The Solid-State Michael Addition of Indole to 4-Arylidene-3-methyl-5-pyrazolone

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The Michael addition reactions of indole to 4-arylidene-3-methyl-1-phenyl-5-pyrazolone **1** were investigated in the solid state, by which a series of new compounds, 1-aryl-1-(3-indolyl)-1-(3'-methyl-1'-phenyl-5'-pyrazolon-4'-yl)methanes **2**, were easily obtained. This provides a feasible method of preparing novel compounds containing two heterocyclic groups at the same carbon.

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Solid state organic reactions have recently attracted considerable attention and have been applied to various types of organic reactions because many solid state organic reactions often proceed with high efficiency and selectivity [1,2,3] and in some cases even enantioselectivity [4,5]. They are very economical and effective synthetic methods. As a part of our research on the solid-state reactions of heterocycles [6,7,8], we have recently found that the heterocycles an acidic C-H, such as pyrazolone and indole, could undergo condensation with carbonyl compounds [9,10,11] and Michael addition with α,β-unsaturated carbonyl compounds [12] more efficiently and selectively in the solid state than in solution.

As a nucleophile indole can undergo various types of reactions in solution, such as substitutions, Mannich reaction and Michael addition, producing 3-indolyl derivatives [13]. The Michael addition reaction of indole to an olefin conjugated with an electron-withdrawing group such as a carbonyl, carboxyl, cyano, or nitro group is known to occur under acidic [14] or basic [15] conditions in solution. The Michael addition reaction of α,β-unsaturated carbonyl compounds and indoles in dichloromethane solution proceeded efficiently in the presence of Montmorillonite clay as the catalyst [16]. Now we wish to present our new finding on the solid-state Michael addition of indole to 4-arylidenepyrazolones **1**, by which a series of novel Michael adducts **2** containing two different heterocyclic groups at the same carbon are obtained.

Results and Discussion.

The solid-state Michael reactions between 4-arylidene-3-methyl-1-phenyl-5-pyrazolones **1** and indole were feasibly carried out with grinding a mixture of **1** and excess indole and allowing it to stand for a certain number of hours at ambient temperature. The 1:1 Michael adducts, 1-aryl-1-(3-indolyl)-1-(3'-methyl-1'-phenyl-5'-pyrazolon-4'-yl)methanes **2a**-**n**, were given in reasonable yields as shown in Table 1 (Scheme 1).

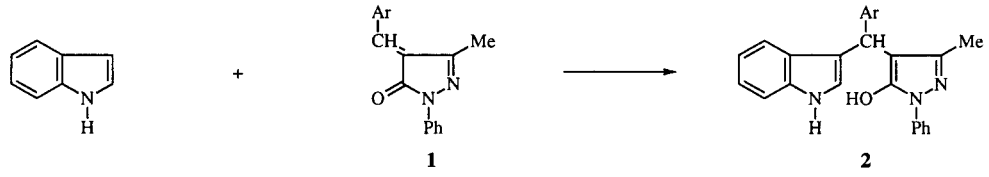
Table 1

The Michael Addition of Indole to **1** in the Solid State and in Solution

Product **2**	Physical State	mp of **2** [a] (°C)	Grinding Time [b] Minutes	Reaction Time [b] Hours	Yield of **2** in the Solid State [c]	Yield of **2** in Methanol Solution [c]
2a	white solid	236	30	15	54	no reaction
2b	white solid	207	30	15	56	no reaction
2c	white solid	176	30	15	54	20
2d	white solid	188	30	20	51	18
2e	white solid	169	40	20	40	no reaction
2f	white solid	200	30	15	58	no reaction
2g	white solid	178	30	15	49	no reaction
2h	white solid	168	40	20	41	no reaction
2i	pale yellow solid	184	30	10	67	32
2j	pale yellow solid	246	30	10	62	31
2k			60	40	no reaction	no reaction
2l			60	40	no reaction	no reaction
2m			60	40	no reaction	no reaction
2n	white solid	206	30	15	50	no reaction

[a] Decomposition temperature; [b] Accumulated time; [c] Based upon the amount of **1** used.

Scheme 1



1

2

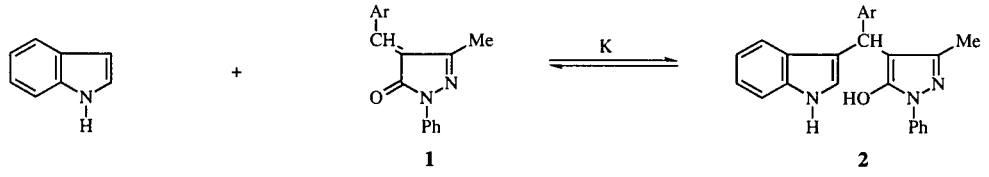
1a:	Ar = Ph	**f**:	Ar = 4-$BzOC_6H_4$	**k**:	Ar = 2-$O_2NC_6H_4$
b:	Ar = 4-FC_6H_4	**g**:	Ar = 4-MeC_6H_4	**l**:	Ar = 4-$Et_2NC_6H_4$
c:	Ar = 4-ClC_6H_4	**h**:	Ar = 4-$MeOC_6H_4$	**m**:	Ar = 4-HOC_6H_4
d:	Ar = 4-BrC_6H_4	**i**:	Ar = 4-$O_2NC_6H_4$	**n**:	Ar = 4-HO, 3-$MeOC_6H_3$
e:	Ar = 4-IC_6H_4	**j**:	Ar = 3-$O_2NC_6H_4$		

The reaction occurred more efficiently in the solid state than in solution and showed similar electronic and steric effects to the Michael addition of 3-methyl-1-phenyl-5-pyrazolone to **1** reported previously [12]. While the electron-withdrawing substituents on *para*-position (*e.g.* 4-nitro) made the addition easier, the electron-donating substituents decreased the reactivity due to the increase of the electron density on the methylidene carbon of **1** (*e.g.* in **1l** and **1m**, the hydroxyl and diethylamino groups made the electron density increase too high to react), and the *ortho*-nitro group (as **1k**) hindered the indole attack to the methylidene carbon of **1**. Besides increasing the reactivity of **1**, the electron-withdrawing group could also increase the stability of **2** by means of decreasing the electron density of the methylidene carbon.

In solution the reaction showed more enhanced substituent effects on the reactivity of **1** than that in the solid state. Only pyrazolones **1** containing an electron-withdrawing group (such as **1c**, **1d**, **1i** and **1j**) reacted with indole in methanol solution to give the Michael adducts **2**. The reactivity was also affected by the polarity of solvents. Thus the Michael addition occurred in the cases of **1c**, **1d**, **1i** and **1j** in methanolic solution, but not in chloroform solution. The polar solvent may be helpful for accelerating the formation of **2**, as this is reflected by the determination of the equilibrium constants shown in Scheme 2.

The equilibrium between **1** and **2** observed in the Michael addition of indole in solution was similar to that of 3-methyl-l-phenyl-5-pyrazolone in solution [12]. The equilibrium constants (K_{obs}) were determined by uv spectra measurements using representative 4-(4'-substituted arylidene)pyrazolones **1** in methanol solution (Scheme 2). Compounds **1** and **2** have different λ_{max} because of their different conjugated systems, the concentration changes of **1** can be obtained by the absorbance (A) changes of **1** at λ_{max}. The K_{obs} is calculated from the initial concentration ($C^1{}_o$) and the equilibrium concentration ($C^1{}_{eq}$) of **1**.

Scheme 2



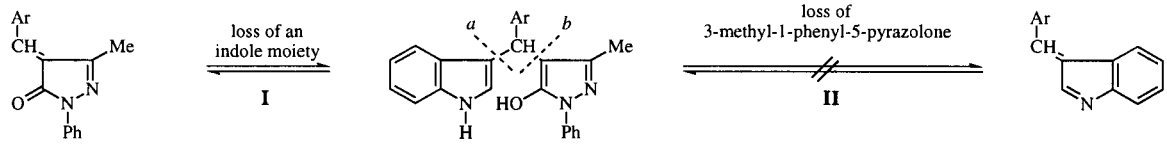
1

2

	1h	**1a**	**1c**	**1d**	**1i**
Ar	$MeOC_6H_4$	Ph	ClC_6H_4	BrC_6H_4	$O_2NC_6H_4$
K_{obs} ($CHCl_3$)	0	0	0	0	36.8
K_{obs} (CH_3OH)	48.5	82.4	121.0	165.0	360.5

Since compound **2** contained two different heterocyclic groups, it is probable that the equilibrium shown in Scheme 3 is accurate. The Michael adducts having structures such as **2** are unstable when heated [17]. They may eliminate a heterocyclic group to reproduce deeply colored conjugated compounds in two possible cleavages: *a*, leaving out an indole to form **1** (equilibrium **I**), and *b*, eliminating 3-methyl-1-phenyl-5-pyrazolone to produce **3** (equilibrium **II**).

Scheme 3



1 **2** **3**

In order to gain further information about the equilibrium shown in Scheme 3, we carried out the time-resolved uv measurement of **2a** at 50° in dimethyl sulfoxide solution (Figure 1). It was found that the absorption maximum of **2a** at 262 nm decreased with the appearance of the absorption maximum of **1a** at 325.5 nm, being accompanied by the isosbestic point at 283 nm, indicating the existence of equilibrium **I**. In this equilibration experiment, no absorption maximum corresponding to **3a** was observed. If **3a** was formed by the equilibrium **II**, we should observe the appearance of a new absorption band of **3a** at 409.5 nm [18].

The structure of **2** was established on the basis of elemental, ir, ^{1}H nmr and ms analyses. The ir spectra of **2** showed bands at *ca.* 3410, 3200 and 1600 cm^{-1}, due to the absorption of the N-H of the 3-indolyl group, the enolic hydroxyl and the ethylenic moiety in the pyrazolone ring, respectively. The absorption of the conjugated carbonyl (~1650 cm^{-1}) in **1** was not observed in **2**, suggesting that the pyrazolone ring in **2** existed in an enolic form. In the ^{1}H nmr spectra, the signal at *ca.* δ = 1.6-1.8 ppm (s, 3H) is due to the 3-methyl group on the pyrazolone ring; the signal at δ = 1 0.8 ppm (s, 1H) was attributable to the absorption of the N-*H* proton in the 3-indolyl, but the signal of the OH proton in 3-methyl-1-phenyl-5-pyrazolonyl group was not observed in dimethyl-d_6 sulfoxide solution; the methylene proton (C-*H*) of **2** appeared downfield (δ = 5.5 ppm) in comparison with that in aryl-4,4'-bis(3-methyl-1-phenyl-5-pyrazolonyl)methanes (δ = 4.90 ppm), as a result of the deshielding effect of the 3-indolyl group on this proton. The mass spectra of the adducts showed clearly the quasi-molecular ion (m/z = M+1). Furthermore, the values of (M-117+1) and (M-174+1) are attributable to the removals of an indole and a pyrazolone from the adducts, respectively. The results establish that the Michael addition occurred at the 3-position of indole to afford the 3-indolyl derivatives exclusively in accordance with previous reports [13].

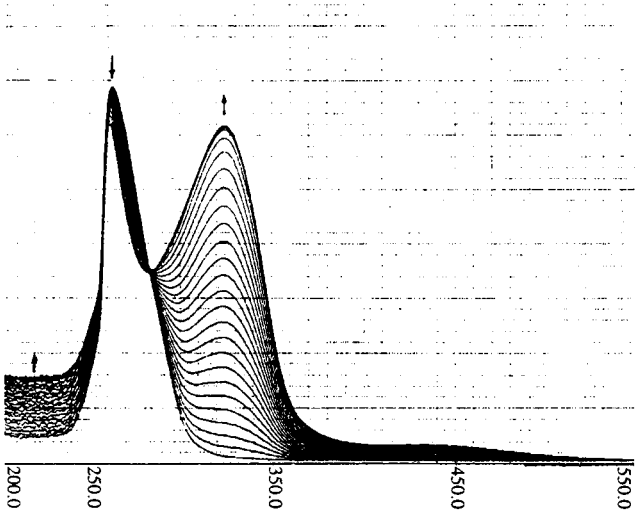
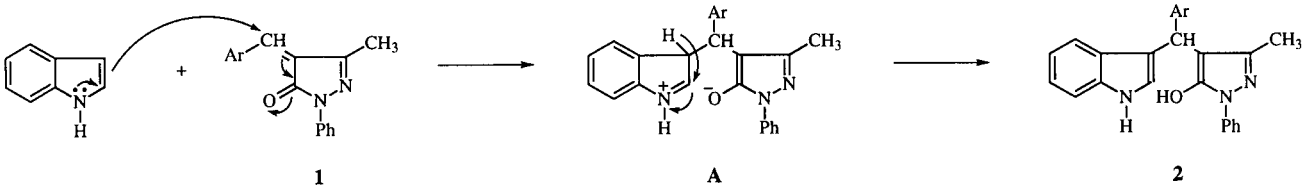


Figure 1. The time-resolved uv spectra of **2a** at 50° in dimethyl sulfoxide solution; concentration = 5.04 x 10^{-5} mol/l; interval: 20 minutes.

Indole has a high electron density and a low delocalized energy for eletrophilic substitution [13]; most of the electrophilic substitutions of indole can be correlated with the supposition that its N-1, C-2, C-3 system should behave as an enamine triad. The C-2—C-3 bond has considerable double bond character and disruption of aromaticity in its benzene ring is an unfavorable process, suggesting that indole can be viewed with some confidence as an enamine fused at both ends to adjacent positions on a benzene ring [13]. This feature renders indole susceptible to attack by a wide variety of electrophiles including such weak ones as α,β-unsaturated carbonyl compounds. In view of the electronic character of indole, the reaction mechanism is ascribed as follows (Scheme 4), in which the intermediate zwitterion **A** is formed *via* nucleophilic attack of indole to pyrazolone **1**. The formation of an intermediate like **A** has been proposed [13,19,20], and with this proposed reaction route the regioselective attack of the C-3 carbon of indole and the substituent effect on the reactivity of **1** would be interpreted.

Scheme 4



1 A 2

EXPERIMENTAL

All melting points were uncorrected. The spectral data were recorded with the following instruments: the ir spectra, NICOLET IFOSX FT-IR spectrophotometer (in potassium bromide pellets); the ^{1}H nmr spectra, JEOLFX-90Q spectrometer in dimethyl-d_6 sulfoxide; the uv spectra, Shimadzu UV-240 UV-Vis spectrophotometer; the mass spectra, HP-5988A spectrometer with Fast Atom Bombardment (FAB) ion source using *m*-nitrobenzyl alcohol as the substrate; and elemental analysis, YANACO CHN CORDER MT-3 analyzer.

General Procedure for the Solid-state Michael Addition of Indole to **1a-n**.

A mixture of **1** (1 mmole) and excess indole (3 mmoles) was ground with an agate motar and a pestle and allowed to stand at room temperature for a specific length of time. The mixture was washed with chloroform to remove colored materials to provide a white solid which was recrystallized from methanol to afford Michael adducts **2a-n**, 1-(5-hydroxyl-3-methyl-1-phenyl-4-pyrazyl)-1-(3'-indolyl)-1-arylmethane. The Michael adducts **2** obtained are shown in Table 1.

1-(5-Hydroxyl-3-methyl-1-phenyl-4-pyrazyl)-1-(3'-indolyl)-1-phenylmethane (**2a**).

This compound was obtained as a colorless solid, mp 236°; ir: ν OH (and NH) 3410 (s), ν C=N (cyclic) 1601 cm^{-1}; ^{1}H nmr: δ 1.80 (s, 3H, CH_3), 5.54 (s, 1H, C-H), 6.78-7.97 (m, 15H, phenyl protons), 10.65 ppm (s, 1H, NH); ms: FAB m/z 380 (M+1), 263 (M-indole+1), 206 (M-pyrazolone+1).

Anal. Calcd. for $C_{25}H_{21}N_3O$: C, 79.13; H, 5.58; N, 11.07. Found: C, 78.96; H, 5.47; N, 10.92.

1-(5-Hydroxyl-3-methyl-1-phenyl-4-pyrazyl)-1-(3'-indolyl)-1-(4"-fluorophenyl)methane (**2b**).

This compound was obtained as a colorless solid, mp 207°; ir: ν OH (and NH) 3427 (s), 3189, ν C=N (cyclic) 1598 cm^{-1}; ^{1}H nmr: δ 1.84 (s, 3H, CH_3), 5.48 (s, 1H, C-H), 6.80-7.97 (m, 14H, phenyl protons), 10.59 ppm (s, 1H, NH); ms: FAB m/z 398 (M+1), 281 (M-indole+1), 224 (M-pyrazolone+1).

Anal. Calcd. for $C_{25}H_{20}FN_3O$: C, 75.55; H, 5.07; N, 10.57. Found: C, 75.62; H, 5.02; N, 10.29.

1-(5-Hydroxyl-3-methyl-1-phenyl-4-pyrazyl)-1-(3'-indolyl)-1-(4"-chlorophenyl)methane (**2c**).

This compound was obtained as a colorless solid, mp 176°; ir: ν OH (and NH) 3412 (s), 3229, ν C=N (cyclic) 1596 cm^{-1}; ^{1}H nmr: δ 1.66 (s, 3H, CH_3), 5.50 (s, 1H, C-H), 6.88-7.79 (m, 14H, phenyl protons), 10.85 ppm (s, 1H, NH); ms: FAB m/z 414 (M+1), 297 (M-indole+1), 240 (M-pyrazolone+1).

Anal. Calcd. for $C_{25}H_{20}ClN_3O$: C, 72.55; H, 4.87; N, 10.15. Found: C, 72.57; H, 4.72; N, 10.20.

1-(5-Hydroxyl-3-methyl-1-phenyl-4-pyrazyl)-1-(3'-indolyl)-1-(4"-bromophenyl)methane (**2d**).

This compound was obtained as a colorless solid, mp 188°; ir: ν OH (and NH) 3425 (s), 3222, ν C=N (cyclic) 1573 cm^{-1}; ^{1}H nmr: δ 1.86 (s, 3H, CH_3), 5.59 (s, 1H, C-H), 6.84-7.86 (m, 14H, phenyl protons), 10.42 ppm (s, 1H, NH); ms: FAB m/z 460, 458 (M+1), 343, 341 (M-indole+1), 286, 284 (M-pyrazolone+1).

Anal. Calcd. for $C_{25}H_{20}BrN_3O$: C, 65.55; H, 4.40; N, 9.17. Found: C, 65.31; H, 4.25; N, 9.08.

1-(5-Hydroxyl-3-methyl-1-phenyl-4-pyrazyl)-1-(3'-indolyl)-1-(4"-iodophenyl)methane (**2e**).

This compound was obtained as a colorless solid, mp 169°; ir: ν OH (and NH) 3410 (s), 3229, ν C=N (cyclic) 1600 cm^{-1}; ^{1}H nmr: δ 1.86 (s, 3H, CH_3), 5.52 (s, 1H, C-H), 6.80-7.86 (m, 14H, phenyl protons), 10.80 ppm (s, 1H, NH); ms: FAB m/z 506 (M+1), 389 (M-indole+1), 332 (M-pyrazolone+ 1).

Anal. Calcd. for $C_{25}H_{20}IN_3O$: C, 59.42; H, 3.99; N, 8.32. Found: C, 59.21; H, 3.70; N, 8.01.

1-(5-Hydroxy-3-methyl-1-phenyl-4-pyrazyl)-1-(3'-indolyl)-1-(4"-benzyloxyphenyl)methane (**2f**).

This compound was obtained as a colorless solid, mp 200°; ir: ν OH (and NH) 3408 (s), 3254, ν C=N (cyclic) 1608 cm^{-1}; ^{1}H nmr: δ 1.63 (s, 3H, CH_3), 5.06 (s, 2H, OCH_2-), 5.45 (s, 1H, C-H), 6.86-7.80 (m, 19H, phenyl protons), 10.79 ppm (s, 1H, NH); ms: FAB m/z 486 (M+1), 369 (M-indole+l), 312 (M-pyrazolone+1).

Anal. Calcd. for $C_{32}H_{27}N_3O_2$: C, 79.15; H, 5.60; N, 8.65. Found: C, 78.87; H, 5.62; N, 8.33.

1-(5-Hydroxy-3-methyl-1-phenyl-4-pyrazyl)-1-(3'-indolyl)-1-(4"-methylphenyl)methane (**2g**).

This compound was obtained as a colorless solid, mp 178°; ir: ν OH (and NH) 3418 (s), 3222, ν C=N (cyclic) 1606 cm^{-1}; ^{1}H nmr: δ 1.84 (s, 3H, CH_3), 2.22 (s, 3H, CH_3), 5.56 (s, 1H, C-H), 6.80-7.96 (m, 14H, phenyl protons), 10.56 ppm (s, 1H, NH); ms: FAB m/z 394 (M+l), 277 (M-indole+1), 220 (M-pyrazolone+1).

Anal. Calcd. for $C_{26}H_{23}N_3O$: C, 79.36; H, 5.89; N, 10.68. Found: C, 79.14; H, 5.68; N, 10.31.

1-(5-Hydroxy-3-methyl-1-phenyl-4-pyrazyl)-1-(3'-indolyl)-1-(4"-methoxyphenyl)methane (**2h**).

This compound was obtained as a colorless solid, mp 168°; ir: ν OH (and NH) 3410 (s), 3238, ν C=N (cyclic) 1606 cm^{-1}; ^{1}H nmr:

δ 1.85 (s, 3H, CH_3), 3.76 (s, 3H, OCH_3), 5.56 (s, 1H, C-H), 6.72-7.92 (m, 14H, phenyl protons), 10.73 ppm (s, 1H, NH); ms: FAB m/z 410 (M+1), 293 (M-indole+1), 236 (M-pyrazolone+1).

Anal. Calcd. for $C_{26}H_{23}N_3O_2$: C, 76.28; H, 5.66; N, 10.26. Found: C, 76.30; H, 5.47; N, 9.88.

1-(5-Hydroxy-3-methyl-1-phenyl-4-pyrazyl)-1-(3'-indolyl)-1-(4"-nitrophenyl)methane (**2i**).

This compound was obtained as a pale yellow solid, mp 184°; ir: ν OH (and NH) 3415 (s), 3223, ν C=N (cyclic) 1603, ν NO_2 1346 (s) cm^{-1}; ^1H nmr: δ 1.92 (s, 3H, CH_3), 5.65 (s, 1H, C-H), 6.81-8.31 (m, 14H, phenyl protons), 10.95 ppm (s, 1H, NH); ms: FAB m/z 425 (M+1), 308 (M-indole+1), 251 (M-pyrazolone+1).

Anal. Calcd. for $C_{25}H_{20}N_4O_3$: C, 70.74; H, 4.75; N, 13.20. Found: C, 70.47; H, 4.39; N, 13.06.

1-(5-Hydroxy-3-methyl-1-phenyl-4-pyrazyl)-1-(3'-indolyl)-1-(3"-nitrophenyl)methane (**2j**).

This compound was obtained as a pale yellow solid, mp 246°; ir: ν OH (and NH) 3422 (s), 3211, ν C=N (cyclic) 1600, ν NO_2 1350 (s) cm^{-1}; ^1H nmr: δ 1.95 (s, 3H, CH_3), 5.66 (s, 1H, C-H), 6.82-8.83 (m, 14H, phenyl protons), 10.95 ppm (s, 1H, NH); ms: FAB m/z 425 (M+1), 308 (M-indole+1), 251 (M-pyrazolone+1).

Anal. Calcd. for $C_{25}H_{20}N_4O_3$: C, 70.74; H, 4.75; N, 13.20. Found: C, 70.30; H, 4.82; N, 13.31.

1-(5-Hydroxy-3-methyl-1-phenyl-4-pyrazyl)-1-(3'-indolyl)-1-(4"-hydroxy-3"-methoxyphenyl)methane (**2n**).

This compound was obtained as a colorless solid, mp 206°; ir: ν OH (and NH) 3242 (s), ν C=N (cyclic) 1597 cm^{-1}; ^1H nmr: δ 1.63 (s, 3H, CH_3), 3.66 (s, 3H, OCH_3), 5.39 (s, 1H, C-H), 6.68-8.31 (m, 13H, phenyl protons), 10.77 ppm (s, 1H, NH); ms: FAB m/z 426 (M+1), 309 (M-indole+1), 252 (M-pyrazolone+1).

Anal. Calcd. for $C_{26}H_{23}N_3O_3$: C, 73.43; H, 5.45; N, 9.88. Found: C, 73.18; H, 5.19; N, 10.02.

The Michael Addition Reaction of Indole to **1** in Solution.

A solution of **1** (2 mmoles) and indole (6 mmoles) in 10 ml of methanol was allowed to stand at room temperature for 48 hours. The crystals of Michael adducts **2** which formed in some cases were collected by filtration, washed with chloroform and recrystallized in methanol, The results are shown in Table 1.

Determination of Equilibrium Constants between Indole + **1** and **2**.

A series of methanolic solutions of indole and **1** in different initial molar ratio ($C^{In}{}_o$:$C^1{}_o$ = 0.00:1.00, 0.25:1.00, 0.50:1.00, 0.75:1.00, 1.00:1.00, 1.50:1.00) with $C^1{}_o$ = 5.0 x 10^{-5} mol•l^{-1} were prepared and allowed to stand for 3 days at room temperature (30°) in order to reach equilibrium. The absorbances (A) of the solutions were determined in the uv spectrophotometer at λ_{max} (methanol) of **1** (**1a**, 324.3 nm; **1b**, 335.5 nm; **1c**, 331.8 nm; **1h**, 359.7 nm; **1i**, 320.0 nm). According to the equation C^1 = A/ε, the ε of **1** was obtained from the solution of C^1 = 0.00, and the equilibrium concentrations of indole, **1** and **2** ($C^{In}{}_{eq}$, $C^1{}_{eq}$ and $C^2{}_{eq}$) in each solution were calculated from A_{eq} of the solution. The equilibrium constants K_{obs} were obtained from K_{obs} = $C^2{}_{eq}/C^{In}{}_{eq}$•$C^1{}_{eq}$. The results are shown in Scheme 2.

Determination of Equilibrium of **2a** in Dimethyl Sulfoxide Solution.

A dimethyl sulfoxide solution of **1a** with a concentration of 5.04 x 10^{-5} mol/l was prepared. The uv spectra were recorded on the UV spectrophotometer with an interval of 20 minutes at 50°. The time-resolved spectrum is shown in Figure 1.

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REFERENCES AND NOTES

[#] Present address: Department of Basic Courses, Agricultural University of Hebei, Baoding, Hebei 071001, China.

[1] G. R. Desiraju, Organic Solid State Chemistry, Elsevier, Amsterdam, 1987.

[2] For reviews on organic solid state reactions, see: [a] F. Toda, *Synlett,* **5**, 303 (1993); [b] N. B. Singh, R. J. Singh and N. P. Singh, *Tetrahedron,* **50**, 6441 (1994); [c] G. R. Desiraju, Organic Solid State Chemistry, Elsevier Science Publishers, Amsterdam, 1987; [d] X. L. Li, Y. M. Wang, J. B. Meng and C. P. Du, *Youji Huaxue,* **18**, 20 (1998).

[3] F. Toda and H. Akai, *J. Org. Chem.,* **55**, 3446 (1990).

[4] F. Toda, K. Tanaka and J. Sato, *Tetrahedron Asymmetry,* **4**, 1771 (1993).

[5] M. Smricina, S. Vyskocil, V. Hanus, M. Polasek, V. Langer, B. G. M. Chew, D. B. Zax, H. Verrier, K. Harper, T. A. Claxton and P. Kocovsky, *J. Am. Chem. Soc.,* **118**, 487 (1996).

[6] J. B. Meng, H. Ma and Y. M. Wang, *Chin. Chem. Letters,* **4**, 475 (1993).

[7a] D. M. Du, S. M. Meng, Y. M. Wang, J. B. Meng and X. Z. Zhou, *Chin. J. Chem.,* **13**, 520 (1995); [b] D. M. Du, S. M. Meng, Y. M. Wang, J. B. Meng, X. Z. Zhou and Y. Zhu, *Chin. J. Struct. Chem.,* **14**, 277 (1995).

[8] J. B. Meng, D. M. Du, Y. M. Wang, R. J. Wang and H. G. Wang, *Chin. Chem. Letters,* **3**, 247 (1992).

[9] J. B. Meng, Z. Wen, Y. M. Wang and H. G. Wang, *Chin. Chem. Letters,* **4**, 865 (1993).

[10] X. L. Li, H. Ma, Y. M. Wang and J. B. Meng, *Chem. J. Chinese Univ.,* **16**, 1903 (1996).

[11] Y. M. Wang, Z. Wen, X. M. Chen, D. M. Du, T. Matsuura and J. B. Meng, *J. Heterocylic Chem.,* **35**, 313 (1998).

[12] X. L. Li, Y. M. Wang, B. Tian, T. Matsuura and J. B. Meng, *J. Heterocylic Chem.,* **35**, 129 (1998).

[13] W. A. Remers, Properties and Reactions of Indoles, Isoindoles and their Hydrogenated Derivatives in Indole, Part One, W. J. Houlihan, ed, John Wiley and Sons Inc., New York, 1972, pp 1-226.

[14] J. Szmuzkovicz, *J. Am. Chem. Soc.,* **79**, 2819, (1957).

[15] W. E. Noland and R. F. Lange, *J. Am. Chem. Soc.,* **81**, 1203, (1959).

[16] Z. Iqeal, A. H. Jaackson and K. R. N. Rao, *Tetrahedron Letters,* **29**, 2577, (1988).

[17] R. Dworczak, W. M. F. Fabian, H. Sterk, C. Kratky and H. Junek, *Liebigs Ann. Chem.,* 7, (1992).

[18] Compound **3** was prepared by the following procedure: To a solution of 0.6 g (5.0 mmoles) of benzaldehyde and 0.6 g (5.0 mmoles) of indole in 10 ml of ethanol was added 0.5 ml of concentrated hydrochloric acid. The mixture was allowed to stand for 2 hours. Compound **3** precipitated as an orange solid, mp 182°; ir: ν Ar-H 3053, 3020, ν C=N (cyclic) 1600, 1452, 745 cm^{-1}; ^1H nmr (dimethyl-d_6 sulfoxide): 5.70 (s, 1H, =CH), 6.80-7.32 ppm (m, 10H, ArH); ms: FAB m/z 222 (M+1); λ_{max} (dimethyl sulfoxide): 409.5 nm (log ε = 3.86).

[19] M. Abdel-Rahman and H. Abdel-Ghany, *Synth. Commun,* **19**, 1987 (1989).

[20] E. D. Berganann, D. Ginsberg and R. Pappo, The Michael Reaction, in Organic Reactions, Vol. **10**, R. Adams, ed, John Wiley and Sons Inc., New York, 1959, p 179.