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N-Phenylurea reacted with benzoylacetone derivatives (I) to give 1,4-diaryl-6-methyl-2-(1H)pyrimidinones (II) in addition to low yields of 1,6-diaryl-4-methyl-2-(1H)pyrimidinones (IV), while *N*-phenylthiourea afforded only 1,6-diaryl-4-methyl-2-(1H)pyrimidinethiones (III) in good yields. Further 1,6-diaryl-4-methyl-2-(1H)pyrimidinethiones (III) were successfully converted in satisfactory yields into the corresponding 2-(1H)pyrimidinones (IV) by the treatment with methyl iodide in the presence of sodium methoxide in methanol at room temperature.

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As a part of investigation about nucleophilic reactions on 2-(1H)pyrimidinones, we required 1,4-diaryl-6-methyl- (II) and 1,6-diaryl-4-methyl-2-(1H)pyrimidinones (IV) which would clarify the reaction sites of 2-(1H)pyrimidinones. Various 2-(1H)pyrimidinones were supplied by the thermal rearrangement of alkoxy pyrimidines (1), the reaction of ureas with tetramethoxypropane (2,3) and acetylacetone (4,5), the condensation of acetylenic ketones with ureas (6), the cyclization of 3-chloro-2-propeniminium salts (7), the reaction of β -aminoenones with ureas (8,9). The great majority of works on *N*-substituted 2-(1H)pyrimidinones have dealt the symmetrical pyrimidinones, having the same substituents at C-4 and C-6 position, while few papers concerning the synthesis of the unsymmetrical pyrimidinones, having the different substituents at C-4 and C-6 position have been reported because of the difficulties of the separation of the two isomers.

In this paper, we wish to report on the selective preparation of the unsymmetrical 1,4-diaryl-6-methyl- (II) and 1,6-diaryl-4-methyl-2-(1H)pyrimidinones (IV).

Previously we reported that the product ratio depended upon the structure of enol form and basicity of ureas on the reaction of β -diketones with ureas (8). Therefore, benzoylacetone (Ia) was treated with *N*-phenylurea in the presence of hydrochloric acid. The yield of IIa was 34%, while that of IVa was only 4%. The ir spectrum of the compound IIa displays a strong band at 1630 cm^{-1} due to C=O stretching and nmr spectrum shows benzoyl pattern at δ 7.1-7.6 (m, 8H) and at δ 8.0-8.3 (m, 2H). Further, C-6 methyl protons exhibit allyl coupling ($J = 0.7$ Hz) with olefinic proton at C-5 position of the pyrimidine ring. On the contrary, the ir spectrum of the compound IVa shows a strong band at 1660 cm^{-1} due to C=O stretching and the nmr spectrum exhibits neither benzoyl pattern nor allyl coupling (*cf.*, Table 2). The reaction of benzoylacetone with *N*-phenylthiourea afforded 1,6-diphenyl-4-methyl-2-(1H)pyrimidinethione (IIIa) in 82% yield without 1,4-diphenyl-6-methyl-2-(1H)pyrimidinethione (VI). The structure of the compound IIIa was determined from the

fact that the nmr spectrum showed neither benzoyl pattern nor allyl coupling, and the chemical shift of methyl protons was similar to that of methyl protons of the compound IVa (*cf.* Table 2). The reaction of other benzoylacetones (Ib-d) with *N*-phenylurea or *N*-phenylthiourea was examined and the results were summarized in Table 1 and Table 2.

Kröger reported that the hydrolysis of 2-alkylthio-4-amino-1-methylpyrimidinium iodide gave the corresponding pyrimidinone in the presence of base (10). Thus, 2-methylthio-1,6-diphenyl-4-methylpyrimidinium iodide (V), which was derived from IIIa by heating with methyl iodide, afforded IVa in 80% yield by the treatment with sodium methoxide in methanol. Further, we tried one pot synthesis of IVa by the treatment of IIIa with methylating agents in the presence of base. The reaction of IIIa with dimethyl sulfate in aqueous sodium hydroxide did not

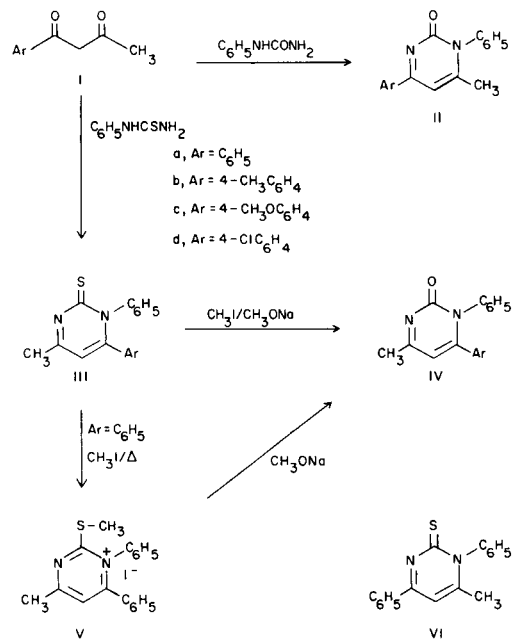


Table 1

Compound No.	M.p. °C dec.	Method	Yield %	Formula	Analysis %		
					C	H	N
IIa	222 (a)	A	34	C ₁₇ H ₁₄ N ₂ O	77.84 (77.71)	5.37 (5.41)	10.67 (10.87)
IIb	259 (a)	A	23	C ₁₈ H ₁₆ N ₂ O	78.23 (78.12)	5.83 (5.65)	10.13 (10.26)
IIc	254 (b)	A	20	C ₁₈ H ₁₆ N ₂ O ₂	73.95 (73.95)	5.51 (5.50)	9.58 (9.61)
IId	238 (a)	A	39	C ₁₇ H ₁₃ N ₂ OCl	68.80 (69.04)	4.41 (4.27)	9.44 (9.44)
IIIa	217 (c)	A	82	C ₁₇ H ₁₄ N ₂ S	73.35 (73.62)	5.06 (5.02)	10.06 (9.77)
IIIb	175 (a)	A	64	C ₁₈ H ₁₆ N ₂ S	73.93 (74.05)	5.51 (5.50)	9.58 (9.48)
IIIc	196 (a)	A	48	C ₁₈ H ₁₆ N ₂ OS	70.10 (70.36)	5.22 (5.16)	9.08 (8.95)
IIId	231 (a)	A	50	C ₁₇ H ₁₃ N ₂ OCl	65.27 (65.53)	4.18 (4.13)	8.95 (8.76)
IVa	151 (c)	A	4	C ₁₇ H ₁₄ N ₂ O	77.84 (78.04)	5.37 (5.42)	10.67 (10.90)
		B	85				
IVb	162 (a)	A	3	C ₁₈ H ₁₆ N ₂ O	78.23 (78.52)	5.83 (5.79)	10.13 (10.04)
		B	79				
IVd	164 (a)	A	9	C ₁₇ H ₁₃ N ₂ OCl	68.80 (69.10)	4.41 (4.34)	9.44 (9.26)
		B	54				

(a) Crystallized from benzene/hexane. (b) Crystallized from ethylacetate/hexane. (c) Crystallized from ethanol.

Table 2

Spectral Analyses of 2-(1H)Pyrimidinones and Pyrimidinethiones

Compound No.	Ir Spectra (cm ⁻¹)		Nmr Chemical Shift δ (ppm)			
	C=O	C=S	=C-CH ₃	Ar-CH ₃	=C-H	Aromatic
IIa	1630	—	2.08 (d, 3H, J = 0.7)	—	6.72 (q, 1H, J = 0.7)	7.1-7.5 (m, 8H) 7.9-8.2 (m, 2H)
IIb	1635	—	2.07 (d, 3H, J = 0.7)	2.40 (s, 3H)	6.80 (q, 1H, J = 0.7)	7.2-7.7 (m, 7H) 8.0-8.2 (m, 2H)
IIc	1630	—	2.03 (d, 3H, J = 0.7)	3.87 (s, 3H)	6.73 (q, 1H, J = 0.7)	6.9-7.6 (m, 7H) 8.1-8.3 (m, 2H)
IId	1640	—	2.07 (d, 3H, J = 0.7)	—	6.72 (q, 1H, J = 0.7)	7.1-7.6 (m, 7H) 7.9-8.2 (m, 2H)
IIIa	—	1260	2.49 (s, 3H)	—	6.60 (s, 1H)	7.1-7.4 (m, 10H)
IIIb	—	1260	2.50 (s, 3H)	2.07 (s, 3H)	6.58 (s, 1H)	7.0-7.4 (m, 9H)
IIIc	—	1270	2.50 (s, 3H)	3.72 (s, 3H)	6.60 (s, 1H)	6.7-7.5 (m, 9H)
IIId	—	1265	2.52 (s, 3H)	—	6.55 (s, 1H)	6.8-7.3 (m, 9H)
IVa	1660	—	2.40 (s, 3H)	—	6.20 (s, 1H)	7.0-7.2 (m, 10H)
IVb	1660	—	2.45 (s, 3H)	2.20 (s, 3H)	6.35 (s, 1H)	6.9-7.6 (m, 9H)
IVd	1650	—	2.50 (s, 3H)	—	6.33 (s, 1H)	6.8-7.5 (m, 9H)

occur. By the treatment with methyl iodide in the presence of sodium methoxide, IIIa was successfully converted in 85% yield into the corresponding 2-(1H)pyrimidinone (IVa) which was the minor product from benzoylacetone and *N*-phenylurea. Other 2-(1H)pyrimidinethiones (IIIb and IIId) were converted in a similar fashion into the corresponding 2-(1H)pyrimidinones (IVb and IVd) in 79% and 54% yield, respectively (cf. Table 1).

It is concluded from these results that *N*-phenylurea reacted with benzoylacetone derivatives to yield mainly

1,4-diaryl-6-methyl-2-(1H)pyrimidinones, while *N*-phenylthiourea gave only 1,6-diaryl-4-methyl-2-(1H)pyrimidinethiones in good yields, and we could selectively obtain unsymmetrical 1,4-diaryl-6-methyl- and 1,6-diaryl-4-methyl-2-(1H)pyrimidinones in satisfactory yields.

EXPERIMENTAL

Melting points were uncorrected. Ir spectra were recorded on Jasco ITA-1 infrared spectrophotometer. Nmr spectra were taken on Hitachi R-20 spectrometer using TMS as an internal standard.

1,4-Diaryl-6-methyl- (II) and 1,6-Diaryl-4-methyl-2-(1H)pyrimidinones (IV) and 1,6-Diaryl-4-methyl-2-(1H)pyrimidinethiones (III).

Method A.

The mixture of benzoylacetones (10 mmoles) and ureas (10 mmoles) in ethanol (30 ml.) was heated for 5 hours in the presence of hydrochloric acid (2.5 ml.). The reaction mixture was neutralized with aqueous sodium hydroxide and extracted with dichloromethane. The crude products II and IV were purified by silica gel chromatography with chloroform/acetone/ethanol (100:20:4). Also, the crude product III was purified by silica gel chromatography with chloroform/acetone/ethanol (100:10:2).

Method B.

The compound III (1 mmole) was dissolved in methanol (20 ml.) in the presence of sodium methoxide (4 mmoles). To the solution, methyl iodide (10 mmoles) was added at room temperature. After stirring for 3 hours, the product IV was obtained by the procedure described above.

2-Methylthio-1,6-diphenyl-4-methylpyrimidinium Iodide (V).

The mixture of IIIa (1 mmole) and methyl iodide (10 mmoles) was heated at 120° in sealed tube for 8 hours. The compound was recrystallized from ethanol and had m.p. 234° dec., 85% yield; ir: 3010, 1260, 1235, 760 and 740 cm^{-1} ; nmr: δ 2.83 (s, 3H), 2.98 (s, 3H), 7.4-7.8 (m, 10H), 8.15 (s, 1H).

Anal. Calcd. for $\text{C}_{18}\text{H}_{17}\text{IN}_2\text{S}$: C, 51.43; H, 4.07; N, 6.66. Found: C,

51.48; H, 3.92; N, 6.82.

Hydrolysis of Pyrimidinium Iodide V.

The compound V (0.2 mmole) was treated with sodium methoxide (0.9 mmole) in methanol (20 ml.) at room temperature for 3 hours. After diluting with water, the product, which was extracted with dichloromethane, was identified with IVa by spectral data and the mixed melting.

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