Quaternization of Imidazoline: Unequivocal Structure Proof

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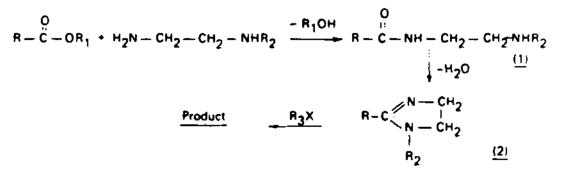
ABSTRACT

Two structures are possible for the product of quaternization of an N-alkylimidazoline, i.e., symmetrical and unsymmetrical. The literature employs both versions, with no unambiguous proof available for either. Proton and ^{13}C nuclear magnetic resonance spectroscopy have been used in this work. The product of quaternization under neutral conditions is shown to be symmetrical. This can be easily rationalized on the basis of resonance stabilization caused by delocalization of the positive charge.

INTRODUCTION

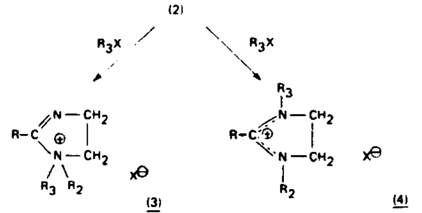
The quaternary salts of imidazolines have long been recognized as useful in the surfactant industry. They find applications in a variety of uses (1). These imidazolinium salts are usually made by the application of the following three-step procedure (Scheme I) or a minor variant thereof (1-3):



SCHEME 1

It is possible, of course, to carry out this sequence in one pot.

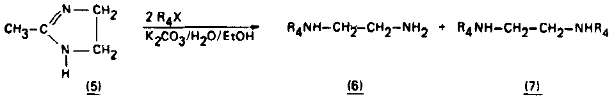
From the structure of the imidazoline, it is easily seen that, due to the presence of two tertiary nitrogen atoms in 2, the quaternization may yield one or both of the isomers, i.e., unsymmetrical 3 and symmetrical 4, as product (Scheme II).



SCHEME 2

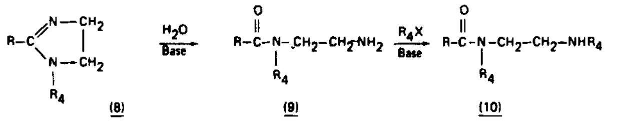
There has been no clear proof in the past regarding the nature of the product of quaternization, i.e., whether the product is symmetrical or unsymmetrical. As a result, either structure can be found in the literature (1). It is possible to prepare structures such as 4 using a symmetrical starting material (4); however, this imposes a bias on the synthesis.

Indirect attempts appear to have been made to resolve the structure. King and McMillan (5), in an effort to synthesize N,N′-dialkylamines, treated imidazoline 5 with two equivalents of an alkylhalide in an aqueous solution of potassium carbonate. The only products they obtained were N-alkylethylenediamine 6 and N,N′-dialkylethylenediamine 7 (Scheme III).



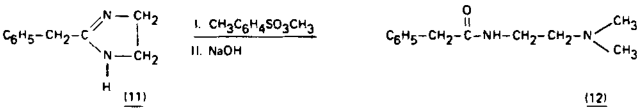
SCHEME 3

Based on the hydrolysis products, symmetrical structure 4 was proposed. This could easily be rationalized by resonance stability (1,5); however, there are a number of unanswered questions. For example, the one pot reaction was conducted in the presence of an excess of base (5). But the imidazolines are known to hydrolyze in the presence of aqueous base (6). Thus, it is not clear what role the alkylation of the partially hydrolyzed derivative 9 to yield 10 played in determining products such as 7 (Scheme IV).



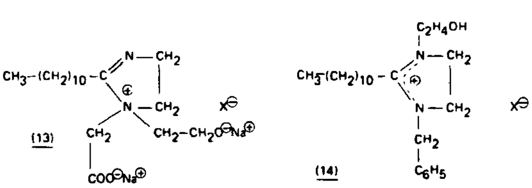
SCHEME 4

Besides, due to the fact that the mass balance was far from quantitative (5) and other products were not identified, no conclusion can be made about the nature of the remaining material. Oxley and Short (7) exhaustively alkylated 2-benzyl-2-imidazoline 11 with methyl *p*-toluenesulfonate (Scheme V). The crude product on alkaline hydrolysis reportedly gave 12. Based on this product, a conclusion opposite to that of King and McMillan (5) may be reached. Again, no mass balance was given.



SCHEME 5

König (8) has reported nuclear magnetic resonance (NMR) data on a number of detergent derivatives. He assigns the unsymmetrical structure such as 13 (Scheme VI). However, the assignments are based on nonequivalent substituents and hence are subject to interpretive error. The mass spectral work of Linhart and Wrabetz (9) led them to assign a symmetrical structure 14 for their compound.



SCHEME 6

This demonstrates existing confusion regarding the structure of the quaternary salt.

MATERIALS AND METHODS

All reagents were analytical reagent grade. N-methylethylenediamine and methyl phenylacetate were purchased from Aldrich Chemical Company. Infrared analyses (IR) were run on a Perkin Elmer 297 instrument. NMR spectra were obtained on a Brucker WP-200 NMR spectrometer equipped with an Aspect 2000 data system. Samples were dissolved in deuterchloroform containing 1% v/v tetramethylsilane (TMS). All spectral data are reported in ppm downfield from TMS. The spectra were accumulated in the Fourier transform mode and broad band irradiation provided proton decoupled ^{13}C spectra. Elemental analyses were performed by Micro-Analysis, Inc., Wilmington, Delaware.

Synthesis of 1-methyl-2-benzyl-2-imidazoline (Product 15)

The compound 1-methyl-2-benzyl-2-imidazoline 15 has been reported previously (10). However, due to the nature of this investigation, a detailed analysis was performed.

Into a 3-neck, round bottom flask equipped with a magnetic stirrer, a thermometer, a subsurface nitrogen inlet and a reflux condenser were introduced 30.0 g (199 mmol) of methyl phenylacetate and 16.2 g (219 mmol) of N-methylethylenediamine. This mixture was heated at 120 C in an oil bath for 6 hr until the ester band (1740 cm^{-1}) in the IR disappeared. The amidoamine so formed was cyclized to the imidazoline by heating the crude reaction mixture at 163-168 C under a stream of nitrogen and full water aspirator vacuum for 6 hr. During this time, the amide bands (1650 cm^{-1}, 1555 cm^{-1}) decreased, and the band caused by the imidazoline ($\sim$1610 cm^{-1}) appeared. The reaction was done for an additional 6 hr, but no further change was observed in the IR. The crude liquid was distilled under vacuum to obtain 22.1 g (63.4%) pale yellow liquid distilling at 78-84 C (0.5-1.0 mm). IR of the product (neat) showed a sharp band at 1615 cm^{-1} with shoulders. From the proton NMR, the following were identified: aromatic protons (multiplet, 7.28-7.22 ppm), ring methylene protons ("apparent triplets," 3.67 ppm and 3.21 ppm), and methyl protons (singlet, 2.63 ppm). The integrated areas support the assignments.

Anal. calcd.: ($C_{11}H_{14}N_2$), C, 75.82; H, 8.10; N, 16.08. Found: C, 75.7; H, 7.19; N, 15.97.

Quaternization of Product 15 with Methyl Bromide

Five ml of liquid methyl bromide was added to a solution of 3.0 g (17.1 mmol) of **15** in 25 ml anhydrous ether in a serum bottle. The mixture was sealed and allowed to stand overnight at room temperature. Upon filtration and washing with three 30-ml portions of anhydrous ether, 4.65 g (100%) crude solid was obtained. A portion of this solid was recyrstallized from chloroform/ethyl acetate to obtain a shiny crystalline product with mp 199.5-201 C.

The following were identified from the ^1H NMR: aromatic protons (multiplet, 7.41-7.17 ppm), benzyl protons (singlet, 4.19 ppm), equivalent ring methylene protons (singlet, 4.10 ppm) and equivalent methyl protons (singlet, 3.22 ppm). The integrated areas support the assignments.

The proton-decoupled ^{13}C spectrum showed the following: C-2 carbon of the imidazoline (167.83 ppm), aromatic carbons (130.59, 129.86, 128.45, 128.21 ppm), equivalent ring methylene carbons (50.78 ppm), equivalent methyl carbons (34.86 ppm), and benzyl carbon (31.12 ppm). Assignments are based on multiplets observed in the coupled spectrum.

Anal. calcd. ($C_{12}H_{17}N_2Br$): C, 53.54; H, 6.36; N, 10.40; Br, 29.68. Found: C, 53.84; H, 6.44; N, 10.56; Br, 29.89.

Preparation of Crude Dimethyl Sulfate Quaternary Salt of Product 15

A solution of 1.17 g (6.4 mmol) of **15** in 50 ml of anhydrous ether was treated with 1.06 g (8.4 mmol) of dimethyl sulfate. A cloudy layer was observed almost instantly. The mixture was allowed to stand overnight. The supernatant was decanted and the viscous oily residue was washed a number of times in ether, followed by toluene, and then was subjected to vacuum 1-2.5 mm at 40 C for 2 hr. The crude product had a sharp band at 1625 cm^{-1}.

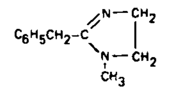
Assignments of peaks in the ^1H spectrum were based on the integrated areas and chemical shifts as follows: aromatic protons (multiplet, 7.35-7.16 ppm), benzyl protons (singlet, 4.05 ppm), equivalent ring methylene protons (singlet, 3.95 ppm), equivalent methyl protons (singlet, 3.07 ppm), and protons due to $CH_3SO_4^-$ (singlet, 6.57 ppm). The remaining unassigned peaks were attributed to unrelated impurities in the crude product.

From the proton-decoupled ^{13}C spectrum, the following were identified: C-2 of the imidazolinium ring (116.13 ppm), aromatic carbons (130.25, 128.89, 127.48, and 127.39 ppm), equivalent ring methylene carbons (49.47 ppm), equivalent methyl carbons (33.40 ppm), benzyl carbon (28.98 ppm), and methyl carbon for $CH_3SO_4^-$ (53.50 ppm).

RESULTS AND DISCUSSION

In view of the uncertainty, it appeared to us that the structure of the quaternary salt needs to be resolved. Since other mesomeric cations are known (3), structures such as 4 would appear reasonable. However, these products have often been made from symmetrical starting materials (4).

Conclusive proof of such a structure can be the preparation of a crystalline model compound and examination of X-ray diffraction pattern. With this intention, we quaternized 1-methyl-2-benzylimidazoline **15** with a number of alkylating agents, e.g., dimethyl sulfate, methyl bromide and methyl *p*-toluenesulfonate. With the exception of methyl bromide, all of them gave glassy liquid products. A well-crystallized sample of the methyl bromide salt of **15** was submitted for X-ray crystallography. To our dismay, we discovered on preliminary examination that the crystal was "twinned," and no useful structural information could be obtained.


(15)

SCHEME 7

A proton NMR of the salt (Fig. 1), however, showed that the two methyl groups were magnetically equivalent. This could occur only if structure **4** were correct, barring any accidental equivalence. Furthermore, the two methylene groups in the ring were also equivalent, further

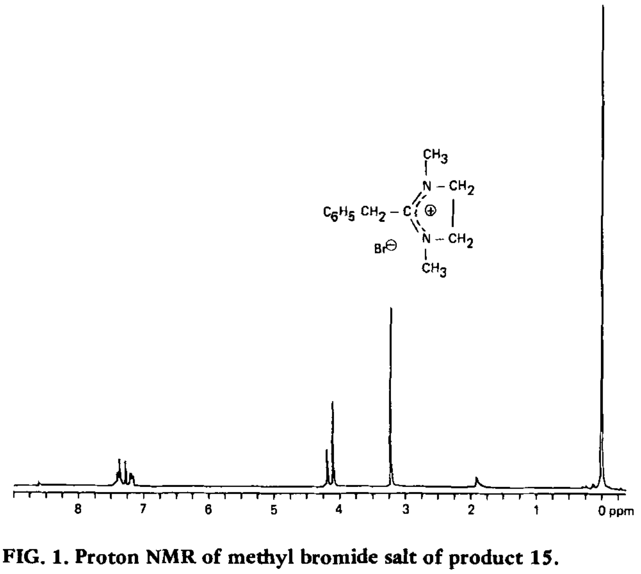


FIG. 1. Proton NMR of methyl bromide salt of product 15.

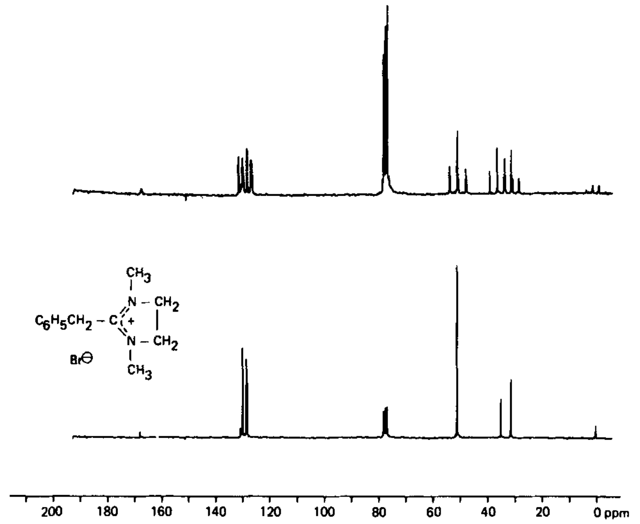


FIG. 2. ^{13}C NMR of methyl bromide salt of product 15: (a) coupled, (b) decoupled.

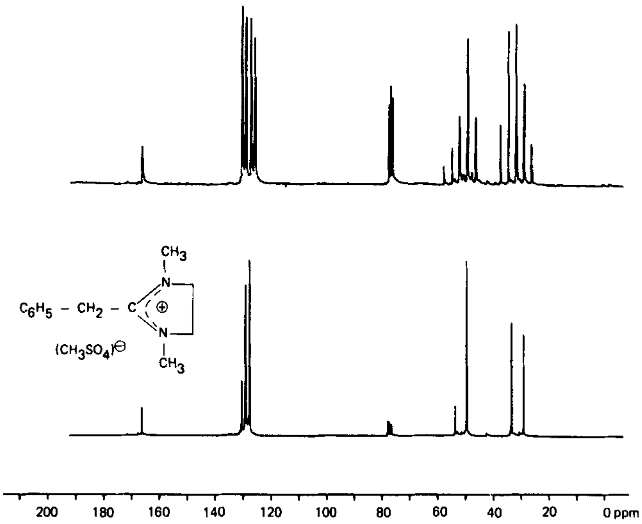


FIG. 4. ^{13}C NMR of dimethyl sulfate salt of product 15: (a) coupled, (b) decoupled.

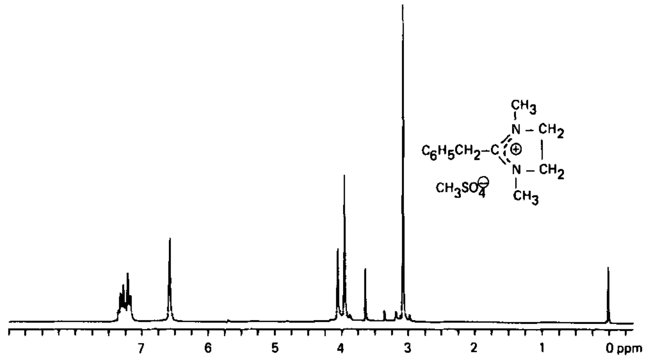


FIG. 3. Proton NMR of dimethyl sulfate salt of product 15.

strengthening the conclusion that the structure could be 4. A similar conclusion was reached from ^{13}C NMR (Fig. 2). However, since the product was crystallized for purification, the possibility that fractionation resulted in the separation of only one isomer could not be ruled out.

To resolve this situation, quaternization of 1-methyl-2-benzylimidazoline 15, was done with dimethyl sulfate. The crude product was washed with, e.g., chilled ether, and treated as described earlier in this report. The crude oily product that was obtained in quantitative yield was examined by both proton and ^{13}C NMR (Figs. 3 and 4). The unmistakable conclusion was that the two methyl groups and two methylene groups were magnetically equivalent. This requirement can be satisfied only with the symmetrical structure 4. Note that the crude product does contain signals caused by unrelated impurities.

Further definitive evidence about the structure of the imidazolinium salt can be obtained using ^{15}N NMR. However, the problems associated with natural abundance ^{15}N NMR are well known. Efforts to obtain ^{15}N data are in progress.

ACKNOWLEDGMENTS

The authors thank R. Grimm and M.L. Deviney for their interest and support.

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[Received October 24, 1980]