBr) 1615 (C=O) cm^{-1}; ^1H NMR δ 3.04 (s, 3, NMe), 4.65 (s, 2, NCH_2), 5.48 (s, 1, >CH), 7.38 (s, 15, ArH), 7.69 (s, 1, =CH); mass spectrum, *m/e* (relative intensity) 381 (M^+, 6), 215 (72), 187 (16), 167 (18), 165 (15), 159 (32), 91 (100).

Anal. Calcd for $C_{25}H_{22}N_2O_2$: C, 78.51; H, 5.80; N, 7.32. Found: C, 78.35; H, 5.76; N, 7.40.

The reaction was also carried out with a 3-fold molar excess of DPK. After 4 h, chromatography of the reaction mixture gave 346 mg (85%) of **4f**.

Reaction of Oxazole 1d with DPK. The reaction was carried out as described above from 500 mg (2.5 mmol) of **1d** in benzene (40 mL) and 430 mg (2.5 mmol) of DPK in the same solvent (40 mL). After 30 min, chromatography of the crude mixture (silica, 9:1 dichloromethane:ethyl acetate) gave 694 mg (71%) of **4g** and 21 mg (4.2%) of unreacted **1d**. The ketone **4g**: mp 139–141 °C (from benzene:petroleum ether); IR (KBr) 1610 (C=O) cm^{-1}; ^1H NMR δ 2.47 (s, 3, =CMe), 3.00 (s, 3, NMe), 4.58 (s, 2, NCH_2), 5.61 (s, 1, >CH), 7.29 (s, 15, ArH); mass spectrum, *m/e* (relative intensity) 396 (M^+, 19), 229 (95), 91 (100).

Anal. Calcd for $C_{26}H_{24}N_2O_2$: C, 78.76; H, 6.10; N, 7.07. Found: C, 78.81; H, 6.08; N, 7.10.

The reaction was also carried out with a 3-fold molar excess of DPK. Chromatography of the reaction mixture gave 812 mg (82%) of **4g**.

Reaction of Oxazole 1c with DCK. To a stirred solution of 800 mg (4.25 mmol) of **1c** and 430 mg (4.25 mmol) of Et_3N in *n*-hexane (100 mL) was added dropwise a solution of 625 mg (4.25 mmol) of dichloroacetyl chloride in the same solvent (200 mL)

in about 4 h. After 40 h the reaction mixture was washed with water, the organic layer was dried over anhydrous Na_2SO_4, and the solvent evaporated under vacuum. The crude mixture was chromatographed (silica, 9:1 dichloromethane:ethyl acetate) using well-dried solvents to give 191 mg (11%) of **11**, 595 mg (47%) of **4l**, and 48 mg (6%) of unaltered **1c**.

The enol ester **11**: oil (decomposed on distillation); IR (film) 1785 (C=O) cm^{-1}; ^1H NMR (C_6D_6) δ 2.55 (s, 3, NMe), 4.23 (s, 2, NCH_2), 5.49 (s, 1, >CH), 7.05 (s, 5, ArH), 7.3 (s, 1, =CH); ^{13}C NMR δ 35.08 (q), 54.11 (t), 63.53 (d), 112.64 (s), 127.94 (d), 128.9 (d), 131.67 (d), 134.01 (s), 135.72 (s), 136.35 (s), 160.94 (s), 162.39 (s); mass spectrum (CI methane), *m/e* (relative intensity) 409 (M^+ + 1, 55), 299 (41), 281 (100), 235 (10), 215 (15), 91 (58); mass spectrum (EI), *m/e* (relative intensity) 408 (M^+, 20), 298 (14), 215 (14), 91 (100).

Anal. Calcd for $C_{15}H_{12}Cl_4N_2O_3$: C, 43.94; H, 2.95; N, 6.83; Cl, 34.57. Found: C, 43.89; H, 2.97; N, 6.88; Cl, 34.49.

The ketone **4l**: mp 103–104 °C (from dichloromethane:*n*-hexane); IR (KBr) 1665 (C=O) cm^{-1}; ^1H NMR δ 3.14 (s, 3, NMe), 4.75 (s, 2, NCH_2), 6.26 (s, 1, >CH), 7.33 (s, 5, ArH), 8.01 (s, 1, =CH); mass spectrum, *m/e* (relative intensity) 298 (M^+, 65), 215 (100), 91 (100).

Anal. Calcd for $C_{13}H_{12}Cl_2N_2O_2$: C, 52.20; H, 4.04; N, 9.37; Cl, 23.69. Found: C, 52.31; H, 4.05; N, 9.35; Cl, 23.73.

The reaction was also carried out in THF and gave only the product **4l** (11% yield) while in dichloromethane the molar ratio of the products **4l** and **11** were 3.2:1 (overall yield 38%).

Reaction of Oxazole 1d with DCK. The reaction was carried out as described above for **1c**. From 700 mg (3.46 mmol) of **1d**, 350 mg (3.46 mmol) of Et_3N in *n*-hexane (100 mL), and 509 mg (3.46 mmol) of dichloroacetyl chloride in the same solvent (180 mL), after 24 h, chromatography (silica, 9:1 dichloromethane:ethyl acetate) gave 656 mg (61%) of **4m** and 8 mg (1%) of **1d**. The ketone **4m**: mp 70–73 °C (from ethyl ether:*n*-hexane); IR (KBr) 1615 (C=O) cm^{-1}; ^1H NMR δ 2.51 (s, 3, =CMe), 3.12 (s, 3, NMe), 4.71 (s, 2, NCH_2), 6.38 (s, 1, >CH), 7.34 (s, 5, ArH); mass spectrum (CI methane), *m/e* (relative intensity) 313 (M^+ + 1, 42), 249 (22), 229 (100), 91 (35).

Anal. Calcd for $C_{14}H_{14}Cl_2N_2O_2$: C, 53.69; H, 4.51; N, 8.95; Cl, 22.63. Found: C, 53.82; H, 4.53; N, 8.90; Cl, 22.60.

Reaction of Oxazole 1c with CCK. To a refluxing solution of 502 mg (2.66 mmol) of 4-azido-3-chloro-5-methoxy-2(5*H*)-furanone in benzene (100 mL) was added dropwise a solution of 500 mg (2.66 mmol) of **1c** in the same solvent (100 mL). After 2 h the solvent was removed under vacuum and the crude mixture was chromatographed (silica, 7:3 dichloromethane:ethyl acetate) to give 630 mg (82%) of the ketone **4h**: decomposable oil; IR (CCl_4) 1620 (C=O) cm^{-1}; ^1H NMR δ 3.12 (s, 3, NMe), 4.73 (s, 2, NCH_2), 5.47 (s, 1, >CH), 7.31 (s, 5, ArH), 8.06 (s, 1, =CH).

Anal. Calcd for $C_{14}H_{12}ClN_3O_2$: C, 58.04; H, 4.18; N, 14.50. Found: C, 58.11; H, 4.09; N, 14.52.

Reaction of Oxazole 1d with CCK. The reaction was carried out as described above. From 470 mg (2.5 mmol) of the azido-2(*H*)-furanone in benzene (100 mL) and 500 mg (2.5 mmol) of **1d** in the same solvent (50 mL), after 2 h, chromatography (silica, 9:1 dichloromethane:ethyl acetate) gave 246 mg (32.5%) of the ketone **4i**: mp 108–109 °C (from ethyl ether: *n*-hexane); IR (CCl_4) 1615 (C=O) cm^{-1}; ^1H NMR δ 2.49 (s, 3, =CMe), 3.13 (s, 3, NMe), 4.72 (s, 2, NCH_2), 5.28 (s, 1, >CH), 7.34 (s, 5, ArH); mass spectrum, *m/e* (relative intensity) 303 (M^+, 55), 229 (97), 201 (9), 173 (38), 91 (100).

Anal. Calcd for $C_{15}H_{14}ClN_3O_2$: C, 59.31; H, 4.65; N, 13.83; Cl, 11.67. Found: C, 59.39; H, 4.60; N, 13.89; Cl, 11.61.

X-ray Crystal Structure Analysis of 8. Crystal data: $C_{28}H_{32}N_4O_3$, M = 448.6, triclinic, a = 11.886 (7) Å, b = 12.054 (8) Å, c = 11.827 (7) Å, α = 124.96 (4)°, β = 90.60 (5)°, γ = 70.02 (5)°, z = 2, D_c = 1.18 g cm^{-3}, space group *P1*. Intensity data were measured up to 70° by the $\omega - 2\theta$ step-scanning mode with Ni-filtered Cu K_α radiation. A total of 3704 reflections were collected and 2618 were used in the analysis. The structure was solved by direct methods and refined by full-matrix anisotropic least-squares techniques. Hydrogen atoms were refined with the constraint C–H = 1.08 Å. The final R index was 0.068 (R_w = 0.073, $w = 1/\sigma^2(F)$). Atomic coordinates have been deposited.

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Registry No. **1a**, 288-42-6; **1b**, 693-93-6; **1c**, 91190-44-2; **1c** (*N*-demethyl deriv), 91190-60-2; **1d**, 91190-45-3; **1d** (*N*-demethyl deriv), 57067-43-3; **1e**, 91190-46-4; **1e** (*N*-demethyl deriv), 91190-61-3; **2a**, 91190-47-5; **2b**, 91190-48-6; **3a**, 91190-63-5; 3b, 91190-64-6; **4c**, 91190-49-7; **4d**, 91190-50-0; **4f**, 91190-51-1; **4g**, 91190-52-2; **4h**, 91190-53-3; **4i**, 91190-54-4; **4l**, 91190-55-5; **4m**, 91190-56-6; **5**, 91190-57-7; **6**, 91237-29-5; **7**, 91190-62-4; **8**, 91190-58-8; **11**, 91190-59-9; DPK, 525-06-4; TBCK, 29342-22-1; CCK, 60010-89-1; DCK, 4591-28-0; hydroxyacetaldehyde, 141-46-8; hydroxyacetone, 116-09-6; 3-hydroxy-2-butanone, 513-86-0; 4-azido-3-chloro-5-methoxy-2(5*H*)-furanone, 60010-88-0; benzyl cyanamide, 622-77-5.

Supplementary Material Available: Table of atomic coordinates, and bond distances of compound **8** (3 pages). Ordering information is given on any current masthead page.