Condensed Pyridazines. VII.[1] Reaction of 7-(Methylsulfonyl)-1-phenyl-1*H*-imidazo[4,5-*d*]pyridazine with Nucleophiles

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The reaction of 7-(methylsulfonyl)- and 7-chloro-1-phenyl-1*H*-imidazo[4,5-*d*]pyridazines (1 and 2) with active methylene compounds (5a—d) or ketones (5e—g) in the presence of sodium hydride gave the corresponding 7-substituted imidazopyridazines (6a—g). A similar substitution of both 1 and 2 with methoxide ion (8) gave the 7-methoxyimidazopyridazine (9). However, 1 and 2 reacted with $BuNH_2$ (10) in a different way from the above substitution, resulting in the formation of the corresponding ring fission products of the imidazole portion, 3-substituted 5-amino-4-anilinopyridazines (11 and 12, respectively). The reaction of 1 with alkylmagnesium halides (13a—d) gave the 4,5- and 2,3-adducts (III and IV) which were converted into the corresponding 4-alkyl- and 2-alkyl-imidazopyridazines (14a—d and 15a, b) by potassium ferricyanide oxidation. A [4+2] cycloaddition occurred in the reaction of 1 with 1-piperidinocyclopentene (16a) to give the tetrahydroindeno[5,6-*d*]imidazoles 17 and 18.

Keywords imidazopyridazine; substitution; addition; ring fission; cycloaddition

It was reported that nucleophilic substitution, ring fission, addition, and cycloaddition, depending on the nature of the reagent, occurred in the reaction of 7-(methylsulfonyl)-1-phenyl-1*H*-1,2,3-triazolo[4,5-*d*]pyridazine (A) with nucleophiles.[1,2] For example, the methylsulfonyl substituent of A was replaced by the carbanion of ethyl cyanoacetate, giving the triazolopyridazineacetate (B).[1] The reaction of A with primary amines gave the ring fission products such as the 4,5-disubstituted triazoles (C).[2] The reaction with alkylmagnesium halides resulted in the formation of the adducts, such as the 4-alkylated 4,5-dihydrotriazolopyridazines (D).[2] Enamines reacted with A, giving the benzotriazoles (E) formed through the [4+2] cycloadducts (F)[1] (Chart 1).

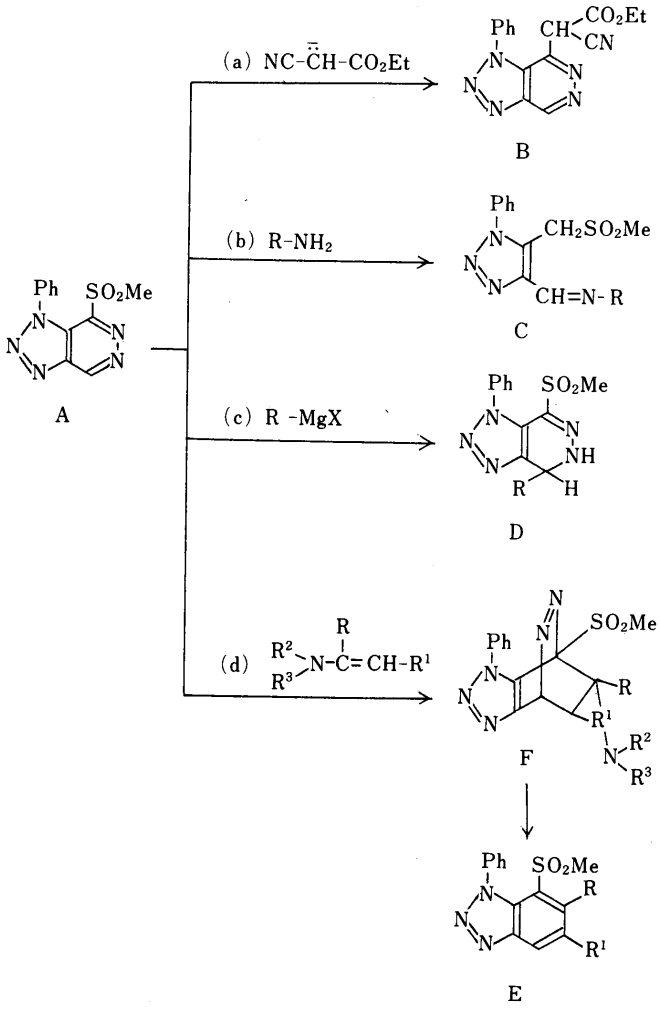


Chart 1

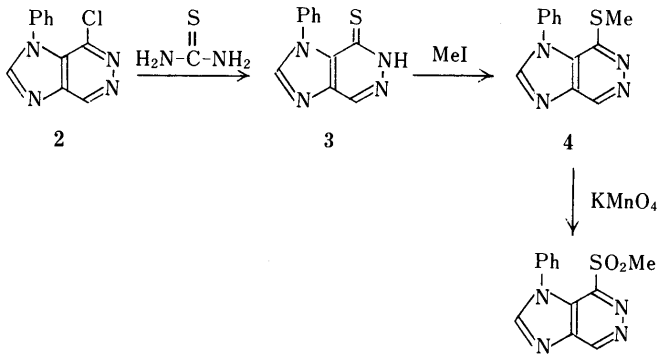


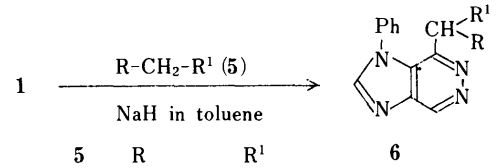
Chart 2

Since 7-(methylsulfonyl)-1-phenyl-1*H*-imidazo[4,5-*d*]-pyridazine (**1**) is a deaza analogue of A, it was expected that **1** might react with nucleophiles in the same ways as A, resulting in substitution (a), ring fission (b), addition (c), and cycloaddition (d). In the present paper, we describe the above reactions in detail, and compare the reactivity of **1** with that of 7-chloro-1-phenyl-1*H*-imidazo[4,5-*d*]pyridazine (**2**).

Compound **1** was prepared from **2**[3] by way of **3** and **4**, as shown in Chart 2, in an overall yield of 40%.

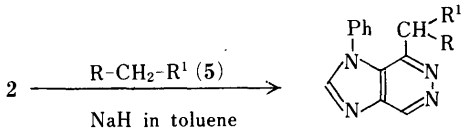
(a) The Nucleophilic Substitution In this study, active methylene compounds and ketones (**5**) used as sources of carbanions were as follows: ethyl cyanoacetate (**5a**), ethyl acetoacetate (**5b**), malononitrile (**5c**), diethyl malonate (**5d**), acetophenone (**5e**), methyl ethyl ketone (**5f**), cyclohexanone (**5g**), and propiophenone (**5h**).

When a mixture of **1**, **5a**—**e**, and sodium hydride in toluene was refluxed for 4 h, the methylsulfonyl group of **1** was easily replaced by carbanions, generated from **5a**—**e**, affording the corresponding 7-substituted imidazopyri-



5	R	R^1
5a	CN	CO_2Et
5b	Ac	CO_2Et
5c	CN	CN
5d	CO_2Et	CO_2Et
5e	H	COPh

Chart 3



5	R	R^1
5a	CN	CO_2Et
5b	Ac	CO_2Et
5c	CN	CN
5d	CO_2Et	CO_2Et
5e	H	COPh
5f	H	COEt
5g	$CH_2(CH_2)_3CO$	

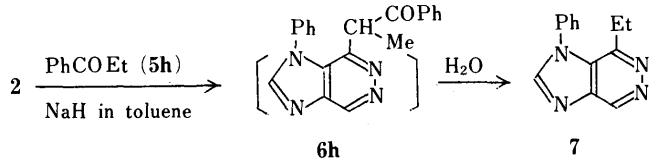


Chart 4

dazines (**6a—e**). However, the reaction of **1** with acetone, phenylacetonitrile, or **5h** in the presence of sodium hydride under the same conditions as used for the above reactions did not give the desired 7-substituted imidazopyridazines (**6**), but resulted in the recovery of **1**. The results are summarized in Chart 3.

The reaction of **2** with **5a—g** in the presence of sodium hydride in toluene resulted in the same substitution as for **1**, affording the corresponding **6a—g**. However, in the reaction with propiophenone (**5h**), 7-ethylimidazopyridazine (**7**) was obtained. The formation of **7** involves the initial substitution of the chlorine atom of **1** by the carbanion of **5h** to form an intermediate (**6h**) which then gives **7** by hydrolysis during work-up of the reaction mixture. A similar hydrolysis is observed in the reaction of 4-chloroquinazoline with **5h**, yielding 4-ethylquinazoline.[4]

The structures of **6a—g** and **7** were suggested by their elemental analytical and mass spectral (MS) data (Table I), and confirmed by their proton nuclear magnetic resonance (^{1}H-NMR) and infrared (IR) absorption spectral data (Table II) (**6a—c** and **6e** exist in enol form).

Both **1** and **2** reacted with sodium methoxide (**8**), giving the 7-methoxyimidazopyridazine (**9**)[3] in 87 and 83% yields, respectively. This substitution is similar to the reaction of A with **8** to the 7-methoxytriazolopyridazine.[2]

(b) The Ring Fission The reaction of **1** and **2** with butylamine (**10**) resulted in the ring fission of the imidazole portion, which is different from the reported ring fission[2] of A with primary amines. Thus, **1** and **2** gave 3-(methylsulfonyl)- and 3-chloro-5-amino-4-anilinopyridazines (**11** and **12**) in 53 and 65% yields, respectively. The struc-

TABLE I. Yields, Melting Points, Elemental Analyses and MS Data for **6** and **7**

Compd.	Yield (%)	mp (°C)	MS *m/z* M^+	Formula	Analysis (%) Calcd (Found) C	H	N
6a	82[a]	199—	307	$C_{16}H_{13}N_5O_2$	62.53	4.26	22.79
	(78)[b]	201[c,i]			(62.48	4.21	22.57)
6b	38	133—	324	$C_{17}H_{16}N_4O_3$	62.95	4.97	17.28
	(19)	135[d,i]			(63.01	4.96	17.24)
6c	11	284—	260	$C_{14}H_8N_6$	64.61	3.10	32.29
	(13)	287[e,j]			(64.39	3.14	32.06)
6d	73	180—	354	$C_{18}H_{18}N_4O_4$	61.01	5.12	15.81
	(72)	182[f,i]			(61.00	5.12	15.67)
6e	29	160—	314	$C_{19}H_{14}N_4O$	72.60	4.49	17.83
	(52)	161[e,i]			(72.60	4.52	17.71)
6f		179—	266	$C_{15}H_{14}N_4O$	67.65	5.30	21.04
	(2)	182[c,j]			(67.29	5.23	21.13)
6g		205—	292	$C_{17}H_{16}N_4O$	69.84	5.52	19.17
	(29)	207[g,i]			(69.82	5.64	19.42)
7		176—	224	$C_{13}H_{12}N_4$	69.62	5.39	24.99
	(38)	180[h,i]			(69.63	5.34	24.97)

a) Yield in the reaction of **1** with **5**. *b*) Yield in the reaction of **2** with **5**. *c*) Pale yellow needles. *d*) Yellow prisms. *e*) Yellow needles. *f*) Colorless plates. *g*) Pale yellow plates. *h*) Colorless needles. *i*) Recrystallization from MeOH. *j*) Recrystallization from dimethyl sulfoxide (DMSO).

TABLE II. IR and ^{1}H-NMR Spectral Data for **6** and **7**

Compd.	IR ν_{max}^{KBr} cm^{-1}	^{1}H-NMR ($CDCl_3$) ppm
6a	2200 (CN)	15.30—14.75[a] (1H, br, NH), 8.58 (1H, s, C^4-H),
	1650 (CO)	8.14 (1H, s, C^2-H), 7.58—7.00 (5H, m, Ph-H), 4.20 (2H, q,[b] $O\underline{CH_2}CH_3$), 1.29 (3H, t,[b] $OCH_2\underline{CH_3}$)
6b	1645 (CO)	12.87[a] (1H, br, enolic H), 9.61 (1H, s, C^4-H), 8.20 (1H, s, C^2-H), 7.69—7.05 (5H, m, Ph-H), 4.23—3.25 (2H, m, $O\underline{CH_2}CH_3$), 1.88 (3H, s, C=C-CH_3), 1.00 (3H, t,[b] $OCH_2\underline{CH_3}$)
6c	2210,	15.50—14.83 (1H, br, NH), 8.89 (1H, s, C^4-H),
	2190 (CN)	8.77 (1H, s, C^2-H), 7.48 (5H, s, Ph-H)
6d	1760,	9.62 (1H, s, C^4-H), 8.14 (1H, s, C^2-H), 7.80—7.28
	1730 (CO)	(5H, m, Ph-H), 4.86 (1H, s, $CH(CO_2Et)_2$), 4.12 (4H, q,[b] 2×$O\underline{CH_2}CH_3$), 1.18 (6H, t,[b] 2×$OCH_2\underline{CH_3}$)
6e	1620 (CO)	16.42—15.60[a] (1H, br, NH), 8.44 (1H, s, C^4-H), 7.95 (1H, s, C^2-H), 7.77—6.72 (10H, m, 2×Ph-H), 5.32 (1H, s, C^α-H)
6f	1625 (CO)	16.32—15.48[a] (1H, br, NH), 8.45 (1H, s, C^4-H), 7.94 (1H, s, C^2-H), 7.59—7.07 (5H, m, Ph-H), 4.60 (1H, s, C^α-H), 2.14 (2H, q,[b] $\underline{CH_2}CH_3$), 0.93 (3H, t,[b] $CH_2\underline{CH_3}$)
6g	1710 (CO)	9.35 (1H, s, C^4-H), 8.01 (1H, s, C^2-H), 7.74—7.15 (5H, m, Ph-H), 3.91—3.57 (1H, m, CHCO), 2.88—1.05 (8H, m, $(CH_2)_4$)
7		9.54 (1H, s, C^4-H), 8.11 (1H, s, C^2-H), 7.95—7.04 (5H, m, Ph-H), 2.81 (2H, q,[b] $\underline{CH_2}CH_3$), 1.12 (3H, t,[b] $CH_2\underline{CH_3}$)

a) Exchangeable with CD_3OD. *b*) J=7.0 Hz.

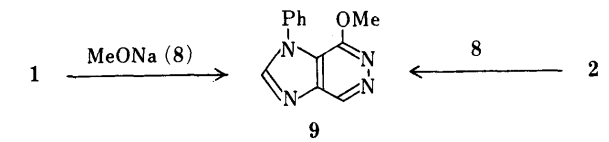


Chart 5

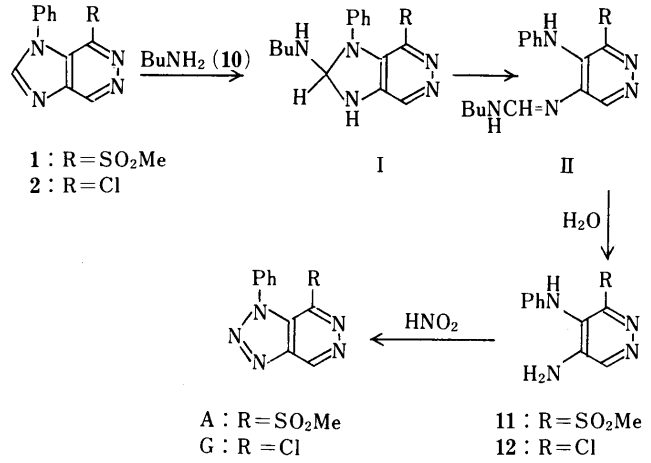


Chart 6

tures of **11** and **12** were confirmed by the reported ring closure with nitrous acid to the known compounds A[2] and 7-chlorotriazolopyridazine (G),[3] respectively. The formation of **11** and **12** is considered to occur through the mechanism shown in Chart 6. The initial step is an addition of butylamine **10** to the double bond in the imidazole portion, leading to an adduct (I), which then undergoes the ring fission, giving an intermediate (II). Then II is readily hydrolyzed to the aminopyridazines **11** and **12** during work-up of the reaction mixture.

Many examples of the ring fission of the imidazole portion in other imidazodiazine ring systems are found in the 9*H*- and 7*H*-purine ring systems, affording the aminopyrimidine derivatives.[5]

(c) The Nucleophilic Addition Grignard reagents used in this study were as follows: phenylmagnesium bromide (**13a**), methylmagnesium iodide (**13b**), benzylmagnesium chloride (**13c**), and ethylmagnesium bromide (**13d**). Reaction of **1** with **13a—d** in dioxane gave tarry products which showed absorption peaks due to amino (NH) and sulfonyl (SO_2) groups in the IR spectra. This suggested that the initial step in the reaction is the formation of the adducts (III and IV), which could not be isolated due to their high susceptibility to oxidation. When the reaction mixture was subjected to oxidation with potassium ferricyanide, the corresponding 4-alkylimidazopyridazines

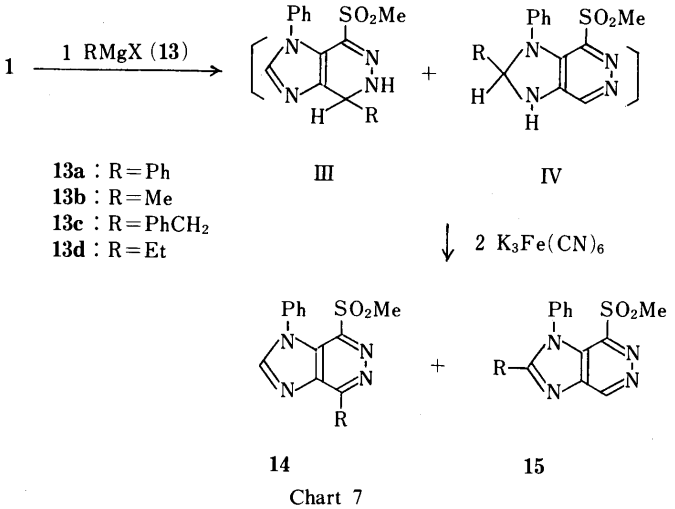


Chart 7

(**14a—d**) and 2-alkylimidazopyridazines (**15a, b**) were obtained, although in poor yields. The results (Chart 7) show that, in the reaction with alkylmagnesium halide (**13a—d**), **1** favors the nucleophilic addition rather than the nucleophilic substitution of the methylsulfonyl substituent.

(d) The [4+2] Cycloaddition Many reports on the [4+2] cycloaddition of monocyclic pyridazines with electron-rich enamines (**16**) have been published.[6] Results on the [4+2] cycloaddition of pyridazine ring system up to 1983 have been summarized in a comprehensive review.[7] In the condensed pyridazine ring systems, it has been reported by us that the triazolopyridazine A reacts with electron-rich dienophiles, *i.e.*, enamines **16**, affording the products E through [4+2] cycloaddition (Chart 1) and this cycloaddition is the first such finding in condensed pyridazine ring systems.[1]

In the imidazo[4,5-*d*]pyridazine ring system, a [4+2] cycloaddition took place between electron-deficient **1** and

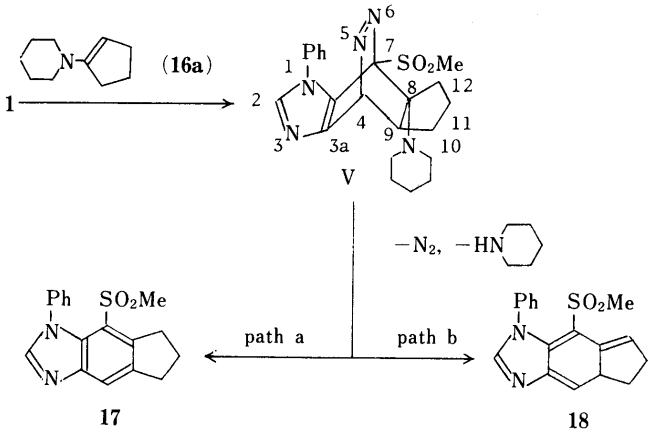


Chart 8

electron-rich 1-piperidinocyclopentene (**16a**). This was demonstrated by the following results. When a mixture of **1** and **16a** in a sealed tube was heated at 180 °C for 12 h, the tetrahydroindeno[5,6-*d*]imidazoles **17** and **18** were obtained in 35 and 18% yields, respectively. Compounds **17** and **18** gave the elemental analytical, and the IR, ^{1}H- and ^{13}C-NMR spectral data detailed in the experimental section. (Although we propose the structure of **18** to be as shown in Chart 8, its fine structure has not been determined yet.) On the other hand, in the reaction of **1** with other enamines **16** such as 1-methoxy-*N*,*N*-dimethylvinylamine (**16b**), 1-piperidinocyclohexene (**16c**), and *N*,*N*-diethyl-1-propynylamine (**16d**), a [4+2] cycloaddition did not take place, and **1** was recovered.

It has been proposed that the mechanism of the [4+2] cycloaddition of A involves regioselective addition of the enamines **16** across C^4/C^7 of the triazolopyridazine nucleus and a preference for the nucleophilic carbon of **16** to attack the C^4-ring atoms, as shown in Chart 1. The same mechanism may be applicable to the formation of **17** and **18**, as shown in Chart 8. Thus, the dienophile **16a** prefers attachment to the C^4-ring atom of **1**. Loss of a nitrogen molecule accompanied with the elimination of piperidine with hydrogen at C^9 from the initially formed [4+2] cycloadduct (V) leads to **17** (path a), while the successive loss of a nitrogen molecule and piperidine with hydrogen at

C^{12} from V gives **18** (path b).

In the reaction of **2** with the enamines **16a—d** under the same conditions as used for the reaction of **1** with **16a**, no product formed through [4+2] cycloaddition, and **2** was recovered in good yields.

Experimental

All melting points are uncorrected. IR spectra were recorded on a Jasco A-102 diffraction grating IR spectrometer. ^{1}H-NMR spectra were measured at 60 MHz on a Hitachi R-24B high-resolution NMR spectrometer, and ^{13}C-NMR spectra were taken at 22.5 MHz on a JEOL JNM-FX90Q FTNMR spectrometer. Chemical shifts are quoted in parts per million (ppm) with tetramethylsilane as an internal standard, and coupling constants (J) are given in Hz. The following abbreviations are used: s=singlet, d=doublet, t=triplet, q=quartet, m=multiple, br=broad and br s=broad singlet. MS were recorded on a JEOL JMS D-100 mass spectrometer. Samples were vaporized in a direct inlet system. Column chromatography was carried out on SiO_2, Wakogel C-200 (200 mesh).

1-Phenyl-1*H*-imidazo[4,5-*d*]pyridazine-7(6*H*)-thione (3) A mixture of 7-chloro-1-phenyl-1*H*-imidazo[4,5-*d*]pyridazine (**2**, 1.0 mmol, 250 mg) and thiourea (1.2 mmol, 91 mg) in EtOH (6 ml) was refluxed for 1 h. On cooling, crystals separated. They were collected by suction and recrystallized from MeOH to give a slightly yellow powder, mp 232—234 °C, in 77% yield (190 mg). *Anal.* Calcd for $C_{11}H_8N_4S$: C, 57.88; H, 3.53; N, 24.54. Found: C, 57.76; H, 3.44; N, 24.47. IR ν_{max}^{KBr} cm^{-1}: 3160—3000 (NH). ^{1}H-NMR ($(CD_3)_2SO$): 14.53—14.14 (1H, br s, NH), 8.72 (1H, s, C^4-H), 8.51 (1H, s, C^2-H), 7.37 (5H, s, C_6H_5).

7-(Methylthio)-1-phenyl-1*H*-imidazo[4,5-*d*]pyridazine (4) Methyl iodide (0.88 mmol, 124 mg) was added to a solution of **3** (0.44 mmol, 100 mg) in 2 N KOH (5 ml), and the mixture was shaken for 10 min at room temperature. The reaction mixture was extracted with $CHCl_3$. The extract was washed with H_2O, dried over Na_2SO_4, and concentrated to dryness. The residue was recrystallized from benzene–petroleum benzin to give pale yellow needles, mp 223 °C, in 73% yield (77 mg). *Anal.* Calcd for $C_{12}H_{10}N_4S$: C, 59.49; H, 4.16; N, 23.12. Found: C, 59.35; H, 4.13; N, 23.04. ^{1}H-NMR ($CDCl_3$): 9.39 (1H, s, C^4-H), 8.05 (1H, s, C^2-H), 7.83—7.32 (5H, m, C_6H_5), 2.65 (3H, s, SCH_3).

7-(Methylsulfonyl)-1-phenyl-1*H*-imidazo[4,5-*d*]pyridazine (1) A solution of 3% $KMnO_4$ (2 ml) was added drop by drop to a stirred solution of **4** (0.19 mmol, 45 mg) in AcOH (1 ml) over a period of 1 h. The reaction mixture was decolorized with Na_2SO_3 and extracted with $CHCl_3$. The extract was washed with H_2O, dried over Na_2SO_4, and concentrated to dryness. The residue was recrystallized from benzene–$CHCl_3$ to give colorless needles, mp 212—213 °C (dec.), in 71% yield (40 mg). *Anal.* Calcd for $C_{12}H_{10}N_4O_2S$: C, 52.55; H, 3.67; N, 20.43. Found: C, 52.87; H, 3.59; N, 20.76. IR ν_{max}^{KBr} cm^{-1}: 1315, 1140 (SO_2). ^{1}H-NMR ($CDCl_3$): 9.79 (1H, s, C^4-H), 8.27 (1H, s, C^2-H), 7.74—7.22 (5H, m, C_6H_5), 3.47 (3H, s, SO_2CH_3).

Reaction of 1 with Active Methylene Compounds or Ketones (5a—e) A mixture of **1** (0.36 mmol, 100 mg), **5** (0.72 mmol), and 60% NaH (in oil, 0.88 mmol, 35 mg) in toluene (4 ml) was refluxed for 4 h. After cooling, the reaction mixture was poured into H_2O (5 ml), neutralized with AcOH, and extracted with $CHCl_3$. The $CHCl_3$ extract was washed with H_2O, dried over Na_2SO_4, concentrated, and chromatographed on a column of SiO_2 with $CHCl_3$. The first fraction gave 7-substituted 1-phenyl-1*H*-imidazo[4,5-*d*]pyridazine (**6**), which was purified by recrystallization from an appropriate solvent (Table I). The yield, elemental analytical, and spectral data for **6** are listed in Tables I and II.

Reaction of 2 with 5a—g i) A mixture of **2** (0.43 mmol, 100 mg), **5** (0.86 mmol), and 60% NaH (in oil, 1.0 mmol, 40 mg) was refluxed for 15 h. The same work-up of the reaction mixture as described for the reaction of **1** with **5** gave **6**. The yield of **6** is shown in Table I, and the elemental analytical, and spectral data for **6f** and **6g** are summarized in Tables I and II.

ii) From the reaction with propiophenone (**5h**), 7-ethyl-1-phenyl-1*H*-imidazo[4,5-*d*]pyridazine (**7**) was obtained in 38% yield (37 mg). The elemental analytical and spectral data for **7** are listed in Tables I and II.

7-Methoxy-1-phenyl-1*H*-imidazo[4,5-*d*]pyridazine (9) i) Compound **1** (0.36 mmol, 100 mg) was added to a solution of MeONa (**8**) [prepared from Na (1.3 mmol, 30 mg) and MeOH (3 ml)], and the mixture was refluxed for 1 h. After removal of MeOH under reduced pressure, the residue was poured into H_2O (5 ml), neutralized with AcOH, and extracted with $CHCl_3$. The extract was washed with H_2O, dried over Na_2SO_4, and concentrated to dryness. The residue was recrystallized from benzene–petroleum benzin to give colorless needles, mp 184—185 °C, in 87% yield (72 mg). The melting point of **9** was undepressed on admixture with an authentic sample prepared by another route.[3]

ii) Compound **9** was obtained in 83% yield (81 mg) from the reaction of **2** (0.43 mmol, 100 mg) with **8** [prepared from Na (1.73 mmol, 40 mg) and MeOH (5 ml)] in essentially the same manner as described for the reaction of **1** with MeONa.

Reaction of 1 with $BuNH_2$ (10) A mixture of **1** (0.36 mmol, 100 mg) and **10** (1 ml) in a sealed tube was heated at 150 °C for 4 h. After the mixture had cooled, the excess of **10** was removed under reduced pressure, and ether was added. The separated crystals were recrystallized from MeOH to give 5-amino-4-anilino-3-(methylsulfonyl)pyridazine (**11**) as colorless needles, mp 160—162 °C (dec.), in 53% yield (51 mg). *Anal.* Calcd for $C_{11}H_{12}N_4O_2S$: C, 49.99; H, 4.58; N, 21.20. Found: C, 49.84; H, 4.52; N, 21.13. IR ν_{max}^{KBr} cm^{-1}: 3450—3200 (NH), 1305, 1140 (SO_2). MS m/z: 264 (M^+). ^{1}H-NMR ($CDCl_3$): 8.52 (1H, s, C^6-H), 7.33 (1H, br s, exchangeable with CD_3OD, NH), 7.30—6.59 (5H, m, C_6H_5), 4.51—4.19 (2H, br, exchangeable with CD_3OD, NH_2), 3.41 (3H, s, SO_2CH_3).

Reaction of 2 with 10 A mixture of **2** (0.43 mmol, 100 mg) and **10** (0.2 ml) in a sealed tube was heated at 180 °C for 6 h. The same work-up of the reaction mixture as described for the reaction of **1** with **10** afforded 5-amino-4-anilino-3-chloropyridazine (**12**) as colorless needles, mp 196—197 °C (dec.), in 65% yield (62 mg). *Anal.* Calcd for $C_{10}H_9ClN_4$: C, 54.43; H, 4.11; N, 25.39. Found: C, 54.56; H, 4.15; N, 25.24. MS m/z: 222 (M^++2), 220 (M^+). IR ν_{max}^{KBr} cm^{-1}: 3440—3100 (NH). ^{1}H-NMR ($(CD_3)_2SO$): 8.50 (1H, s, C^6-H), 7.37 (1H, br s, exchangeable with CD_3OD, NH), 7.52—6.30 (5H, m, C_6H_5), 6.16 (2H, br, exchangeable with CD_3OD, NH_2).

Reaction of 1 with RMgX (13) The procedure for the reaction of **1** with PhMgBr (**13a**) is described in detail as a typical example.

1,4-(**14a**) and 1,2-(**15a**)Diphenyl-7-(methylsulfonyl)-1*H*-imidazo[4,5-*d*]pyridazine: A solution of **13a** [prepared from PhBr (2.23 mmol, 350 mg) and Mg (2.26 mmol, 55 mg) in ether (3 ml)] was added to **1** (0.73 mmol, 200 mg), and the ether was removed under reduced pressure. The residue was dissolved in dioxane (2 ml) and refluxed for 1 h. After cooling of the reaction mixture, aqueous NH_4Cl–NH_3 (a solution of NH_4Cl (3 g) and 28% NH_3 (0.5 ml) in H_2O (10 ml)) was added. The aqueous solution was extracted with $CHCl_3$. The $CHCl_3$ solution was combined with the dioxane solution, and the combined solution was dried over Na_2SO_4, and then concentrated to dryness. A solution of $K_3Fe(CN)_6$ (1 g) in 2 N KOH (5 ml) was added to a suspension of the residue in benzene (5 ml), and the mixture was shaken for 1 h at room temperature. The reaction mixture was neutralized with AcOH and extracted with $CHCl_3$. The extract was washed with H_2O, dried over Na_2SO_4, and concentrated to dryness. The residue was chromatographed on a column of SiO_2 with $CHCl_3$. The first and second fractions gave **14a** and **15a** in 4 (11 mg) and 10% yields (25 mg), respectively.

Compound **14a** was recrystallized from benzene–petroleum benzin to give colorless needles, mp 238—239 °C. *Anal.* Calcd for $C_{18}H_{14}N_4O_2S$: C, 61.70; H, 4.03; N, 15.99. Found: C, 61.97; H, 4.09; N, 15.60. MS m/z: 350 (M^+). IR ν_{max}^{KBr} cm^{-1}: 1310, 1150 (SO_2). ^{1}H-NMR ($CDCl_3$): 8.30 (1H, s, C^2-H), 8.94—7.08 (10H, m, $2C_6H_5$), 3.47 (3H, s, SO_2CH_3).

Compound **15a** was recrystallized from MeOH to give colorless prisms, mp 212—214 °C. *Anal.* Calcd for $C_{18}H_{14}N_4O_2S$: C, 61.70; H, 4.03; N, 15.99. Found: C, 61.48; H, 4.06; N, 15.79. MS m/z: 350 (M^+). IR ν_{max}^{KBr} cm^{-1}: 1320, 1140 (SO_2). ^{1}H-NMR ($CDCl_3$): 9.66 (1H, s, C^4-H), 7.80—6.70 (10H, m, $2C_6H_5$), 3.42 (3H, s, SO_2CH_3).

From MeMgI (**13b**), 4-methyl- and 2-methyl-7-(methylsulfonyl)-1-phenyl-1*H*-imidazo[4,5-*d*]pyridazines (**14b** and **15b**) were obtained in 7 (14 mg) and 8% yields (16 mg), respectively. Compound **14b** was recrystallized from MeOH to give colorless needles, mp 200—201 °C. *Anal.* Calcd for $C_{13}H_{12}N_4O_2S$: C, 54.16; H, 4.19; N, 19.43. Found: C, 54.28; H, 4.17; N, 19.35. MS m/z: 288 (M^+). IR ν_{max}^{KBr} cm^{-1}: 1315, 1150 (SO_2). ^{1}H-NMR ($CDCl_3$): 8.17 (1H, s, C^2-H), 7.65—7.34 (5H, m, C_6H_5), 3.43 (3H, s, SO_2CH_3), 3.11 (3H, s, CH_3). Compound **15b** was recrystallized from MeOH to give colorless scales, mp 224—226 °C. *Anal.* Calcd for $C_{13}H_{12}N_4O_2S$: C, 54.16; H, 4.19; N, 19.43. Found: C, 53.91; H, 4.13; N, 19.15. MS m/z: 288 (M^+). IR ν_{max}^{KBr} cm^{-1}: 1305, 1140 (SO_2). ^{1}H-NMR ($CDCl_3$): 9.64 (1H, s, C^4-H), 7.78—7.19 (5H, m, C_6H_5), 3.42 (3H, s, SO_2CH_3), 2.49 (3H, s, CH_3).

From $PhCH_2MgCl$ (**13c**), 4-benzyl-7-(methylsulfonyl)-1-phenyl-1*H*-imidazo[4,5-*d*]pyridazine (**14c**) was obtained as colorless needles from MeOH, mp 191—192 °C, in 20% yield (52 mg). *Anal.* Calcd for $C_{19}H_{16}N_4O_2S$: C, 62.62; H, 4.43; N, 15.37. Found: C, 62.44; H, 4.38; N, 15.21. MS m/z: 363 (M^+−1). IR ν_{max}^{KBr} cm^{-1}: 1310, 1145 (SO_2). ^{1}H-NMR

($CDCl_3$): 8.18 (1H, s, C^2-H), 7.72—7.10 (10H, m, $2C_6H_5$), 4.78 (2H, s, CH_2Ph), 3.40 (3H, s, SO_2CH_3).

From EtMgBr (**13d**), 4-ethyl-7-(methylsulfonyl)-1-phenyl-1*H*-imidazo[4,5-*d*]pyridazine (**14d**) was obtained as colorless needles from MeOH, mp 206—208 °C, in 2% yield (5 mg). *Anal.* Calcd for $C_{14}H_{14}N_4O_2S$: C, 55.62; H, 4.67; N, 18.53. Found: C, 55.78; H, 4.66; N, 18.32. MS *m/z*: 302 (M^+). IR ν_{max}^{KBr} cm^{-1}: 1315, 1145 (SO_2). ^{1}H-NMR ($CDCl_3$): 8.12 (1H, s, C^2-H), 7.81—7.14 (5H, m, C_6H_6), 3.53 (2H, q, J=7.0 Hz, Ar-CH_2CH_3), 3.45 (3H, s, SO_2CH_3), 1.58 (3H, t, J=7.0 Hz, CH_2CH_3).

Reaction of 1 with 1-Piperidinocyclopentene (16a) A mixture of **1** (0.38 mmol, 100 mg) and **16a** (0.3 ml) in a sealed tube was heated at 180 °C for 12 h. After cooling, the reaction mixture was poured into H_2O (5 ml), neutralized with AcOH, and extracted with $CHCl_3$. The extract was washed with H_2O, dried over Na_2SO_4, and concentrated to dryness. The residue was chromatographed on a column of SiO_2 with $CHCl_3$. The first and second fractions gave 8-(methylsulfonyl)-1-phenyl-1,5,6,7-tetrahydroindeno[5,6-*d*]imidazole (**17**) and 8-(methylsulfonyl)-1-phenyl-1,4a,5,6-tetrahydroindeno[5,6-*d*]imidazole (**18**) in 35 and 18% yields (40 mg and 21 mg), respectively.

Compound **17** was recrystallized from MeOH to give colorless plates, mp 216—218 °C. *Anal.* Calcd for $C_{17}H_{16}N_2O_2S$: C, 65.36; H, 5.16; N, 8.97. Found: C, 65.09; H, 5.20; N, 8.89. MS *m/z*: 312 (M^+). IR ν_{max}^{KBr} cm^{-1}: 1300, 1125 (SO_2). ^{1}H-NMR ($CDCl_3$): 7.92 (1H, s, C^2-H), 7.86 (1H, s, C^4-H), 7.64—7.18 (5H, m, C_6H_5), 3.38 (2H, t, J=7.0 Hz, C^7H_2), 3.06 (2H, t, J=7.0 Hz, C^5H_2), 2.86 (3H, s, SO_2CH_3), 2.15 (2H, quintet, J=7.0 Hz, C^6H_2). ^{13}C-NMR ($CDCl_3$): 147.26 (d, C^2), 146.07 (s), 142.98 (s), 141.30 (s), 139.25 (s), 130.95 (s), 129.06 (d, Ph), 128.95 (d, Ph), 127.33 (d, Ph), 121.91 (d, C^4), 121.63 (s), 44.21 (q, SO_2CH_3), 34.24, 32.24 (each t, C^5 and C^7), 26.28 (t, C^6).

Compound **18** was recrystallized from MeOH to give colorless needles, mp 171—172 °C. *Anal.* Calcd for $C_{17}H_{16}N_2O_2S$: C, 65.36; H, 5.16; N, 8.97. Found: C, 65.20; H, 5.06; N, 8.97. MS *m/z*: 312 (M^+). IR ν_{max}^{KBr} cm^{-1}: 1300, 1125 (SO_2). ^{1}H-NMR ($CDCl_3$): 8.12 (1H, s, C^2-H), 7.78, 7.73 (each 1H, s, C^4-H) and C^7-H), 7.58—7.19 (5H, m, C_6H_5), 4.61 (1H, t, J=6.0 Hz, C^{4a}-H), 3.37—2.95 (2H, m, C^6H_2), 2.86—2.33 (2H, m, C^5H_2), 2.64 (3H, s, SO_2CH_3). ^{13}C-NMR ($CDCl_3$): 145.79 (s), 143.52 (d, C^2), 139.68 (s), 136.05 (s), 133.39 (s), 130.41 (s), 130.14 (d, Ph), 128.19 (d, Ph), 123.97 (d, Ph), 116.43, 108.85 (each d, C^4 and C^7), 69.68 (d, C^{4a}),*) 36.68 (q, SO_2CH_3), 30.40, 28.01 (each t, C^6 and C^5). *) Assignment based on selective decoupling.

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