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Addition Reactions of Heterocumulenes. IV.[1] Reactions of Diketene and Diphenylketene with N-Aryl-S,S-dimethylsulfilimines[2]

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The reactions of diketene with S,S-dimethyl-N-2-pyridinylsulfilimine (IVa) and N-2-benzothiazolyl-S,S-dimethylsulfilimine (IVb) gave 2-(2-dimethylsulfuranylideneaceto-acetamido)pyridine (VIa) and 2-(2-dimethylsulfuranylideneacetoacetamido)benzothiazole (VIb), respectively. However, the reaction of diketene with S,S-dimethyl-N-(4-nitrophenyl)sulfilimine (IVc) and N-2-benzoxazolyl-S,S-dimethylsulfilimine (IVd) gave 3-acetyl-4-hydroxy-6-methyl-1-(4-nitrophenyl)-2-pyridone (VIIc) and 3-acetyl-1-(2-benzoxazolyl)-4-hydroxy-6-methyl-2-pyridone (VIId), respectively.

On the other hand, the reaction of diphenylketene with sulfilimines (IVa, IVb, and IVd) gave the corresponding 1,3-cyclization products (VIII, IX, and X).

Keywords——sulfilimine; diketene; diphenylketene; cyclization; addition

We have previously reported that N′-2-benzothiazolyl-N,N-dimethylformamidine (I) reacts with diketene to give 3-acetyl-4H-pyrimido[2,1-*b*]benzothiazol-4-one (II).[1] A similar reaction of 2-(4-dimethylaminobenzylideneamino)benzothiazole (III) occurs with diphenylketene.[4]

The present paper deals with the reactions of diketene and diphenylketene with N-aryl-S,S-dimethylsulfilimines such as N-2-benzothiazolyl-S,S-dimethylsulfilimine (IVb). Sulfilimines $R\bar{N}-\overset{+}{S}R'_2$ bearing a nucleophilic nitrogen atom and a good leaving group have unique properties, and are useful for organic synthesis.[5]

1. Reaction of Diketene with N-Aryl-S,S-dimethylsulfilimines

The reaction of S,S-dimethyl-N-2-pyridinylsulfilimine (IVa) with diketene in benzene gave the known compound, 2-acetoacetamidopyridine (Va), mp 111—112° (lit.[6] mp 111—112°), and 2-(2-dimethylsulfuranylideneacetoacetamido)pyridine (VIa), mp 201—202° in 22% and 55% yields, respectively. Structural assignment was based on elemental analyses and the spectroscopic data described in the experimental section. Treatment of VIa in 5% hydrochloric acid afforded Va. The reaction involves the addition of diketene to the $-\bar{N}-\overset{+}{S}\!<$ bond of IVa, forming a four-membered cyclic intermediate followed by prototropy to give VIa.

A similar reaction of IVb with diketene afforded 2-(2-dimethylsulfuranylideneacetoacetamido)benzothiazole (VIb) in 54% yield in addition to 2-acetoacetamidobenzothiazole (Vb) in 6% yield.

On the other hand, S,S-dimethyl-N-(4-nitrophenyl)sulfilimine (IVc) reacted with diketene to give N-(4-nitrophenyl)-2-dimethylsulfuranylideneacetoacetamide (VIc) and 3-acetyl-4-hy-

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1) Part III: M. Sakamoto, K. Miyazawa, and Y. Tomimatsu, *Chem. Pharm. Bull.* (Tokyo), **25**, 3360 (1977).
2) A part of this work was reported in a preliminary communication. M. Sakamoto, K. Miyazawa, K. Kuwabara, and Y. Tomimatsu, *Heterocycles*, **12**, 231 (1979).
3) Location: *35-23, Nozawa 1-chome, Setagaya-ku, Tokyo, 154, Japan.*
4) M. Sakamoto, K. Miyazawa, and Y. Tomimatsu, *Chem. Pharm. Bull.* (Tokyo), **24**, 2532 (1976).
5) T.L. Gilchrist and C.J. Moody, *Chem. Rev.*, **77**, 409 (1977).
6) T. Kato, H. Yamanaka, T. Niitsuma, K. Wagatsuma, and M. Oizumi, *Chem. Pharm. Bull.* (Tokyo), **12**, 910 (1964).

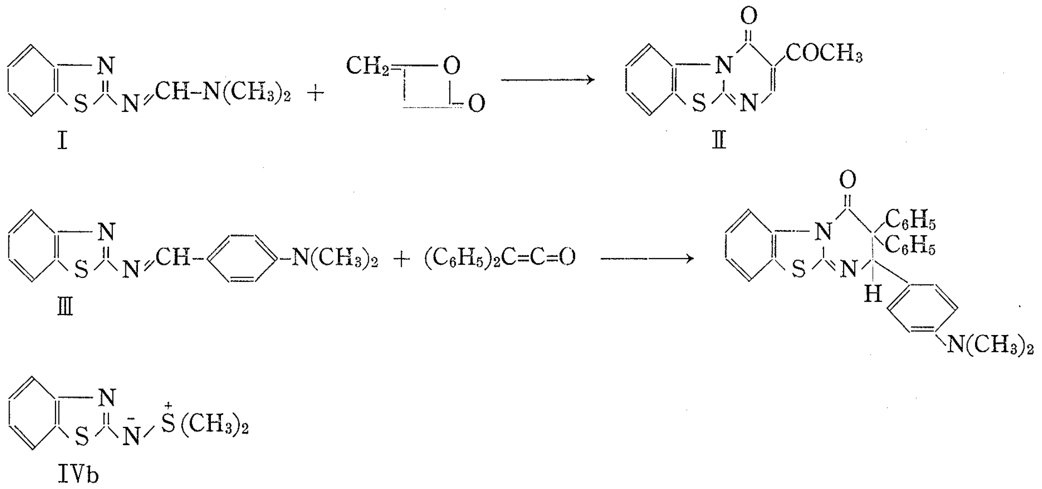

Chart 1

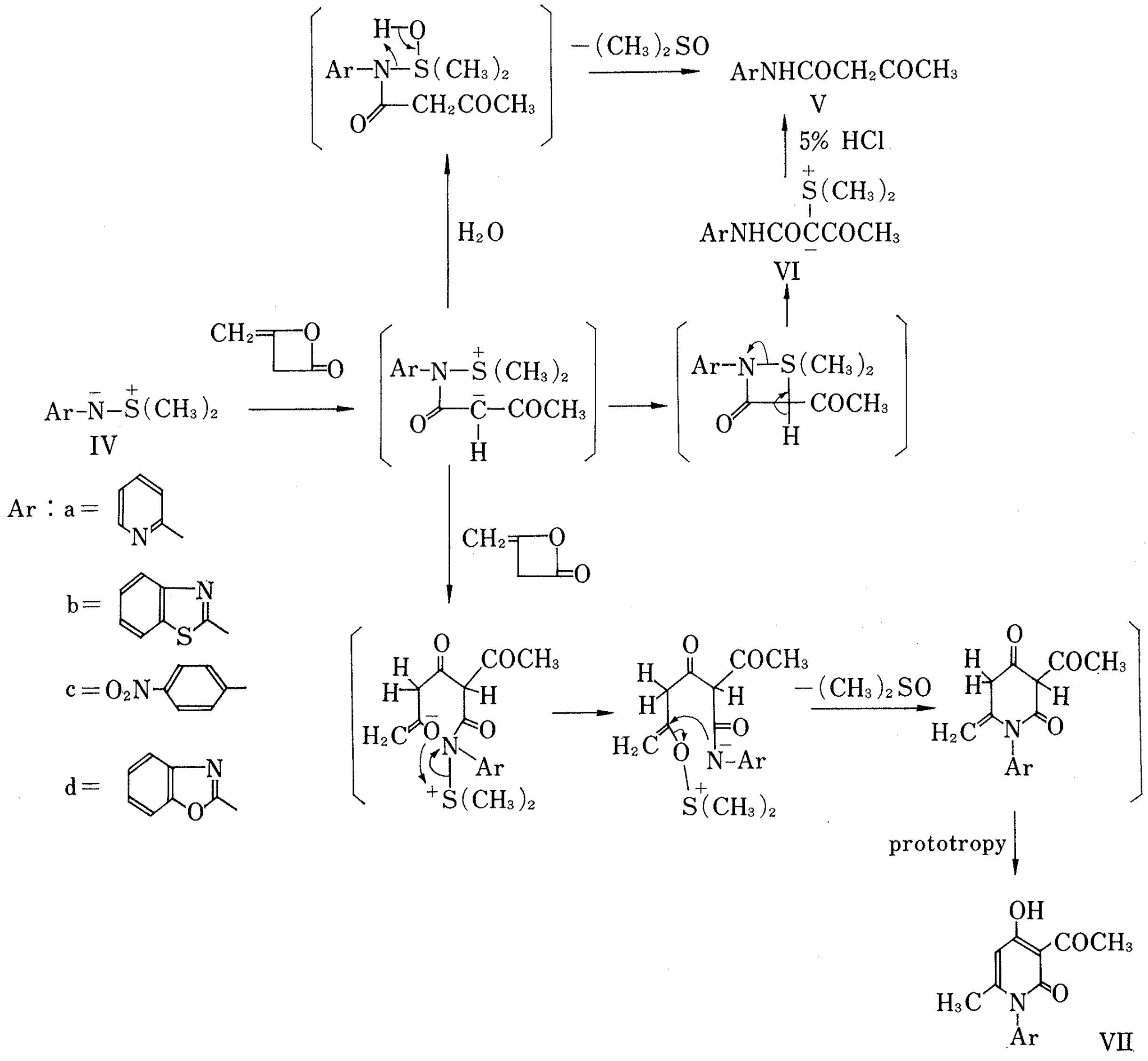

Chart 2

droxy-6-methyl-1-(4-nitrophenyl)-2-pyridone (VIIc) in 34% and 21% yields, respectively. The reaction of N-2-benzoxazolyl-S,S-dimethylsulfilimine (IVd) with diketene afforded only 3-acetyl-1-(2-benzoxazolyl)-4-hydroxy-6-methyl-2-pyridone (VIId) in 25% yield. The structures of VIIc and VIId were assigned by comparison of the spectral data with those for similar compounds.⁷⁾ Kato *et al.*⁷⁾ reported that aniline reacted with diketene, in the presence of a basic catalyst such as triethylamine, to afford acetoacetanilide (V: where Ar is C_6H_5-) and 3-acetyl-4-hydroxy-6-methyl-1-phenyl-2-pyridone (VII: where Ar is C_6H_5-), but 4-nitroaniline gave only N-(4-nitrophenyl)-2,6-dimethyl-4-oxo-4H-pyran-3-carboxamide.

2. Reaction of Diphenylketene with N-Aryl-S,S-dimethylsulfilimines

The reaction of IVa with diphenylketene in xylene gave 3,3-diphenylimidazo[1,2-*a*]-pyridin-2(3H)-one (VIII), mp 214—215°, in 48% yield. The product was unequivocally identified by comparison of the infrared (IR) spectrum, and by a mixed melting point test with an authentic sample prepared from 2-aminopyridine and 2-chloro-2,2-diphenylacetyl chloride, using the synthetic procedure for 2-hydroxy-3-methylimidazo[1,2-*a*]pyridine.⁸⁾

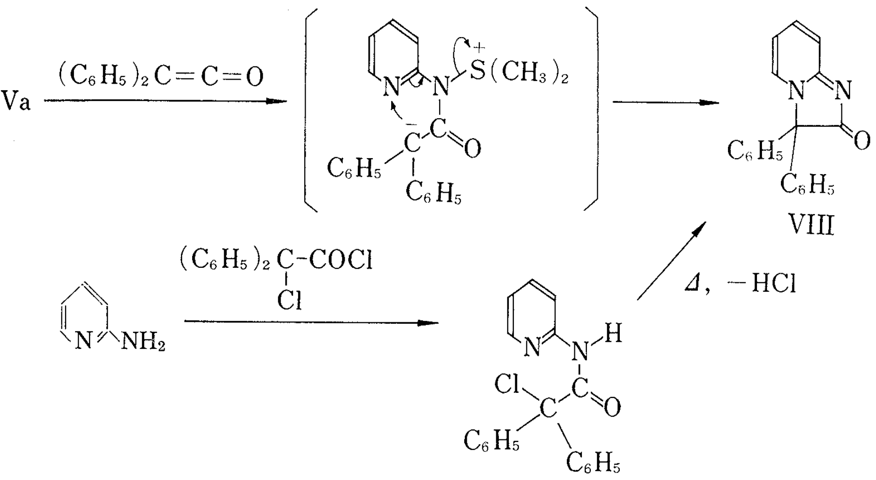

Chart 3

A similar reaction of IVb with diphenylketene afforded 3,3-diphenylimidazo[2,1-*b*]benzothiazol-2(3H)-one (IX), mp 249—251°, in 15% yield. The product was unequivocally identified by comparison of the IR spectrum, and by a mixed melting point test with an authentic sample prepared from 2-aminobenzothiazole and 2-chloro-2,2-diphenylacetyl chloride by a method similar to that described above.⁸⁾

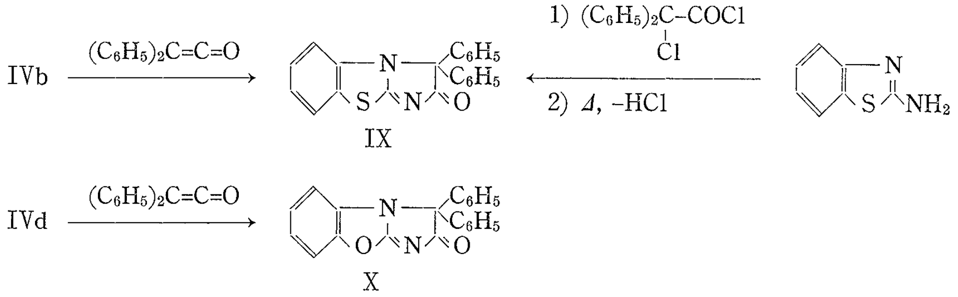

Chart 4

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7) T. Kato and Y. Kubota, *Yakugaku Zasshi*, **87**, 1212 (1967).
8) S. Sugiura, H. Kakoi, S. Inoue, and T. Goto, *Yakugaku Zasshi*, **90**, 436 (1970).

Lastly, IVd was allowed to react with diphenylketene, giving 3,3-diphenylimidazo[2,1-*b*]benzoxazol-2(3H)-one (X) in 74% yield. Attempts to obtain X from 2-aminobenzoxazole in the same way were unsuccessful.

Experimental

All melting points were measured with a Yanagimoto micro melting point apparatus and are uncorrected. Nuclear magnetic resonance (NMR) spectra were measured with a JEOL PS-100 (100 MHz) spectrometer with tetramethylsilane as an internal standard. The following abbreviations are used: s=singlet, m=multiplet, b=broad. Mass spectra were taken on a JEOL JMS-OISG-2 spectrometer. IR absorption spectra were measured with a Nihon Bunko Jasco DS-701G spectrometer.

Reaction of Diketene with S,S-Dimethyl-N-2-pyridinylsulfilimine (IVa)——Diketene (2.2 g, 26 mmol) was added to 2.0 g (13 mmol) of IVa⁹⁾ dissolved in 20 ml of dry benzene. The reaction mixture was stirred at room temperature for 24 hr and the resulting precipitates were collected by filtration. Recrystallization from acetone gave 1.69 g (55%) of 2-(2-dimethylsulfuranylideneacetoacetamido)pyridine (VIa) as colorless granules, mp 201—202°. MS *m/e*: 238 (M$^+$). *Anal.* Calcd. for $C_{11}H_{14}N_2O_2S$: C, 55.45; H, 5.92; N, 11.76. Found: C, 55.34; H, 5.89; N, 11.99. IR ν_{max}^{KBr} cm^{-1}: 1639 (C=O). PMR (in $CDCl_3$) δ: 2.28 (3H, s, $-COCH_3$), 3.12 (6H, s, $S(CH_3)_2$), 12.19 (1H, b, NH). The filtrate of the reaction mixture was evaporated down *in vacuo*, and the residue was purified by column chromatography on silica gel. The fraction eluted with chloroform–acetone (20:1) was evaporated down to give a crystalline substance. Recrystallization from isopropyl alcohol gave 0.5 g (22%) of 2-acetoacetamidopyridine (Va) as colorless plates, mp 111—112° (lit.⁶⁾ mp 111—112°). MS *m/e*: 178 (M$^+$). *Anal.* Calcd. for $C_9H_{10}N_2O_2$: C, 60.66; H, 5.66; N, 15.72. Found: C, 60.44; H, 5.70; N, 15.81. IR ν_{max}^{KBr} cm^{-1}: 3240 (NH), 1719, 1664 (C=O). PMR (in $CDCl_3$) δ: 2.36 (3H, s, CH_3), 3.70 (2H, s, CH_2), 9.76 (1H, b, NH).

Hydrolysis of VIa with HCl——A mixture of 0.36 g of VIa and 40 ml of 5% HCl was stirred at room temperature for 5 hr, then the reaction mixture was extracted with AcOEt. The aqueous layer was made alkaline with 10% aqueous NaOH and extracted with AcOEt. The organic layer was washed with water, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The resulting residue was purified by recrystallization from ligroin to give 0.026 g (10%) of Va, mp 113—114° (lit.⁶⁾ mp 111—112°). The IR spectrum was identical with that of an authentic sample prepared by the above method.

N-2-Benzothiazolyl-S,S-dimethylsulfilimine (IVb)——*t*-Butyl hypochlorite (4.4 g, 40 mmol) in 20 ml of dry dichloromethane was added dropwise over 45 min to a solution of the 2-aminobenzothiazole (6 g, 40 mmol) in 220 ml of dry dichloromethane, with stirring at −50°. After a further 1 hr, dimethylsulfide (2.5 g, 40 mmol) was added dropwise over 5 min. The mixture was stirred for 1 hr at −50°, then sodium methoxide [formed from sodium (48 mmol) and methanol (20 ml)] was added. After stirring at −50° for 1 hr, the mixture was allowed to warm up to room temperature and was then washed with water, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was subjected to silica gel column chromatography, eluting with AcOEt–benzene (10:1) then with AcOEt, to yield unreacted 2-aminobenzothiazole and the sulfilimine (IVb), respectively. Recrystallization of the latter from *n*-hexane–chloroform (2:1) gave 1.8 g (21%) of IVb, mp 85—86°. MS *m/e*: 210 (M$^+$). *Anal.* Calcd. for $C_9H_{10}N_2S_2$: C, 51.42; H, 4.80; N, 13.33. Found: C, 51.38; H, 4.71; N, 13.65. PMR (in $CDCl_3$) δ: 2.82 (6H, s, $S(CH_3)_2$), 6.89—7.51 (4H, m, aromatic protons).

Reaction of Diketene with IVb——Diketene (0.8 g, 9.6 mmol) was added to 1 g (4.8 mmol) of IVb dissolved in 30 ml of dry benzene, together with six drops of AcOH. The reaction mixture was stirred at room temperature for 48 hr and the resulting precipitates were collected by filtration. Recrystallization from acetone gave 0.7 g of 2-(2-dimethylsulfuranylidenacetoacetamido)benzothiazole (VIb) as colorless plates, mp 239—242°. The filtrate of the reaction mixture was concentrated *in vacuo*, and the residue was recrystallized from acetone to give another 0.06 g of VIb. Total yield, 0.76 g (54%). MS *m/e*: 294 (M$^+$). *Anal.* Calcd. for $C_{13}H_{14}N_2O_2S_2$: C, 53.06; H, 4.80; N, 9.52. Found: C, 53.35; H, 4.79; N, 9.69. IR ν_{max}^{KBr} cm^{-1}: 1639 (C=O). PMR (in d_6-DMSO) δ: 2.21 (3H, s, $COCH_3$), 3.04 (6H, s, $S(CH_3)_2$), 12.21 (1H, s, NH). The filtrate after recrystallization was evaporated down *in vacuo*, and the residue was purified by recrystallization from MeOH to give 0.094 g (6%) of 2-acetoacetamidobenzothiazole (Vb) as colorless prisms, mp 220—221° (lit.¹⁰⁾ mp 219°). The IR spectrum was identical with that of an authentic sample prepared by the method of Allen *et al.*¹⁰⁾

Reaction of Diketene with S,S-Dimethyl-N-(4-nitrophenyl)sulfilimine (IVc)——Diketene (1.3 g, 15.5 mmol) was added to 1.5 g (7.6 mmol) of IVc¹¹⁾ dissolved in 90 ml of dry benzene. After refluxing for 5 hr, the reaction mixture was concentrated *in vacuo*, and the residue was washed with MeOH. Recrystallization

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9) P.G. Gassman and C.T. Huang, *J. Am. Chem. Soc.*, **95**, 4453 (1973); T.L. Gilchrist, C.J. Harris, D.G. Hawkins, C.J. Moody, and C.W. Rees, *J. Chem. Soc. Perkin I*, **1976**, 2166.

10) C.F.H. Allen, J. Van Allan, and C.V. Wilson, *J. Am. Chem. Soc.*, **66**, 1805 (1944).

11) P. Claus and W. Vycudilik, *Monatsh. Chem.*, **101**, 396 (1970).

from EtOH gave 0.72 g (34%) of N-(4-nitrophenyl)-2-dimethylsulfuranylideneacetoacetamide (VIc) as pale yellow plates, mp 218—220°. MS *m/e*: 282 (M$^+$). *Anal.* Calcd. for $C_{12}H_{14}N_2O_4S$: C, 51.06; H, 5.00; N, 9.93. Found: C, 50.68; H, 5.03; N, 9.73. IR ν_{max}^{KBr} cm^{-1}: 1641 (C=O). PMR (in $CDCl_3$) δ: 2.32 (3H, s, $COCH_3$), 3.14 (6H, s, $S(CH_3)_2$), 12.14 (1H, b, NH). The filtrate (which was washed with MeOH) was evaporated down *in vacuo*, and the residue was purified by preparative thin-layer chromatography (TLC) using chloroform–acetone (20: 1) as a developing solvent. Recrystallization from isopropyl alcohol gave 0.47 g (21%) of 3-acetyl-4-hydroxy-6-methyl-1-(4-nitrophenyl)-2-pyridone (VIIc) as colorless plates, mp 253—255°. MS *m/e*: 288 (M$^+$). *Anal.* Calcd. for $C_{14}H_{12}N_2O_5$: C, 58.33; H, 4.20; N, 9.72. Found: C, 58.34; H, 4.39; N, 9.64. IR ν_{max}^{KBr} cm^{-1}: 1653 (C=O). PMR (in $CDCl_3$) δ: 2.04 (3H, s, CH_3), 2.70 (3H, s, $COCH_3$), 6.00 (1H, s, pyridone ring proton), 15.62 (1H, s, OH).

Reaction of Diketene with N-2-Benzoxazolyl-S,S-dimethylsulfilimine (IVd)——1) Diketene (0.44 g, 5.2 mmol) was added to 0.5 g (2.6 mmol) of IVd[12] dissolved in 15 ml of dry benzene, together with a few drops of AcOH. After refluxing for 7 hr, the reaction mixture was concentrated *in vacuo*, and the residue was washed with acetone. Recrystallization from acetone gave 0.18 g (25%) of 3-acetyl-1-(2-benzoxazolyl)-4-hydroxy-6-methyl-2-pyridone (VIId) as colorless plates, mp 177—178°. MS *m/e*: 284 (M$^+$). *Anal.* Calcd. for $C_{15}H_{12}N_2O_4$: C, 63.38; H, 4.26; N, 9.86. Found: C, 63.40; H, 4.37; N, 10.08. IR ν_{max}^{KBr} cm^{-1}: 1675, 1633 (C=O). PMR (in $CDCl_3$) δ: 2.18 (3H, s, CH_3), 2.71 (3H, s, $COCH_3$), 6.00 (1H, s, pyridone ring proton), 15.93 (1H, s, OH).

2) Diketene (0.87 g, 10.4 mmol), together with six drops of AcOH, was added to 1 g (5.2 mmol) of IVd dissolved in 30 ml of dry benzene. After stirring at room temperature for 48 hr, the reaction mixture was concentrated *in vacuo*, and the residue was washed with acetone. Recrystallization from acetone gave 0.33 g (22%) of VIId, mp 177—178°, undepressed on admixture with a sample obtained in the first run.

Reaction of Diphenylketene with IVa——A mixture of 0.5 g (3.2 mmol) of IVa and 0.63 g (3.2 mmol) of diphenylketene in 10 ml of dry xylene was refluxed for 6.5 hr. After cooling, crystals that separated were collected by filtration. Recrystallization from EtOH gave 0.52 g (48%) of 3,3-diphenylimidazo[1,2-*a*]pyridin-2(3H)-one (VIII) as colorless plates, mp 214—215°. MS *m/e*: 286 (M$^+$). *Anal.* Calcd. for $C_{19}H_{14}N_2O \cdot C_2H_5OH$: C, 75.88; H, 6.07; N, 8.43. Found: C, 75.74; H, 5.94; N, 8.42. IR ν_{max}^{KBr} cm^{-1}: 1696 (C=O), 1625 (C=N).

Synthesis of VIII from 2-Aminopyridine——A solution of 2-chloro-2,2-diphenylacetyl chloride (5.3 g, 20 mmol) in 10 ml of dry ether was added to a solution of 2-aminopyridine (1.88 g, 20 mmol) in 15 ml of dry ether containing dry pyridine (1.57 g, 20 mmol) at −2°. The reaction mixture was stirred at −2° for 1.5 hr, then allowed to warm up to room temperature. Stirring was continued for 3 hr, then the reaction mixture was washed with water. The ether layer was separated, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was purified by recrystallization from *n*-hexane to give 0.6 g (9%) of 2-(2-chloro-2,2-diphenylacetylamino)pyridine, mp 82—85°. MS *m/e*: 322 (M$^+$). *Anal.* Calcd. for $C_{19}H_{15}ClN_2O$: C, 70.70; H, 4.68; N, 8.68. Found: C, 70.91; H, 4.78; N, 8.71. IR ν_{max}^{KBr} cm^{-1}: 3405 (NH), 1695 (C=O). PMR (in $CDCl_3$) δ: 9.42 (1H, b, NH). 2-(2-Chloro-2,2-diphenylacetylamino)pyridine (1 g, 3.1 mmol) was heated directly at 120° in an oil bath for 11 hr. The reaction mixture was neutralized with 10% aqueous $NaHCO_3$ and extracted with chloroform. The organic layer was washed with water, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was purified by recrystallization from acetone to give 0.1 g (11%) of VIII, mp 210—214°. MS *m/e*: 286 (M$^+$). *Anal.* Calcd. for $C_{19}H_{14}N_2O$: C, 79.70: H, 4.93; N, 9.78. Found: C, 79.42; H, 5.15; N, 9.73. IR ν_{max}^{KBr} cm^{-1}: 1696 (C=O), 1625 (C=N).

Reaction of Diphenylketene with IVb——A mixture of 0.3 g (1.4 mmol) of IVb and 0.28 g (1.4 mmol) of diphenylketene in 15 ml of dry benzene was refluxed for 5 hr. The solvent was evaporated off *in vacuo*, and the residue was washed with ether. Recrystallization from acetone gave 0.07 g (15%) of 3,3-diphenylimidazo[2,1-*b*]benzothiazol-2(3H)-one (IX), mp 249—251°. MS *m/e*: 342 (M$^+$). *Anal.* Calcd. for $C_{21}H_{14}N_2OS$: C, 73.67; H, 4.12; N, 8.18. Found: C, 73.63; H, 4.14; N, 8.26. IR ν_{max}^{KBr} cm^{-1}: 1731 (C=O).

Synthesis of IX from 2-Aminobenzothiazole——A solution of 2-chloro-2,2-diphenylacetyl chloride (2.65 g, 10 mmol) in 5 ml of dry ether was added to a solution of 2-aminobenzothiazole (1.5 g, 10 mmol) in 10 ml of dry ether containing dry pyridine (0.8 g, 10 mmol) at 0°. The reaction mixture was stirred at 0° for 1 hr, then allowed to warm up to room temperature. Stirring was continued for 5 hr, then the reaction mixture was washed with water. The ether layer was separated and dried over anhydrous Na_2SO_4. From the ether filtrate, 1.8 g (48%) of crude 2-(2-chloro-2,2-diphenylacetylamino)benzothiazole was obtained. The product was recrystallized from ligroin, mp 139—142°. MS *m/e*: 378 (M$^+$). *Anal.* Calcd. for $C_{21}H_{15}ClN_2OS$: C, 66.57; H, 3.99; N, 7.39. Found: C, 66.38; H, 4.06; N, 7.26. IR ν_{max}^{KBr} cm^{-1}: 1680 (C=O). 2-(2-Chloro-2,2-diphenylacetylamino)benzothiazole (0.7 g, 1.85 mmol) was heated at 150° in an oil bath for 11 hr, then the reaction mixture was neutralized with 10% aqueous $NaHCO_3$ and extracted with chloroform. The organic layer was washed with water, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was purified by recrystallization from acetone to give 0.2 g (32%) of 3,3-diphenylimidazo[2,1-*b*]benzothiazol-2(3H)-one (IX), mp 250—252°. MS *m/e*: 342 (M$^+$). *Anal.* Calcd. for $C_{21}H_{14}N_2OS$: C, 73.67; H, 4.12; N, 8.18. Found: C, 73.59; H, 4.38; N, 8.48. IR ν_{max}^{KBr} cm^{-1}: 1731 (C=O).

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[12] T.L. Gilchrist, C.J. Harris, C.J. Moody, and C.W. Rees, *J. Chem. Soc. Perkin I*, **1975**, 1969.

Reaction of Diphenylketene with IVd——A mixture of 0.5 g (2.6 mmol) of IVd and 0.5 g (2.6 mmol) of diphenylketene in 20 ml of dry benzene was refluxed for 5 hr. The reaction mixture was concentrated *in vacuo*, and the residue was washed with ether. Recrystallization from acetone gave 0.62 g (74%) of 3,3-diphenylimidazo[2,1-*b*]benzoxazol-2(3H)-one (X), mp 211—212°. MS *m/e*: 326 (M^+). *Anal.* Calcd. for $C_{21}H_{14}N_2O_2$: C, 77.28; H, 4.32; N, 8.58. Found: C, 76.99; H, 4.42; N, 8.47. IR ν_{max}^{KBr} cm^{-1}: 1742 (C=O).

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