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CYCLIC CARBALKOXY AMINIMIDES. SYNTHESIS AND THERMAL DECOMPOSITION TO GIVE N,N-DIMETHYLAMINO ISOCYANATE

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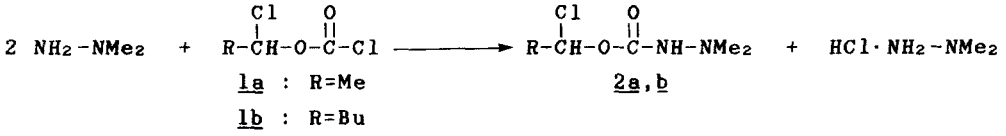
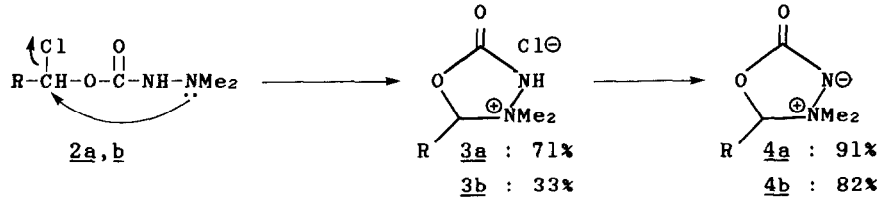
Five membered ring carbalkoxy aminimides are prepared from 1,1-dimethylhydrazine and α-chloroalkyl chloroformates in three steps. Upon heating, these aminimides give high yields of N,N-dimethylamino isocyanate. This intermediate dimerizes or can be trapped in the presence of a nucleophile.

Although acyl and sulfonyl aminimides have been extensively studied[1], carbalkoxy aminimides have received little attention[2,3] and, to our knowledge, cyclic carbalkoxy aminimides have never before been synthesized.

In continuation of our studies on the synthesis[4] and reactivity[5a-e] of α-chloroalkyl chloroformates, we have examined the preparation of 5-membered ring carbalkoxy aminimides. Thus, when 1,1-dimethylhydrazine (26.6 g, 0.44 mole) in anhydrous THF (50 mL) is added (25 min) to a solution of α-chloroethyl chloroformate (1a, ACE-Cl, 31.6 g, 0.22 mole) in THF (150 mL) kept at 10-20 °C with an ice bath, the intermediate carbazate (2a) is formed. The hydrochloride salt is filtered off and the cyclization is accomplished by





refluxing 2a in the THF solution for 1 hour, precipitating the hygroscopic salt (3a) as it is formed. Upon filtration and drying in vacuo, 3a is obtained pure in 71% overall yield. In the solid form, 3a is stable indefinitely at room temperature. However, in solution after several days, it decomposes to give the hydrazone hydrochloride (MeCH=N-NMe2·HCl).[6] This is also the major side product in the formation of the cyclic carbazate (3a).

The cyclization of hindered carbazates is much difficult. The carbazate from ACE-Cl (1a) and N-aminomorpholine gave only decomposition to the hydrazone

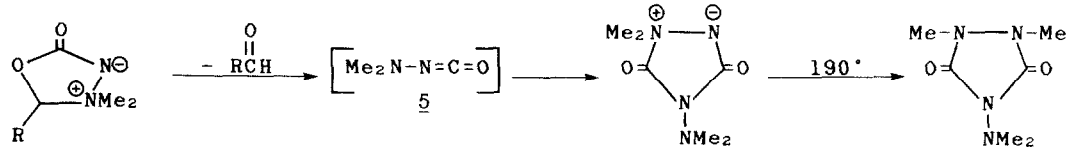
hydrochloride under various reaction conditions. The α-chloropentyl derivative (2b) gave only a 33% overall yield of 3b.[7] The ^{1}H NMR spectrum[8] of 3b illustrates the steric crowding in this molecule. The β-CH_2 protons (Hb,Hc) are inequivalent as is seen in the coupling constants with the α-CHa proton (Jab=1.5,Jac=10.5 Hz) and in the anisotropic shielding of Hc by the carbonyl group (Hb:m,δ2.34; Hc:m,δ1.95). The IR spectra[8] also show increased ring strain in 3b and 4b as compared with 3a and 4a (C=O frequency 15 cm^{-1} higher in b series).

The aminimides (4) are easily prepared from 3 by reaction with base. Thus, 4a is obtained pure in 91% yield by stirring 3a (35.0 g, 0.21 mole) in water (200 mL) with 250 mL of Amberlite IRA-400(OH) ion-exchange resin followed by filtration, washing of the resin (5 x 200 mL H_2O), and evaporation of the water at 50 °C in vacuo. If desired, 4a can be prepared with aqueous NaOH or anhydrously with a tertiary amine (such as Et_3N). However, due to the insolubility of 4a in most organic solvents, this aminimide cannot be easily isolated from the NaCl or trialkylammonium salts. The aminimide, 4b, is thermally less stable than 4a and is best prepared with a tertiary amine at 0-20 °C.[9] The ^{1}H NMR spectrum[8] of 4b again shows hindered rotation of the butyl group (as with 3b).

It is also interesting to note the change in C=O frequency in passing from 3 to 4. The frequency drops by 105 cm^{-1} due to the delocalization of the negative charge into the carbonyl group.

Since the cyclic, 5-membered ring, carbalkoxy aminimides (4) are now easily prepared, we have studied their thermolysis. Unlike acyclic carbalkoxy aminimides which have been shown to thermolytically rearrange (150-200 °C) by alkyl group migration[3], these cyclic carbalkoxy aminimides (4) undergo a rearrangement in which dimethylamino isocyanate (5) and aldehyde are formed at moderate temperatures and in good yields. Heating 4b in solution at 40 °C for 1 hour gives 50% thermal decomposition, whereas a much higher temperature of 65-70 °C is needed for the same rate of decomposition of 4a.

Dialkylamino isocyanates are known transient intermediates and, in the absence of other reagents, have been shown to dimerize.[10] Thus when 4a is heated at 130°/0.03 mm for 3 hours, 6 sublimes and is obtained in 89% yield.



Alternatively, 6 was prepared quantitatively by refluxing 4a in CH_3CN for 2 hours followed by evaporation of the solvent. At higher temperatures, 6 is

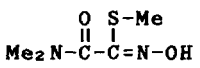
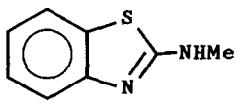
formed but rearranges to 7[10]. Thus 4a is heated to 190° for 5 minutes and then vacuum distilled (pot temp. at 190°, bp 100°/0.06 mm) to give 7 (92%).

At present, dimethylamino isocyanate (5) can be prepared by two different methods. The preparation through phosphoramidate anions with CO_2 is slow and the yield is not very good[10]. Alternatively, 5 can be prepared via a Curtius rearrangement by the gas phase vacuum pyrolysis[11] (300-360°) or the photolysis[12] (300 nm) of carbamoyl azides. The inconvenience of this method lies in the potential danger of the azide and also the special equipment needed for the pyrolysis or photolysis.

Thus, our new method represents a simple, rapid, and high yield preparation of dimethylamino isocyanate. This interesting intermediate has been the subject of several publications[10-14] and is useful for the preparation of a wide variety of heterocycles, carbazates, semicarbazides, and other molecules containing a hydrazine group.

We have prepared several carbazates and semicarbazides (see Table) and are currently testing some of these products for pesticidal activity. These hydrazine derivatives were easily prepared by heating 4a and the nucleophile (:Nu-H) for 1 hour in refluxing 1,2-dichloroethane.

TABLE

Example	:Nu-H	Nu-CO-NHNMe$_2$ Yield
1	EtOH	87%
2		95%
3	$PhCH_2NHMe$	89%
4		74%
5	$EtO_2CCH_2NH_2$	76%

The only drawback in this method is that the released aldehyde can react with certain substrates (such as primary amines), thus giving side products. Otherwise, this method gives an excellent, high yield source of dimethylamino isocyanate.

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References and Notes

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6. MeCH=N-NMe_2·HCl was identified by preparation of an authentic sample by reaction of MeCHO and Me_2NNH_2 (in a stirred $CHCl_3$ & $MgSO_4$ mixture) followed by addition of HCl. ^{1}H NMR(DMSO-d^6 & $CDCl_3$): 8.85(q,J=5.5,1H), 3.02(s,6H), 2.08(d,J=5.5,3H).
7. 2b was prepared in t-butyl methyl ether, filtered, and concentrated. 2b was then refluxed in MeCN for 10 min, cooled, and concentrated giving a mixture of BuCH=N-NMe_2·HCl & 3b. 3b was purified by washing with $CHCl_3$, filtration, and drying in vacuo.
8. Spectral and physical properties (IR C=O, cm^{-1}; 200 MHz NMR).
   3a: mp 145-150 °C (dec.); IR 1800 (KBr); ^{1}H NMR (DMSO-d^6): 8.60(br s, 1H), 6.05(q,J=6,1H), 3.65(s,3H), 3.54(s,3H), 1.88(d,J=6,3H); ^{13}C NMR (DMSO-d^6): 150.28(C=O), 97.27(CH), 52.08 & 47.75($N(CH_3)_2$), 11.57(CH_3).
   3b: mp 115 °C (dec.); IR 1815 (KBr); ^{1}H NMR (DMSO-d^6): 12.84 (br s,1H), 6.02 (d of d,J=10.5;1.5,1H), 3.65(s,3H),3.54(s,3H), 2.34(m,1H), 1.95(m, 1H), 1.42(m,4H), 0.92(t,J=7,3H); ^{13}C NMR (DMSO-d^6): 151.56(C=O), 100.56 (CH), 53.18 & 49.07($N(CH_3)_2$), 26.04 & 25.54 & 21.46($(CH_2)_3$),13.46(CH_3).
   4a: mp 170-172 °C; IR 1696 (KBr); ^{1}H NMR (DMSO-d^6): 5.18(q,J=6,1H), 3.10(s,3H), 2.90(s,3H), 1.57(d,J=6,3H); ^{13}C NMR (DMSO-d^6): 164.67(C=O), 98.69(CH), 56.58 & 52.26($N(CH_3)_2$), 17.54(CH_3).
   4b: mp 112 °C (dec.); IR 1710 ($CHCl_3$); ^{1}H NMR ($CDCl_3$): 4.98(d of d, J=9;3,1H), 3.26(s,3H), 3.06(s,3H), 1.9(m,2H), 1.5(m,4H), 0.95(t,J=7,3H); ^{13}C NMR ($CDCl_3$): 161.97(C=O), 99.47(CH), 53.56 & 48.97($N(CH_3)_2$), 28.04 & 27.53 & 22.30($(CH_2)_3$),13.77(CH_3).
9. Separation of 4b from Et_3N·HCl is difficult even though 4b is soluble in 1,2-dichloroethane and $CHCl_3$.
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