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A Method of Synthesizing Pyrimidine Derivatives. II

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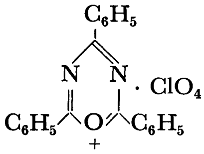
2,4,6-Triphenyl-1,3,5-oxadiazin-1-ium perchlorate (**1**), a six-membered heterocycle, is an oxonium salt similar to 2,4,6-triphenylpyrylium salt. Since **1** has two nitrogen atoms, more negative than carbon, in the ring, it is expected that there might be some difference in the reactivity between the two salts, though **1** would, on the whole, behave toward many nucleophiles in a manner similar to the pyrylium salt. Several papers[1–3] and the review[4] by Dimroth *et al.* have shown that the pyrylium salt reacts with active methylene compounds to give benzene derivatives. On the other hand, present authors have reported that **1** gave 4-benzoylamino-5-substituted-2,6-diphenylpyrimidine (**2a**, **b**, **c**) when **1** was refluxed with substituted acetonitrile.[5] This work was undertaken in an attempt to make clear the behavior of **1** toward a variety of active methylene compounds as well as the substituted acetonitriles by comparison with the behavior of the pyrylium salt.



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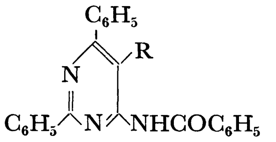
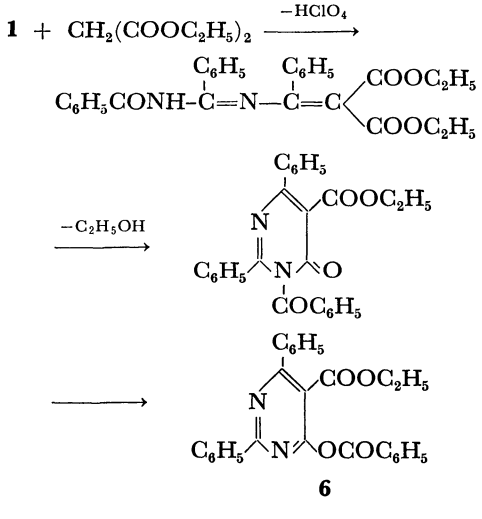


2a: $R=CN$ **2b**: $R=COOCH_3$ **2c**: $R=COC_6H_5$

Results and Discussion

Ethyl Benzoylacetate, Benzoylacetonitrile, and Dibenzoylmethane. When ethyl benzoylacetate was refluxed with **1**,5-ethoxycarbonyl-2,4,6-triphenylpyrimidine (**3**)[6] was obtained. The mass and IR spectra of **3** agreed with those of an authentic sample. The reaction of the pyrylium salt with ethyl acetylacetate, which is analogous to this reagent, was also examined and found to give ethyl 2,4,6-triphenylbenzoate.[1] Benzoylacetonitrile with **1** afforded another product (**4**), together with **2c**,[5] when allowed to stand at room temperature for a week. The mol. wt of **4** was determined by mass spectroscopy to be 333. The IR spectrum of **4** was indicated absorptions assignable to a cyano group (2200 cm^{-1}) and a pyrimidine ring (1520 cm^{-1}) alone. These results and those of the elemental analysis provide a basis for the identification of **4** with 5-cyano-2,4,6-triphenylpyrimidine. On the other hand, benzoylacetonitrile with the pyrylium salt gave only 2,4,6-triphenylbenzonitrile. Dibenzoylmethane with **1** gave **5** under conditions similar to the above. The mol. wt of **5** was determined to be 412; its IR spectrum was similar to that of **4** except for the difference between their absorptions assigned to the cyano and benzoyl groups. Therefore, **5** was determined to be 5-benzoyl-2,4,6-triphenylpyrimidine. Every reaction of **1** with these three reagents possessing a benzoyl group gives 5-substituted-2,4,6-triphenylpyrimidine, with the liberation of benzoic acid.

Diethyl Malonate. Upon refluxing in dioxane, diethyl malonate with **1** gave **6** in a low yield. Its mol. wt was 424. The major peaks of the mass spectrum, 395, 380, 351, and 105, were ascribed to $M^+-C_2H_5$, M^+-CO_2, $M^+-COOC_2H_5$, and the benzoyl cation respectively. 4-Benzoyloxy-5-ethoxycarbonyl-2,6-diphenylpyrimidine satisfied these data. The reaction course is assumed to be in which this reagent attacks the 2-position of the oxadiazinium ring, the 1–2 bond of the ring is broken, and then the resulting open-chain intermediate cyclizes, with the liberation of ethanol followed by the benzoyl migration to afford **6**. This reaction is analogous to the formation of **2a** from malonitrile and **1** with the shift of the benzoyl group. In regard to the pyrylium salt, this reagent gives 2-hydroxy-3-ethoxycarbonyl-4,6-diphenylbenzophenone, with the liberation of ethanol.[3]



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Cyanoacetamide and Benzoylacetamide. Cyanoacetamide with **1** afforded **7** at room temperature, while benzoylacetamide gave **8** upon refluxing. The measurement of the mass spectra resulted in failure since their vapor pressures are very low. Their IR spectra are very similar to each other. **7** was identified with 4-hydroxy-5-cyano-2,6-diphenylpyrimidine,[7] and con-

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[1] K. Dimroth and G. Neubauer, *Chem. Ber.*, **92**, 2042 (1959).

[2] K. Dimroth and G. Neubauer, *ibid.*, **92**, 2046 (1959).

[3] K. Dimroth and G. Neubauer, *Angew. Chem.*, **69**, 720 (1957).

[4] K. Dimroth and G. Neubauer, *ibid.*, **72**, 331 (1960).

[5] I. Shibuya and M. Kurabayashi, This Bulletin, **42**, 2382 (1969).

[6] Y. Asahina and E. Kuroda, *Ber.*, **42**, 1815 (1914).

[7] R. R. Schmidt, *ibid.*, **98**, 346 (1965).

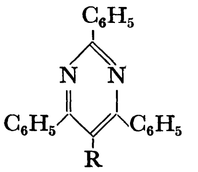
Table 1. Pyrimidine derivatives (**3**—**8**)

Compound	Reaction condition	Solvent for recryst.	Mp (°C)	Yield (%)	Elemental analysis Found (Calcd)			(IR cm^{-1})	Mass (m/e)
					C(%)	H(%)	N(%)		
3	a[a)]	MeOH	108.5	76	78.99 (78.93)	5.37 (5.30)	7.46 (7.36)	1729, 1709, 1524, 1260 1144, 1054.	380, 351, 336, 129, 103.
4	b[b)]	DMF	260.5	28	82.69 (82.86)	4.49 (4.54)	12.61 (12.60)	2200, 1520, 1487, 1380, 1370.	333, 332, 230, 229, 166.5, 127.
5	b	MeCN	181.2	69	84.44 (84.46)	4.89 (4.93)	6.79 (7.01)	1663, 1520, 1491, 1441, 1385, 1260.	412, 129, 105, 103.
6	a	EtOH	157.5	12	73.53 (73.57)	4.59 (4.75)	6.83 (6.60)	1756, 1730, 1558, 1525, 1263, 1243, 1023, 1008.	424, 395, 380, 351, 129, 105.
7	b	DMF	>300	45	74.71 (74.55)	4.06 (4.23)	15.38 (15.30)	3060, 2925, 2200, 1651, 1530, 1376, 1303, 1224.	
8	a	DMF	296.0	88	78.18 (78.39)	4.66 (4.58)	8.15 (7.95)	3030, 2925, 1673, 1629, 1559, 1544, 1447, 1380.	

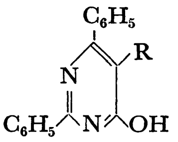
a) Under refluxing. b) Under allowing to stand at room temperature.

sequently **8** was determined to be 4-hydroxy-5-benzoyl-2,6-diphenylpyrimidine. These results showed that the reaction of **1** with reagents possessing a carbamoyl group gives 4-hydroxypyrimidines.

Thus, it was proved that the 1,3,5-oxadiazinium salt gives pyrimidines with a number of functional groups on the 4 and 5-positions when it is treated with several active methylene compounds.



3: $R=COOC_2H_5$
4: $R=CN$
5: $R=COC_6H_5$



7: $R=CN$
8: $R=COC_6H_5$

Experimental

The melting point of all products were measured by means of a Mettler FPI apparatus in capillary tubes with the elevating rate of 2 °C/min. The IR spectra were recorded in KBr disks on a JASCO DS-403G apparatus. The mass spectra were obtained on a Hitachi RMU6E mass spectrometer, with a direct inlet and an ionization energy of 70 eV.

*General Procedures for Preparing Pyrimidines (**3**—**8**).* To a solution of 4 mmol of an active methylene compound and 6 mmol of triethylamine in 20 ml of dioxane, 4 mmol of **1** were added; the mixture was subsequently stirred for ten minutes and then (a); refluxed for an hour or (b); allowed to stand for a week at room temperature. The resulting mixture was poured into dilute hydrochloric acid. The precipitate was collected by filtration and purified by recrystallization from an appropriate solvent. The reaction conditions, the yields, the melting points, the solvents for recrystallization, the results of elemental analyses, the main absorptions of the IR spectra, and the major peaks of the mass spectra are all listed in Table 1.