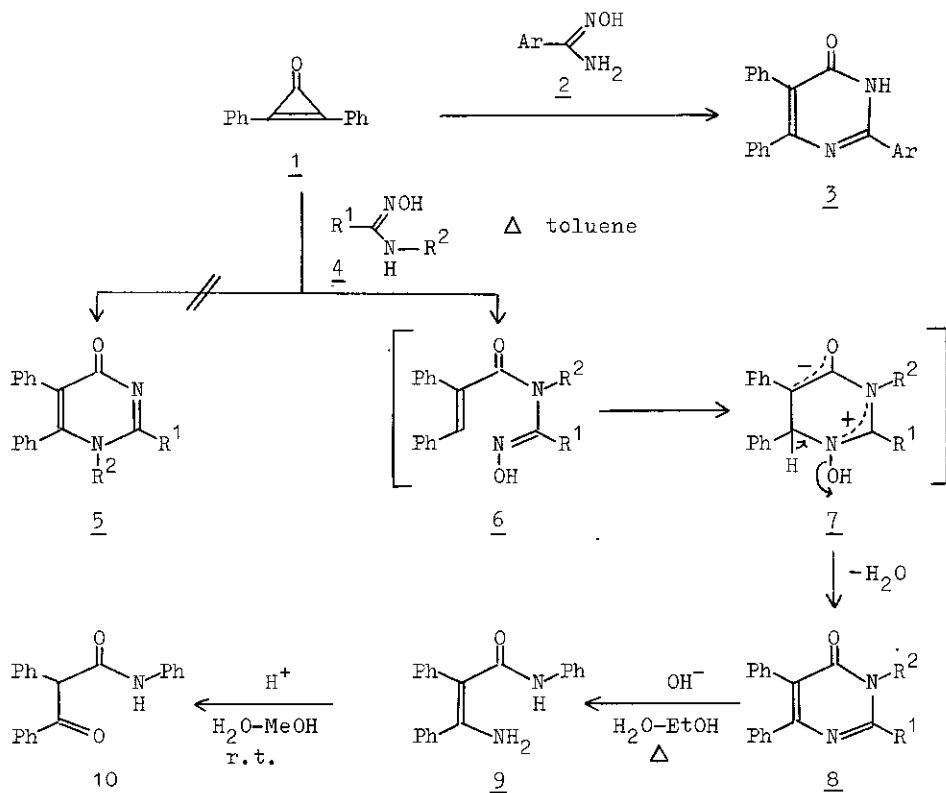


SYNTHESIS OF 3-SUBSTITUTED 5,6-DIPHENYLPYRIMIDIN-4-ONES FROM  
DIPHENYLCYCLOPROPENONE AND N-SUBSTITUTED AMIDE OXIMES

Masahiko Takahashi\*, Takayuki Nogami, and Ken-ichi Nidaira  
Department of Industrial Chemistry, Faculty of Engineering,  
Ibaraki University, Hitachi, Ibaraki 316, Japan

Abstract — 3-Substituted 5,6-diphenylpyrimidin-4-ones were prepared regioselectively from diphenylcyclopropenone and N-substituted amide oximes.

Diphenylcyclopropenone (1) is a readily available and useful synthon for heterocycles.<sup>1,2</sup> There have been some reports about the formation of two isomeric pyrimidin-4-ones 5 and 8 from 1. 1-Substituted pyrimidin-4-ones 5 were formed on treatment of 1 with benzo[c]cinnolinium-5-(N-benzimido-imides)<sup>3</sup>, N-imidoyl sulfoximides<sup>4</sup>, or N-phenylbenzamidines.<sup>3,5</sup> On the other hand, isomeric 3-substituted pyrimidin-4-ones 8 were obtained from 1 and N-imidoyl sulfimides.<sup>6</sup> These reactions, however, do not seem preparative because of the low yields<sup>4</sup>, two step operations in the experiments<sup>3,5</sup>, or limited availability of the reagents.<sup>3,4,6</sup> In a previous report<sup>7</sup>, we described a facile and general synthesis of 2-aryl-5,6-diphenylpyrimidin-4-ones (3) from 1 and arylamide oximes 2. As a continuation of this work, we have examined the reaction of 1 with N-substituted amide oximes 4 and found a method to introduce substituents on the 3-position of pyrimidin-4-ones regioselectively. Treatment of 1 with N-phenylformamide oxime (4a) in refluxing toluene afforded an addition-dehydration product. The structure of the product was presumed to be either 1,5,6-triphenylpyrimidin-4-one (5a) or 3,5,6-triphenylpyrimidin-4-one (8a) on the basis of the spectral and analytical data. The structure, however, was finally found to be 8a as follows; Alkaline hydrolysis of the product in refluxing aqueous ethanol gave a ring-opened product 9, which was further hydrolyzed in the presence of sulfuric acid in aqueous methanol at room temperature to yield the known  $\beta$ -ketoamide 10.<sup>8</sup> Moreover, the IR spectrum of



<u>4-8</u>	R <sup>1</sup>	R <sup>2</sup>
a	H	C <sub>6</sub> H <sub>5</sub> -
b	H	4-MeO-C <sub>6</sub> H <sub>4</sub> -
c	H	4-Me-C <sub>6</sub> H <sub>4</sub> -
d	H	4-Cl-C <sub>6</sub> H <sub>4</sub> -
e	C <sub>6</sub> H <sub>5</sub> -	C <sub>6</sub> H <sub>5</sub> -
f	C <sub>6</sub> H <sub>5</sub> -	4-Me-C <sub>6</sub> H <sub>4</sub> -
g	H	H

the product from 1 and 4e was identical with that of the authentic 8e<sup>9</sup>, but not with that of the authentic 5e.<sup>3</sup> Thus, regioselective formation of 3-substituted pyrimidin-4-ones 8 from 1 and 4 has been established and the physical and spectral data of these pyrimidinones are shown in the Table. 2,4-Unsubstituted derivative 8g was also obtained.

The tentative reaction pathway is shown in the Scheme. Intramolecular

Table. 3-Substituted 5,6-diphenylpyrimidin-4-ones (8)

Pro- duct	Yield %	mp °C	MS (M <sup>+</sup> ) m/e	IR (KBr) cm <sup>-1</sup>	NMR (Solvent) δ
<u>8a</u>	69	206-207 (MeOH)	324	1650, 1600, 1580, 1565, 1525, 1490	8.20 (s, 1H), 7.20-7.47 (m, 15H) (CDCl <sub>3</sub> )
<u>8b</u>	46	180-181 (MeOH)	354	1655, 1600, 1580, 1565, 1515, 1505	8.23 (s, 1H), 6.89-7.43 (m, 14H), 3.82 (s, 3H) (CDCl <sub>3</sub> )
<u>8c</u>	64	188-189 (MeOH)	338	1645, 1600, 1585, 1565, 1530, 1505	8.21 (s, 1H), 7.23-7.31 (m, 14H), 2.43 (s, 3H) (CDCl <sub>3</sub> )
<u>8d</u>	60	241-242 (MeOH-CHCl <sub>3</sub> )	357	1640, 1590, 1580, 1565, 1515, 1480	9.01 (s, 1H), 6.87-7.17 (m, 14H) (CF <sub>3</sub> COOH)
<u>8e</u>	76	298-300 (DMF)	400	1650, 1605, 1575, 1545, 1530, 1500	
<u>8f</u>	50	264-266 (MeOH-CHCl <sub>3</sub> )	414	1655, 1580, 1550, 1525, 1510, 1490	7.05-7.53 (m, 19H), 2.28 (s, 3H) (CDCl <sub>3</sub> )
<u>8g</u>	77	254-257 (MeOH)	248	2650, 1620, 1595, 1560, 1520, 1485	8.92 (s, 1H), 6.92 (s, 10H) (CF <sub>3</sub> COOH)

Satisfactory microanalytical data (C  $\pm$ 0.40%, H  $\pm$ 0.16%) were obtained.

conjugate addition of nitrogen atom of oxime 6 affords resonance-stabilized zwitterion intermediate 7, which extrudes water, giving 8.

#### EXPERIMENTAL

Starting amide oximes 4<sup>10</sup>: N-Arylamide oximes 4b-d were prepared according to the literature method for 4a<sup>11</sup>. Thus, treatment of 4g<sup>11</sup> (3.0 mmol) and arylamine hydrochloride (3.0 mmol) in refluxing ethanol (9 ml) for several hours gave N-arylamide oximes in 50-60% yields. 4b: mp 135-137°C. 4c: mp 138-140°C. 4d: mp 152-154°C.

3-Substituted 5,6-diphenylpyrimidin-4-ones 8: A general procedure. A mixture of 1 (3.0 mmol) and 4 (3.0 mmol) in toluene (9 ml) was refluxed for 3-5 h.

After cooling, the precipitates were collected by filtration, washed with a small amount of methanol, and recrystallized to give 8.

N-Phenyl-3-amino-2,3-diphenyl-2-propene-1-carboxamide (9): A mixture of 8 (970 mg, 3.0 mmol) in aqueous ethanol (30 ml, water:ethanol=1:9) containing 1% potassium hydroxide was refluxed for 10 h. After evaporation of the solvent, the residue was washed with water and recrystallized from methanol to give 9 (580 mg, 61% yield), white plates, mp 124-126°C. IR (KBr)  $\text{cm}^{-1}$ : 3450, 3400, 1635, 1585, 1570, 1510, 1480. MS m/e: 314 ( $\text{M}^+$ ). Anal. Calcd. for  $\text{C}_{21}\text{H}_{18}\text{ON}_2$ : C, 80.23; H, 5.77. Found: C, 80.54; H, 5.87.

N-Phenyl-2,3-diphenylpropan-3-one-1-carboxamide (10): A mixture 9 (314 mg, 1.0 mmol) in aqueous methanol consisting of methanol (10 ml) and 10% sulfuric acid (10 ml) was stirred at room temperature for 2 h. The precipitates were collected by filtration and recrystallized from methanol to give 10 (222 mg, 71% yield), mp 168-169°C (lit.<sup>8</sup> mp 168-169°C). IR (KBr)  $\text{cm}^{-1}$ : 3250-3030, 1670, 1655, 1590, 1545, 1490. MS m/e: 315 ( $\text{M}^+$ ).

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#### REFERENCES

1. K. T. Pott and J. S. Baum, *Chem. Rev.*, 74, 189 (1974).
2. M. L. Deem, *Synthesis*, 701 (1982).
3. J. J. Bar, R. C. Storr, and V. K. Tandon, *J. Chem. Soc. Perkin Trans. 1*, 1147 (1980).
4. H. Yoshida, D. Sogame, Y. Takishita, and T. Ogata, *Bull. Chem. Soc. Jpn.*, 56, 2438 (1983).
5. T. Eicher, G. Franke, and F. Abdesaken, *Tetrahedron Lett.*, 4067 (1977).
6. T. L. Gilchlist, C. J. Harris, C. J. Moody, and C. W. Rees, *J. Chem. Soc. Perkin Trans. 1*, 1969 (1975).
7. M. Takahashi and S. Watanabe, *Chem. Lett.*, 1213 (1979).
8. A. Kascheres and D. Marchi, Jr., *J. Org. Chem.*, 40, 2985 (1975).
9. R. A. Y. Jones and N. Sadighi, *J. Chem. Soc. Perkin Trans. 1*, 2259 (1976).
10. For a review; F. Eloy and R. Lenaers, *Chem. Rev.*, 62, 155 (1962).
11. J. Nef, *Justus Liebigs Ann. Chem.*, 280, 294 (1891).

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