

AN EFFICIENT METHOD FOR SYNTHESIS OF 1,1-DIARYLHYDRAZINES
AS AN INTERMEDIATE FOR INDOLE SYNTHESIS

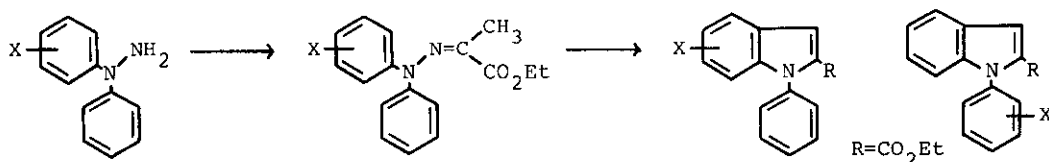
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Abstract—The Hofmann reaction of 1,1-diarylureas(2) to afford the corresponding hydrazines(3) is described.

Diarylamines(1) were converted to 1,1-diarylureas(2) with sodium cyanate and trifluoroacetic acid, or chlorosulfonyl isocyanate. The Hofmann reaction of 2 with alkaline sodium hypochlorite in ethanol successfully gave the corresponding hydrazines(3) in good yields. This method is especially effective for the preparation of easily reducible 1,1-diarylhydrazine derivatives.

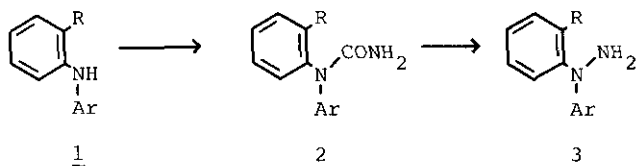
In the course of the studies on the mechanism of abnormal Fischer indolization¹⁾, we needed to carry out the Fischer indolization of 1,1-diarylhydrazones. However, all efforts²⁾ to synthesize some key intermediate 1,1-diarylhydrazines



by various methods were failed. This situation forced us to develop another novel route for preparing 1,1-diarylhydrazines.

Recently, O'Connor reported³⁾ a synthetic method of 1,1-diphenylhydrazine by a Curtius rearrangement of *N,N*-diphenylcarbonyl azide. However, in order to find an easier method, we examined the Hofmann reaction⁴⁾ of 1,1-diarylureas and obtained a satisfactory result. The Hofmann reaction of some mono-substituted ureas has been reported,⁵⁾ but no systematic report about 1,1-diarylureas.

Thus ureas(2) were prepared by the reaction of the corresponding amines(1)

Table I⁶⁾

a: R=methoxy, Ar=o-methoxyphenyl

b: R=H, Ar=phenyl

c: R=nitro, Ar=phenyl

d: R=H, Ar=α-naphthyl

starting materials	Urea derivatives (2) (yield, %)			Hydrazines (3)	
	method a ^{a)}	method b ^{b)}	mp	(yield, % from 2)	mp
<u>1a</u>	78.9	—	188.5-190°	85.0 % ^{c)}	89-91°
<u>1b</u>	66.9	—	196-197° ⁷⁾	62.0 ^{d)}	196-198° ³⁾
<u>1c</u>	6.2	66.4	186-188°	73.0 ^{d,e)}	180-181°
<u>1d</u>	50.3	—	185-186.5° ⁷⁾	62.8 ^{d)}	173-174.5°

a): NaOCN/CF₃CO₂H, b): ClSO₂NCO, c): hydrazone with ethyl pyruvate, d): salt with TsOH, e): Higher temperature (70-80°) was used for the reaction.

in benzene with sodium cyanate and trifluoroacetic acid.⁷⁾ However, since this method did not give satisfactory result in the case of 1c, a reaction with chlorosulfonyl isocyanate⁸⁾ was examined to give 2c in a moderate yield. These results were summarized in Table I.

The Hofmann reaction was carried out with alkaline aq. NaOCl in ethanol at room temperature for 1 to 2 hr. The yields and the identification of the hydrazines (3) in Table I were based on their hydrazone derivative or salts with TsOH.

General procedure for the Hofmann reaction of urea is as follows.

To an ice-cooling solution of an urea (2, 1.0 mmol) in ethanol (5 ml) was slowly added a mixture of 14 % aq. NaOH (1.5 ml) and aq. NaOCl (0.86 ml) containing 10.2 % active chlorine, and the resulted suspension (or solution) was stirred for 1 to 2 hr. at room temperature. After the reaction had been completed, the mixture was diluted with water, and then extracted with appropriate solvent to remove the amine (1) which formed as by-product. The aqueous layer was acidified with aq. HCl, then basified with aq. K₂CO₃, extracted with appropriate solvent, and dried over anhyd. K₂CO₃. The removal of solvent gave crude hydrazine (3), which was treated with ethyl pyruvate in ethanol to afford ethyl pyruvate [di(o-methoxyphenyl)-hydrazone] or with TsOH in a mixture of ether and benzene to afford TsOH salt.

The yields were good in all cases, and our method is especially effective for preparing easily reducible 1,1-diarylhydrazine. It should be noted that this procedure can be a general method of amination of 1,1-diarylamines to the corresponding hydrazines, which were difficult to be obtained even by the aminating reagents.^{2b)} Although there is only one report⁹⁾ on the Hofmann reaction of 1,1-disubstituted urea derivatives for preparing some triazanes, we would like to emphasize that this is the first synthetic study of the Hofmann reaction of 1,1-diarylureas, which is interesting from a point of view of the C-N bond migration. Application of our reaction for 1-alkyl-1-aryl- or 1,1-dialkylureas is now in progress in our laboratory.

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