Nucleophilic Ring Openings of 1-Aryl-3-methyl-1,3-diazetidine-2,4-diones

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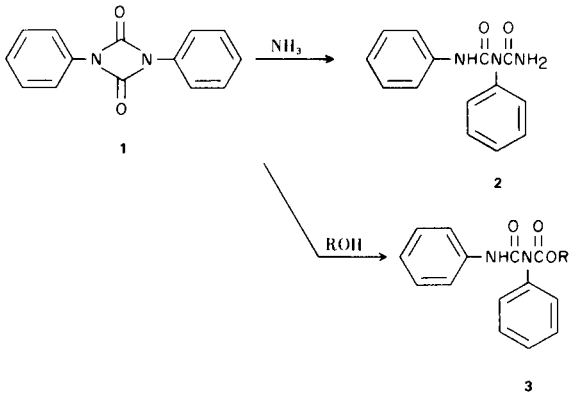
Sir:

Hoffmann noted as early as 1871 that the phenyl isocyanate dimer **1** is converted by ammonia into 1,3-diphenylbiuret (**2**) and by alcohols into 2,4-diphenyl-allophanates (**3**) (1). This reaction has since been utilized to prepare 1,3-disubstituted biurets from 1,3-symmetrically disubstituted-1,3-diazetidine-2,4-diones and ammonia and 1,3,5-trisubstituted biurets by the use of alkylamines in place of ammonia (1-6).



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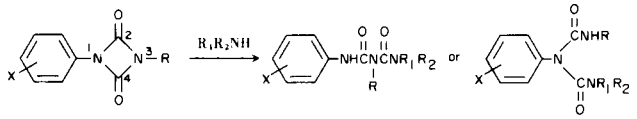
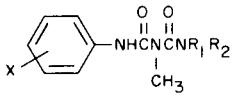
Unsymmetrical 1-aryl-3-alkyl-1,3-diazetidine-2,4-diones (**4**) are only a very recent synthetic development and nothing has been published about their reactions (7,8). In priniciple, the four membered ring of the unsymmetrical diazetidines **4** can be opened by amines at two locations, between positions 1 and 2 or 2 and 3, to give, respectively, the isomeric biurets **5** and **6** (9). We have found, however, that isomer **5** is the only biuret product



4, R = alkyl 5 6

TABLE I

1-Aryl-3-Methyl-5-Alkylbiurets (a)



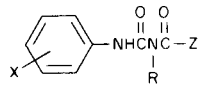
X	R_1	R_2	M.p., °C	Chemical Shifts δ in ppm (b) 3-⩾N-CH_3 (c)	5-NHCH_3 (d)
H	H	CH_3	93-95	3.25	2.78
4-Cl	H	CH_3	140-141	3.27	2.81
4-Br	H	CH_3	131-133	3.28	2.81
4-OCH_3	H	CH_3	104-106	3.26	2.80
4-NO_2	H	CH_3	219-220	3.31	2.84
3,4-$(Cl)_2$	H	CH_3	136-137	3.28	2.81
3-CF_3	H	CH_3	101-102	3.30	2.83
4-Cl	*n*-C_3H_7	*n*-C_3H_7	syrup	3.11	(e)

(a) Satisfactory C, H, and N analyses were obtained for each biuret; no attempts were made to optimize yields. (b) Spectra obtained at 60 MHz in acetone-d_6. (c) All absorptions are singlets. (d) Each absorption is a doublet with J = 4.5 cps. (e) The 5-N-$(C_3H_7)_2$ group had a triplet at 0.9 ppm (6H), a multiplet at 1.57 ppm (4H), and a quartet at 3.23 ppm (4H). Several of the diazetidines **4** prepared in this study are novel; the synthesis of these diazetidines will be published elsewhere.

isolated from the reaction of amines with the unsymmetrical diazetidines **4**. The biurets **5** were characterized by their nmr spectra and by comparison with authentic samples prepared from the reaction of anilines with allophanoyl chlorides. None of the isomeric biurets **6** could be detected in the nmr spectra of either the isolated product or the crude reaction product. The following procedure is illustrative.

A molar excess of 40% aqueous methylamine was added slowly to a stirred solution of 1-(4′-chlorophenyl)-3-methyl-1,3-diazetidine-2,4-dione (**4**, X = 4′-Cl, R = CH_3) (8) in acetonitrile at 25°. The mixture was then warmed to 50° for 10 minutes, cooled, concentrated *in vacuo*, and the solid obtained was recrystallized from ethyl acetate/*n*-hexane to give a 79% yield of 1-(4′-chlorophenyl)-3,5-dimethylbiuret (**5**, X = 4′-Cl, R = CH_3) (10). The nmr spectrum of this biuret (acetone-d_6) displayed a singlet at δ 3.27 ppm (3H) for the >N-CH_3 protons; a doublet at δ 2.81 ppm (3H, J = 4.5 cps) for the -NH-CH_3 methyl protons; an AA′BB′ multiplet at δ 7.18-7.70 ppm (4H) for the aryl protons, and broad absorptions at δ 7.02 and 11.55 ppm (1H each) for the >N-*H* absorptions. A mixed melting point of this biuret and that obtained from 4-chloroaniline and 2,4-dimethylallophanoyl chloride was undepressed. Additional biurets **5** prepared by this technique are summarized in Table I.

Other nucleophiles also open the diazetidines **4** primarily at the 1-2 linkage to give products generalized by **7**. Thus the methyl allophanate **7** (Z = CH_3O-, R = CH_3, X = H) was obtained by the reaction of 1-phenyl-3-



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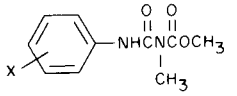
methyl-1,3-diazetidine-2,4-dione (8) with methanol in refluxing carbon tetrachloride in the presence of a catalytic amount of trimethylamine. The m.p. and nmr spectrum of this methyl allophanate were identical with those obtained for the allophanate prepared from the reaction of 2,4-dimethylallophanoyl chloride with methanol in pyridine. Table II summarizes various methyl allophanates prepared by this technique.

TABLE II

Methyl 2-Methyl-4-Arylallophanates (a)



X	M.p., °C	Chemical Shifts δ in ppm (b) 3-$>$N-CH_3 (c)	-OCH_3 (c)
H	60-61	3.20	3.73
4-Cl	132-134	3.27	3.87
3,4-$(Cl)_2$	140-141	3.25	3.88

(a) Satisfactory C, H, and N analyses were obtained for each allophanate. (b) Spectra obtained at 60 MHz in deuteriochloroform. (c) Each absorption is a singlet.

Acknowledgment.

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(9) H. Gehlenand and M. Just, *Ann. Chem.*, 692, 151 (1966), have reported that 1-(1,3,4-oxadiazole-2-yl)-3-phenyl-1,3-diazetidine-2,4-diones are opened by amines to give 1-(1,3,4-oxadiazole-2-yl)-3-phenyl-5-substituted biurets.

(10) This biuret has been reported by P. L. Salzberg, U. S. Patent, 3,189,431, June 15, 1965, assigned to E. I. duPont de Nemours and Co., but no physical data were reported.