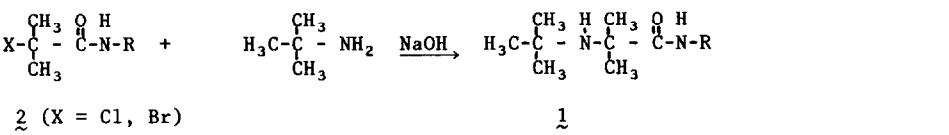
Tetrahedron Letters,Vol.23,No.6,pp 595-598,1982 0040-4039/82/060595-04$03.00/0
Printed in Great Britain

HINDERED AMINES.[1] GENERAL SYNTHESIS OF α-(TERT-BUTYLAMINO)-ISOBUTYRAMIDES

John T. Lai
BFGoodrich Co., R&D Center
9921 Brecksville Rd., Brecksville, OH 44141

ABSTRACT: α-(tert-Butylamino)-isobutyramides (1) can be prepared from α-haloisobutyramides (2) and tert-butylamine with sodium hydroxide in Favorskii-like reactions.

Hindered amines are very useful compounds.[2] We are interested in finding new routes for making hindered amines because of their ability to stabilize polymers against ultraviolet light.[3] In this paper, we would like to report a general synthesis of α-(tert-butylamino)-isobutyramides (1) from α-haloisobutyramides[4] (2) and tert-butylamine with sodium hydroxide as the base:



(1)

2 (X = Cl, Br) 1

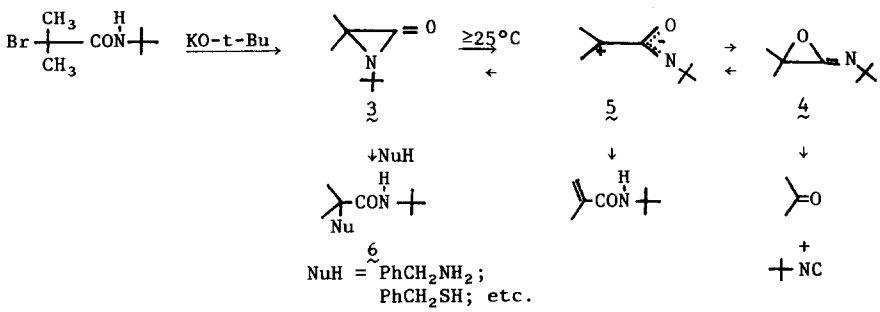
It is interesting to note that phase-transfer catalysts do not accelerate the reaction. Sodium hydroxide in powder form is more efficient than the 50% aqueous solution. The following illustrates a typical procedure: α-haloisobutyramide (2) (5 mmole) and tert-butylamine (100 mole) were mixed and cooled in a water-bath. Powdered sodium hydroxide (10 mmole) was added in small portions in 5 minutes and the reaction was refluxed under argon till the conversion was complete as indicated by gas chromatograph. Dilution with water, extraction with solvent, drying, concentration and recrystallization afforded the product (1) in very pure form.

TABLE I
Synthesis of 1

Compound[a]	X	R	Time(hr)[b]	Yield(%)[c]	mp (bp), °C
1 a	Cl	Ph	2	74	77.5-9
b	Br	Ph	1	65	77-9
c	Cl	$-CH_2CH_2-$	3	74	93-6
d	Br	$-CH_2CH_2-$	2	80	96.5-8.5
e	Br	t-Bu	4(7)	65	70-2[d]
f	Br	H	2	55	110.5-3
g	Br		6(20)	74	139-41
h	Cl	n-Pr	7(15)	71	(125-7/5 torr)

a. all new compounds have correct spectral data and acceptable elemental analysis.
b. powdered NaOH (50% NaOH)
c. of isolated products
d. ref.[7] 68-70°C

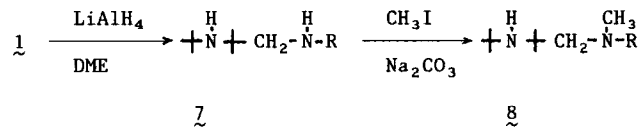
In earlier reports,[8] N-tert-butyl-α-isobutyramide underwent Favorski-type elimination with potassium tert-butoxide to form the α-lactam (3) which could be isolated at 0°C. At ambient or higher temperature, 3 rearranges to its valence tautomer, the imino-α-lactone (4), followed by rapid decomposition to the isonitrile and ketone, presumably through an open-chain intermediate 5, or its delocalized form.



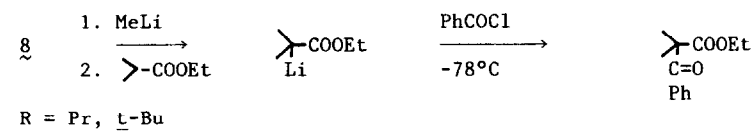
The α-lactam (3) could react with nucleoplic reagents to form the α-substituted-isobutyramides 6, although tert-butylamine was never employed as the nucleoplile.[9]

We believe a similar mechanism is involved in reaction (1), with 5 as the more likely reactive species which was trapped by tert-butylamine.

Compound 1 can be reduced with 2-5 molar equivalent of lithium aluminum hydride in refluxing dimethoxyethane to afford the β-aminosubstiuted di-tert-butylamine derivatives (7). The less hindered amino group in 7 can be selectively methylated with methyl iodide - a.q. sodium carbonate solution.



The lithium salts of 8 (R = n-Pr, t-Bu) act almost identically as lithium 2,2,6,6-tetramethylpiperidinide[10] in the deprotonation of ethyl isobutyrate:



The aforementioned new synthesis of α-(tert-butylamino)-isobutyramides offers the advantage over the one we described earlier[7] since an R group different than the tert-butyl group can be placed in 1. We are currently exploring the possibility that lithium salts of 8 are stronger bases than the lithium salts of either tetramethylpiperidine or di-tert-butylamine.[11]

ACKNOWLEDGMENT

The author wishes to thank Prof. Leo Paquette of Ohio State University for useful discussions and Mr. Craig Krieger for his laboratory work.

REFERENCES AND NOTES

1. Part 5 of a series. For Part 4, see J. T. Lai, Synthesis, in press.

2. I. E. Kopka, Z. A. Fataftah and M. W. Rathke, J. Org. Chem., 45, 4616 (1980) and references cited therein.

3. "Developments in Polymer Stabilization - I", Scott, G. Ed., Chapters 7 and 8. Applied Science Publishers, London, 1979.

4. α-Chloroisobutyramides were prepared from amidation of α-chloroisobutyric acid[5] through the acyl chloride while α-bromoisobutyramides were prepared from α-bromoisobutyryl bromide.[6]

5. Y. Ogata, et al., J. Org. Chem., 40, 2960 (1975).

6. G. W. Smith and D. G. Norton, Org. Syn. Coll. Vol. V, p. 348.

7. J. T. Lai, J. Org. Chem., 45, 3671 (1980).

8. I. Lengyel and J. C. Sheehan, Angew Chem. Internat. Ed., 7, 25 (1968) and references cited therein.

9. tert-Butylamine did react with 2e to yield 1e when potassium tert-butoxide was used as the base.

10. R. A. Olofson and C. M. Dougherty, J. Am. Chem. Soc., 95, 581 (1973).

11. M. W. Rathke and R. Kow, J. Am. Chem. Soc., 94, 6854 (1972).

(Received in USA 15 October 1981)