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A REGIOSELECTIVE SYNTHESIS OF PYRROLO- AND PYRIDO[2,3-d]-PYRIMIDINE-2,4-DIONES

Yasumitsu Tamura,* Toshiko Sakaguchi, Tomomi Kawasaki,
and Yasuyuki Kita
Faculty of Pharmaceutical Sciences, Osaka University, Toneyama,
Toyonaka, Osaka, Japan

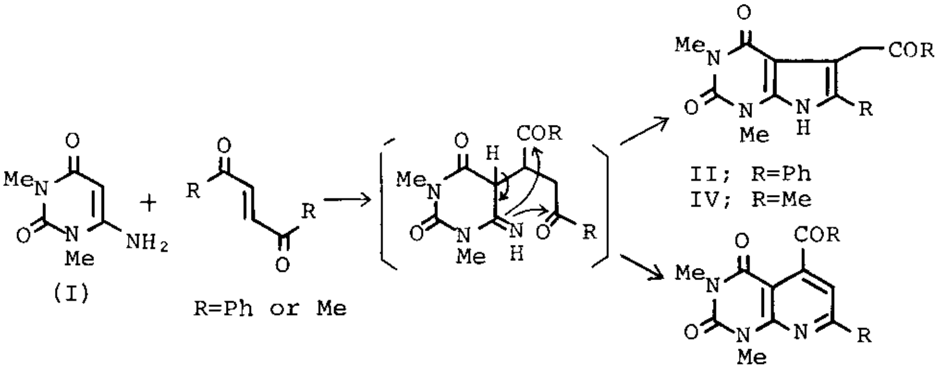
Reaction of diacylethylene with 6-amino-1,3-dimethyluracil gives rise to either pyrrolo-or pyrido-[2,3-d]pyrimidine-2,4-dione by the selection of reaction conditions.

We reported previously[1] the regioselective reaction of dibenzoylethylene (DBE) with 3-amino-2-cyclohexen-1-ones, which under acidic condition gave the 4-oxotetrahydroindoles, while under dehydrogenation condition gave the 5-oxotetrahydroquinolines. It seems of quite interest to examine the generality of this method and applicability to other heterocyclic systems. In the present communication, we report here that diacylethylene (RCOCH=CHCOR, R=Ph or Me) reacts also with 6-amino-1,3-dimethyluracil to give pyrrolo- and pyrido[2,3-d]pyrimidines regioselectively.

DBE was found to react readily with 6-amino-1,3-dimethyluracil (I) in a refluxing ethanolic solution for 6h to give a 60% yield of pyrrolo[2,3-d]pyrimidine-2,4-dione (II), mp 222-223.5°. The structure was determined by its elemental, mass [m/e 373 (M^+)], nmr (NH at τ -0.35 and $PhCOC\underline{H}_2$ at τ 5.45) and ir data (two carbonyl absorptions at 1690 and 1635 cm^{-1}).

On the other hand, refluxing the pyridine solution of DBE and (I) under oxygen bubbling gave a 47% yield of pyrido[2,3-d]-pyrimidine-2,4-dione (III), mp 288-290°, whose structural assignment was based on its elemental, ir (two carbonyl bands at 1700 and 1650 cm^{-1}) and nmr data (no other signals were observed besides eleven aromatic protons and two methyl signals). The above reaction condition of condensation and simultaneous dehydrogenation was proved to give better yield than the previously reported[1] condition as refluxing in xylene in the presence of Pd-C. 1,3-Dimethyluracil(I) was likewise converted by the reaction with diacetylethylene into the corresponding pyrrolo- and pyrido[2,3-d]pyrimidine derivatives, (IV; mp 182-184°) and (V; mp 203-204°).

The reaction of diacylethylene with (I) is supposed to proceed as analogous to the mode realised in the reaction of DBE with 3-amino-2-cyclohexen-1-ones.[1] These regioselective reactions using diacylethylene would promise to be widely applicable to further heterocycles.



(I)

R=Ph or Me

II; R=Ph
IV; R=Me

III; R=Ph
V; R=Me

R	Reaction Conditions	% yield of (II, IV)	% yield of (III, V)
Ph	EtOH reflux 6h	60	—
	$(CH_3)_2C_6H_4$, Pd-C reflux 7h	20	12
	$(CH_3)_2C_6H_4$, DDQ reflux 6h	5	26
	$(CH_3)_2C_6H_4$, O_2 reflux 5h	8	30
	C_5H_5N, I_2 reflux 2h	—	24
	C_5H_5N, O_2 reflux 5h	—	47
Me	AcOH reflux 5h	48	—
	$(CH_3)_2C_6H_4$, DDQ reflux 5h	—	21
	C_5H_5N, O_2 reflux 3h	—	37

Reference

1 Y. Tamura, T. Sakaguchi, T. Kawasaki, and Y. Kita, Heterocycles, 2, 645 (1974).

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