The Cycloaddition Reaction of *N*-Imidoyl Sulfoximides with Diphenylcyclopropenone to Yield Pyrimidinone or Pyrrolinone Derivatives

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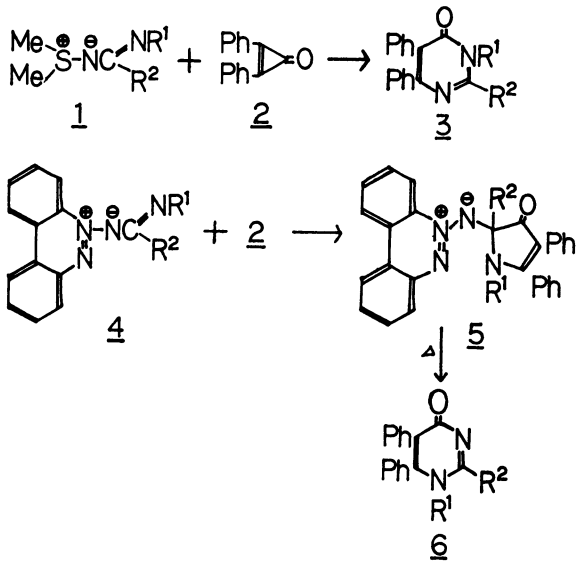
N-Imidoyl sulfoximide (**7**) reacted with diphenylcyclopropenone (**2**) at 130 °C to yield a mixture of 1,2-disubstituted 5,6-diphenyl-4(1*H*)-pyrimidinone (**6**) and *N*-(4-oxo-2-pyrrolin-5-yl)sulfoximide (**10**), which might be formed by [3+3] and [2+3] cycloaddition reactions between **2** and **7**. The yields of **6** and **10** depended on the electronic and steric effects of the substituents of **7**.

Diphenylcyclopropenone (**2**) and its analogs react with a variety of ylides and imides to give heterocycles.[1] *N*-Imidoyl sulfimides (**1**)[2] reacts with **2** to yield pyrimidine (**3**). In contrast, the reaction of benzo[*c*]cinnolium imide (**4**) with **2** gives the adduct (**5**),[3] which on pyrolysis yields the isomeric pyrimidine (**6**) (Scheme 1).

In a continuation of our earlier works of the chemical and physical properties of *N*-, *P*-, and *S*-ylides and imides substituted with C=S or C=N groups,[4] we have found an easy route for the preparation of the new *N*-imidoyl sulfoximide (**7**). In this paper, the reaction of **7** with **2** was carried out in order to compare it with those of **1** and **4**.



Scheme 1.

Results and Discussion

The reaction of acid chloride with unsubstituted sulfoximide (**8**) to give *N*-acylsulfoximide has been well known.[5] On the similar treatment of **8** with imidoyl chloride (**9**) in the presence of triethylamine, the sulfoximides **7** were prepared in moderate yields. The imides **7** were fairly stable at room temperature; their physical properties are collected in Table 1.

It has been reported that propenone **2** decomposes over 140 °C.[6] Thus, an equimolar mixture of **2** and **7d** in xylene was heated at 130 °C. The disappearance of **2** was checked by TLC at suitable time intervals. The subsequent purification of the product by chromatography over silica gel yielded two products: the colorless 4(1*H*)-pyrimidinone (**6d**) and the yellow sulfoximide (**10d**). The structure assignment is based on the following evidence.

The former product had the same physical properties as the previously reported compound,[3] but quite different from those of the **3a** isomer (R^1=4-MeC_6H_4, R^2=Ph) obtained from the reaction of **1a** (R^1=4-MeC_6H_4, R^2=Ph) with **2**.[2,7] The mass spectroscopic studies of **3a** and **6d** clarified the ambiguity of the structure elucidation. The **6d** isomer showed a characteristic peak corresponding to MeC_6H_4N–C(Ph)=CPh; in contrast, **3a** showed no such peak.

The latter product, **10d**, gave satisfactory elemental analysis, ^{1}H-NMR, MS, and chemical transformation. Upon treatment with ethanol in the presence of trifluoroacetic acid, **10d** yielded the pyrrolinone derivative **11b** in quantitative yield. The hydrolysis of **11b** in a mixture of aqueous sulfuric and acetic acids yielded the known furanone **12**,[8] not the isomeric acid **13**.[9]

The reaction of other sulfoximides with **2** yielded two kinds of products, corresponding to **6** and **10**. The product ratios **10**/**6** and physical properties of **6** and **10**

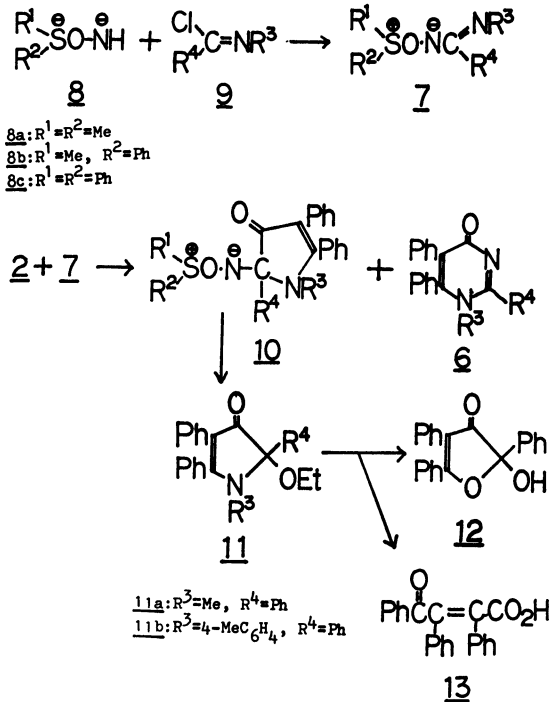


TABLE 1. PREPARATION OF SULFOXIMIDE 7

	R^1	R^2	R^3	R^4	Yield %	Mp θ_m/°C	M^+	^{1}H-NMR δ in $CDCl_3$[a]	Found (Calcd) (%) C	H	N
7a	Me	Me	Me	Ph	36	84—86	210	3.03 (3H, s, NMe), 3.28 (6H, s, Me_2S)	57.02 (57.11	6.63 6.71	13.64 13.32)
7b	Me	Me	C_2H_5	Ph	67	75—78	224	1.03 (3H, t, J=7 Hz, CH_3), 3.21 (2H, q, CH_2), 3.17 (6H, s Me_2S)	58.49 (58.90	7.08 7.19	12.09 12.49)
7c	Me	Me	Ph	t-Bu	74	95—96	252	1.20 (9H, s, t-Bu), 2.65 (6H, s, Me_2S)	61.57 (61.87	8.13 7.99	11.04 11.10)
7d	Me	Me	4-MeC_6H_4	Ph	63	143—145	286	2.23 (3H, s, $\underline{Me}C_6H_4$), 3.35(6H, s, Me_2S)	67.06 (67.10	6.38 6.38	9.83 9.78)
7e	Me	Me	4-$MeOC_6H_4$	Ph	73	145—146	302	3.43 (6H, s, Me_2S), 3.75 (3H, s, MeO)	63.69 (63.55	6.05 6.00	9.34 9.26)
7f	Me	Me	2,6-$Me_2C_6H_3$	Ph	50	125—128	300	2.08(6H, s, $\underline{Me}_2C_6H_3$), 3.39 (6H, s, Me_2S)	68.07 (67.97	6.64 6.71	8.97 9.32)
7g	Me	Me	4-$NO_2C_6H_4$	Ph	72	152—153	317	3.45 (6H, s, Me_2S)	56.88 (56.77	4.73 4.76	13.06 13.24)
7h	Me	Me	Ph	4-MeC_6H_4	86	118—119	286	2.23 (3H, s, $\underline{Me}C_6H_4$), 3.31 (6H, s, Me_2S)	67.32 (67.10	6.37 6.33	10.09 9.78)
7i	Me	Me	Ph	4-$MeOC_6H_4$	82	145—146	302	3.30 (6H, s, Me_2S), 3.69 (3H, s, MeO)	63.51 (63.55	6.08 6.00	9.48 9.26)
7j	Me	Me	Ph	2,4,6-$Me_3C_6H_2$	77	94—95	314	2.15 (3H, s, Me), 2.20 (6H, s, Me_2), 3.36 (6H, s, Me_2S)	68.24 (68.76	7.14 7.05	8.82 8.91)
7k	Me	Me	Ph	4-$NO_2C_6H_4$	45	128—129	317	3.40 (6H, s, Me_2S)	56.64 (56.77	4.62 4.76	12.95 13.24)
7l	Me	Me	Ph	4-ClC_6H_4	73	114—115	306	3.35 (6H, s, Me_2S)	58.39 (58.72	4.77 4.93	9.01 9.13)
7m	Me	Ph	4-MeC_6H_4	Ph	73	138—140	348	2.20 (3H, s, $\underline{Me}C_6H_4$), 3.32 (3H, s, Me_2S)	72.46 (72.38	5.69 5.79	8.31 8.04)
7n	Ph	Ph	4-MeC_6H_4	Ph	35	139—140	410	2.32 (3H, s, Me)	75.93 (76.07	5.38 5.40	6.67 6.82)

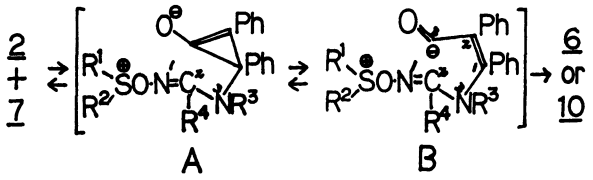
a) Phenyl-ring protons were observed at δ 6.6—8.0.

TABLE 2. THE REACTION OF 7 WITH 2 AT 130 °C IN XYLENE

Reactant	Time/h			Yield/%		Ratio 10/6
7a	2	—		10a	60	
7b	2	6b	1	10b	79	79
7c	100[a]	—		—		
7d	2	6d	15	10d	45	3.0
7e	2	6e	10	10e	50	5.0
7f	80[a]	—		—		
7g	90	6g	4	10g	11	2.8
7h	2	6h	19	10h	58	3.1
7i	2	6i	17	10i	51	3.0
7j	50[a]	—		—		
7k	27	6k	13	10k	45	3.5
7l	6	6l	11	10l	60	5.5
7m	4	6d	22	10m	63	2.9
7n	20	6d	1	10n	37	37

a) None of the products corresponding to **6** or **10** were found.

are shown in Tables 2 and 3. Since **2** decomposed slowly at the reaction temperature,[6] half a molar excess **2** was added in the course of the reaction for the cases of imides of a low reactivity: **7c**, **7f**, **7g**, and **7j**. From the reaction mixtures of such imides, none of the expected products **6** and **10** was isolated, or they were isolated only in low yields, together with an unidentifiable tarry mass. *N*-Alkylbenzimidoyl sulfoximides, **7a** and **7b**, gave **10a** and **10b** in an overwhelming majority. In contrast, the *N*-arylbenzimidoyl sulfoximides **7d**, **7e**, **7g—i**, and **7k—m** yielded the corresponding **6** and **10** in nearly similar ratios, although much rate retardation was observed for the imides substituted with the electron-withdrawing groups: **7k** and **7g**.



Scheme 2.

Upon heating at 140 °C for 12 h, the isolated **10b** or **10d** did not yield **6b** or **6d**, and long-time heating of the reaction mixtures of **7b** or **7d** with **2** did not improve the yields of **6b**/**10b** or **6d**/**10d**. These observations seem to indicate that **10** was not the precursor or intermediate of the production of **6**.

The ^{1}H-NMR spectroscopic studies for the sulfoximides **7** and **10** were interesting. The signal of the *S*-methyl groups of **7** appeared as a singlet at around δ 3.3, while those of the pyrrolinone-substituted sulfoximide **10** appear as two singlets at around δ 2.9 and 3.2 (Tables 1 and 3). The resolution of the two methyl groups for the *N*-alkyl substituted imides **10a** and **10b** was small. These observations seem to indicate that the free rotation around the S–N bond of **10** might be highly hindered by the bulky aryl substituents on the pyrrolinone ring.

Aldimine, ketimine, and amidine, which have C=N bonds, react with **2** to give 2-pyrrolin-4-one derivatives[8,10] *via* a [2+3] cycloaddition reaction. Considering the results obtained, the most plausible mechanism is that shown in Scheme 2. The nucleophilic attack of he terminal nitrogen (N^3) on the cyclopropenone **2**

Table 3. Physical properties of **6** and **10**

	Mp θ_m/°C	M^+	^{1}H-NMR δ in $CDCl_3$[c]	Found (Calcd) (%)		
				C	H	N
6b	252—254[a]	352	0.83 (3H, t, J=7 Hz, CH_3), 4.82 (2H, q, CH_2)	81.78 (81.79	5.66 5.72	7.78 7.95)
6d	203—205[b]	414	2.10 (3H, s, MeC_6H_4)	83.85 (84.03	5.24 5.35	6.60 6.76)
6e	193—195	430	3.57 (3H, s, MeO)	81.19 (80.91	5.29 5.15	6.46 6.51)
6g	256—259	445		75.46 (75.49	4.14 4.30	9.45 9.43)
6h	213—214	414	2.18 (3H, s, MeC_6H_4)	84.34 (84.03	5.27 5.35	6.39 6.76)
6i	170—171	430	3.73 (3H, s, MeO)	80.97 (80.91	5.26 5.15	6.85 6.51)
6k	118—120	445		74.92 (75.49	4.18 4.30	9.54 9.43)
6l	168—169	434		77.51 (77.33	4.72 4.40	6.63 6.44)
10a	191—193	416	2.80 (3H, s, MeN), 3.17 (3H, s, MeS), 3.18 (3H, s, MeS)	71.96 (72.09	5.77 5.81	6.68 6.73)
10b	145—146	430	0.61 (3H, t, J=7 Hz, CH_3CH_2), 3.34 (2H, dq, J=3 and 7 Hz), 3.10 (3H, s, MeS), 3.18 (3H, s, MeS)	72.26 (72.53	6.05 6.09	6.55 6.51)
10d	221—222	492	2.09 (3H, s, MeC_6H_4), 2.88 (3H, s, MeS), 3.25 (3H, s, MeS)	75.38 (75.58	5.68 5.73	5.53 5.69)
10e	208—209	508	2.95 (3H, s, MeS), 3.29 (3H, s, MeS), 3.62 (3H, s, MeO)	73.14 (73.20	5.48 5.55	5.53 5.51)
10g	283—285	523	2.88 (3H, s, MeS), 3.20 (3H, s, MeS)	68.65 (68.82	4.84 4.81	7.73 8.02)
10h	161—162	492	2.15 (3H, s, MeC_6H_4), 2.74 (3H, s, MeS), 3.12 (3H, s, MeS)	75.81 (75.58	5.78 5.73	5.59 5.69)
10i	188—189	508	2.90 (3H, s, MeS), 3.26 (3H, s, MeS), 3.76 (3H, s, MeO)	73.00 (73.20	5.48 5.55	5.55 5.51)
10k	252—254	523	2.93 (3H, s, MeS), 3.22(3H, s, MeS)	69.32 (68.82	4.82 4.81	7.97 8.03)
10l	123—124	513	2.86 (3H, s, MeS), 3.21 (3H, s, MeS)	69.91 (70.23	5.10 4.91	4.82 5.46)
10m	201—203	554	2.00 (3H, s, MeC_6H_4), 3.21 (3H, s, MeS)	77.63 (77.95	5.49 5.45	4.96 5.05)
10n	233—235	616	2.10 (3H, s, Me)			

a) The reported[5] mp for the **3b** isomer (R^1=Et, R^2=Ph) was 175 °C. b) The reported[2] mp for **6d** was 204—205 °C. The isomer **3d** (R^1=MeC_6H_4, R^2=Ph) had 262—265 °C. c) Phenyl-ring protons were observed at δ 6.4—8.3.

yields the intermediate **A**, followed by the ring-opening of the cyclopropenone and the nucleophilic attack of the carbonyl carbon (C^3) on the imino nitrogen (N^1) or the imino carbon (C^2) to yield either **6** or **10** *via* [3+3] or [2+3] cycloaddition. The pyrrolinone **10** is not an intermediate for the formation of **6**.

Table 2 indicates that bulkiness and electronic nature of the substituents R^1—R^4 on **7** controlled the reactivity of **7**. The nucleophilicity of the terminal nitrogen N^3 decreased with the electron-attracting substituents on N^3 (*i.e.*, R^3) and C^2 (*i.e.*, R^4) through the C=N bond. Bulky substituents lowered the reactivity of **7** (**7c**, **7f**, and **7j**), indicating that steric hindrance might contribute not only to the initial nucleophilic attack, but also to the ring-forming step to yield **6** or **10**.

The product ratios **10**/**6** also seem greatly affected by the bulkiness of the substituents R^1—R^4. Two phenyl groups of **7n** and alkyl groups for R^3 (**7a** and **7b**) increased the product ratios. These results seem to indicate that the ring formation of **10** would be easier than the formation of **6** due to the steric crowding between the substituents.

Barr *et al.* have indicated that the nature of the cationic center of the imide can profoundly affect the character of an ambident anionic portion.[3] This finding agrees well with our present results. The free *S*,*S*-dimethylsulfimide and *S*,*S*-dimethylsulfoximide (**8a**) have pK_a values of 7.28 and 3.24 respectively.[11,12] This big difference seems to affect the imino nitrogens of **1** and **7** (N^1 in Scheme 2). The imide **1** reacts with **2** at imino nitrogen (N^1); in contrast, the sulfoximide **7** reacts with **2** at the terminal nitrogen (N^3).

Experimental

General. The melting points were not corrected. ^{1}H-NMR spectra were recorded on a Hitachi-Perkin-Elmer R-20(60 MHz) spectrometer, using TMS as the internal standard; the IR spectra, on a Japan Spectroscopic Co. Ltd., A-3 infrared spectrophotometer, and the mass spectra, on a Hitachi RMU-7M mass spectrometer.

*Preparation of Unsubstituted Sulfoximides (**8a**—**c**).* *S*,*S*-Dimethyl-, *S*-methyl-*S*-phenyl-, and *S*,*S*-diphenylsulfoximides (**8a**—**c**) were prepared according to the literature.[13—15]

*Preparation of N-Imidoyl Sulfoximides (**7**).* A solution of

unsubstituted sulfoximide **8** (10 mmol) in benzene (30 cm³) and triethylamine (11 mmol) was dried over sodium carbonate (1 g). To the stirred mixture we then added, drop by drop, imidoyl chloride **9** (10 mmol) in benzene (10—20 cm³) over a 2-h period, the temperature being kept at around 15 °C. After the reaction, the precipitate was separated by filtration and the benzene solution was washed with water, dried over sodium carbonate, and evaporated *in vacuo* to yield the crude sulfoximide **7**, which was then recrystallized from benzene–petroleum ether. The physical properties of the products **7** are shown in Table 1.

The Reaction of ***7*** *with* ***2***. An equimolar mixture of **2** and **7** (1 mmol) in a minimum amount of xylene (*ca.* 3 cm³) was heated at 130 °C. The reaction was checked by means of TLC (silica gel, ethyl acetate–petroleum ether 2 : 1) at suitable time intervals. After the reaction, the cooled mixture was chromatographed over silica gel. Elution with a mixture of chloroform and ethyl acetate (5 : 1) gave **6** and **10**. The physical properties of the products are collected in Table 3.

The Reaction of ***10a*** *and* ***10d*** *with Ethanol*. To a solution of **10a** (0.1 mmol) in dry ethanol (10 cm³) we added 3 drops of trifluoroacetic acid at room temperature. One hour later, the reaction mixture was quenched with water and extracted with chloroform. The chloroform extract was dried under reduced pressure to yield a crystalline mass, which was then recrystallized from ethanol to give **11a** in a 90% yield. **11a** (R^3=Me, R^4=Ph): mp 157—158 °C; NMR ($CDCl_3$) δ=1.37 (3H, t, J=7 Hz, $C\underline{H}_3CH_2$), 2.80 (3H, s, MeN), 3.59 (2H, q, CH_2), and 6.8—7.8 (15H, m, Ph). Found: C, 81.51; H, 6.18; N, 3.83%; M^+ 369. Calcd for $C_{25}H_{23}NO_2$: C, 81.27; H, 6.27; N, 3.79%; M 369.

When **10d** was treated similarly **11d** (R^3=4-MeC_6H_4, R^4=Ph) was obtained in a 94% yield. **11d**: mp 178—180 °C; NMR ($CDCl_3$) δ=1.27 (3H, t, J=7 Hz, $C\underline{H}_3CH_2$), 2.16 (3H, s, $\underline{Me}C_6H_4$), 3.86 (2H, q, CH_2), and 6.6—7.8 (19H, m, Ar). Found: C, 83.29; H, 6.22; H, 3.21%; M^+ 445. Calcd for $C_{31}H_{27}NO_2$: C, 83.57; H, 6.11; N, 3.14%; M 445.

Hydrolysis of ***11a*** *and* ***11d***. A solution of **11a** or **11d** (0.2 mmol) in a mixture of acetic acid, sulfuric acid, and water (50 : 2 : 25 v/v) (10 cm³) was refluxed for 24 h. The cooled mixture was quenched with water and extracted with chloroform. The extract was dried under reduced pressure to yield a colorless mass, which, on crystallization, from benzene–petroleum ether gave needles of **12**; mp 190 °C (lit,[8] mp 191 °C).

Preparation of ***3a*** *(R^1=4-MeC_6H_4, R^2=Ph)*. A solution of **1a** (R^1=4-MeC_6H_4, R^2=Ph) and **2** in benzene was refluxed for 24 h. Layer chromatography (silica gel, chloroform–ethyl acetate 1 : 1 v/v) and crystallization from ethyl acetate–petroleum ether afforded **3a** in a 21% yield. **3a**: mp 262—264 °C; NMR ($CDCl_3$) δ=2.19 (3H, s, Me) and 6.8—7.8 (19H, m, Ar). Found: C, 83.96; H, 5.64; N, 6.88%; M^+ 414. Calcd for $C_{29}H_{22}N_2O$: C, 84.03; H, 5.35; N, 6.76%; M 414.

References

1) K. T. Potts and J. S. Baum, *Chem. Rev.*, **74**, 189 (1974); M. L. Deem, *Synthesis*, **1982**, 701.

2) T. L. Gilchrist, C. J. Harris, C. J. Moody, and C. W. Rees, *J. Chem. Soc., Perkin Trans. 1*, **1975**, 1969,

3) J. J. Barr, R. Storr, and V. K. Tandon, *J. Chem. Soc., Perkin Trans. 1*, **1980**, 1147.

4) H. Yoshida, T. Ogata, and S. Inokawa, *Bull. Chem. Soc. Jpn.*, **52**, 1541 (1979).

5) P. D. Kennewell and J. B. Taylor, *Chem. Soc. Rev.*, **4**, 189 (1975).

6) R. Breslow, T. Eicher, A. Krebs, R. A. Peterson, and J. Posner, *J. Am. Chem. Soc.*, **87**, 1320 (1965).

7) L. Giammanco and F. P. Invidiata, *Ann. Chim. (Rome)*, **60**, 188 (1970).

8) T. Eicher, J. W. Weber, and G. Chatila, *Justus Liebigs Ann. Chem.*, **1978**, 1203.

9) J. Hoch and R. Teixier, *C. R. Acad. Sci., Ser. A*, **261**, 4132 (1965).

10) T. Eicher, F. Abdesaken, G. Franke, and J. L. Weber, *Tetrahedron Lett.*, **1975**, 3915; T. Eicher, G. Franke, and F. Abdesaken, *ibid.*, **1977**, 4067; T. Eicher and G. Franke, *Liebigs Ann. Chem.*, **1982**, 1337.

11) F. Knoll, J. Gronebaum, and R. Appel, *Chem. Ber.*, **102**, 848 (1969).

12) R. G. Laughlin and W. Yellin, *J. Am. Chem. Soc.*, **89**, 2435 (1967).

13) C. R. Johnson and D. E. Roger, *J. Org. Chem.*, **38**, 1793 (1973).

14) T. R. Williams and D. J. Cram, *J. Org. Chem.*, **38**, 20 (1973).

15) T. W. Fair and L. Reiver, *J. Am., Chem. Soc.*, **73**, 459 (1951).