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Studies on Organometallic Compounds. I. Insertion Reaction of Diketene into N-Si Bond of Silylated Amides

YUTAKA YAMAMOTO[1a] and HITOSHI KIMURA[1b]

Tohoku College of Pharmacy[1a] and Pharmaceutical Institute, Tohoku University[1b]

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Insertion of diketene into the N–Si bond of silylated secondary amides (Ia—d) followed by hydrolysis afforded N-acetoacetyl derivatives (IVa—d) of the corresponding amides in good yields, respectively.

In the reaction with silylated primary amides (Va—c), insertion of diketene into the N–Si bond with subsequent reaction of another mole of diketene resulted in the formation of the corresponding 4-pyrone derivatives (VIa—c), respectively.

Insertion reaction of ketene,[2,3] isocyanate[4] and β-propiolactone[5] into N-Si bond of silylated amines has recently appeared in literatures. On the other hand, reaction of diketene with amide has been reported to give N-acetoacetylamide derivatives.[6,7] However, re-investigation of this reaction did not proved consistently successful. Namely, no reaction was observed except in the cases of formamide and benzamide.[8] Since it was of special interest to us as a general preparative method of N-acetoacetylamide, our attention was focused on insertion of diketene into N-Si bond of activated amide by silylation, which is the subject of the present paper.

The reaction of diketene with N-trimethylsilyl-2-pyrrolidone (Ia) gave rise to an oily product, which was highly sensitive to moisture and purified with difficulty. This was distilled with partial decomposition to give a colorless oil, bp 88° (0.003 Torr.), whose nuclear magnetic resonance (NMR) spectrum suggested the structure of the products being O-trimethylsilyl derivative of IVa (II or III). Structure II was resulted from insertion reaction of diketene into N-Si bond of Ia, which isomerizes to III by prototropy.

Hydrolysis of the oil gave N-acetoacetyl-2-pyrrolidone (IVa) in an excellent yield, which was also obtained without distillation of an oily product by addition of water to the reaction mixture as a colorless crystals, quantitatively, as shown in Chart 1. The structure of IVa was assigned on the basis of the spectral and analytical data.

In the same manner as above, reactions of diketene with N-trimethylsilyl-2-piperidone (Ib), N-trimethylsilyl-ε-caprolactam (Ic) and N-trimethylsilyl-N-methylacetamide (Id) followed by hydrolysis afforded the corresponding N-acetoacetyl derivatives (IV) of 2-piperidone, ε-caprolactam and N-methylacetamide in 84%, 87% and 56% yields, respectively.

In the reaction of N-trimethylsilyl primary amide with diketene, results obtained were at variance with those mentioned above. When N-trimethylsilylacetamide was likewise treated with an equimolar amount of diketene followed by hydrolysis, the main products were

1) Location: *a) 4-4-1, Komatsushima, Sendai, 983, Japan; b) Aobayama, Sendai, 980, Japan.*
2) I. Matsuda, K. Itoh, and Y. Ishii, *J. Chem. Soc.*, **1969**, 701.
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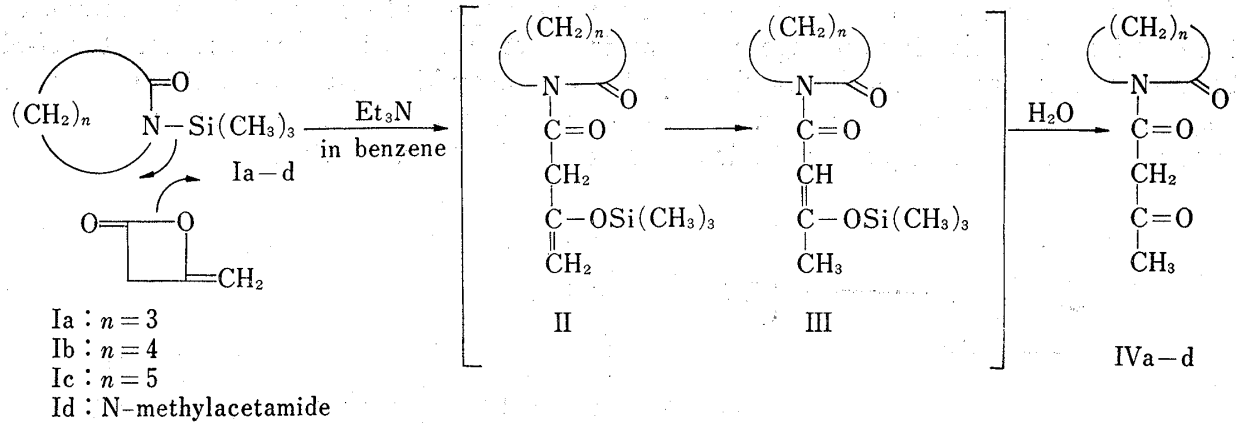

Chart 1

compound VIa and acetamide (VIIIa) besides a low yield of the expected N-acetylaceto-acetamide[9] (VIIa).

Compound VIa was identified as N-acetyl-2,6-dimethyl-4-pyrone-3-carboxamide by following chemical and spectroscopic evidences. Namely, IR spectrum of compound VIa showed absorption bands of imido C=O groups (1750, 1716 sh, 1687 cm^{-1}) and 4-pyrone C=O (1664 cm^{-1}). NMR spectrum showed particular signals of three methyl-protons singlets each at 2.32 ppm, 2.40 ppm and 2.78 ppm, a ring proton singlet at 6.28 ppm, and broad one NH proton at 12.1 ppm. Important mass spectral fragments besides molecular ion were $C_4H_5O_2^+$ (*m/e* 85) due to typical retro Diels-Alder fission of 4-pyrone derivatives, $C_8H_7O_3^+$ (*m/e* 151, M^+-CH_3CONH) and $C_7H_8O_2^+$ (*m/e* 124, M^+-CH_3CONCO).[10,11]

Hydrolysis of VIa with 10% HCl gave 3-acetyl-6-methylpyridin-2,4(1*H*, 3*H*)-dione (IX), 2,6-dimethyl-4-pyrone (X), ammonium chloride and acetic acid. Product IX was identified by comparison of its infrared (IR) spectrum with that of IX prepared according to the literature.[12]

In the reaction of diketene with N-trimethylsilylbenzamide (Vb), two kinds of the products were obtained, which were N-benzoyl-2,6-dimethyl-4-pyrone-3-carboxamide (VIb) and benzamide (VIIIb) in 32% and 42% yield, respectively. Also, reaction of N-trimethylsilyl-phenylacetamide (Vc) yielded 4-pyrone type compound (VIc, 28%) and phenylacetamide (VIIIc, 46%).

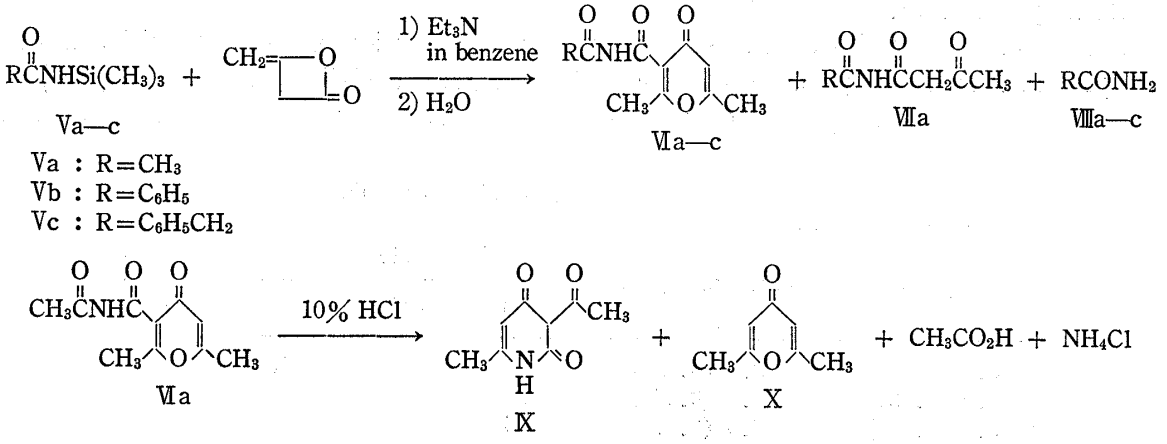

Chart 2

9) T. Kato, H. Yamanaka, Y. Yamamoto, and M. Kondo, *Yakugaku Zasshi*, **92**, 886 (1972).
10) H. Nakata and A. Tatematsu, *Mass Spectroscopy*, **15**, 5 (1967).
11) T. Kato, H. Yamanaka, N. Katagiri, and S. Masuda, *Chem. Pharm. Bull.* (Tokyo), **20**, 133 (1972).
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A consideration of the mechanism of the reaction suggests that formation of VI involves the reaction proceeding in two stages as shown in Chart 3; first, diketene inserts into the N-Si bond of starting amide to give 3-trimethylsiloxycrotonamide derivative (XI), in the next stage, an electrophilic attack of another mole of diketene proceeds at the α-carbon of XI and trimethylsilanol is subsequently eliminated to form the 4-pyrone ring.

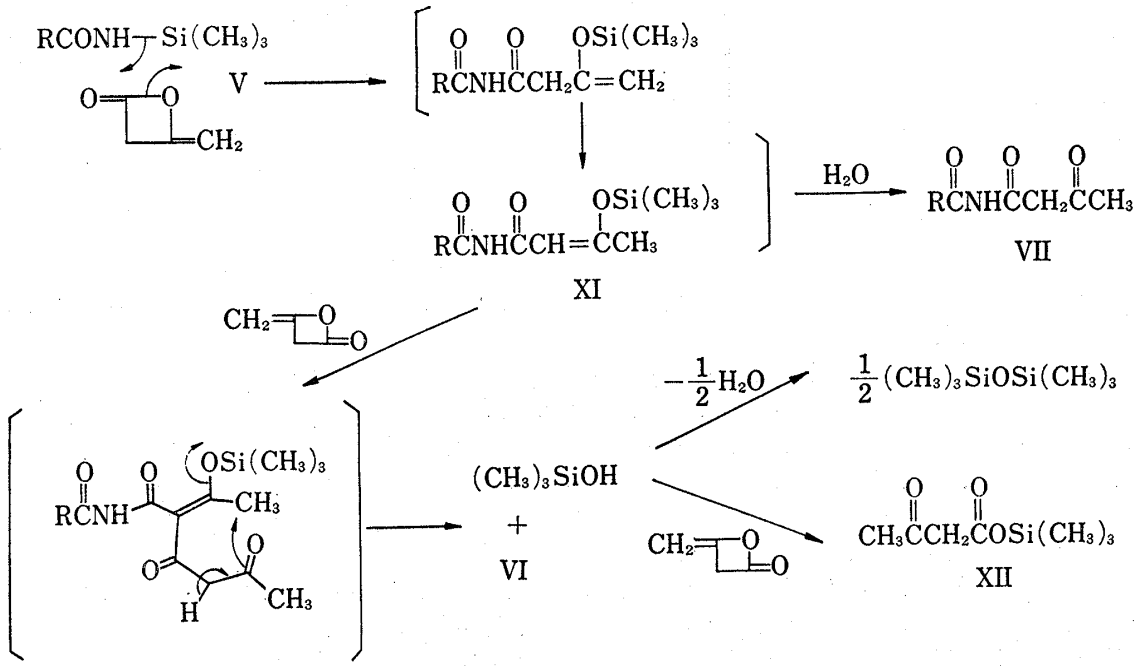

Chart 3

In these reactions mentioned above, the main product was always amide (VIII) produced by hydrolysis of the starting V with water, which was generated while formation of hexamethyldisiloxane from trimethylsilanol as shown in Chart 3. This speculation also can explain the low yield of VI and VII.

In fact compound VI was obtained in a good yield in the reaction of diketene with N-acetyl-3-trimethylsiloxycrotonamide (XI), which was prepared from N-acetylacetoacetamide by the usual silylation method.[13] This finding provides that an excess of diketene is necessary to increase yield of VI.

Use of three equimolar amounts of diketene in the reaction of N-trimethylsilylacetamide accomplished increase of yields of compound VI and trimethylsilyl acetoacetate (XII) up to 85% and 50%, respectively, and decrease of recovery of acetamide as shown in Table I.

Table I. Reaction of Diketene with Va

Va g (mole)	Diketene g (mole)	Yields (%) of			
		VIa	VIIa	VIIIa	XI
3.0 (0.023)	2.0 (0.024)	20	9	51	0
3.0 (0.023)	4.0 (0.048)	54	0	33	43
3.0 (0.023)	6.0 (0.072)	85	0	0	48

It is of interest to note that the 3-trimethylsiloxy derivative of N-acetoacetyl cyclic amide (III) did not undergo the similar reaction with diketene any more under the same reaction

13) H.J. Hurwitz and P.L. De Benneville, U.S.Patent 2876234 (1959) [*C.A.*, 53, 12238*e* (1959)].

condition as stated above. Also, it is already reported[8] that N-acetylacetoacetamide was unreactive to diketene under these conditions.

Experimental

IR spectra were taken with a JASCO model IR-S spectrophotometer. NMR spectra were measured on a Hitachi R-20 instrument. Chemical shifts are reported as δ-value, parts per million downfield from tetramethylsilane as an internal standard. Mass spectra were measured on a Hitachi Double Focusing Mass Spectrometer RMU-7L. All melting points were uncorrected.

N-Trimethylsilyl-2-pyrrolidone (Ia)——N-Trimethylsilyl-2-pyrrolidone (Ia) was prepared according to the method reported by Hurwitz, *et al.*[13] To a solution of 2-pyrrolidone (8.5 g) and Et_3N (10.1 g) in dry benzene, was added dropwise trimethylchlorosilane (11.0 g). The mixture was refluxed with stirring for 2 hr. $Et_3N \cdot HCl$ precipitated was filtered off. The benzene layer was evaporated *in vacuo*, and the residue was distilled to give 12.3 g (78%) of Ia, bp 87° (12 Torr.) (lit.[13] bp77—81° (6 Torr.)). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1678, 850 (ν, $Si(CH_3)_3$). NMR (CCl_4) ppm: 0.21 (9H, s, $Si(CH_3)_3$), 1.95—2.22 (4H, m), 3.18—3.42 (2H, m).

N-Trimethylsilyl-2-piperidone (Ib)——N-Trimethylsilyl-2-piperidone (Ib) was prepared from 2-piperidone (5.0 g), trimethylchlorosilane (5.5 g) and Et_3N (5.0 g) by similar procedure described above, bp 88° (15 Torr.). Yield, 7.13 g (84%). *Anal.* Calcd. for $C_8H_{17}ONSi$ (Ib): C, 56.11; H, 9.94. Found: C, 55.44; H, 10.05. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1668, 1629, 850. NMR (CCl_4) ppm: 0.13 (9H, s), 1.38—1.95 (4H, m), 1.90—2.35 (2H, m), 2.93—3.38 (2H, m).

N-Trimethylsilyl-ε-caprolactam (Ic)——N-Trimethylsilyl-ε-caprolactam (Ic) was prepared from ε-caprolactam (4.5 g), trimethylchlorosilane (4.5 g) and Et_3N (4.1 g) by similar procedure as above, bp 83° (5 Torr.). Yield, 6.3 g (85%). *Anal.* Calcd. for $C_9H_{19}ONSi$ (Ic): C, 58.35; H, 10.27. Found: C, 58.00; H, 10.25. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1633, 848. NMR (CCl_4) ppm: 0.13 (9H, s), 1.30—1.78 (6H, m), 2.22—2.48 (2H, m), 2.98—3.23 (2H, m).

N-Trimethylsilyl-N-methylacetamide (Id)——N-Trimethylsilyl-N-methylacetamide (Id) was prepared from N-methylacetamide (7.3 g), trimethylchlorosilane (11.8 g) and Et_3N (10.1 g) by similar procedure as above, bp 57—59° (17 Torr.) (lit.[13] bp 48—49° (11 Torr.)). Yield, 7.41 g (51%).

N-Trimethylsilylphenylacetamide (Vc)——Following the similar procedure given for Ia, Vc was prepared from phenylacetamide (5.0 g), trimethylchlorosilane (4.02 g) and Et_3N (3.75 g), as colorless crystals, bp 110° (1 Torr.). Yield, 6.0 g (78%). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3400, 1655, 862. NMR ($CDCl_3$) ppm: 0.20 (9H, s), 3.55 (2H, s), 4.65—5.15 (1H, broad), 7.25 (5H, ring protons).

Reaction of N-Trimethylsilyl-2-pyrrolidone (Ia) with Diketene——a) A solution of Ia (3.0 g, 0.02 mole) and diketene (1.6 g, 0.02 mole) in 10 ml of dry benzene was refluxed for 4 hr in the presence of a catalytic amount of Et_3N. The reaction mixture was evaporated *in vacuo*, and the oily residue was distilled under reduced pressure to give 3.3 g of a colorless oil (II, III), bp 88° (0.003 Torr.), whose NMR (CCl_4) showed methyl-protons as a singlet due to structure II at 2.18 ppm and terminal methylene-protons as a singlet due to structure III at 4.00 ppm[3] (ratio; II: III=1: 9). Attempts to further purify the oil failed. A solution of the oil (3.30 g) in 95% EtOH (10 ml) was warmed for 10 min. The reaction mixture was evaporated *in vacuo*, and the oily residue was solidified by addition of a small amount of ether and scrubbing with a glass rod. The resulting crystalline solid was recrystallized from ether to give N-acetoacetyl-2-pyrrolidone (IVa) as colorless prisms of mp 52—53°. Yield, 1.15 g (35%). *Anal.* Calcd. for $C_8H_{11}O_3N$ (IVa): C, 56.79; H, 6.55; N, 8.28. Found: C, 56.76; H, 6.51; N, 8.35. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1728, 1687. NMR ($CDCl_3$) ppm: 1.80—2.25 (2H, m), 2.29 (3H, s), 2.60 (2H, t, J=7 Hz), 3.88 (2H, t, J=7 Hz), 4.02 (2H, s). b) A solution of Ia (3.0 g) and diketene (1.6 g) in 10 ml of dry benzene was refluxed for 4 hr in the presence of a catalytic amount of Et_3N. Then a small amount of H_2O was added, and the mixture was warmed on a water bath (60°) for 10 min. The reaction mixture was evaporated *in vacuo*, and the oily residue was solidified by addition of a small amount of ether and scrubbing with a glass rod. The resulting crystalline solid was recrystallized from ether to give IVa. Yield, 2.88 g (89%).

Reaction of N-Trimethylsilyl-2-piperidone (Ib) with Diketene——Following the similar procedure given for IVa, Ib (3.0 g, 0.017 mole) was allowed to react with diketene (1.4 g, 0.017 mole) to give N-acetoacetyl-2-piperidone (IVb) as colorless prisms (ether–petroleum ether) of mp 41—42°. Yield, 2.69 g (84%). *Anal.* Calcd. for $C_9H_{13}O_3N$ (IVb): C, 59.00; H, 7.15; N, 7.65. Found: C, 59.12; H, 7.24; N, 7.59. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1717, 1681. NMR (CCl_4) ppm: 1.68—1.95 (4H, m), 2.14 (3H, s), 2.28—2.60 (2H, m), 3.57—3.80 (2H, m), 3.81 (2H, s).

Reaction of N-Trimethylsilyl-ε-caprolactam (Ic) with Diketene——Following the similar procedure given for IVa, Ic (1.95 g, 0.01 mole) was allowed to react with diketene (0.84 g, 0.01 mole) to give N-acetoacetyl-ε-caprolactam (IVc) as colorless prisms (ether–petroleum ether) of mp 46—47°. Yield, 1.80 g (87%). *Anal.* Calcd. for $C_{10}H_{15}O_3N$ (IVc): C, 60.89; H, 7.67; N, 7.10. Found: C, 60.41; H, 7.50; N, 7.29. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1718, 1682. NMR ($CDCl_3$) ppm: 1.50—1.98 (6H, m), 2.24 (3H, s), 2.52—2.85 (2H, m), 3.75—4.09 (2H, m), 3.98 (2H, s).

Reaction of N-Trimethylsilyl-N-methylacetamide (Id) with Diketene——Following the similar procedure given for IVa, Id (1.45 g, 0.01 mole) was allowed to react with diketene (0.84 g, 0.01 mole) for 3 hr to give N-

acetyl-N-methylacetoacetamide (IVd) as colorless prisms (ether) of mp 41°. Yield, 0.88 g (56%). *Anal.* Calcd. for $C_7H_{11}O_3N$ (IVd): C, 53.47; H, 7.05; N, 8.91. Found: C, 53.46; H, 6.95; N, 8.81. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1718, 1700, 1686. NMR ($CDCl_3$) ppm: 2.23 (3H, s), 2.30 (3H, s), 3.22 (3H, s), 3.92 (2H, s).

Reaction of N-Trimethylsilylacetamide (Va) with Diketene——a) A solution of Va (3.0 g, 0.023 mole) and diketene (2.0 g, 0.024 mole) in 10 ml of dry benzene was refluxed for 2 hr in the presence of a catalytic amount of Et_3N. A small amount of H_2O was added and the mixture was warmed on a water bath (60°) for 10 min. The reaction mixture was evaporated *in vacuo*, the resulting residue was washed with ether. The ether insoluble solid was taken by filtration and recrystallized from benzene to give acetamide (VIIIa). Yield, 0.64 g (51%). The ether layer was condensed and the residue was purified by column chromatography on silica gel. From the petroleum ether–ether eluate a crystalline substance was obtained. Recrystallization from petroleum ether–ether gave N-acetylacetoacetamide (VIIa) as colorless needles of mp 87—88° (lit.[9] mp 88—89°). Yield, 0.38 g (9%). The IR spectrum was identical with that of VIIa prepared according to the literature.[9] The ether eluted fraction was purified by recrystallization from cyclohexane to give N-acetyl-2,6-dimethyl-4-pyrone-3-carboxamide (VIa) as colorless needles of mp 90—91°. Yield, 0.9 g (20%). *Anal.* Calcd. for $C_{10}H_{11}O_4N$ (VIa): C, 56.94; H, 5.14; N, 6.43. Found: C, 57.41; H, 5.30; N, 6.70. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1750, 1716 (sh), 1687, 1664. NMR ($CDCl_3$) ppm: 2.32 (3H, s), 2.40 (3H, s), 2.78 (3H, s), 6.28 (1H, s), 11.90—12.30 (1H, broad). Mass Spectrum *m/e*: 209 (M^+), 194, 151, 150, 124, 109, 86, 85, 81, 67, 43.

b) According to the procedure described in a), a solution of Va (3.0 g, 0.023 mole) and diketene (4.0 g, 0.048 mole) in dry benzene was refluxed for 2 hr in the presence of a catalytic amount of Et_3N. The reaction mixture was evaporated *in vacuo*, and the resulting residue was washed with petroleum ether. VIa (2.6 g, 54%) and VIIIa (0.45 g, 33%) were obtained as the petroleum ether insoluble crystals. The petroleum ether layer was condensed, and the oily residue was distilled under reduced pressure to give trimethylsilyl acetoacetate (XII) as a colorless oil, bp 91° (30 Torr.) (lit.[14] bp 32° (0.01 Torr.)). Yield, 1.70 g (43%). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1728, 1708. The IR spectrum was identical with that of XII prepared according to the literature.[14]

c) According to the procedure described in b), reaction of Va (3.0 g, 0.023 mole) with diketene (6.0 g, 0.072 mole) gave VIa (4.05 g, 85%) and XII (1.92 g, 48%).

Hydrolysis of VIa——A solution of VIa (100 mg) in 10% HCl (10 ml) was refluxed 1 hr. After cooling, the crystals separated were collected by filtration and recrystallized from 95% EtOH to give 3-acetyl-6-methylpyridin-2,4(1*H*, 3*H*)-dione (IX) as colorless needles of mp 260° (decomp.) (lit.[12] mp 256° (decomp.)). Yield, 30 mg (38%). The IR spectrum was identical with that of IX prepared according to the literature.[12]

The HCl layer was made alkaline with 10% NaOH, and the mixture was extracted with chloroform. The chloroform layer was dried over Na_2SO_4 and filtered. The filtrate was condensed to give a trace of 2,6-dimethyl-4-pyrone (X). The IR spectrum was identical with that of the authentic sample. In this reaction, ammonia (Nessler's reagent was positive) and acetic acid were identified.

Reaction of N-Trimethylsilylbenzamide (Vb) with Diketene——A solution of Vb (3.0 g, 0.016 mole) and diketene (1.4 g, 0.016 mole) in 20 ml of dry benzene was refluxed for 1 hr in the presence of a catalytic amount of Et_3N. The reaction mixture was treated in the same manner as described above. The ether insoluble crystals were recrystallized from benzene to give benzamide (VIIIb). Yield, 0.8 g (42%). The ether soluble fraction was condensed and the residue was recrystallized from cyclohexane to give N-benzoyl-2,6-dimethyl-4-pyrone-3-carboxamide (VIb) as colorless needles of mp 178—180°. Yield, 1.15 g (32%). *Anal.* Calcd. for $C_{15}H_{13}O_4N$ (VIb): C, 66.38; H, 5.03; N, 5.27. Found: C, 66.41; H, 4.83; N, 5.16. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1735, 1658. NMR ($CDCl_3$) ppm: 2.35 (3H, s), 2.88 (3H, s), 6.31 (1H, s, olefinic proton), 7.43—7.65 (3H, m, ring protons), 7.97—8.17 (2H, m, ring protons), 13.35—13.60 (1H, broad, N–H). Mass Spectrum *m/e*: 271 (M^+), 151, 150, 141, 124, 109, 105, 85, 67, 43.

Reaction of N-Trimethylsilylphenylacetamide (Vc) with Diketene——A solution of Vc (2.0 g, 0.01 mole) and diketene (0.84 g, 0.01 mole) in 10 ml of dry benzene was refluxed for 2 hr in the presence of a catalytic amount of Et_3N. The reaction mixture was treated in the same manner as described above. The ether insoluble crystals were recrystallized from benzene to give phenylacetamide (VIIIc). Yield, 0.62 g (46%). The ether soluble fraction was condensed, and the residue was recrystallized from benzene–cyclohexane to give N-phenacyl-2,6-dimethyl-4-pyrone-3-carboxamide (VIc) as pale yellow prisms of mp 80—81°. Yield, 0.73 g (26%). *Anal.* Calcd. for $C_{16}H_{15}O_4N$ (VIc): C, 67.03; H, 5.54; N, 4.88. Found: C, 67.36; H, 5.30; N, 4.91. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1743, 1681, 1640. NMR ($CDCl_3$) ppm: 2.30 (3H, s), 2.76 (3H, s), 3.92 (2H, s), 6.22 (1H, s, olefinic proton), 7.29 (5H, s), 12.1—12.4 (1H, broad, N–H). Mass Spectrum *m/e*: 285 (M^+), 194, 151, 150, 124, 118, 109, 67, 43.

Reaction of N-Acetyl-3-trimethylsiloxycrotonamide (XI) with Diketene——According to Hurwitz's method,[13] to a solution of VIIa (1.0 g) and Et_3N (0.71 g) in 20 ml of dry benzene, was added a solution of trimethylchlorosilane (0.76 g) in 5 ml of dry benzene dropwise. The mixture was refluxed with stirring for 1 hr. $Et_3N \cdot HCl$ precipitated was filtered. Evaporation of the benzene layer *in vacuo* gave XI as light red crystals. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3390, 1719, 1700, 1680, 853. NMR (CCl_4) ppm: 0.33 (9H, s), 2.25 (3H, s), 2.30 (3H, s), 5.75 (1H, s, olefinic proton), 9.80 (1H, broad, N–H).

14) U. Schmidt and M. Schwochau, *Monatsh. Chem.*, **98**, 1492 (1967).

A solution of XI (which was used without purification) and diketene (0.60 g) in 10 ml of dry benzene was refluxed for 1 hr in the presence of a catalytic amount of Et_3N. After cooling, the reaction mixture was evaporated *in vacuo*. The crystalline residue was purified by recrystallization from cyclohexane to give VIa. Yield, 1.20 g (82%, based on VIIa).

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