Reaction of Enamines, Imines, and Ketones with Acrylamide

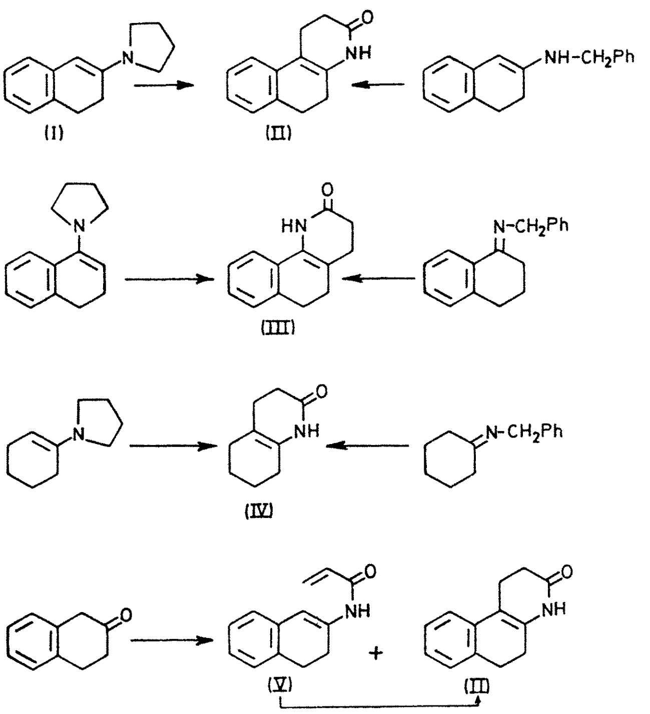
By I. NINOMIYA,* T. NAITO, S. HIGUCHI, and T. MORI
(*Kobe Women's College of Pharmacy, Motoyama, Higashinada, Kobe, Japan*)

Summary The aza-annelation of imines with acrylamide occurs smoothly, as in the cases of enamines, illustrating the versatility of imines as an effective substitute for enamines.

THE reaction of cyclohexanone enamine with acrylamide in dioxan ("aza-annelation") was described by Stork.[1] We have found a convenient procedure for this aza-annelation employing enamines of cyclic ketones, and further studied the reactions of the corresponding imines and ketones with acrylamide.

The procedure used throughout this work involved stirring a molten mixture of the enamine, the imine, or the ketone (1 mole) and acrylamide (1·5—2·0 moles) in the presence of TsOH. For example, a mixture of β-tetralone pyrrolidine-enamine (I) and acrylamide was warmed at 80° for 1—1·5 h, followed by 30 min. heating at 130° to polymerize the excess of acrylamide. After cooling, the reaction mixture was treated with water, yielding (II),[2] which was collected, washed, dried, and recrystallized. This simple procedure afforded the results shown in the Table, using the enamines and the imines of cyclohexanone and α- and β-tetralones, and the ketones themselves.† The use of imines shows a distinct advantage over use of enamines.

	Yield % from:			ν_{max} ($CHCl_3$)	δ ($CDCl_3$)
	Enamine	Imine	Ketone		
(II)	75	85	52	3430 1682 1659	8·25 (1H br. NH) 7·1 (4H s. arom H)
(III)	20	54	trace	3410 1676	8·1 (1H br. NH) 7·3—7·0 (4H arom H
(IV)	83	77	0	3430 1665	



However, from the reaction of β-tetralone with acrylamide under similar conditions, the uncyclized N-acryloylenamine (V) was isolated in poor yield, along with the cyclized lactam (II). The yield of (V) was higher at lower temperatures (50° and 60°), while that of (II) was lower. Compound (V) was thermally unstable and decomposed without cyclization when heated at 80°—100° in the absence of TsOH, but cyclized to the lactam (II), though in poor yield, upon heating in the presence of TsOH.[3] The structure of (V) was confirmed by its spectral properties: i.r. ν_{max}; ($CHCl_3$) 3470(w), 1683(s), 1645(w), 1627(w), 1510(vs); n.m.r. δ ($CDCl_3$); 7·6 (1H, broad, NH), 7·2 (1H, olefinic H), 7·05 (4H, s, aromatic H), and 6·6—5·5 (3H, ABC type, $CH_2{=}CH{\cdot}CO$).

The results clearly suggest that the reaction of the enamine and the imine with acrylamide proceeds through the Michael-type adduct suggested by Stork,[1] whereas the N-acryloylenamine such as (V) could be involved as an intermediate in the ketone–acrylamide reaction.

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† All the products showed satisfactory analyses and spectral data.

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