pounds used to derive the c_i values listed in Table I.

Different procedures were followed in calculating c_i values in the different series. The alkane $c(\text{C C H H H })$ and $c(\text{C C C H H })$ values are based on just the *n*-alkanes in order to provide highest accuracy for these important values. The other two alkane values were determined as simple averages of residuals.

For the alcohols and the alkenes it was more convenient to use an overall least-squares adjustment.[44] For the other compounds it was possible to examine the residuals remaining after subtracting out the c_i values of the standard groups. The remaining c_i values could then be obtained as averages from selected residuals. The results were checked by calculating the ΔH_f values; there are a few fairly large discrepancies. Among the reported compounds the largest deviations of calculated ΔH_f are 0.7 kcal/mol. A few omitted compounds showed discrepancies of the order of 4 kcal/mol; these are presumably errors because the data also fail the test of internal consistency. For purposes of illustration a few of these discordant values have been left in Table II, although the discordant series were not used to get the reported C_i values.

Relationships between c_i Values. The relationships between the c_i values in the earlier study[7,8] and the present values are as follows:

$$c(\text{CH}_3\text{O}) = c(\text{C H H H O }) + 0.5c(\text{O C C })$$

$$c(\text{CH}_2\text{O}) = -5.141 + 0.5c(\text{O C C })$$

$$c(\text{CHO}) = c(\text{C C C H O }) + 0.5c(\text{O C C })$$

$$c(\text{CO}) = c(\text{C C C C O }) + 0.5c(\text{O C C })$$

$$c(\text{HO}) = c(\text{O C H }) - 0.5c(\text{O C C })$$

$$c(\text{CH}_3\text{-}\alpha) = c(\text{C CDH H H }) - 10.00 + 5.14$$

$$c(\text{CH}_2\text{-}\alpha) = -10.00$$

$$c(\text{CH-}\alpha) = c(\text{C C C CDH }) - 10.00 + 5.14$$

$$c(\text{C-}\alpha) = c(\text{C C C C CD}) - 10.00 + 5.14$$

$$c(=\text{CH}_2) = c(\text{CDCDH H })$$

$$c(=\text{CCH}) = c(\text{CDC CDH }) + 10.00 - 5.14$$

$$c(=\text{C}_2) = c(\text{CDC C CD}) + 20.00 - 10.28$$

Two sets of programs have been developed to aid in identification of representative groups and in systematic assignment of FSE values to standards.[47]

Registry No. 2-Methylbutane, 78-78-4; 2,2-dimethylbutane, 75-83-2; 2-methylpentane, 107-83-5; 2-methylhexane, 591-76-4; 2-methylheptane, 592-27-8; 2,2-dimethylpentane, 590-35-2; 2,2-dimethylhexane, 590-73-8; 2-butanol, 78-92-2; 2-methyl-2-butanol, 75-85-4; methyl isopropyl ether, 598-53-8; diisopropyl ether, 108-20-3; methyl *tert*-butyl ether, 1634-04-4; 3-methyl-1-butene, 563-45-1; 3,3-dimethyl-1-butene, 558-37-2; 3-methyl-1-pentene, 760-20-3; 2-methyl-1-butene, 563-46-2; 2-methyl-1-pentene, 763-29-1; ethyl propanoate, 105-37-3; ethyl acetate, 141-78-6; ethyl 2-methylbutanoate, 7452-79-1; ethyl 2,2-dimethylpropanoate, 3938-59-2; methyl acetate, 79-20-9; butyl acetate, 123-86-4; methyl pentanoate, 624-24-8; ethyl pentanoate, 539-82-2; methyl 2-methylbutanoate, 868-57-5; ethyl 3-methylbutanoate, 108-64-5; methyl hexanoate, 106-70-7; *tert*-butylbenzene, 98-06-6; isobutylbenzene, 538-93-2.

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[44] DeTar, D. F., Ed. *Computer Programs for Chemistry*; Academic Press: New York, 1972; Vol. 4, p 71, GENLSS.

[45] Pedley, J. B.; Rylance, J. Sussex - N.P.L. Computer Analyzed Thermochemical Data, Sussex University, 1977.

[46] Beckhaus, H.-D. *Chem. Ber.* **1983**, *1983*, 86.

[47] FSIELD(QCMPO26) and FSEUNIT(QCMPO27), Quantum Chemistry Program Exchange, Department of Chemistry, Indiana University, Bloomington, IN 47405.

Notes

The Reaction of Amines with Methylene Chloride. Evidence for Rapid Aminal Formation from *N*-Methylenepyrrolidinium Chloride and Pyrrolidine

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Received October 9, 1986

Several papers dealing with the reaction of amines with methylene chloride have recently appeared in the literature.[1-8] The conclusions drawn by the authors are markedly different. Some chemists report that the reaction of methylene chloride with amines is negligible or nonexistent at atmospheric pressure,[3,4] while others recommend caution when using this solvent for extractions of amines.[1,2] Here, we shall attempt to dispel the myth that methylene chloride is unreactive with amines by providing additional evidence for the rapid reaction of methylene chloride with a secondary amine at room temperature and atmospheric pressure. In addition, this note describes studies which establish that, in methylene chloride or chloroform, the reaction of a tertiary chloromethylamine (1-methylenepyrrolidinium chloride) with pyrrolidine is rapid.

The rate of the reaction of methylene chloride with a

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[1] Mills, J. E.; Maryanoff, C. A.; Cosgrove, R. M.; Scott, L.; McComsey, D. F. *Org. Prep. Proc. Int.* **1984**, *16* (2), 97.

[2] Nevstad, G. O.; Songstad, J. *Acta Chem. Scand., Ser. B* **1984**, *38*, 469.

[3] Matsumoto, K.; Hashimoto, S.; Ikemi, Y.; Otani, S. *Heterocycles* **1984**, *22*, 1417.

[4] Almarzoqi, B.; George, A. V.; Isaacs, N. S. *Tetrahedron* **1986**, *42*, 601.

[5] Julia, S.; del Mazo, J. M.; Avila, L.; Elguero, J. *Org. Prep. Proc. Int.* **1984**, *16*, 299.

[6] Balsells, R. E.; Frasca, A. R. *Tetrahedron Lett.* **1984**, *25*, 5363.

[7] Heskey, W. A. *Chem. Eng. News* **1986**, *May 26*, 2.

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Table I. ^{13}C and ^{1}H Spectral Data for Pure Compounds

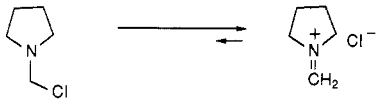
compound	^{13}C, ppm	^{1}H, ppm
aminal 1	77.5, 52.7, 23.8	3.2 (s), 2.56 (m), 1.72 (m)
iminium chloride 2	160.1, 56.6, 24.9	8.81 (m), 4.29 (m), 2.21 (m)
pyrrolidine	47.9, 25.5	2.80 (m), 1.60 (m)

number of primary, secondary, and tertiary amines has been quantitated[2] by following the production of ionic chloride; however, the organic products were not identified. The condensation of secondary amines with methylene chloride was qualitatively examined by a study[1] in which the organic reaction products were carefully identified. The conclusions reached by both groups are in general agreement; however, the rate paper[2] states that for secondary amines "reactions leading to bis(dialkylamino)methanes, $(R_2N)_2CH_2$, and products from $ClCH_2NR_2$ can apparently be neglected". This assumption may be correct for derivation of the kinetic equation for the reaction, but it is invalid with respect to the actual products produced. In fact, it has been our experience and the experience of others[9] that the reaction of 1-chloromethylpyrrolidine with secondary amines is extremely rapid (vide infra).

In order to establish the course of the reaction of methylene chloride with pyrrolidine without the possibility of introducing impurities during sampling, several NMR experiments were performed. These experiments were run at room temperature in methylene chloride with the addition of a small amount of benzene-d_6 as internal standard for ^{13}C NMR spectroscopy. The initial concentration of pyrrolidine in the reaction was 1.7 M. The reaction was checked periodically up to 24 h after mixing the reagents. Pyrrolidine was partially consumed, and new resonances at 77.2, 52.7, and 23.8 ppm were observed. (See Table I for reference chemical shift values.) The resonances for the pyrrolidine shifted downfield slightly as the reaction proceeded, presumably due to protonation by the hydrogen chloride liberated in the reaction. Since the reaction was run in a sealed tube, none of the acid could escape from the reaction, and the final composition of the reaction was ca. 33 mol % 1,1′-methylenebis(pyrrolidine) (1) and 66 mol % starting pyrrolidine (i.e., approximately half of the pyrrolidine was converted to aminal). It is obvious that if the formation of aminal can be observed in these NMR experiments, then the high-pressure conditions reported by Matsumoto et al.[3] are not necessarily required. Indeed, for certain secondary amines, higher yields of aminal have been obtained at atmospheric pressure[1] than under Matsumoto's conditions.

No direct evidence for the formation of 1-(chloromethyl)pyrrolidine was obtained in our experiments;[10] a number of factors may account for the lack of observation of this species. 1-(Chloromethyl)pyrrolidine could have been formed in the reaction, but its chemical shifts could have been affected by the presence of the pyrrolidine, aminal, or hydrogen chloride in the reaction mixture. Alternatively, 1-(chloromethyl)pyrrolidine may have been formed in the reaction but reacted so rapidly that its concentration remained too low for the compound to be observed. A series of experiments was performed to determine the chemical and spectral properties of this compound.

1-(Chloromethyl)pyrrolidine was synthesized by Böhme's procedure.[11] Treatment of 1,1′-methylenebis(pyrrolidine) (1), with acetyl chloride in diethyl ether resulted in the formation of a white flocculant precipitate of the chloromethylamine which was isolated by filtration under argon. Exposure of the solid to humid air resulted in rapid formation of a tacky glass and the detection of the odor of formaldehyde. The chloromethylamine was soluble in both chloroform and methylene chloride. ^{1}H NMR at 60 MHz in $CDCl_3$ of the white flocculant chloromethylamine showed a sharp singlet at 8.7 ppm (2 H) as well as broad multiplets at 4.2 (4 H) and 2.2 ppm (4 H) downfield from Me_4Si. Fully decoupled ^{13}C NMR in CH_2Cl_2 showed a broad resonance at ca. 160 ppm as well as singlets at 56.6 and 24.9 ppm. Both sets of NMR data are consistent with the iminium chloride 2 as the major species present in these solvents. The broadening of the exocyclic methylene resonance in the ^{13}C NMR spectra can be interpreted as evidence for an equilibrium involving the covalent chloromethyl compound 3 as shown in eq 1. Since the physical and spectroscopic properties are more consistent with this compound being ionic, future references to it in this paper shall be made using the name 1-methylenepyrrolidinium chloride.[12]



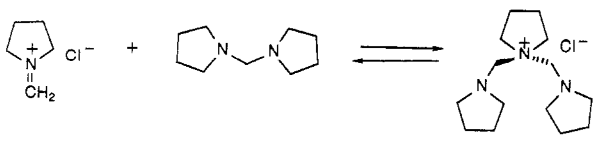
3 2

(1)

Experiments run in $CDCl_3$ using ^{1}H NMR showed that the chemical shifts of both the 1-methylenepyrrolidinium chloride and 1,1′-methylenebis(pyrrolidine) were changed in the presence of each other. Addition of small increments of aminal 1 to a solution of 1-methylenepyrrolidinium chloride initially showed dramatic broadening and a slight upfield shift of all resonances associated with the iminium chloride. No resonance could be observed for the formaminal methylene bridge protons, and the ring methylene protons adjacent to the nitrogens appeared as a broad resonance between 3.5 and 2.8 ppm. Additional increments of aminal caused further upfield shifts of the proton resonances assigned to iminium chloride. At a 1:1 molar ratio, the exocyclic methylene resonances assigned to both compounds coalesced into a singlet shifted downfield by ca. 0.8 ppm from those observed for the pure aminal.

Similar experiments run in CH_2Cl_2 using ^{13}C NMR showed the disappearance of the resonance at 160.1 ppm with formation of a broad resonance at ca. 76.4 ppm when 0.5 mol equiv of aminal was added. At a 1:1 molar ratio of 1-methylenepyrrolidinium chloride to aminal, three sharp resonances were observed at 76.2, 52.5, and 24.4 ppm.

These data are interpreted as evidence for the equilibrium shown in eq 2. Evidence for a similar equilibrium has been provided by work[13] in which methylenebis(dimethylamine) (4) was added to a suspension of 4-methylenemorpholinium chloride (5) in acetonitrile at −20°C. Addition of ether to the resulting solution precipitated a mixture of 80% *N*-methyl-*N*-methylene-



(2)

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[9] Böhme, H.; Eichler, D. *Chem. Ber.* **1967**, *100*, 2131.

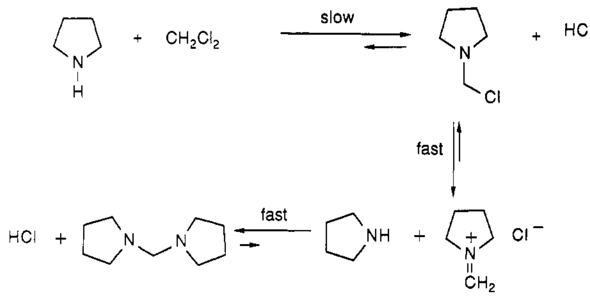
[10] The same reaction intermediate has previously been postulated in the reaction of secondary amines with bis(chloromethyl) ether to yield aminals: Iovu, M.; Iqbal, M. *Rev. Roum. Chim.* **1984**, *29* (4), 333.

[11] Böhme, H.; Hartke, K. *Chem. Ber.* **1960**, *93*, 1305.

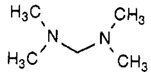
[12] For a discussion of the NMR chemical shifts of methyleneiminium species, see: Böhme, H.; Viehe, H. G. *Advances in Organic Chemistry*; Wiley: New York, 1976; Vol. 9, Part 1, p 152 and references cited therein.

[13] Böhme, H.; Höver, W. *Chem. Ber.* **1970**, *103*, 3918.

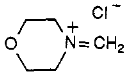
Scheme I



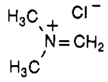
methanaminium chloride (**6**) and 20% 4-methylenemorpholinium chloride.



4



5



6

These data provide evidence that 1-methylenepyrrolidinium chloride could have been produced in the ^{13}C NMR experiments described above, but remained unobserved due to a change in the chemical shift. However, they do indicate that **2** is not the major species in solution at the end of the reaction.

Experiments run by addition of excess pyrrolidine to pure 1-methylenepyrrolidinium chloride (**2**) showed immediate loss of the resonance at 8.81 ppm with formation of a broad singlet at 3.2 ppm in the ^1H NMR. Upon quenching the reaction with $NaOD/D_2O$, this resonance remained. These data indicate that the formation of aminal from 1-methylenepyrrolidinium chloride and pyrrolidine is very rapid.

A mechanism which accounts for the kinetics observed by Songstad[2] as well as for the products observed in these and other studies is shown in Scheme I. If the condensation of methylene chloride with a secondary amine is the rate-determining step in the sequence leading to aminal, pseudo-first-order kinetics will be observed for this reaction. Whether or not the absolute values of the rate constants for the reactions of amine with methylene chloride determined by Nevstad and Songstad turn out to be correct, the values may serve as an indicator of relative reactivity of the amines.

From our study we conclude (1) that pyrrolidine rapidly reacts with methylene chloride solvent molecules at room temperature, (2) that in the absence of additional base, the major products in this reaction are 1,1′-methylenebis(pyrrolidine) and pyrrolidinium hydrochloride, and (3) that 1-methylenepyrrolidinium chloride, a presumed intermediate in the formation of the aminal, reacts so rapidly with pyrrolidine and/or aminal that its presence as a distinct species can not be established. These conclusions are what is expected based upon literature precedent.[1,9,13,14]

Methylene chloride has been reported[14] to be one of the best solvents for the reaction of tertiary amines with alkyl halides. It should not be surprising, then, that reactions of primary, secondary, and tertiary amines with this solvent are common. Although quantitative work in this area is difficult due to the frequent formation of inhomogeneous reaction mixtures, quantitative,[2] and qualitative[1] studies have been reported. Tertiary amines frequently form quaternary chloromethylammonium salts with methylene chloride. Secondary amines can react rapidly to yield mixtures of amine hydrochloride and aminal or in the presence of additional base to give high yields of pure aminal. Aminal formation from secondary amines is apparently occurring through the intermediacy of the corresponding methyleneiminium chloride which reacts rapidly with another molecule of the starting amine.

Since methylene chloride is frequently used in extractions and those solutions are, on occasion, allowed to stand at room temperature for extended periods, reaction yields can be adversely affected through formation of undesired byproducts. Care should be exercised when this solvent is used with amines to avoid conditions which can favor byproduct formation.

Experimental Section

AR grade methylene chloride was used without additional purification. The solvent was shown not to contain bromochloromethane by mass spectrometry. ^1H NMR spectra were obtained on a Varian EM390 spectrometer. ^{13}C NMR spectra were obtained on a JEOL JNM-FX60Q (60 MHz) instrument. As noted above, $CDCl_3$ or CH_2Cl_2 was used as the solvent in all NMR studies. Tetramethylsilane was used as internal reference for ^1H NMR spectra. The internal reference for ^{13}C NMR spectra was $CDCl_3$ or benzene-d_6.

1,1′-Methylenebis(pyrrolidine) (1) was prepared by stirring pyrrolidine (7.1 g, 0.1 mol) with methylene chloride (60 mL) in the presence of 30% aqueous sodium hydroxide (10 mL) for 18 h at room temperature.[1] The product was purified by distillation under reduced pressure.

1-Methylenepyrrolidinium chloride (2) was prepared by the method of Böhme[11] in 94% yield from 1,1′-methylenebis(pyrrolidine). The compound is extremely hygroscopic and gradually decomposes to formaldehyde and pyrrolidine hydrochloride when exposed to humid air.

Acknowledgment. We acknowledge the work done by Susan Campbell and Martin Mutter in obtaining ^{13}C NMR spectra and thank Dr. Vasken Paragamian, Martin Mutter, and Dr. Ruth Inners for helpful discussions.

Registry No. 1, 7309-47-9; 2, 52853-03-9; pyrrolidine, 123-75-1; methylene chloride, 75-09-2.

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[14] Abraham, M. H.; Grellier, P.L. *J. Chem. Soc., Perkin Trans. 2* **1976**, 1735.

Tertiary Amine Microaggregate Control of (Ethoxycarbonyl)nitrene Regioselectivity[1]

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Received September 11, 1986

It is well-known that nitrenes are interesting reagents for the introduction of a nitrogen functionality in many organic compounds.[2] Despite this fact, nitrenes are rarely used in synthetic chemistry owing to their poor selectivity.

Our recent results[3] encouraged us to try a new approach to induce selectivity in reactions involving nitrenes. There

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[1] A preliminary account has been presented at the Fourth European Symposium on Organic Chemistry (ESOC IV), Aix-en-Provence, France, Sept 2-6, 1985; Abstract PB-14.

[2] Scriven, E. F. V., Ed. *Azides and Nitrenes, Reactivity and Utility*; Academic: Orlando, FL, 1984.

[3] (a) Fioravanti, S.; Loreto, M. A.; Pellacani, L.; Tardella, P. A. *J. Org. Chem.* **1985**, *50*, 5365. (b) Bertolaccini, R.; Cerichelli, G.; Loreto, M. A.; Pellacani, L.; Tardella, P. A. *Gazz. Chim. Ital.* **1986**, *116*, 587.