PYRIMIDINES

XIX. Synthesis of Pyrimidine Derivatives from Phenylacetone*

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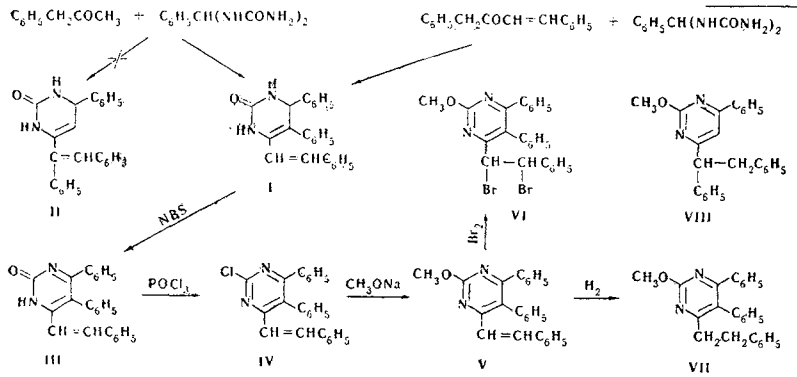
The reaction of phenylacetone with benzylidenebisurea (BBM) has given 2-hydroxy-4,5-diphenyl-6-styryl-3,4-dihydropyrimidine (I). The structure of I has been confirmed by its independent synthesis from 1,4-diphenylbut-3-en-2-one and BBM and also by a number of subsequent transformations.

We have previously shown that the condensation of benzylidenebisurea (BBM) with compounds having the $-CH_2COCH_2-$ grouping forms pyrimidine derivatives containing the benzylidene group in a side chain [2] or spiro compounds [3], depending on the conditions. Continuing a study of the behavior of unsymmetrically-substituted ketones in this reaction, we have investigated phenylacetone, which, as is well known, can give derivatives both with respect to the $-CH_2-$ and with respect to the CH_3 group (Mannich reaction [4, 5], condensation with aldehydes [6–8], etc.).

When BBM was condensed with phenylacetone, a compound was obtained which, on the basis of analytical and spectroscopic data and by analogy with the structure of the product obtained from cyclohexane [2], could be ascribed the structure of 2-hydroxy-4,5-diphenyl-6-styryl-3,4-dihydropyrimidine (I) or 6-(α,β-diphenylisopropenyl)-2-hydroxy-4-phenyl-3,4-diphydropyrimidine (II). The choice between these structures in favor of compound I was made on the basis of the synthesis of an identical compound from 1,4-diphenylbut-3-en-2-one and BBM.



The dehydration of compound I with the formation of 2-hydroxy-4,5-diphenyl-6-styrylpyrimidine (III) was achieved by the action of N-bromosuccinimide. High-temperature dehydrogenation with Pd/C led either to pronounced resinification or to a mixture of compounds I and III that was difficult to separate.

By the action of phosphorus oxychloride, III yielded 2-chloro-4,5-form 2-methoxy-4,5-diphenyl-6-styrylpyrimidine (V). The double bond in the styryl group of compound V possesses the properties usual for styryl derivatives of heterocyclic compounds [2, 9]. Thus, when V was treated with bromine a quantitative yield of 6-(α,β-dibromo-β-phenylethyl)-2-methoxy-4,5-diphenylpyrimidine (VI) was obtained, while the catalytic hydrogenation of V over Pd/C yielded 2-methoxy-4,5-diphenyl-6-(β-phenylethyl)pyrimidine (VII).

The PMR spectrum of the latter compound, recorded in deuterochloroform confirms the structure of VII and does not agree with that of 6-(α,β-diphenylethyl)-2-methoxy-4-phenylpyrimidine (VIII). It was possible to obtain compound VIII in a similar manner to VII, but compound II was also present in the initial condensation product; for VIII one could expect four bands with an intensity ratio of 16 ($C-H_{arom}$) : 1 (triplet) : 2 (doublet) : 3 (singlet). However, the PMR spectrum of the hydrogenation product had three bands with a ratio of the intensities of 15 : 3 : 4 at δ 7.05, 4.04, 2.87, which confirms the structure VII completely. The absence of splitting for the $-CH_2-CH_2$ group and the presence of a broadened signal can be explained by the very similar nature of the CH_2 groups.

The UV spectra of compounds I and III–VII and also the positions of the absorption bands of the C=O and N—H groups in the IR spectra of I and III and the change in the spectra on passing from one compound to the other are similar to those obtained previously for the products of the condensation of BBM with α-tetralone [10], cyclohexanone [2], and other ketones and the products of their transformations.

EXPERIMENTAL

Phenylacetone was obtained by Magidson and Garkusha's method with a yield of 51%, bp 71–73° C (2 mm), n_D^{20} 1.5165. According to the literature [12], bp 214–215° C, n_D^{20} 1.5168.

1,4-Diphenylbut-3-en-2-one was obtained by the method of Southwick et al. [7]; mp 73.5–74° C; according to the literature [7], mp 73–74° C.

*For part XVIII, see [1]

2-Hydroxy-4, 5-diphenyl-6-styryl-3, 4-dihydropyrimidine (I). A) A mixture of 9.0 g (0.15 mole) of urea and 15.7 g (0.15 mole) of benzaldehyde was heated in 50 ml of absolute ethanol containing 3.0 g (0.082 mole) of dry HCl until a precipitate of benzylidenebisurea appeared. Then 9.9 g (0.075 mole) of phenylacetone was added to the reaction mixture and boiling was continued for 2.5 hr. The precipitate was filtered off and was washed with ethanol, ether, and saturated sodium bicarbonate solution to give 18.4 g (70%) of **I**, mp 261–265° C (from a mixture of ethanol and acetic acid). Found, %: C 81.9, 81.7; H 5.85, 5.81; N 8.13, 8.08; mol. wt. 352 (mass spectrometrically). Calculated for $C_{24}H_{20}N_2O$, %: C 81.8; H 5.72; N 7.95%; mol. wt. 352. UV spectrum, λ_{max}, nm (log ε): 232 (4.17); 262 (4.34); 324 (4.32).

B). A mixture of 0.53 g (2.4 mM) of 1, 4-diphenylbut-3-en-2-one and 0.5 g (2.4 mM) of BBM was boiled in 8 ml of absolute ethanol in the presence of 10 drops of conc HCl for 1.5 hr. The BBM dissolved during the first 20 min., and the precipitate appeared almost immediately afterwards. The precipitate was filtered off and washed with ethanol and ether to give 0.68 g of **I** (yield 81%), mp 261–265° C (from a mixture of ethanol and acetic acid).

2-Hydroxy-4, 5-diphenyl-6-styrylpyrimidine (III). A mixture of 2.0 g (5.7 mM) of **I**, 1.10 g (6.2 mM) of N-bromosuccinimide, 50 mg of benzoyl peroxide, and 50 ml of CCl_4 was boiled for 50 min. The precipitate was filtered off and dissolved in 30 ml of methanol, and, after the addition of 1 ml of pyridine, the solution was boiled for 1 hr. The precipitate was filtered off to give 0.5 g of **III** (yield 25%), mp 268–270° C (from a mixture of ethanol and acetic acid). Found, %: C 82.3, 82.3; H 5.47, 5.34; N 8.21; 8.19. Calculated for $C_{24}H_{18}N_2O$, %: C 82.3; H 5.18; N 7.99. UV spectrum, λ_{max}, nm (log ε): 238 (4.36); 350 (4.23).

2-Chloro-4, 5-diphenyl-6-styrylpyrimidine (IV). A mixture of 0.5 g (1.4 mM) of **III** and 7 ml of phosphorus oxychloride was boiled for 1.5 hr. The excess of phosphorus oxychloride was distilled off in vacuum. The residue was dissolved in benzene and the solution was washed with saturated sodium bicarbonate solution and with water. The benzene was distilled off and the residue was recrystallized from ethanol, giving 0.33 g of **IV** (yield 63%), mp 147–150° C. Found, %: C 78.2, 77.9; H 4.60, 4.71; Cl 9.77, 9.53, N 7.87, 7.71. Calculated for $C_{24}H_{17}ClN_2$, ClN_2, %: C 78.1; H 4.64; Cl 9.61; N 7.59. UV spectrum, λ_{max} nm (log ε): 238 (4.25); 266 (4.20); 346 (4.39).

2-Methoxy-4, 5-diphenyl-6-styrylpyrimidine (V). A solution of 1.50 g (4.0 mM) of **IV** in 70 ml of absolute ethanol was added to a solution containing 0.40 g (15.0 mM) of sodium methoxide in 20 ml of absolute methanol. The mixture was boiled for 6 hr, and the precipitate was filtered off and washed with water to give 1.4 g of **V** (95%), mp 146–148° C (from methanol). Found, %: C 82.7, 82.7; H 5.68, 5.56; N 7.86, 7.76. Calculated for $C_{25}H_{20}N_2O$, %: C 82.4; H 5.53; N 7.69. UV spectrum, λ_{max}, nm (log ε): 232 (4.35); 256 (4.20); 346 (4.45).

6-(α, β-Dibromo-β-phenylethyl)-2-methoxy-4, 5-diphenylpyrimidine (VI). A solution of 0.13 g (0.8 mM) of bromine in 3 ml of chloroform was added to a solution of 0.30 g (0.8 mM) of **V** in 5 ml of chloroform. The solution was evaporated, giving a precipitate of **VI** with mp 161–163° C (from ethanol). Found, %: C 57.8, 57.6; H 3.84, 3.97; Br 30.3, 30.5; N 5.83, 5.98. Calculated for $C_{25}H_{20}Br_2N_2O$, %: C 57.3; H 3.84; Br 30.5; N 5.34. UV spectrum, λ_{max}, nm (log ε): 302 (4.04).

2-Methoxy-4, 5-diphenyl-6-(β-phenylethyl)pyrimidine (VII). In the presence of 0.10 g of 5% Pd/C at room temperature and atmospheric pressure, 0.60 g (1.6 mM) of **V** was hydrogenated in a mixture of 40 ml of ethanol and 5 ml of acetic acid. The catalyst was filtered off, the filtrate was evaporated, and the residue was recrystallized from petroleum ether (bp 40–60° C), giving **VII**, mp 80–82° C. Found, %: C 81.9, 82.0; H 6.15, 6.13; N 7.91, 7.61. Calculated for $C_{25}H_{22}N_2O$, N_2O, %: C 81.9; H 6.06; N 7.64. UV spectrum λ_{max}, nm (log ε): 288 (4.01).

The UV spectra were taken on an SF-4 spectrophotometer in ethanol at a concentration of 10^{-4}M.

The NMR spectrum was recorded on a JNM • 4H-100 instrument with $CDCl_3$ as solvent at a concentration of 15%, the chemical shifts being given in ppm taking the TMS signal as 0.

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