ANIONIC HETERO[3,3]REARRANGEMENTS. *N*-ACYL-*N'*-ENYLHYDRAZINES TO PYRROLIDINONES

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Abstract-*N*-Acyl-*N'*-enylhydrazines rearrange upon treatment with base to afford 5-amino-2-pyrrolidinones. The rearrangement can be rationalized in terms of initial stereospecific [3,3]sigmatropic shifts of the enolates followed by intramolecular addition of the nitrogen atom of the amide group to the imino group.

The 3,4-diaza [3,3]sigmatropic rearrangement is important in the fields of synthetic and mechanistic organic chemistry.[1] Both aromatic and aliphatic versions of 3,4-diaza [3,3]sigmatropic shifts are well known. An example of the former is the first step in the conversion of *N*-aryl-*N'*-enylhydrazines to indole.[2] An example of the latter is the acid-catalyzed rearrangement of bis(enyl)hydrazine, derived from cyclohexanone and *N,N'*-dimethylhydrazine, to a pyrrole derivative.[3]

We previously reported anionic rearrangements of *N,O*-diacylhydroxylamines [4] and *N,N'*-diacylhydrazines [5] to succinic acid derivatives. The C-C bond-forming rearrangement can be rationalized in terms of hetero [3,3]sigmatropic shifts of dienolated precursors. These investigations indicate that the carboxamide enolate can be employed as a component of [3,3]sigmatropic rearrangement precursors. From the viewpoint described above, an *N*-acyl-*N'*-enylhydrazine enolate, corresponding to the *N*-aryl-*N'*-enylhydrazine intermediate in the Fischer indole synthesis, should undergo a similar [3,3]sigmatropic rearrangement. In this paper, we wish to report the facile anionic [3,3] sigmatropic rearrangement of *N,N'*-dimethyl-*N*-acyl-*N'*-enylhydrazines to afford the 5-methylamino-*N*-methyl-2-pyrrolidinones and related reactions.

N,N'-Dimethyl-*N*-acylhydrazines, readily available by partial acylation of *N,N'*-dimethylhydrazine, were transformed into *N,N'*-dimethyl-*N*-acyl-*N'*-enylhydrazines by condensation with suitable ketones in the presence of a catalytic amount of pyridinium *p*-toluenesulfonate in benzene at refluxing temperature. After purification by alumina column chromatography,[6] several *N*-acyl-*N'*-enylhydrazines in which the enyl group is stabilized by a neiboring phenyl group or a cyclic structure (**1**,**6**,**9** and **12**) were isolated as relatively stable liquid. These compounds were characterized chiefly by nmr spectral data.[7] When the *N*-phenacetyl-*N'*-cyclohexenylhydrazine (**1a**) was treated with 1.5 eq.of LDA at 0°C for 30 min and 20°C for 2 h in THF, the product isolated was a bicyclic compond (**2a**) as a single stereoisomer in a yield of 40 %. The structure was confirmed by ^{1}H- and ^{13}C-nmr and nuclear Overhauser experiments.[8] The other *N*-acyl-*N'*-enylhydrazines (**1b**,**6**,**9** and **12**) smoothly rearranged with the same conditions to give the corresponding 5-methylamino-*N*-methylpyrrolidinone derivatives (**2b**, **7**, **10**, **13**) in 41-64 % yields (Table 1).

The first step of the rearrangement can be rationalized in terms of [3,3]sigmatropic shifts of the transition state (**3**), which consists of E-enamine-Z-enolate, according to the Fischer reaction. However, the basic and mild conditions of the rearrangement suggests participation of the anionic character in a similar manner to the oxy-Cope rearrangement.[9] The resulting rearranged intermediate (**4**) is transformed to **2** by intramolecular addition of the nitrogen atom of the amide group to the imino group.

Scheme 1

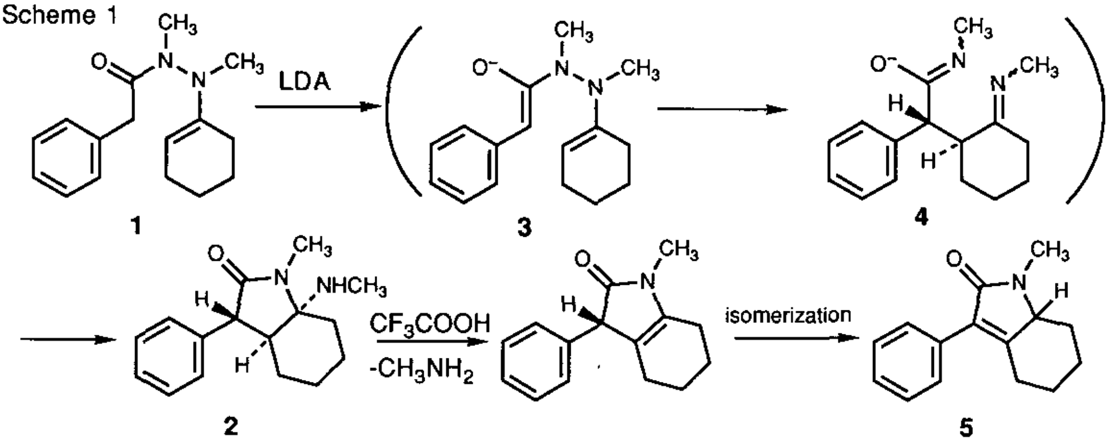
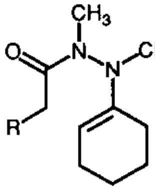
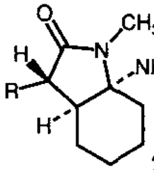
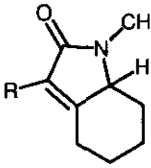
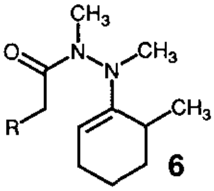
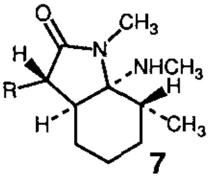
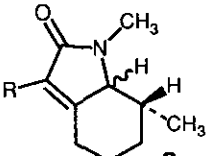
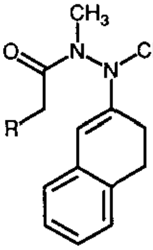
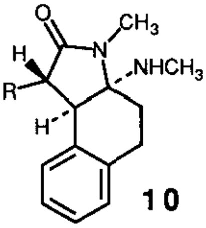
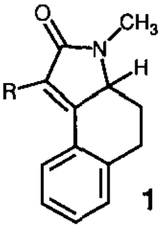
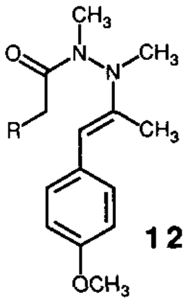
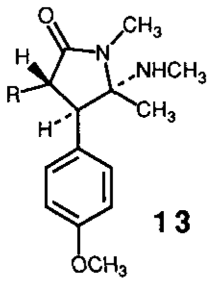
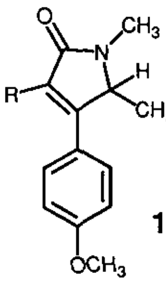
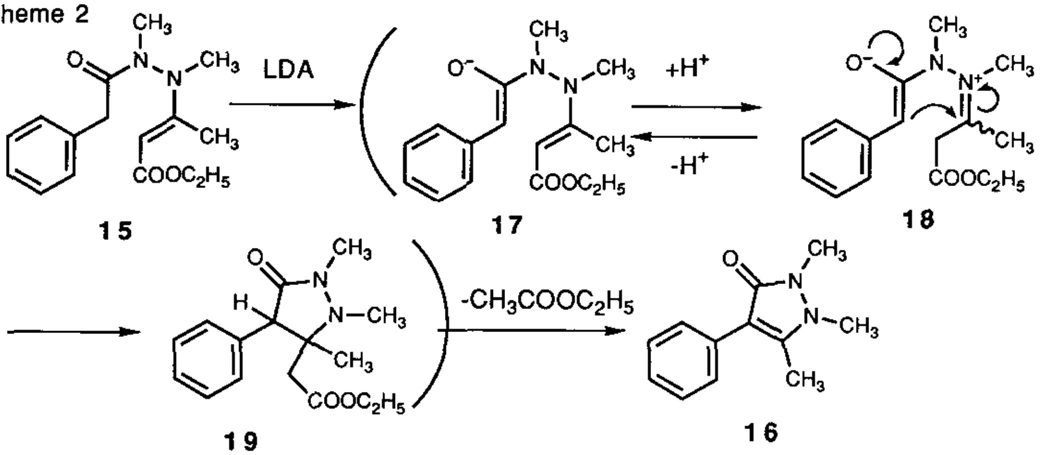


Table 1

N-Acyl-*N'*-enylhydrazine	Rearranged and Cyclized Product	Deaminated Product
 **1**	 **2** **a** R = C_6H_5 40% **b** R = CH_3 41%	 **5** **a** R = C_6H_5 79%
 **6**	 **7** **a** R = C_6H_5 42%	 **8** **a** R = C_6H_5 79% (α : β = 1 : 5)
 **9**	 **10** **a** R = C_6H_5 46% **b** R = CH_3 45%	 **11** **a** R = C_6H_5 82%
 **12**	 **13** **a** R = C_6H_5 64% **b** R = CH_3 43%	 **14** **a** R = C_6H_5 88%

Treatment of phenyl-substituted analogs of 5-methylamino-*N*-methyl-2-pyrrolidinones (**2a**, **7a**, **10a**, **13a**) with trifluoroacetic acid gave 2,5-dihydro-*N*-methylpyrrol-2-ones (**5a**, **8a**, **11a**, **14a**). The reaction can be explained by protonation at the methylamino group followed by elimination of methylamine to give a cationic intermediate, in which the relatively acidic proton between the phenyl and carbonyl groups is abstracted to give the products.

Scheme 2



Another reaction was observed in the case of the reaction of *N*,*N'*-dimethyl-*N*-phenacetyl-*N'*-enylhydrazine (**15**), derived from *N*,*N'*-dimethyl-*N*-phenacetylhydrazine and ethyl acetoacetate. Treatment of **15** with 1.5 eq of LDA in THF at 20°C for 2 h and 40°C for 2 h gave 1,2,5-trimethyl-4-phenylpyrrazol-3-one (**16**) in a yield of 32 %. The formation of **16** can be rationalized in terms of intramolecular addition of the carbon atom of the enolate to the iminium group in the transition state (**18**) followed by the elimination of ethyl acetate.

In conclusion, we have demonstrated the base-catalyzed 3,4-diaza [3,3]sigmatropic rearrangement of *N*-acyl-*N'*-enylhydrazines. The rearrangement is a new example of hetero [3,3]sigmatropic shifts and should be applicable to the synthesis of heterocycles.

REFERENCES AND NOTES

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6. The *N*-acyl-*N'*-enylhydrazines (**1**,**6**,**9** and **12**) were completely decomposed on a silica gel column and on tlc. The use of halogenated solvents should be avoided.

7. The measurements of nmr spectra were carried out employing CD_3OD as a solvent because the *N*-acyl-*N'*-enylhydrazines were decomposed in $CDCl_3$. The *N*-enyl structure is characterized by the olefinic proton at 4.5-5.5 ppm. The nmr spectral data of a representative product **1a** are given below. ^{1}H-Nmr (CD_3OD, 400 MHz): 1.50-1.70 (m, 4H), 1.80 (m, 2H), 2.08 (m, 2H), 2.58 (s, 3H), 2.79 (s, 3H), 3.73 (d, J= 14.3 Hz,1H), 3.89 (d, J=14.3 Hz,1H), 4.78 (t, J=4.0 Hz,1H), 7.20-7.30 (m, 5H); ^{13}C-nmr (CD_3OD, 100 MHz): 23.37 (CH_2), 23.93 (CH_2), 25.21 (CH_2), 26.41 (CH_2), 27.66 (CH_3), 38.17 (CH_3), 40.71 (CH_2), 104.49 (CH), 127.61 (Ar), 129.36 (Ar), 130.41 (Ar), 136.75 (Ar), 143.37 (C), 176.15 (C=O). The structure of **1a** is characterized by a vinylic carbon signal at 104.49 ppm.

8. The nmr spectral data of **2a** are given below. The stereochemistry of **2a** is supported by the nuclear Overhauser difference spectra of **2a**. Saturation of the proton signal at 2.30 ppm ($NHCH_3$) results in a characteristic enhancement of the proton signal at 2.37 ppm which is due to the 4-position of the pyrrolidinone. ^{1}H-Nmr ($CDCl_3$, 400 MHz): 1.40-1.80 (m, 8H), 2.30 (s, 3H), 2.37 (bd, 1H, J=11.8 Hz), 2.74 (s, 3H), 3.47 (d, 1H, J=11.8 Hz), 7.20-7.35 (m, 5H); ^{13}C-nmr ($CDCl_3$, 100 MHz): 20.55 (CH_2), 21.63 (CH_2), 21.80 (CH_2), 23.76 (CH_3), 27.32 (CH_3), 34.73 (CH_2), 42.56 (CH), 50.52 (CH), 76.50 (C), 126.92 (Ar), 128.74 Ar), 128.83 (Ar), 138.77 (Ar), 173.75 (C=O). The structure of **2a** is characterized by a quaternary carbon signal at 76.50 ppm.

9. S. Swaminathan, K. G. Srinivasan and P. S. Venkataramani, Tetrahedron, **1970**, 26, 1453; D. A. Evans and A. M. Golub, J. Am. Chem. Soc., **1975**, 97, 4765; L. A. Paquette, G. D. Crouse and A. K. Sharina, J. Am. Chem. Soc., **1982**, 104, 4411.

10. The nmr spectral data of a representative product **5a** are given below. ^{1}H-Nmr ($CDCl_3$, 400 MHz): 1.13 (dddd, J=3.3, 3.3, 12.1, 12.1 Hz,1H), 1.31 (ddddd, J=4.0, 4.0, 12.8, 12.8, 12.8Hz,1H), 1.53 (ddddd, J=3.3,3.3,13.5,13.5,13.5Hz1H), 1.92 (bd,J=13.5Hz,1H), 1.98 (m,1H), 2.26 (ddd, J=4.0,4.0, , 14.6 Hz,1H), 3.71 (dd, J=5.5, 11.5 Hz,1H), 7.32 (t, J=7.3 Hz,1H), 7.41 (t, J=7.3 Hz 2H), 7.48 (d, J=7.3Hz,2H).

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