many, and the assistance of Mr. William Foxenberg and Wade Nasholds in the preparation of 6-allyl-2-piperidone.

Registry No. 2a, 73789-08-9; **2b**, 73789-09-0; **3**, 74282-88-5; **4**, 55038-60-3; *cis*-**5**, 74282-89-6; *trans*-**5**, 74282-90-9; *cis*-**6**, 74282-91-0; *trans*-**6**, 74282-92-1; **7**, 60924-91-6; **8**, 4868-25-1; **9**, 71203-69-5; **10**, 71203-75-3; **11**, 74282-93-2; **12**, 74282-94-3; **13**, 42988-47-6; **14**, 74282-95-4; *cis*-**15**, 74282-96-5; *trans*-**15**, 74282-97-6; *cis*-**16**, 74282-98-7; *trans*-**16**, 74282-99-8; **17**, 74283-00-4; **18**, 74283-01-5; **19**, 74298-03-6; *cis*-**20**, 74283-02-6; *trans*-**20**, 74283-03-7; **21**, 74283-04-8; **22**, 74298-04-7; **23**, 74283-05-9; **24**, 74283-06-0; **25**, 74283-07-1; **26** isomer 1, 74283-08-2; **26** isomer 2, 74283-09-3; **27** isomer 1, 74283-10-6; **27** isomer 2, 74311-05-0; **28**, 74283-11-7; **29**, 74283-12-8; **30**, 74283-13-9; **31**, 74283-14-0; **32**, 74283-15-1; **33**, 74283-16-2; **34**, 74283-17-3; dimethyl carbonate, 616-38-6; 6-methyl-6-hepten-2-one, 10408-15-8; bromoacetone, 598-31-2; 2-(carbomethoxy)-2-(4-pentenyl)cyclopentanone, 74283-18-4; 2-(carbomethoxy)cyclopentanone, 53229-93-9; 1-iodo-4-pentene, 7766-48-5; 3-bromofuran, 22037-28-1.

Hindered Amines. Synthesis of Hindered Acyclic α-Aminoacetamides[1]

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Received February 14, 1980

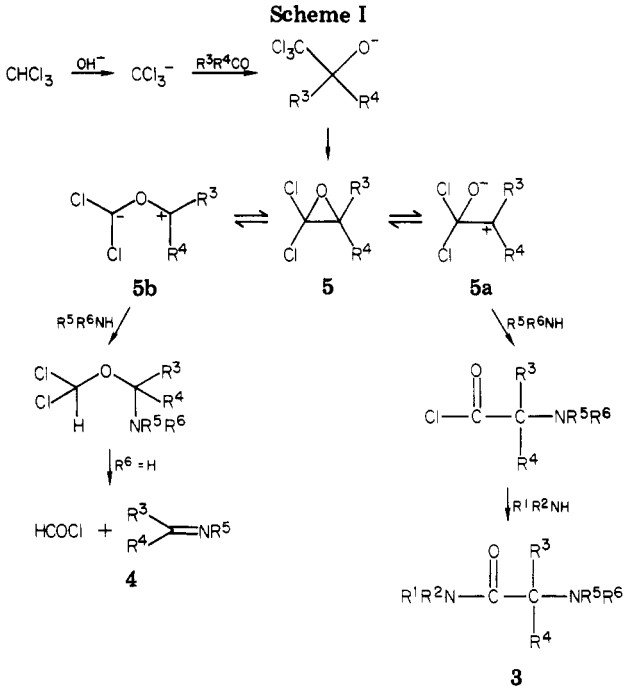
Hindered amines and their nitroxyl radicals are useful in spin-label studies as nonnucleophilic bases and as stabilizers for polymers against UV degradation. Hindered acyclic α-aminoacetamides (**3**, R^5 = aryl, *tert*-butyl; R^6 = H) can be synthesized from amines, ketones, and chloroform with 50% sodium hydroxide solution in phase-transfer-catalyzed reactions. Nucleophilic secondary amines will undergo the same reactions while bulky ones fail. Mixed **3** can be prepared from different amines according to their nucleophilicities. 1,1-Dialkyl-2,2-dichlorooxirane (**5**) is believed to be the reactive intermediate. Imines are sometimes formed as byproducts through the opening of a carbon–carbon bond in the oxirane ring by amines. Thus, *tert*-butylcyclohexylamine (**7**) is obtained in 62% yield after hydrogenation of the crude imine from *tert*-butylamine, cyclohexanone, and chloroform.

Hindered amines are versatile compounds. Their lithio salts attract considerable synthetic interest as strong and nonnucleophilic bases.[2] Their nitroxyl radicals have been used extensively as spin labels in biological studies.[3] Their *N*-chloro derivatives regioselectively chlorinate alkanes at the 2-position in acidic media.[4] Industrially, hindered amines are able to prolong polymer life against UV light.[5] We described[1a] a novel synthesis of 1,3,3,5,5-pentasubstituted 2-piperazinones from N^1,2,2-trisubstituted 1,2-ethanediamines, chloroform, and ketones in phase-transfer-catalyzed (PTC) reactions.[6] We now report the synthesis of several types of acylic hindered amines (**3**) by extending these reactions to monoamines (**1** and **2**), chloroform, and ketones under similar conditions.

$$\underset{\mathbf{1}}{R^1R^2NH} + CHCl_3 + R^3R^4CO + \underset{\mathbf{2}}{R^5R^6NH} \xrightarrow[NaOH]{PTC} \underset{\mathbf{3}}{R^1R^2NC(O)CR^3R^4NR^5R^6}$$

When aniline and its para-substituted derivatives (**1**, **2** = substituted anilines) are subjected to these reaction conditions, α-anilinoacetanilide derivatives[7] (**3a–e**) are formed in generally good yields. However, when *o*-toluidine or ketones other than acetone are used, a large amount of Schiff bases[8] (**4f–h**) is observed in addition to

Scheme I



(1) (a) Part 2 of a series; for part 1, see: Lai, J. T. *J. Org. Chem.* **1980**, *45*, 754. (b) Presented in part at the 179th American Chemical Society National Meeting, Phase Transfer Catalysis Symposium, Houston, TX, March 25, 1980.

(2) (a) Olofson, R. A.; Dougherty, C. M. *J. Am. Chem. Soc.* **1973**, *95*, 581, 582. (b) Olofson, R. A.; Lotts, K. D.; Barber, G. N. *Tetrahedron Lett.* **1976**, 3779 and references cited therein.

(3) (a) "Spin Labelling, Theory and Applications"; Berliner, L. J., Ed.; Academic Press: New York, 1976. (b) Roaztsev, E. G. "Free Nitroxyl Radicals"; Plenum: New York, 1970.

(4) Deno, N. C.; Gladfelter, E. J.; Pohl, D. G. *J. Org. Chem.* **1979**, *44*, 3728.

(5) "Developments in Polymer Stabilization - I"; Scott, G., Ed.; Applied Science Publishers: London, 1979; Chapters 7 and 8.

(6) (a) Weber, W. P.; Gokel, G. W. "Phase Transfer Catalysis in Organic Synthesis"; Springer-Verlag: New York, 1977. (b) Stark, C. M.; Liotta, C. "Phase Transfer Catalysis: Principles and Techniques"; Academic Press: New York, 1978.

(7) α-Anilinoacetanilide (**3a**) was reportedly prepared in ~20% yield from aniline and α-(trichloromethyl)-2-propanol in alcoholic potassium hydroxide solution: Banti *Gazz. Chim. Ital.* **1929**, *59*, 819; *Chem. Abstr.* **1930**, *24*, 1632.

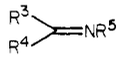
(8) These Schiff bases are identical in spectroscopic data with the ones prepared with molecular sieves as catalyst: (a) Taguchi, K.; Westheimer, F. *J. Org. Chem.* **1971**, *36*, 1570; (b) Kyba, E. P. *Org. Prep. Proced.* **1970**, *2*, 149.

0022-3263/80/1945-3671$01.00/0

Table I. Synthesis of $R^1R^2NC(O)CR^3R^4NR^5R^6$ (3)

product	R^1	R^2	R^3	R^4	R^5	R^6	mp or bp (mm), °C	yield, %
3a	Ph	H	Me	Me	Ph	H	157-159	85
b	*p*-ClPh	H	Me	Me	*p*-ClPh	H	139-141	65
c	*p*-MePh	H	Me	Me	*p*-MePh	H	125-127	87
d	*p*-OEtPh	H	Me	Me	*p*-OEtPh	H	128-130	100
e	*o*-MePh	H	Me	Me	*o*-MePh	H	140-142	70
f	Ph	H	$(CH_2)_5$		Ph	H	135-138	35
g	*o*-MePh	H	Me	Et	*o*-MePh	H	118-120	40
h	*o*-MePh	H	Me	*i*-Bu	*o*-MePh	H	91-93	35
i	Me	Me	Me	Me	Me	Me	86-87 (3)	85
j	Me	Me	Me	Ph	Me	Me	115-116 (1.1)	84
k	Me	Me	Me	Et	Me	Me	102-105 (15)	57
l	$CH_2CH_2OCH_2CH_2$		Me	Me	$CH_2CH_2OCH_2CH_2$		56-59	75
m	Et	Et	Me	Me	Ph	H	151-152	65
n	Et	Et	Me	Me	*o*-MePh	H	77-79	41
o	*n*-Bu	*n*-Bu	Me	Me	Ph	H	105-107	49
p	Et	Et	Me	Me	*p*-OEtPh	H	83-86	55
q	Et	Et	Me	Me	*p*-MePh	H	124-127	81
r	*t*-Bu	H	Me	Me	*t*-Bu	H	68-70	45
s	*t*-Bu	H	Me	Ph	*t*-Bu	H	104-105 (0.2)	51
t	*t*-Bu	H	Me	Et	*t*-Bu	H	107-108 (0.9)	10

3f–h. Without chloroform or the catalyst, little or no 4 could be detected.



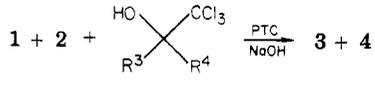
4

When nucleophilic and nonbulky secondary amines (e.g., Me_2NH or morpholine) are used in place of aniline derivatives under similar conditions, the "normal" products, α-dialkylamino-α,α-dialkyl-*N*,*N*-dialkylacetamides (**3i–l**) are isolated. However, larger amines (i.e., 1 and 2 = Et_2NH or larger) will totally retard the formation of **3**, presumably due to the steric hindrance encountered between the amine and the dialkyl carbon in the oxirane intermediate **5**. This finding led to the synthesis of the mixed α-anilino-α,α-dialkyl-*N*,*N*-dialkylacetamides (**3m–q**) from a mixture of the aforementioned bulky secondary amines (1 = dialkylamine) used in excess and the substituted anilines (2 = $ArNH_2$). The aniline opens the oxirane **5** by cleaving the dialkyl carbon–oxygen bond followed by attack of the secondary amine at the resulting acyl chloride (see Scheme I).

Finally, when a large excess of *tert*-butylamine is employed in the reaction, it affords a fair yield of α-(*tert*-butylamino)-α,α-disubstituted-*N*-*tert*-butylacetamides (**3r** and **s**) when acetone or acetophenone is used as the ketone while imine (4, R^5 = *tert*-butyl) formation predominates when 2-butanone or cyclohexanone is used. The overall reaction mechanisms are proposed in Scheme I.

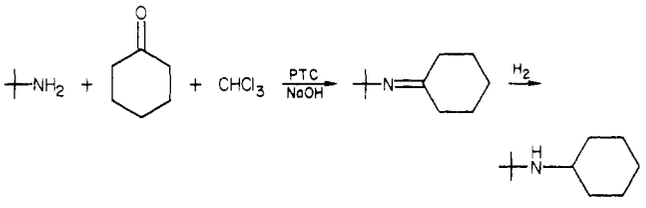
Normally, breaking of the C–O bond in 5[9] (i.e., **5a**) predominates because of the better charge separation. But when steric hindrance becomes a factor in the reaction pathway, cleavage of the C–C bond in **5** (i.e., **5b**) becomes important since this reduces the steric interactions among the substituents on the two oxirane carbons in **5** and the incoming amine.

When α-(trichloromethyl)-2-alkanols (**6**) react with different amines under similar PTC conditions, the same products **3** and **4** are obtained.



6

Cyclohexanone, chloroform, and *tert*-butylamine give a 62% yield of *N*-*tert*-butylcyclohexylamine 7[10] after hydrogenation of the crude imine. The synthetic use of the lithio salt of **7** has been reported in the literature[11] as a nonnucleophilic base while the lithio salt of other hindered amines, including 2,2,6,6-tetramethylpiperidine, showed nucleophilic character.



7

We believe this reaction route offers a preferred alternative for preparing compounds such as **7**. Investigations are under way to further expand the synthetic methodology and to explore the applications of these new hindered amines.

Experimental Section

The spectrometers and solvent used were the following: ^1H NMR, Varian A60 ($CDCl_3$, Me_4Si as internal standard); IR, Perkin-Elmer 467; (KBr pellet for solid, neat for oil); mass spectra, Varian MAT 311A. Boiling points were not corrected. Melting points were obtained on a Melt-Temp apparatus from Laboratory Devices, Cambridge, MA, and were not corrected. Microanalyses were performed by the Huffman Laboratories, Wheatridge, CO, or BFGoodrich Company, Avon Lake Technical Center.

General Procedure for Preparing 3a–h and 4f–h. In a cooled 500-mL three-neck flask were placed the aniline derivatives (0.2 mol), the ketone (0.3 mol), chloroform (0.3 mol), 100 mL of CH_2Cl_2, and benzyltriethylammonium chloride (BTEAC, 0.005 mol). With stirring, 50% aqueous NaOH (1.0 mol) was added dropwise to keep the temperature below 5 °C and the reaction was stirred at 5 °C overnight. Water was added to dissolve the solid and the two layers were separated. The aqueous layer was extracted twice with 50 mL of CH_2Cl_2 and the combined organic layers were washed once with 20 mL of H_2O, dried over Na_2SO_4, and concentrated. The residue was stirred with cold hexanes, filtered, and rinsed with hexanes to afford white powders which proved to be pure **3** by GC and ^1H NMR. The hexanes filtrate

(9) This dichlorodialkyloxirane intermediate was proposed before; cf.: (a) Kuhl, P.; Muhlstadt, M.; Graefe, J. *Synthesis* **1976**, 825; (b) Weizman, Ch.; Sulzbacher, M.; Bergman, E. *J. Am. Chem. Soc.* **1948**, *70*, 1153.

(10) (a) Girault-Vexlearschi, G. *Bull. Soc. Chim. Fr.* **1956**, 582. (b) Stowell, J. C.; Padegimas, J. J. *Synthesis* **1974**, 127.

(11) Lowenthal, H.; Schatlmiller, S. *J. Chem. Soc., Perkin Trans. 1* **1976**, 944.

could be concentrated and distilled to isolate pure **4f-h**. The yields of 4 were better if powdered NaOH was used.

General Procedure for Preparing α-Dialkylamino-α,α-dialkyl-*N*,*N*-dialkylacetamides (3i-e). Dimethylamine (either 40% aqueous solution or neat) or morpholine (0.4 mol), the ketone (0.2 mol), chloroform (0.1 mol), and BTEAC (0.005 mol) were mixed and cooled while 50% NaOH (0.5 mol) was added as described before. The reaction mixture was worked up in the same manner and the residue was either washed with hexanes to collect the solid or distilled.

General Procedure for Preparing α-Anilino-α,α-dialkyl-*N*,*N*-dialkylacetamides (3m-q). The aniline derivative (0.1 mol), the dialkylamine (0.4 mol), acetone (0.2 mol), chloroform (0.15 mol), BTEAC (0.005 mol), and 100 mL of CH_2Cl_2 were placed in the flask and 50% NaOH (0.5 mol) was added dropwise to keep the reaction temperature below 5 °C as described before. The reaction mixture was worked up in the usual manner.

General Procedure for Preparing α-(*tert*-Butylamino)-α,α-disubstituted-*N*-*tert*-butylacetamines (3r-t). *tert*-Butylamine (1.0 mol), chloroform (0.1 mol), the ketone (0.15 mol), BTEAC (0.005 mol), and 50% NaOH (0.5 mol) were used in the same procedure as described before. The products were distilled.

***N*-*tert*-Butylcyclohexylamine (7).** *tert*-Butylamine (58.5 g, 0.8 mol), cyclohexanone (14.7 g, 0.15 mol), chloroform (11.9 g, 0.1 mol), and BTEAC (1.14 g, 0.005 mol) were mixed and cooled. Powdered NaOH (20.0 g, 0.5 mol) was added in small portions to keep the temperature below 5 °C. After 2 h, the mixture was filtered and the solid was washed thoroughly with hexanes. The filtrate was dried over Na_2SO_4 and hydrogenated immediately with 2.0 g of 10% Pt on carbon at room temperature and 30 atm for 1 h. The reaction mixture was filtered and fractionally distilled to collect 9.6 g (62% yield based on $CHCl_3$ used) of colorless oil at 170-173 °C (lit.[10a] bp 172-174 °C): IR (neat) 3350 cm^{-1}; ^1H NMR δ 2.75-2.15 (m, 1 H), 2.00-1.15 (m, 10 H), 1.08 (s, 9 H), 0.82 (m, 1 H).

Acknowledgment. I thank Mr. Ed Sabo and Mr. Craig Krieger for their lab work, Dr. Jerry Westfahl and Dr. Robert Lattimer for their spectroscopic services, and Dr. Dwight Chasar for editorial corrections of the manuscript.

Registry No. 1 (R^1 = Ph, R^2 = H), 62-53-3; 1 (R^1 = *p*-ClPh, R^2 = H), 106-47-8; 1 (R^1 = *p*-MePh, R^2 = H), 106-49-0; 1 (R^1 = *p*-OEtPh, R^2 = H), 156-43-4; 1 (R^1 = *o*-MePh, R^2 = H), 95-53-4; 1 (R^1, R^2 = Me), 124-40-3; 1 (R^1, R^2 = $CH_2CH_2OCH_2CH_2$), 110-91-8; 1 (R^1, R^2 = Et), 109-89-7; 1 (R^1, R^2 = *n*-Bu), 111-92-2; 1 (R^1 = *t*-Bu, R^2 = H), 75-64-9; **3a**, 74262-30-9; **3b**, 74262-31-0; **3c**, 74262-32-1; **3d**, 74262-33-2; **3e**, 74262-34-3; **3f**, 74262-35-4; **3g**, 74262-36-5; **3h**, 74262-37-6; **3i**, 71172-30-0; **3j**, 74262-38-7; **3k**, 74282-41-0; **3l**, 74262-39-8; **3m**, 74262-40-1; **3n**, 74262-41-2; **3o**, 74262-42-3; **3p**, 74262-43-4; **3q**, 74262-44-5; **3r**, 74262-45-6; **3s**, 74282-42-1; **3t**, 74262-46-7; **4f**, 1132-38-3; **4h**, 74262-47-8; **7**, 51609-06-4; acetone, 67-64-1; cyclohexanone, 108-94-1; 2-butanone, 78-93-3; 4-methyl-2-butanone, 108-10-1; 1-phenylethanone, 98-86-2.

Supplementary Material Available: Melting and/or boiling points, elemental analyses, IR and ^1H NMR spectral data of compounds **3a-t** and **4f,h** (5 pages). Ordering information is given on any current masthead page.

Reaction of *N*-Nitrosamides with Metal Hydrides[1a]

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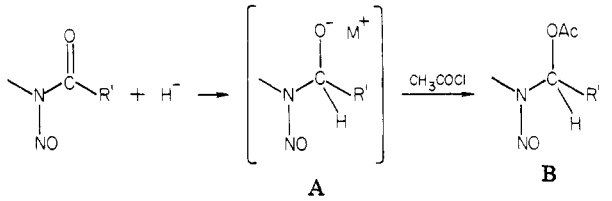
Received February 22, 1980

The reaction of *N*-nitrosamides with lithium aluminum hydride results mainly in attack of hydride at the carbonyl group to give the aldehyde and the diazotate ion (syn?) as the primary products. Products resulting from *N*-nitrene fragmentation (by reduction of the nitroso group) and from hydride-induced denitrosation were also characterized.

α-Acyloxy-*N*-nitrosamines (B, Scheme I) have become important as precursors of the putative α-hydroxy-*N*-nitrosamines.[1b,c] As part of our interest in *N*-nitrosamines,[2] we thought that the addition of hydrides to *N*-nitrosamides should lead to alkoxides A, which might then be intercepted by acylating agents to afford the desired α-acyloxy-*N*-nitrosamines (B).[3a] While this work was in progress, Saavedra reported the reductive cleavage of *N*-methyl-*N*-nitrosamides to the alcohols derived from the acyl portion of the nitrosamides with sodium borohydride ($NaBH_4$) in glyme at room temperature.[3b]

However, examination of the structure of *N*-nitrosamides suggests that the carbonyl group is only one of other possible sites of attack by hydride. Thus, reaction at the amino nitrogen could lead to denitrosation while removal of an α-hydrogen, though unlikely, might result in the formal loss of HNO; a fourth possibility involves

Scheme I



attack at the nitroso group (Scheme II).

Results and Discussion

The addition of *N*-nitroso-*N*-benzylbenzamide (NBB) to lithium aluminum hydride (LAH) in ether at ~0 °C followed by quenching with dilute hydrochloric acid gave benzaldehyde, detected by TLC. This reaction was repeated at room temperature and quenched with acetyl chloride instead of hydrochloric acid. In addition to a mixture of benzyl benzoate and recovered starting material, benzyl acetate (15%) was isolated. The same reaction carried out at -60 °C developed a reddish color. Since the crude reaction mixture which displayed a prominent absorption at 2050 cm^{-1} decomposed on attempted chromatography on silica gel, the presence of phenyldiazomethane was confirmed by repeating the reaction and quenching

(1) (a) This is the sixth in a series of papers dealing with *N*-nitrosamines and related compounds; for the previous paper see ref 2. (b) J.-P. Anselme, *ACS Symp. Ser.*, **No. 101**, Chapters 3 and 4 (1979). (c) B. Gold and W. B. Linder, *J. Am. Chem. Soc.*, **101**, 6772 (1979), and references therein.

(2) M. Nakajima and J.-P. Anselme, *Tetrahedron Lett.*, 4037 (1979).

(3) (a) R. A. Moss, *Acc. Chem. Res.*, **7**, 421 (1974); M. Regitz in "The Chemistry of Diazonium and Diazo Groups", S. Patai, Ed., Interscience, New York, 1978, 659. (b) J. E. Saavedra, *J. Org. Chem.*, **44**, 860 (1979).

0022-3263/80/1945-3673$01.00/0