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

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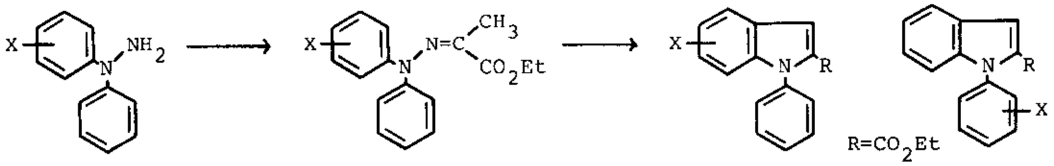
Abstract——The Hofmann reaction of 1,1-diarylureas(2) to afford the corresponding hydrazines(3) is described. Diarylamines(1) were converted to 1,1-diarylureas(2) with sodium cyanate and trifluoroacetic acid, or chlorosulfonyl isocyanate. The Hofmann reaction of 2 with alkaline sodium hypochlorite in 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.

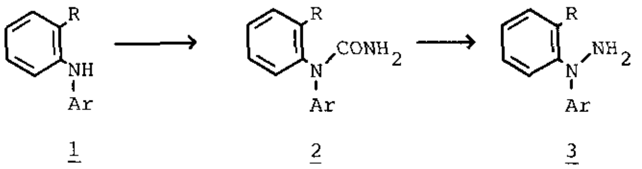
In the course of the studies on the mechanism of abnormal Fischer indolization[1)], we needed to carry out the Fischer indolization of 1,1-diarylhydrazones. However, all efforts[2)] to synthesize some key intermediate 1,1-diarylhydrazines by various methods were failed. This situation forced us to develop another novel route for preparing 1,1-diarylhydrazines.



Recently, O'Connor reported[3)] a synthetic method of 1,1-diphenylhydrazine by a Curtius rearrangement of N,N-diphenylcarbamoyl azide. However, in order to find an easier method, we examined the Hofmann reaction[4)] 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 I[6]



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, %) method a[a]	method b[b]	mp	Hydrazines(3) (yield,% from 2)	mp
1a	78.9	——	188.5-190°	85.0 %[c]	89-91°
1b	66.9	——	196-197°[7]	62.0[d]	196-198°[3]
1c	6.2	66.4	186-188°	73.0[d,e]	180-181°
1d	50.3	——	185-186.5°[7]	62.8[d]	173-174.5°

a):$NaOCN/CF_3CO_2H$, b):$ClSO_2NCO$, 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 isocyanate[8] 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 1 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.K_2CO_3, extracted with appropriate solvent, and dried over anhyd. K_2CO_3. 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 report[9)] 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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