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Mechanism of Cycloaddition of Nitroso Compounds with Diphenylketene

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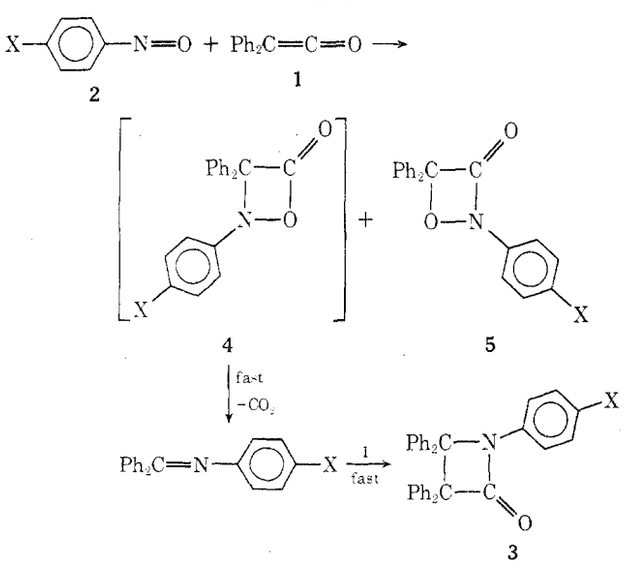
The cycloaddition of aromatic nitroso compounds *p*-X-C_6H_4NO with diphenylketene occurs in all cases rapidly and with relatively low regioselectivity, which is little affected by solvents or substituents. With X = CH_3O, CH_3, H, and CH_3O_2C, the principal product is the 2-aryl-4,4-diphenyl-1,2-oxazetidin-3-one. The isomeric oxazetidin-4-one, the main primary product for X = $(CH_3)_2N$, is unstable in all cases and decomposes to carbon dioxide and a Schiff base, which reacts *in situ* to form an azetidinone. The oxazetidin-3-ones undergo a very facile solvolysis reaction, apparently *via* a nitrenium ion-like intermediate. The cycloaddition results suggest a near-concerted mechanism.

Like most reactions of ketenes, the cycloaddition with nitroso compounds was discovered by Staudinger, who reported in 1911[1] that diphenylketene (**1**) reacted with *p*-dimethylaminonitrosobenzene (**2a**) to yield ultimately the β-lactam **3a** (65%). Staudinger proposed that **3a** arose *via* an unstable oxazetidin-4-one, **4a,** which decomposed to a Schiff base; the latter was shown to give the product **3a** (Scheme I). In contrast to **2a,** nitrosobenzene (**2b**) gave the oxazetidin-3-one **5b** in 63% yield.[1]

Scheme I



a, X = NMe_2
b, X = H
c, X = OMe
d, X = Me
e, X = CO_2Me
f, X = Br
g, X = Cl

These results were extended by Kresze and Trede,[2] who obtained oxazetidin-3-ones **5d, 5f,** and **5g** in 19–48% yields from **2d, 2f,** and **2g,** and the β-lactam **3c** (40%) from reaction of **2c** with **1.** These workers deduced from the effect of the dimethylamino and methoxy groups on the products that the unstable **4** was produced by a dipolar mechanism and **5** by a concerted process.

Mechanisms of ketene cycloadditions have received substantial theoretical[3-5] and experimental study in recent years. Alkenes,[6-10] vinyl ethers,[11,12] and azo compounds[13-15] react with ketenes by essentially concerted [$_\pi2_s + _\pi2_a$] mechanisms, whereas enamines (at least in part),[16-18] imines,[19-21] carbodiimides,[22] and sulfodiimides[23] react *via* dipolar intermediates.

In contrast to these extensive studies on ketene cycloadditions, nitroso compound cycloadditions have been relatively little studied. Nitroso compounds function as dienophiles in Diels–Alder reactions,[24,25] but their involvement in [2 + 2] cycloadditions, despite a number of erroneous early reports,[26-31] is fairly rare. They do yield [2 + 2] adducts (oxazetidines) with highly halogenated[32,33] and methoxylated[34] alkenes, presumably by diradical processes. More recently, the [2 + 2] cycloaddition of nitroso compounds with ketenimines has been reported and studied by Barker.[35] We report here a study of the mechanism of cycloaddition of diphenylketene (**1**) with substituted nitrosobenzenes, **2.**

Results

The principal tool used in this investigation has been the regioselectivity of the cycloaddition, as affected by substituents and solvents. Previous investigators[1,2] had generally reported the formation of *either* **4** *or* **5** from a given nitrosobenzene derivative, which might be taken to imply a completely regiospecific cycloaddition, had the material balances been better.

In our study, the reaction was run by titrating a solution of **1** with a solution of **2** until the end point was indicated by persistent blue or green color of **2** and the complete disappearance of ketene absorption at 2090 cm^{-1} in the ir. (This procedure was made practical by the great speed of the reaction.) In some cases (X = H, CO_2Me) the primary product **5** was stable and was isolated as such; in

Table I
Products of Reaction of 1 with Nitroso Compounds p-XC_6H_4NO[a] (2)

X	σ_p	% 3[b]	% 5[b]	% urethane[b,c]	% urea[b,d]	% Ph_2CO[b]	% 4[e,f]	% 5[f,g]
NMe_2	−0.83	61	0	28	0	36	61 (68)	28 (32)
OMe	−0.27	22	0	81	0	69	22 (21)	81 (79)
Me	−0.17	13	0	0	86	30	13 (13)	86 (87)
H[h]	0.00	13	60	0	10	19	13 (16)	70 (84)
CO_2Me[i]	0.31	(28)	(72)	0	0	0	(28)	(72)

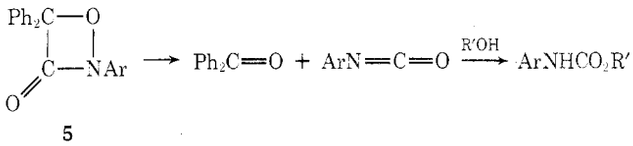
[a] In chloroform at 25°. [b] Isolated yields, based on **2**. [c] Formed by addition of ethanol or methanol to the reaction mixture. [d] Formed by hydrolysis of isocyanate (from **5**) on chromatography. [e] Based on yield of **3**, derived from **4**. [f] Yields in parentheses normalized to 100%. [g] Based on combined yields of **5** and products derived therefrom. [h] Diphenylacetic acid (11%) also isolated. [i] Yields by nmr.

Table II
Effect of Solvents in Product Ratio in Reaction of 1 with 2

X	Solvent	E_T[a]	% 3 = % 4[b]	% urethane = % 5[b]	% Ph_2CO[b]
OMe	Hexane	30.9	22 (25)	67 (75)	68
OMe	Chloroform	39.1	22 (21)	81 (79)	69
OMe	Dimethylformamide	43.8	17 (21)	65 (79)	64
OMe	Acetonitrile	46.0	9 (9)	91 (91)	74
NMe_2	Benzene	34.5	78 (79)	21 (21)	32
NMe_2	Chloroform	39.1	61 (68)	28 (32)	35
NMe_2	Acetonitrile	46.0	83 (94)	5 (6)	4

[a] Solvent polarity parameter: ref 36. [b] Isolated yields, based on **2**; yields in parentheses normalized to 100%.

others (X = NMe_2, OMe) it decomposed *in situ* to benzophenone and an isocyanate, which was isolated as the urethane or urea. Thus the quantity of **4** formed in the initial

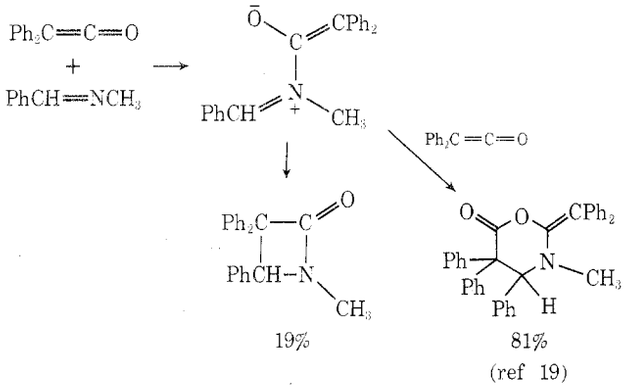


cycloaddition was measured by the quantity of β-lactam **3** isolated; the quantity of **5** was measured either directly or from the quantity of urethane or urea. The results are summarized in Table I.

Except for the case of **2a**, the major primary product is the oxazetidin-3-one, whether X is electron donating or electron withdrawing. Moreover, the regioselectivity is in no case very great, ranging from 1:2 to 6:1; both primary products, **4** and **5**, are produced and detected in every case. The very strongly electron-donating dimethylamino group, as previously reported,[1] causes **4** to become the predominant primary product, but only by a modest 2:1 ratio. To test Kresze's hypothesis[2] that **4** arises by a dipolar and **5** by a concerted process, the effect of solvents on the product distribution was investigated (Table II) using **2a** and **2c**, which should be most prone to react by a dipolar mechanism, and most sensitive therefore to solvent effects.

It is evident that, for both **2a** and **2c**, the solvent, like the substituent X, has only a modest effect on the product ratio. There is no consistent increase in the amount of **4** with increasing solvent polarity as required by Kresze's proposal. The concept[2] that one primary product, **4**, is produced by one mechanism and the other, **5**, by a fundamentally different mechanism is not supported by these facts. We therefore conclude for the remainder of the discussion that a common type of mechanism leads to both primary products in every case. This common mechanism might be a dipolar, diradical, or concerted mechanism, as limiting cases (Scheme II).

Dipolar intermediates are well established in some [2 + 2] cycloadditions.[16-23] In these cases, the reactions have been found to be regiospecific, strongly affected by solvents, and prone to formation of 2:1 adducts by reaction of the 1,4-dipolar intermediate with an additional ketone molecule. As between the two possible dipolar intermedi-

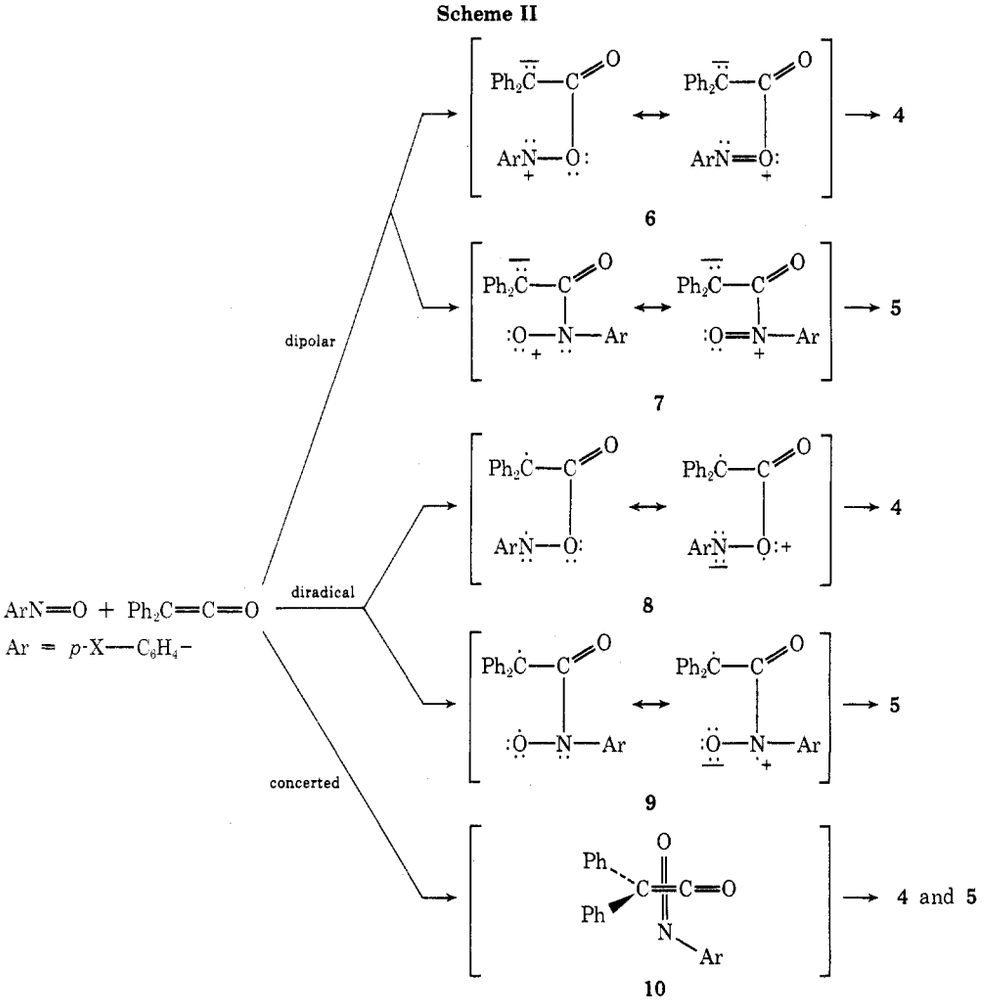


ates, **6** and **7**, the nitrenium ion[37] **6** seems less unreasonable than the oxenium ion **7**, at least in the absence of strong electron-withdrawing groups X. One would therefore expect **4** to be the predominant primary product in most cases, accompanied by 2:1 adduct(s).

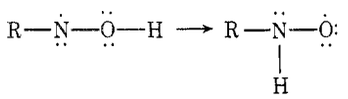
Clearly none of the above expectations for a dipolar mechanism accords with the experimental observations: no 2:1 adducts are detectable in the reaction mixtures, despite the presence of a large excess of ketene **1** in the early stages; the major primary product is generally **5**, not **4**; and solvent and substituent effects on the regioselectivity are modest. We are therefore led to reject the dipolar mechanism.

In contrast to **6** and **7**, diradical intermediates **8** and **9** would appear *a priori* relatively favorable. Nitroxyl radicals (such as **9**) are probably the most stable and best characterized of radicals;[38] a number of stable oxaminyl radicals like **8** have also recently been characterized.[39-44] However, addition of radicals to nitroso compounds occurs only at N, to give nitroxyls, rather than at O, in the absence of extraordinary steric hindrance at N.[41,43] This indicates the greater stability of nitroxyls relative to oxaminyls, as does the rearrangement of the latter.[39,40] We

Scheme II

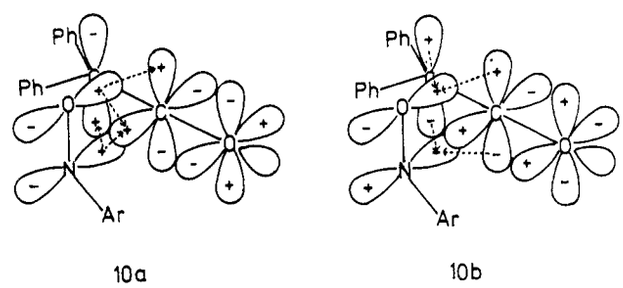


would thus expect the diradical **9** to be substantially more stable than **8**, and thus **5** to be the sole (or at least predominant) primary product. Diradical **9** being the more polar of the two, polar solvents should increase the **5**:**4** ratio relative to nonpolar solvents.[45] Relative substituent effects on **8** and **9** are difficult to predict, however.



The observed preferential formation of **5** over **4** is *qualitatively* consistent with a diradical mechanism; however, the low regioselectivity of the cycloaddition is difficult to reconcile with the normal regiospecificity of radical additions to nitroso compounds, as is the preference for **4a** over **5a**.

However, the experimental observations are consistent with an essentially concerted mechanism, analogous to that proposed by Woodward and Hoffmann[3] for the ketene + alkene cycloaddition. The transition state **10** is quite free of steric hindrance, and is stabilized by interactions of the π_{NO} OMO of the nitroso compound with the π_{CC}^* and π_{CO}^* (UMO) orbitals of the ketene (**10a**), complimented by interaction of the π_{NO}^* LUMO of the nitroso group with the π_{CC} HOMO of the ketene (**10b**). The low-lying nature of the π_{NO}^* LUMO of nitrosobenzene is indicated by its facile electrochemical reduction.[46] In view of the fairly weak N=O double bond and its relationship to singlet oxygen,[47] one may expect a relatively high-lying π_{NO} orbital.[48]

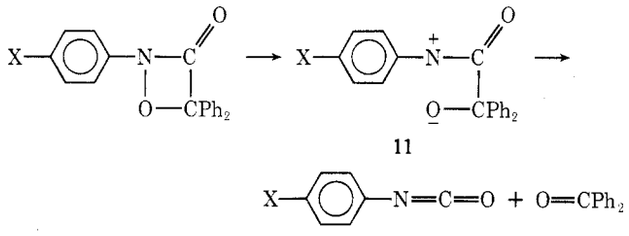


10a **10b**

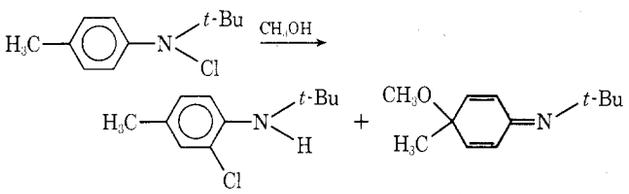
If the regioselectivity is ketene LUMO controlled[49] (as in **10a**), then **4** should be the major primary product, as in fact found with **2a**. In the absence of the strong electron-donating (HOMO- and LUMO-raising) effect of the dimethylamino group of **2a**, however, the reaction must be more nearly ketene HOMO controlled (**10b**), giving a moderate preference for **5** in most cases. The concept of ketene HOMO control is also in full accord with the relative reactivities of various ketenophiles (*e.g.*, ArN=O > ArN=NR ≫ ArCH=CH_2) in concerted reactions, which parallel their reducibilities.

Stabilities of 1,2-Oxazetidin-3-ones. The thermal stabilities of **5a-e** exhibit a marked dependence on the substituents X, ranging from the readily isolable **5e** and **5b** (X = CO_2CH_3, H) through **5d** (X = CH_3), stable in the reaction mixture but not to chromatography, and **5c** (X = OCH_3), in part decomposed in the reaction mixture, to **5a** (X = NMe_2), entirely undetectable except through its decomposition products. Thus, the thermal stabilities of the oxazetidin-3-ones decrease dramatically as X becomes

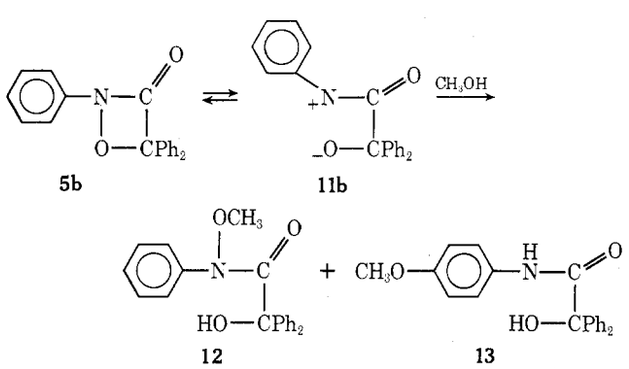
more electron donating. This is most consistent with thermal decomposition *via* a nitrenium ion-like intermediate, **11**.[50]



Analogous nitrenium ions have been detected in the solvolyses of *N*-chloroanilines, for which a ρ^+ of −6.35 has been measured, by trapping with methanol.[51] Similarly,

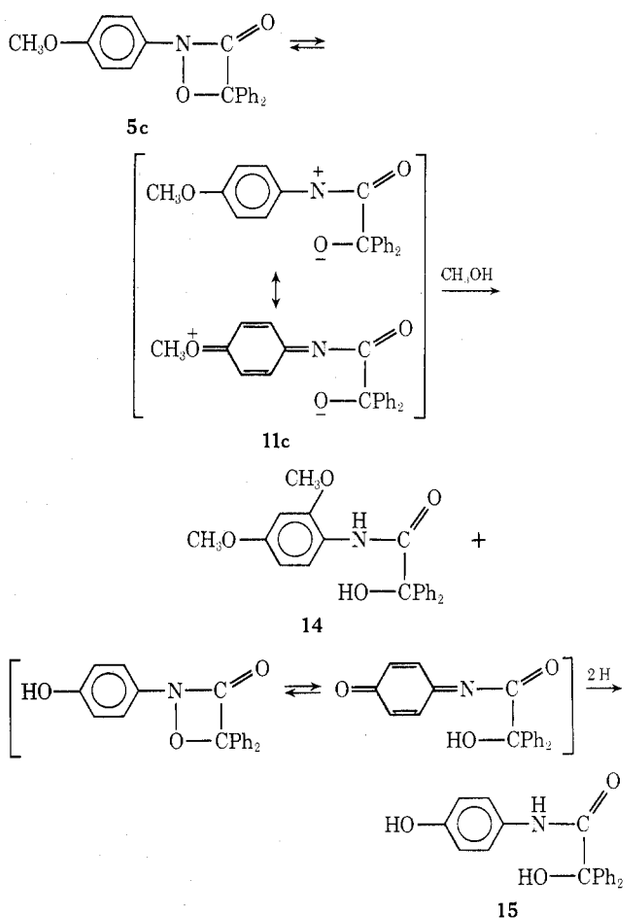


addition of methanol to product mixtures from reaction of **1** with **2a** and **2c** resulted in solvolysis of the oxazetidin-3-ones *via* **11**, as shown by the nature of the products formed. Thus, two additional products not present upon completion of the reaction (ir) were isolated from the reaction mixture of **1** with **2b** after adding methanol. One of these, **12**, was a white solid whose ir [2940 (s, br, OH), 1634 (s, amide C=O), 760 and 700 cm^{-1} (s, C_6H_5)], nmr [δ 3.00 (s, 3 H), 7.2 (m, 15 H), 8.5 (br s, 1 H, exchangeable with D_2O)], and analysis indicated the structure *N*-methoxybenzilanilide.[52] The other, **13**, was identified as benzil-*p*-anisidide by its ir [1664 (s, amide C=O), 833 cm^{-1} (s, *p*-C_6H_4)] and nmr data [δ 3.68 (s, 3 H), 6.72 (d, $J \approx 10$ Hz, 2 H), 7.2 (m, 13 H), 8.2 (br s, 1 H)] and comparison with an authentic sample.

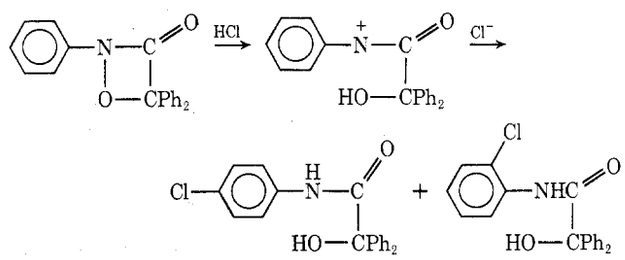


Two additional products (Scheme III) were also obtained from methanolysis of the transient oxazetidin-3-one **5c**. One, **14**, was identified as *N*-(2,4-dimethoxyphenyl)benzilamide by its ir [1669 (s, amide C=O), 909 and 839 (1,2,4-C_6H_3), 752 and 700 cm^{-1} (C_6H_5)] and nmr data [δ 3.65 (s, 3 H), 3.67 (s, 3 H), 3.95 (s, 1 H), 6.41 (m, 2 H), 7.33 (m, 10 H), 8.30[53] (d, $J \approx 9$ Hz, 1 H), 8.89 (br s, 1 H)] and comparison with an authentic sample. The other product, **15**, was identified as *N*-(4-hydroxyphenyl)benzilamide by its ir [1640 (s, amide C=O), 820 cm^{-1} (s, *p*-C_6H_4)], nmr [δ 6.02 (d, $J \approx 10$ Hz, 2 H), 6.45 (d, $J \approx 10$ Hz, 2 H), 7.25 (m, 12 H), 8.24 (s, exchangeable with D_2O, 1 H)], and mass spectra [*m/e* 319 (P^+), 274 (P − OH − CO^+), 194 (Ph_2CCO^+), 183 (Ph_2COH^+), 135 (HO-$C_6H_4NCO^+$), 105 ($PhCO^+$)].

Scheme III



Related reactions have also been reported by Sheradsky,[54] who isolated ring-chlorinated products on treating **5b** with HCl. The nature of the product in all of these



cases implicates nitrenium ion-like intermediates **11** in the solvolyses and supports their intermediacy in the thermal decompositions to isocyanates and benzophenone.

Experimental Section[55]

Materials. Diphenylketene (**1**),[13] 4-nitrosoanisole (**2c**),[56] 4-nitrosotoluene (**2d**),[57] and methyl 4-nitrosobenzoate (**2e**)[58] were prepared by literature methods. *N,N*-Dimethyl-4-nitrosoaniline, nitrosobenzene, 4-aminophenol, *N,N*-dimethyl-*p*-phenylenediamine, and 2,4-dimethoxyaniline were used as obtained from Aldrich Chemical Co. *p*-Anisidine (Aldrich) was recrystallized from cyclohexane.

Reaction of 2a with 1 in Chloroform. A chloroform solution of *N,N*-dimethyl-4-nitrosoaniline (**2a**, 2.700 g in 25 ml) was added dropwise to a stirred solution of diphenylketene (3.471 g, 17.9 mmol) in 25 ml of chloroform, under a nitrogen atmosphere, until the ketene absorbance at 2090 cm^{-1} in the ir disappeared. The amount of **2a** actually consumed was 1.670 g (11.1 mmol). The ir spectrum indicated isocyanate (2270 cm^{-1}), lactam **3a** (1730 cm^{-1}), and benzophenone (1655 cm^{-1}). Ethanol (10 ml) was added to convert isocyanate to urethane, and after 5 hr the sol-

vents were stripped off. The residue was chromatographed on 65 g of silica gel. Elution with benzene yielded a binary mixture of lactam **3a** and benzophenone (ir). Lactam **3a** was isolated (2.23 g) by dissolving out the benzophenone with hexane–benzene, followed by recrystallization from acetone: mp 191–196° dec (lit.[1] mp 196–200°); nmr ($CDCl_3$) δ 3.17 (s, 6 H), 6.79 (d, $J \approx 10$ Hz, 2 H), 7.28 (m) and 7.60 (d, $J \approx 10$ Hz) (combined integral 22 H); mass spectrum *m/e* (rel intensity) 494 (0.1, P), 300 (100, $Ph_2C{=}NC_6H_4NMe_2$), 223 (34, $PhC{\equiv}NC_6H_4NMe_2$), 194 (26, Ph_2CCO), 165 (59, $C_{12}H_9$). The hexane–benzene filtrate left 1.81 g residue upon evaporation, which was dissolved in ethanol and treated with excess 2,4-dinitrophenylhydrazine reagent[59] to precipitate the 2,4-dinitrophenylhydrazone derivative of benzophenone (1.43 g, 3.95 mmol), which indicated the residue to have contained 3.95 mmol (0.72 g, 36%) of benzophenone and 1.09 g of lactam **3a**, for a total of 3.32 g (6.72 mmol, 61%) of the latter.

Elution of the column with 60% ether–benzene gave 0.651 g (3.13 mmol, 28%) of a green solid, mp 71–73°, which afforded a white solid, mp 77–78°, upon recrystallization from hexane, identical (ir, nmr, mixture melting point) with authentic ethyl 4-(*N,N*-dimethylamino)carbanilate. The latter was prepared from ethyl chloroformate and *N,N*-dimethyl-*p*-phenylenediamine: mp 79–81°; ir (KBr) 3210 (s), 2860 (s, br), 1670 (s), 1640 (s, br), 943 (m, br), 813 (s), and 758 cm^{-1} (m); nmr ($CDCl_3$) δ 1.30 (t, $J \approx 8$ Hz, 3 H), 2.90 (s, 6 H), 4.23 (q, $J \approx 8$ Hz, 2 H), 6.74 (d, $J \approx 9$ Hz, 2 H), 7.32 (d, $J \approx 9$ Hz, 2 H).

A previous run of the reaction gave 46% isolated **3a**, 42% benzophenone, and 28% of the urethane. Reactions in acetonitrile and benzene were run as above, with results as in Table II.

Reaction of 2c with 1 in Chloroform. A solution of 1.900 g of 4-nitrosoanisole (**2c**) in 25 ml of chloroform was added dropwise to a stirred solution of **1** (2.764 g, 14.3 mmol) in 25 ml of chloroform in a 250-ml three-neck flask equipped with a reflux condenser and nitrogen inlet tube, until the blue-green color persisted and the ketene absorbance at 2090 cm^{-1} in the ir disappeared. This left 0.40 g of unreacted **2c**, whence the amount consumed was 1.50 g (10.4 mmol). After 2 hr of stirring at room temperature, an ir spectrum showed strong peaks due to oxazetidin-3-one **5c** (1764 cm^{-1}) and lactam **3c** (1730 cm^{-1}), and weak peaks due to isocyanate (2260 cm^{-1}) and benzophenone (1655 cm^{-1}). Refluxing for 4 hr resulted in loss of the oxazetidin-3-one and large increases in the isocyanate and benzophenone peaks. Methanol (10 ml) was added, the solution was stirred for 10 min, and the solvents were stripped off. Methanol (30 ml) was added to the partially crystalline residue, which mixture was then filtered to give 1.07 g of white solid, mp 213–218°. Recrystallization from hexane–benzene gave white crystals of lactam **3c:** mp 226–227° (lit.[2] mp 222–225°); ir (KBr) 1730, 1520, 1350, 1250, and 850 cm^{-1} (all s); nmr ($CDCl_3$) δ 3.62 (s, 3 H), 6.59 (d, $J \approx 10$ Hz), 6.95 (m), 7.27 (d, $J \approx 10$ Hz) (doublets and multiplet, 24 H).

The residue from the methanol filtrate, 3.05 g brown oil, was chromatographed on 60 g of silica gel. Elution with benzene gave a binary mixture of benzophenone and lactam **3c** (ir), 1.485 g. Hexane precipitated 0.10 g of **3c,** mp 212–218°, for a total yield of 1.17 g (2.44 mmol, 22%). The remainder was benzophenone (1.37 g, 7.56 mmol, 69%) by ir.

Elution of the column with 10% ether–benzene afforded methyl 4-methoxycarbanilate (1.60 g, 8.86 mmol, 81%), mp 82–88°. Recrystallization from hexane–benzene gave a white solid: mp 90–91.5° (lit.[60] mp 90°); ir (KBr) 3230 (m), 1740 (s), 1540 (s, br), 1235 (s, br), 1080 (m), and 851 cm^{-1}; nmr ($CDCl_3$) δ 3.65, 3.68 (two singlets, total 6 H), 6.72 (d, $J \approx 10$ Hz, superimposed on br s, total 3 H), 7.16 (d, $J \approx 10$ Hz, 2 H).

Reactions in acetonitrile, dimethylformamide, and hexane were run as above, with results as in Table II.

Reaction of 2d with 1 in Chloroform. The reaction was run as above, using 2.99 g (15.4 mmol) of **1** and 1.25 g (10.3 mmol) of **2d.** An ir spectrum of the reaction mixture at completion showed peaks due to oxazetidin-3-one **5d**[2] (1779 cm^{-1}) and lactam **3d** (1735 cm^{-1}). The chloroform was stripped from the mixture, and 15 ml of hexane was added. Filtration after 18 hr yielded **3d** (0.242 g) as a white solid, mp 186–195°. Crystallization from hexane–benzene gave white crystals: mp 199–205°; ir (KBr) 1735 (s), 1515 (m), 1366 (s), 820 (m), 704 cm^{-1} (br m); nmr ($CDCl_3$) δ 2.21 (s, 3 H), 7.1 (m, 24 H).

The residue from the hexane filtrate, 4.10 g of brown oil, was chromatographed on 65 g of silica gel. Elution with benzene afforded a yellow oil, fractional crystallization of which from hexane yielded first 0.365 g of lactam **3d,** then 0.100 g of a yellow solid, and further recrystallization of which gave a white solid, mp 158–161°, whose spectral data [ir (KBr) 3240 (s), 1670 (vs), 1605 (s), 1518 (s), 700 cm^{-1} (s); nmr ($CDCl_3$) δ 2.30 (s, 3 H), 3.96 (s, 1 H), 5.01 (s, <1 H), 7.40 (m, *ca.* 13 H), 8.31 (d, <1 H, $J \approx 9$ Hz), and 9.08 (s, 1 H)] did not suggest a unique structure.[61] Treatment of the residue from the crystallizations with 2,4-dinitrophenylhydrazine reagent[59] gave 1.63 g (4.50 mmol) of 2,4-dinitrophenylhydrazone derivative, whence the yield of benzophenone was also 4.50 mmol (0.83 g, 44%). Some additional **3d** also contained in the residue could not be isolated. The total isolated amount of **3d** was 0.607 g (1.34 mmol, 13%).

Elution of the column with 50% ether–benzene gave 1.07 g (4.40 mmol, 86%) of crude di-*p*-tolylurea, mp 245–261°. Recrystallization from ether–benzene gave a white solid, mp 270–271° (lit.[62] mp 277°), identical (ir, nmr, mixture melting point) with authentic material.

Reaction of 2b with 1 in Chloroform. The reaction was run as above, using 3.556 g (18.3 mmol) of **1** and 1.240 g (11.6 mmol) of **2b.** An ir spectrum at completion showed large amounts of oxazetidin-3-one **5b** (1776 cm^{-1}) and lactam **3b** (1733 cm^{-1}), and traces of phenyl isocyanate (2240 cm^{-1}) and benzophenone (1655 cm^{-1}). Evaporation of the chloroform left a yellow oil, which on standing for 18 hr in hexane precipitated 0.415 g of lactam **3b,** mp 181–190°. Recrystallization from ethanol gave pure **3b,** mp 189–190° (lit.[63] mp 190–191°), ir identical with that of an authentic[64] sample. The residue from the hexane filtrate (4.40 g) was chromatographed on 65 g of silica gel. Elution with benzene yielded a yellow oil, fractional crystallization (hexane) of which yielded first 0.287 g of **3b,** mp 188–189° (total yield 0.702 g, 1.55 mmol, 13%), then 1.943 g of **5b:** mp 72–73° (lit.[2] mp 73.0–73.5°); ir (KBr) 1773 (s), 1600 (m), 1493 (s), 1360 (s), 763 (s), 747 (s), and 694 cm^{-1} (s). The residue from the recrystallizations (0.539 g), a binary mixture of oxazetidin-3-one **5b** and benzophenone by ir, was treated to obtain the 2,4-dinitrophenylhydrazone of benzophenone[59] (2.15 mmol, 19%), whence an additional 0.148 g of **5b** was also present by difference. The total yield of **5b** was thus 2.017 g (6.90 mmol, 60%).

Elution of the column with 8% ether–benzene gave 0.425 g (2.0 mmol, 11%) of crude diphenylacetic acid, mp 127–140°, mp 142–146° after recrystallization from hexane–benzene (lit.[65] mp 146°). Elution with 50% ether–benzene gave 0.128 g (0.605 mmol, 10%) of 1,3-diphenylurea, mp 219–222°, mp 240–241° after recrystallization from hexane–benzene (lit.[66] mp 237–237.5°).

Reaction of 2e with 1 in Chloroform. The reaction was run as above, using 1.507 g (7.70 mmol) of **1** and 1.065 g (6.50 mmol) of **2e.** The ir spectrum indicated oxazetidin-3-one **5e** (1779 cm^{-1}) and lactam **3e** (1742 cm^{-1}), in addition to the ester groups at 1712 cm^{-1}. No change occurred in the ir after 18 hr. The chloroform was stripped off and the residue, 3.62 g, was chromatographed on silica gel. Elution with benzene yielded a mixture of **3e** and **5e,** which proved inseparable by preparative layer chromatography as well as column chromatography. Fractional crystallization of the mixture from hexane–benzene yielded lactam **3e** as opaque white crystals: mp 195–196°; ir (KBr) 1742 (s), 1712 (s), 1597 (s), 1332 (s), 1271 (s), 1180 (m), 1104 (m), 830 (m, br), 770 (m), 725 (m), and 694 cm^{-1} (m); nmr ($CDCl_3$) δ 3.78 (s, 3 H), 7.10 (br m, 20 H), 7.58 (d, $J \approx 10$ Hz, 2 H), 7.92 (d, $J \approx 10$ Hz, 2 H).

Anal: Calcd for $C_{35}H_{27}NO_3$: C, 82.51; H, 5.31; N, 2.75; Found: C, 82.64; H, 5.35; N, 2.70.

The reaction was rerun as above, using 0.603 g (3.11 mmol) of **1** and 0.364 g (2.21 mmol) of **2e.** The ratio of the products was determined by careful integration of the two methyl ester peaks at δ 3.78 (**3e**) and 3.82 (**5e**), using sweep widths of 108 and 54 Hz. This showed the quantities to be 28% lactam **3e** and 72% oxazetidinone **5e,** ±2%. Fractional crystallization of the mixture from acetone afforded the oxazetidin-3-one **5e** as colorless, transparent crystals: mp 122–123°; ir (KBr) 1770, 1724, 1600, 1372, 1274, 823, 700 cm^{-1} (all strong); nmr ($CDCl_3$) δ 3.82 (s, 3 H), 7.26 (m, 12 H), 7.88 (d, $J \approx 9$ Hz, 2 H).

Anal: Calcd for $C_{22}H_{17}NO_4$: C, 73.54; H, 4.73; N, 3.90. Found: C, 73.75; H, 4.58; N, 3.82.

Reaction of 2b with 1, with Methanolysis of 5b. The reaction was run as previously described, using 4.221 g (21.7 mmol) of **1** and 1.373 g (12.8 mmol) of **2b.** Evaporation of the chloroform left a light brown oil, to which was added 25 ml of methanol. Filtration of the resulting mixture gave solid lactam **3b** (0.694 g, 1.54 mmol, 12%), mp 177–186°. Evaporation of the methanol left 4.86 g of brown oil which was chromatographed as before. Elution with benzene gave a mixture (3.80 g) which contained benzophenone and **5b;** further chromatography yielded 0.737 g (2.4 mmol, 19%) of **5b** from this mixture. Elution with 8% ether–benzene gave first

a white solid (0.705 g), mp 96–96.5° after recrystallization from hexane, whose spectra (see text) and analysis suggested the structure *N*-methoxybenzilanilide (**12**, 2.12 mmol, 17%).

Anal. Calcd for $C_{21}H_{19}NO_3$: C, 75.67; H, 5.71; N, 4.20. Found: C, 75.51; H, 5.85; N, 4.19.

Continued elution with 8% ether–benzene gave benzil-*p*-anisidide (**13**), mp 178–179.5° after recrystallization from carbon tetrachloride (0.259 g, 0.78 mmol, 6%); for ir and nmr spectra, see text. The material was identical (ir, nmr, mixture melting point) with an authentic sample, mp 177–179.5° (lit.[67] mp 170–172°), synthesized by reaction of chlorodiphenylacetyl chloride and *p*-anisidine, followed by hydrolysis.[54] Elution of the column with ether gave 0.23 g (1.07 mmol, 5%) of diphenylacetic acid.

Reaction of 2c with 1, with Methanolysis of 5c. The reaction was run as previously described, using 3.27 g (16.9 mmol) of **1** and 2.040 g (14.9 mmol) of **2c**. After removal of the solvent, the residue was taken up in 25 ml of methanol. Filtration gave 1.675 g of lactam **3c**, mp 212–218°. The residue from evaporation of the filtrate, 3.99 g of brown oil, was chromatographed on 65 g of silica gel. Elution with benzene yielded initially a mixture of benzophenone and **3c**; analysis as before indicated 6.1 mmol (41%) of benzophenone and 0.81 g of **3c** (total yield 2.49 g, 5.16 mmol, 35%). Further elution with benzene yielded a green-yellow solid, mp 117–119°, identified as 4,4′-azoxydianisole by ir.[68] Elution with 6% ether–benzene gave a brown oil (0.418 g, 1.15 mmol, 8%), recrystallization of which from hexane–benzene gave a white solid, mp 122.5–123.5°; for spectra, see text. This was identical (ir, nmr, mixture melting point) with authentic *N*-(2,4-dimethoxyphenyl-)benzilamide (**14**), mp 123–124°, synthesized by reaction of chlorodiphenylacetyl chloride with 2,4-dimethoxyaniline, followed by hydrolysis.[54,69]

Anal. Calcd for $C_{22}H_{21}NO_4$: C, 72.72; N, 5.80; N, 3.85; O, 17.63. Found: C, 73.12; H, 5.70; N, 3.99; O, 17.20.

Further elution of the column with 6% ether–benzene gave methyl 4-methoxycarbanilate (0.665 g, 3.67 mmol, 25%), mp 90–91.5° after recrystallization from hexane–benzene. Elution with 12% ether–benzene gave **15** as a brown solid (1.28 g, 4.02 mmol, 27%), mp 173–177° after recrystallizations from hexane–benzene; for ir, nmr, and mass spectra, see text. A good carbon analysis could not be obtained on this difficultly purified material.

Anal. Calcd for $C_{20}H_{17}NO_3$: C, 75.24; H, 5.33; N, 4.39. Found: C, 77.63, 77.32; H, 4.87, 5.19; N, 3.85, 4.14.

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Registry No.—**1**, 525-06-4; **2a**, 138-89-6; **2b**, 586-96-9; **2c**, 1516-21-8; **2d**, 623-11-0; **2e**, 13170-28-0; **3a**, 51751-63-4; **3b**, 14313-14-5; **3c**, 51751-64-5; **3d**, 51751-65-6; **3e**, 51751-66-7; **5c**, 51751-67-8; **5e**, 51751-68-9; **12**, 51751-69-0; **13**, 20594-45-0; **14**, 51751-74-7; **15**, 51751-75-8; ethyl 4-(*N*,*N*-dimethylamino)carbanilate, 41116-23-8; methyl 4-methoxycarbanilate, 14803-72-6.

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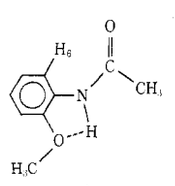

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were obtained using a Varian Aerograph Series 1200 chromatograph equipped with a flame ionization detector or a Varian Aerograph Model 90-P chromatograph equipped with a thermal conductivity detector. The mass spectra were determined by the Morgan-Schaffer Corp., Montreal, Quebec, Canada, on a Hitachi Perkin-Elmer RMU-6D spectrometer. Elemental analyses were obtained from Galbraith Laboratories, Inc., Knoxville, Tenn., or from Meade Microanalytical Laboratory, Amherst, Mass. The chloroform used in each experiment was distilled from barium oxide, passed through a basic alumina column, and dried over magnesium sulfate just prior to use, except as noted. Benzene and hexane were distilled from phosphorus pentoxide prior to use. Dimethylformamide (DMF) was shaken for 3 days over phosphorus pentoxide and 5 g of fresh phosphorus pentoxide was added each day. The DMF was then decanted, shaken for 5 hr over potassium hydroxide to neutralize any formic acid, decanted again, and distilled from Type 4A molecular sieves under a stream of nitrogen at reduced pressure (bp 56°). All transferring of DMF was done under a nitrogen atmosphere. Acetonitrile was distilled from phosphorus pentoxide directly into the reaction vessel.

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Addition of Nitrosyl Chloride to Trimethylsilyl Enol Ethers. A New General Method for Nitrosation of Carbonyl Compounds[1]

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Addition of nitrosyl chloride to trimethylsilyl enol ethers **1** in dichloromethane at −10 to −15° gives good yields of α-oximinocarbonyl compounds **2**. In the case of aldehydes, these initial products are unstable, but may be trapped by hydroxylamine as the glyoximes **3**. The silyl ether of cyclohexanone **1h** yields 2,6-dioximinocyclohexanone (**4**) upon treatment with excess NOCl, whereas with 1 equiv of NOCl the unstable nitroso dimer **5** is formed. Similarly, the silyl derivatives of esters, lactones, and carboxylic acids are directly converted to α-oximino esters and acids. The results are explained by initial addition of NOCl to the silyl enol ether double bond, followed by elimination of trimethylsilyl chloride and tautomerization to the oxime.

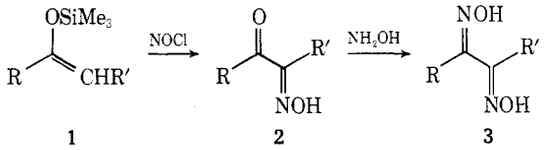
Trimethylsilyl enol ethers are now readily available from ketones or aldehydes,[2a] and their utility as synthetic equivalents of enols[3,4] has recently been demonstrated. Similar derivatives of esters[2b] and acids[2c] have also recently become available. Our interest in the regiospecific and stereospecific introduction of nitrogen functions into organic molecules by additions to double bonds[5] prompted us to study the reaction of silyl enol ethers with nitrosyl chloride. We have found that the reaction is instantaneous at −10 to −15° in dichloromethane and affords good yields of α-oximino carbonyl compounds in a high state of purity.

Results

When the ketone-derived trimethylsilyl enol ethers **1a–c** were treated with excess NOCl for <1 min, good yields of the corresponding α-oximino ketones **2a–c** were formed (Table I). The only by-products were the corresponding ketones, presumably from hydrolysis of **1**. Purification[6] of the NOCl (by removal of HCl, H_2O, and NO_2) led to no improvement in yields or reduction of hydrolysis. If the reaction time was extended to several hours, different products were formed. For instance, when the reaction mixture from **1a** was allowed to stand for 18 hr at −20°, α-oximinophenacyl chloride (**2g**, R = Ph; R′ = Cl) was obtained in 48% yield. Acetophenone (14%) and benzoic acid (21%) were identified as by-products in this reaction. The formation of **2g** is not surprising, since it can also be prepared from acetophenone and excess NOCl in 24.5% yield.[7]

Table I
Oximes from Trimethylsilyl Enol Ethers 1 and Nitrosyl Chloride

Silyl ether	R	R′	Product	Yield, %
1a	Ph	H	**2a**	82
1b	Ph	Me	**2b**	83.5
1c	Et	Me	**2c**	72
1d	H	Et	**3d**	66
1e	H	$PhCH_2$	**3e**	77.5
1f	H	n-C_8H_{17}	**2a**	63



1 2 3

The reaction of the silyl ether of cyclohexanone (**1h**) is somewhat more complicated. With excess NOCl, 2,6-dioximinocyclohexanone (**4**)[8] was obtained in 93% yield. By contrast, treatment with 1 equiv of NOCl yielded the unstable nitroso dimer **5** in quantitative yield. Reaction of the latter with hydroxylamine afforded dimer **6**, which dissociated and tautomerized to dioxime **3h**[9] upon dissolution in dimethyl sulfoxide (DMSO). The establishment of structures **5** and **6** rests upon spectral data and upon the isolation and identification of **3h** (see Experimental Section).

When silyl ethers of aldehydes (**1d–f**) were treated with NOCl, the initially formed α-oximino aldehydes **2d–f** were