Reaction of β-Aminoamides with Aromatic Aldehydes

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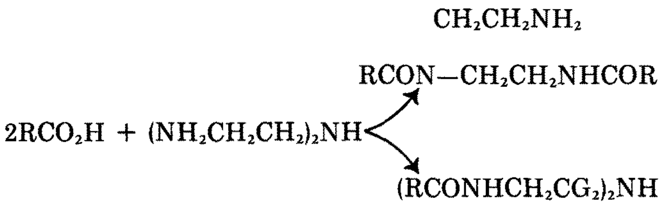
The American Oil Chemists' Society official methods TF 1b-64 and TF 2b-64, "Quantitative Determination of Amines," fail to correctly analyze fatty diethylenetriamine (DETA)-diamides and diamides of 3,3′-iminobispropylamine (DPTA). Primary amine determination through the formation of Schiff base adducts using salicylaldehyde will, in the case of secondary amines that bear amide carbonyl at either the β or γ position, undergo reactions that consume salicylaldehyde despite the absence of primary amine groups. The product of this reaction has been investigated, and a cyclic (2-arylimidazolidine) structure is advanced as the principal adduct of the reaction of aryl aldehydes with DETA-diamides.

Cationic surfactants were previously synthesized in this laboratory for use as water repellents for soils to facilitate water harvesting (1-3). For a study of chemical structure vs physical properties, the cationic surfactants selected had to be available over a wide range of molecular weight. We therefore chose to prepare fatty acid derivatives of diethylenetriamine (DETA) and 3,3′-iminobis-propylamine (DPTA) as model compounds that would meet these criteria. Fatty DETA-derivatives from propionic acid, pelargonic acid, the C_{14}-C_{18} saturated fatty acids and oleic acids were prepared, purified and analyzed by combustion analysis for elemental composition.

Theoretically, two separate diamides could be obtained from this reaction.



$$\begin{array}{l} \qquad\qquad\qquad\qquad\qquad CH_2CH_2NH_2 \\ \qquad\qquad\qquad\qquad RCON{-}CH_2CH_2NHCOR \\ 2RCO_2H + (NH_2CH_2CH_2)_2NH \\ \qquad\qquad\qquad\qquad (RCONHCH_2CG_2)_2NH \end{array}$$

Scheme 1.

Primary amines react quantitatively with salicylaldehyde to form a Schiff base.

$$HOC_6H_4CHO + RNH_2 \rightarrow HOC_6H_4CH{=}NR$$

Scheme 2.

Results from the American Oil Chemists' Society (AOCS) official methods TF 1b-64 and TF 2b-64, "Quantitative Determination of Amines" (4), for the amounts of total, primary, secondary and tertiary amines indicated that the fatty DETA-diamides contained 90–95% of primary amine, which suggested the structural assignment of formula A for the diamides prepared. Subsequently, this assignment was found to be incorrect. ^{13}C NMR spectra indicated that the fatty DETA-diamides were symmetrical molecules with the amido groups on the terminal 1,3 positions and a secondary amino group in the central position. It became necessary therefore to resolve the discrepancy between the results of the wet chemical and NMR methodologies.

According to the AOCS method for amines, three titrations are required. While total and tertiary amines are measured directly, primary and secondary amines are determined by difference. Total amine (a) is determined by titrating a sample of amine, dissolved in isopropanol, using 0.1 N HCl, to a pH 3.0 (yellow) with bromophenol blue indicator. To another sample, salicylaldehyde is added to react with the primary amines present to form a Schiff base, and the sample is then titrated to determine the amounts of secondary and tertiary amines present (b). In the Schiff reaction (5), carbonyl compounds react with primary amines to form an adduct that loses water spontaneously and is converted into the imine $RCH{=}NR$. Subtraction of the value for secondary + tertiary amine (b) from total amine content (a) gives the value for primary amine. The tertiary amine content (c) is determined first by reaction of sample with phenylisothiocyanate and second by titration with 0.1 N HCl.

The objective of this investigation was to establish the chemical structure of the fatty DETA-diamide, to study the reaction of fatty DETA-diamide with salicylaldehyde and other aromatic aldehydes and to determine the chemical structure of the reaction product.

MATERIALS AND METHODS

Materials. The following chemicals were used: diethylenetriamine, 3,3-iminobispropylamine, benzaldehyde, salicylaldehyde, benzene sulfonyl chloride and nonanoic (pelargonic) acid from Aldrich Chemical Co. (Milwaukee, Wisconsin); anisaldehyde from Chem Service (Media, Pennsylvania); p-toluenesulfonylchloride from Eastman Kodak Co. (Rochester, New York); C_{12}, C_{14}, C_{16} and C_{18} saturated fatty acids from Armak Industrial Chemicals Division (Chicago, Illinois); oleic acid from A. Gross and Co. (Newark, New Jersey); and propionic acid from Mallinckrodt (St. Louis, Missouri).

Instrumentation. The following instruments were used: a Model 1610 infrared spectrophotometer from Perkin-Elmer Corp. (Norwalk, Connecticut); a Fisher-Johns melting point apparatus from Fisher Scientific Co. (Pittsburgh, Pennsylvania); a JEOL JNM GX-400

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FT NMR spectrometer (Peabody, Massachusetts); a Finnigan MAT-311A mass spectrometer, from Finnigan Corp. (Sunnyvale, California); and an HP5995B gas chromatography-mass spectrometer from Hewlett-Packard Corp. (Palo Alto, California).

^{13}C nuclear magnetic resonance (NMR). ^{13}C NMR spectra were measured with a JEOL spectrometer for solutions in deuterated chloroform-d or benzene-d_6 with probe temperatures of 21 and 45 C, using chloroform-d or benzene-d_6 as the lock solvent and internal reference (77.0 ppm or 128 ppm), respectively. The spectrometer was operated in the Fourier transform mode at 100.4 MHz, with a 25 KHz sweep width and a digital resolution of 1.53 Hz/point. Spectra were acquired with a 30-45° radio frequency pulse, repeated every 5-10 seconds, using broad band H decoupling. A 1-2 Hz broadening factor was applied in data processing. To identify the multiplicity of each carbon resonance, spectra were accumulated in the coupled mode with gated decoupling, during the recycling time to preserve the Nuclear Overhauser Effect (NOE).

Mass spectrometry. The HP-5995B gas chromatography-mass spectrometry system was used to obtain the electron impact (EI) spectra, while the chemical ionization (CI) data was obtained using a Finnigan MAT 311A. Detailed operational information is reported in a previous publication (6).

Synthetic procedure: preparation of diamide derivatives. A 104.5-g volume of DETA (1.0 mol) was added with caution to 150.0 g propionic acid (2.0 mol). The temperature increased over 30 min from 26 C to 104 C. When the addition was completed, the reaction was continued for 4 hr at 145-155 C. Analysis of the product by titration showed 4.6% free fatty acid and 4.60 meq/g total amine (4.64 theoretical value), according to AOCS official methodology (4). The product was recrystallized from acetone, yielding 96.2 g $(CH_3CH_2CONHCH_2CH_2)_2NH$, a white crystalline powder (mp 86-87 C) in 45% yield (meq/g amine = 4.47). The preparation of DETA derivatives of higher molecular weight fatty acids has been described in previous publications (1,2), while the fatty diamides of DPTA are described in a recent report (3).

Reaction of propionic-DETA-diamide with salicylaldehyde. Twenty g propionic-DETA-diamide (0.09 mol), was dissolved in 250 ml benzene at 55 C and 12.0 g salicylaldehyde (0.10 mol) was added. The reaction mixture was heated for 2 hr at 83 C, and 2 ml water was collected in a Dean Stark tube. Benzene was removed, and the reaction product was recrystallized from 1:1 acetone/hexane to produce a white crystalline product in 94.4% yield (mp 98-99 C) with a combustion analysis of $C_{17}H_{25}N_3O_3$. Similar reactions were carried out between the diamide and benzaldehyde or anisaldehyde with the diamide.

TABLE 1

Amine Analyses of β-Amino Amides (meq/g)[a]

RCOOH	Total amine Theoretical	Total amine Found	Primary	Secondary
Diethylenetriamine (DETA)				
C_2H_5	4.64	4.47	4.27	0.20
C_8H_{17}	2.61	2.60	2.25	0.05
$C_{11}H_{23}$	2.14	1.85	1.76	0.09
$C_{13}H_{27}$	1.96	1.69	1.61	0.08
$C_{15}H_{31}$	1.72	1.70	1.67	0.03
$C_{17}H_{35}$	1.57	1.50	1.49	0.01
$C_{17}H_{33}$,*cis*	1.57	1.57	1.32	0.25
Iminobis-propylamine (DPTA)				
C_2H_5	4.11	4.44	2.69	1.32
C_8H_{17}	2.43	2.47	2.03	0.44
$C_{11}H_{23}$	2.02	1.95	1.34	0.61
$C_{13}H_{27}$	1.81	1.78	1.56	0.22
$C_{15}H_{31}$	1.64	1.62	1.33	0.29
$C_{17}H_{35}$	1.51	1.48	1.23	0.25
$C_{17}H_{33}$,*cis*	1.51	1.58	1.06	0.52

[a] As determined by AOCS official methods TF 1b-64 and TF 2b-64. Theoretical amine = 1000/mol wt.

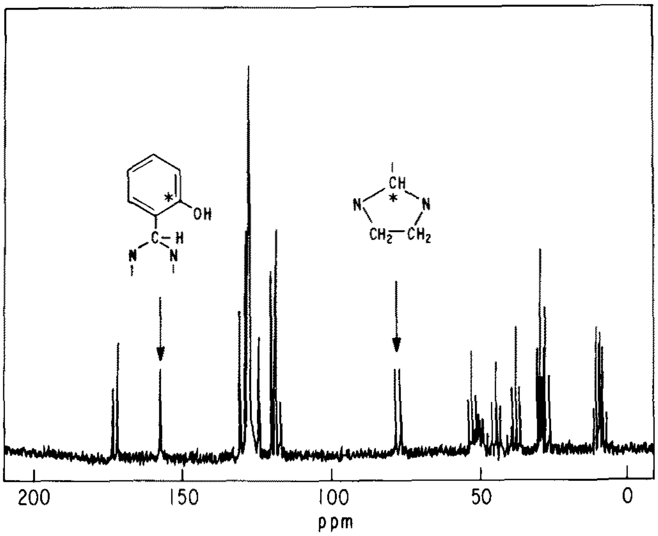

FIG. 1. ^{13}C proton-coupled spectrum of imidazolidine from reaction of propionic-diethylenetriamine-diamide and salicylaldehyde, in benzene-d_6. *, Absorption of specific carbons.

Reaction of pelargonic DETA diamide and p-toluenesulfonyl chloride. Twenty-five g pelargonic-DETA-diamide (0.07 mol) was dissolved at 50 C in 250 ml of toluene containing 25 ml of pyridine, and 15.5 g p-toluenesulfonyl chloride (0.08 mol) dissolved in 100 ml benzene was added dropwise with stirring. The reactants were heated at 100 C for 1 hr to complete the reaction, then cooled, extracted with 6 N HCl to remove excess pyridine, and washed with distilled water until neutral. Sixteen g of a white crystalline product (46% yield, mp 115-116 C) was obtained after several crystallizations from 1,2-dichloroethane. Its elemental analysis corresponded to $C_{29}H_{51}N_3O_4S$, which agreed with the formula for the p-toluenesulfonamide of pelargonic-DETA-diamide. Similar reactions were carried out with propionic-DETA-diamide and pelargonic-DETA-diamide with benzenesulfonyl chloride. The benzenesulfonamide of pelargonic-DETA-diamide was a white powder (mp 97-98 C) obtained in 80% yield. The corresponding propionic analogue, obtained as yellow crystals in 50% crude yield, required further extraction with ethyl ether in a Soxhlet apparatus to produce crystalline needles (mp 92-93 C).

RESULTS AND DISCUSSION

The AOCS official methodology (4) has long been recognized as a standard procedure for analyzing mixtures of amines and had been used by us in the past for simple amines without incident. This method was selected initially to evaluate fatty DETA-diamides and fatty DPTA-diamides. The results, recorded in Table 1, indicated that the diamides were predominantly primary amine. Only small amounts of secondary amine were found in each sample. On this basis we assigned structure A of scheme 1 to the diamide. However, the ^{13}C NMR spectrum indicated that the DETA-diamide of pelargonic acid was in fact symmetrical. To resolve this matter, the propionic-DETA-diamide and derivatives were prepared for ^{13}C NMR and mass spectrometric analyses. The molecular weight and purity of all compounds were confirmed by CI mass spectrometry, and the EI fragmentation patterns were consistent with structures that we ultimately proposed.

The ^{13}C proton-decoupled NMR spectrum of the propionic-DETA-diamide in deuterated chloroform was determined. In addition to the $CDCl_3$ peak at 77 ppm, only five other peaks for carbon were observed. These peaks are assigned as follows:

$(CH_3$	CH_2	CONH	CH_2	$CH_2)_2NH$
9.8	29.5	174.5	39.0	48.4

These are the observed ^{13}C NMR chemical shifts (in ppm from Me_4Si). If the diamide had really possessed large amounts of primary amine, as indicated by the AOCS official method for amines, the NMR spectrum would have indicated the unsymmetrical nature of the molecule, and more than five peaks would have been observed. The ^{13}C NMR data clearly show that the diamides from the reaction of DETA with carboxylic acids are symmetrical compounds as well as secondary amines. This is confirmed by the reaction of the DETA-diamides of propionic and pelargonic acids with benzenesulfonyl chloride.

Although propionic-DETA-diamide is a secondary amine, it reacted readily with salicylaldehyde nonetheless. This product, obtained in excellent yield, had a molecular weight of 319.5 according to mass spectrometry and gave an elemental analysis corresponding to $C_{17}H_{25}N_3O_3$. The ^{13}C proton-coupled NMR spectrum of this compound is shown in Figure 1. In this spectrum, which was determined in deuterated benzene, a doublet appeared at 78 ppm that was assigned to the 2-carbon of an imidazolidine ring, while the singlet at 158 ppm was assigned to the nonprotonated-phenolic ring carbon and not the CH=N resonance. Schiff bases give rise to signals in the same spectral region (7), but their resonances would be doublets due to C-H coupling. Furthermore, brief treatment of the propionic acid-DETA-diamide-salicylaldehyde adduct with one equivalent of HCl (2N, 30 min at reflux) gave salicylaldehyde and the hydrochloride salt of the original symmetrically substituted diamide, in accordance with our proposed structure. The reaction proceeds by the initial reaction of the aldehyde at the basic secondary nitrogen and goes to completion because of the proximity of an amide functionality by forming an imidazolidine ring, (Equation 1, Fig. 2).

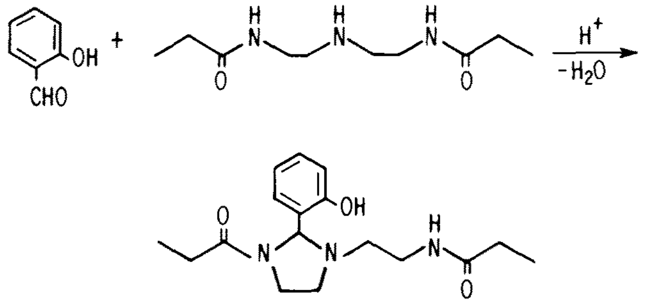

FIG. 2. Reaction of propionic-diethylenetriamine-diamide and salicylaldehyde.

The reaction products of γ-aminoamides and salicylaldehyde were also investigated to determine the scope of this reaction. The adduct of propionic-DPTA-diamide and salicylaldehyde had a molecular weight of 347.4 and a shift of 78 ppm in the ^{13}C NMR, indicating the formation of the hexahydropyrimidine derivative.

We also found that imidazolidine formation occurred in reactions between other aromatic aldehydes that do not contain aromatic hydroxyl groups and the aminoamides. Propionic acid-DETA-diamide was allowed to react with benzaldehyde and anisaldehyde. Both of the oily reaction products yielded similar spectra and were judged likewise to have formed the corresponding heterocyclic structure. The molecular weight of the propionic acid-DETA derivatives was found to be 303.4 for the benzaldehyde derivative and 333.5 for the anisaldehyde derivative. These compounds also possessed a shift of 78 ppm, showing that formation of ring compounds was not the exclusive property of β-amino amides and salicylaldehyde.

These reactions do not appear to have been reported previously. Thus the AOCS methods for "Quantitative Determination of Amines" are invalid for the analysis of β- and γ-aminoamides, because salicylaldehyde reacted with the β-aminoamides to form imidazolidines and with γ-aminoamides to produce hexahydropyrimidines.

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[Received January 28, 1986]