Tetrahedron Letters, Vol.32, No.35, pp 4517-4520, 1991
Printed in Great Britain

0040-4039/91 $3.00 + .00
Pergamon Press plc

ANIONIC 3,4-DIAZA[3,3]SIGMATROPIC REARRANGEMENTS OF N,N'-DIACYLHYDRAZINES

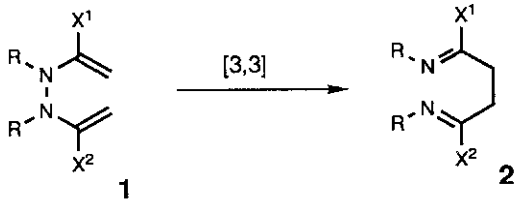
Yasuyuki Endo* and Koichi Shudo

Faculty of Pharmaceutical Sciences, University of Tokyo,
7-3-1, Hongo, Bunkyo-ku, Tokyo, 113 Japan

Summary: N,N'-Diacylhydrazines rearrange under basic conditions to afford 1,2-disubstituted succinamides. The rearrangement can be rationalized in terms of [3,3]sigmatropic shifts of biscarboxamide enolates.

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 (**1**, **2**, X=H,C). An example of the former is the first step in the conversion of 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]

Scheme 1



1 **2**

Compared with the utility of carboxylic ester enolates in a wide variety of synthetic processes, applications of carboxamide enolates in synthetic reactions have been reported in a few cases, i.e., simple α-alkylation of carboxamides,[4] and asymmetric synthesis of α-amino acids.[5] In the case of [3,3]sigmatropic rearrangement, ester enolates have been utilized for rearrangement of allylic ester to α-allylcarboxylic acid by Ireland and Mueller.[6] From the viewpoint of preparing rearrangement precursors, N,N'-diacylhydrazine dienolates (**1**, X=O^-) seem to be widely applicable.

We wish to report the facile anionic [3,3]sigmatropic rearrangement of N,N'-dialkyl-N,N'-diacylhydrazines (**3**) to afford the 1,2-disubstituted N,N'-dialkylsuccinamides(**4** and **5**).

Scheme 2

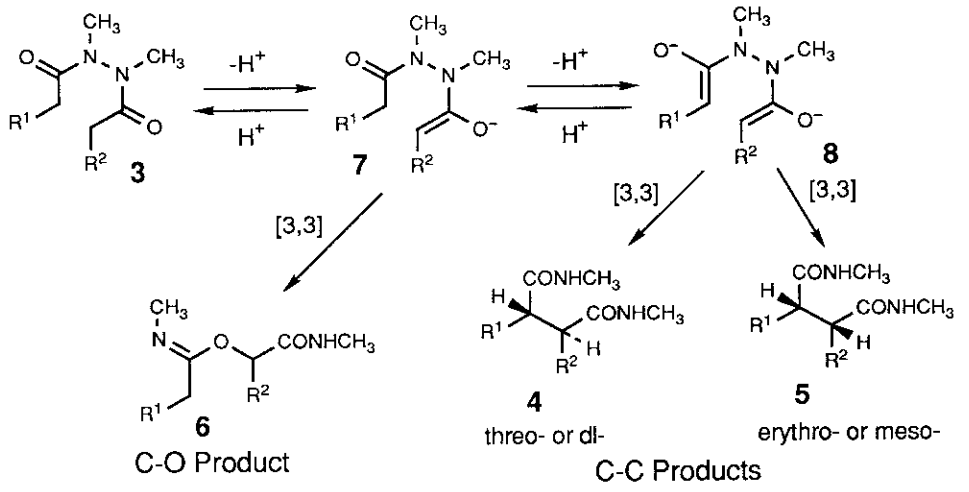


Table 1. Anionic [3,3]Rearrangement of N,N'-Dimethyl-N,N'-diacylhydrazines

	R^1	R^2	Conditions[a]	Yield (%)[b]	
				C - C product (threo **4** :erythro **5**)	C - O product **6**
a	Ph	Ph	A	50 (4:1)	19
b	Ph	H	B	44	29
c	Ph	CH_3	B	41(3:1)	19
d	Ph	$CH{=}CH_2$	A	42(4:1)	10
e	Ph	SCH_3	C	34(3:1)[c]	15
f	Ph	SPh	C	41(4:1)	17
g	Ph	$-S(CH_2)_4S-$	C	51	10
h	$CH{=}CH_2$	$CH{=}CH_2$	C	45(6:1)	
i	$CH{=}CH_2$	H	B	20	
j	SPh	H	B	12[d]	19
k	CH_3	CH_3	B[e]	12(3:1)	10

[a]All starting materials were enolized with LDA at -78°C in THF and the reaction mixture required an additional 30 min for the temperature to rise from -78°C to the indicated as follows. Condition A : 2.5 eq. LDA, 0°C 1 h, 20°C 1.5 h; Condition B : 5.0 eq. LDA, 20°C 5 h; Condition C: 5.0 eq. LDA, 0°C 3h.

[b]Yields are isolated yields.

[c]The erythro product was isolated as N,N'-dimethyl-phenyl-maleinamide.

[d]The isolated product was N,N'-dimethylmaleinamide.

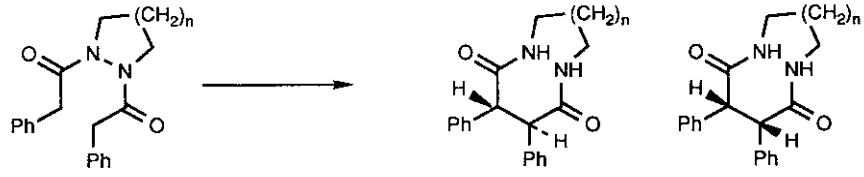
[e]Toluene was used as the solvent.

Treatment of N,N'-dimethyl-N,N'-diphenacetylhydrazine (**3a**) with 2.5 eq. of LDA at 0°C for 1 h and then at 20°C for 1.5 h in THF gave two C-C products (**4a** and **5a**) in 49% yields (threo: erythro 4:1) and a C-O product (**6a**) in a 19% yield. Results on the substituent effects for R^1 and R^2 are listed in Table 1. The N-phenacetylhydrazine derivatives (R^1=Ph, **3a-3g**) rearranged smoothly to give C-C products (**4** and **5**) in 34-51 % yields accompanied with C-O products (**6**).

The presence of a phenyl group enhances the thermodynamic acidity of an adjacent proton by 10^7 over a simple alkane.[7] Similarly, a vinyl group and a sulfenyl group enhance the acidities of adjacent protons by 5 and 3 pK units, respectively.[8,9] The yields of the C-C products seem to reflect the extent of stabilization by substituents α to carbonyl groups (**3h-3j**). A substituent poorly stabilizing the α-carbanion caused a low yield of the C-C products (**3k**).[10] The structures of the C-O products (**6**) indicate that the oxygen atoms of acyl groups forming a less stable carbanion rearrange to the other enolates.

The present rearrangement is applicable to a conversion of cyclic hydrazine diacylate to medium membered lactam. Treatment of hexahydropyridazine[11] bisphenylacetate (**10**) with 2.5 eq. of LDA at 50°C for 3 h in THF gave two 10-membered lactams (**12** and **13**) in 48 % yields (dl:meso 3:1). Similarly, **11**[12] rearranged to give 11-membered lactams in 64 % yields (**14** and **15** 4:1). But, no rearranged product was obtained from tetrahydropyrazole bisphenylacetate (**9**).

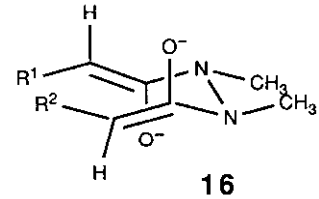
Scheme 3



n = 1 **9**
n = 2 **10**
n = 3 **11**

n = 2 48% **12 : 13** (3 : 1)
n = 3 64% **14 : 15** (4 : 1)

Scheme 4



16

This result is expected from the usual chair model for the cyclic six-centered transition state, such as **16**.[13] The transition state from **9** could be disadvantageous to [3,3] rearrangement because of the rigid 5-membered ring conformation. The stereochemistry of C-C products (threo: erythro 3:1-6:1) is evidence for preferential formation of the Z,Z-enolates **16** compared to E,Z-enolates. The assignment of the enolate stereochemistry is also consistent with a chairlike transition state, taking into account the steric effects in the two transition states.

Although the product yields in these 3,4-diaza[3,3]-rearrangements are moderate, the mild conditions and the ready availability of substrates suggest that carboxamide enolates will be useful in various synthetic applications.

REFERENCES AND NOTES

1. For reviews, see Lutz,R.P., Chem.Rev., **1984**, 84, 205; Heimgartner,H., Hansen,H.-J., Schmid,H., 3,3-Rearrangement of Iminium Salts, In Advances in Organic Chemistry vol 9, part 2, Iminium Salts in Organic Chemistry", Eds. Bohme,H., Viehe,H.G., John Wiley and Sons, New York 1979.
2. This mechanism was proposed by Robinson,G.M., and Robinson,R., J.Chem.Soc., **1918**, 639; For a monograph, see Sundberg,R.J., "The Chemistry of Indoles", pp142-163, Academic Press, New York, 1970
3. Sucrow,W., Chondomatidis,G., Chem.Ber.,**1970**, 103, 1759; Sucrow,W., Bethe,H., Chondromatidis,G., Tetrahedron Lett., **1971**, 1481
4. Gay,R.L., Hauser,C.R., J.Am.Chem.Soc., **1967**, 89, 1647; Trost,B.M., Kunz,R.A., J.Org.Chem., **1974**, 39, 2475; Deslongchamps,P., Cheiyan,U.O., Patterson,D.R., Can.J.Chem., **1975**, 53, 1682
5. Naef,R., Seebach,D., Helv.Chim.Acta., **1985**, 68, 135; Evans,D.A., J.Am.Chem.Soc., **1986**, 108, 6755; Ikegami.S., Hayama,T., Katsuki,T., Yamaguchi,M., Tetrahedron Lett., **1986**, 27, 3403
6. Ireland,R.E., Mueller,R.H., J.Am.Chem.Soc., **1972**, 94, 5897; For a review, see Ziegler,F.E., Chem.Rev., **1988**, 88, 1423
7. Streitwieser,A., Granger,M.R., Mares,F., Wolf,R.A., J.Am.Chem.Soc., **1973**, 95, 4257
8. Boerth,D.W., Streitwieser,A., J.Am.Chem.Soc., **1981**, 103, 6443
9. Coates,R.M., Pigott,H.D., Ollinger,J.,Tetrahedron Lett., **1974**, 3955
10. According to the analogy with the aliphatic Claisen rearrangement, it seemed advantageous to quench the carboxamide dienolates at low temperature with chlorotrimethylsilane before warming. However, in the present case, after treatment of **3k** with 2.5 eq. of LDA at -30°C for 30 min, chlorotrimethylsilane was added to the solution, and the solution was heated to 60°C for 4h to give no C-C products.
11. Groszkowski,S., Wrona,J., Pol.J.Chem., **1982**, 56, 1131
12. Hexahydro-1H-1,2-diazepine monohydrochloride was prepared following the procedure described in ref. 10.
13. Hansen,H.J., Schmid,H., Tetrahedron, **1974**, 30, 1959; Perrin,C.L., Faulkner,D.J., Tetrahedron Lett., **1969**, 2783

(Received in Japan 26 April 1991)