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The separation of *cis*- and *trans*-1,2-diaminocyclohexane via trifluoroacetylation

The use of ethyl trifluoroacetate as trifluoroacetylating agent

One of the impurities formed during the hydrogenation of adiponitrite (ADN) to form hexamethylenediamine (HMD) is 1,2-diaminocyclohexane (DCH). The presence of impurities even at the parts per million level in the refined HMD, which is used as a nylon intermediate, will affect the stability and dying properties of the final polymer. In an effort to study the mechanism of the formation of DCH during the hydrogenation of ADN, it was necessary to determine the DCH *cis/trans* ratio so as to correlate this ratio with hydrogenation and distillation conditions.

SMITH AND RADFORD[1] have previously reported a gas–liquid chromatographic (GLC) separation of the *cis*- and *trans*-DCH isomers by direct injection of the amines. The separation is not complete and the procedure is lengthy due to the use of long columns and is not intended for trace amine analysis.

Due to loss by absorption and decomposition, it is difficult to chromatograph amines quantitatively by GLC techniques at the parts per million level[2]. Thus, it is convenient to convert the basic amine group to the less basic amido group by trifluoroacetylating the amines. DCH, after isolation and purification from production line material, was converted into its trifluoroacetyl (TFA) derivative with ethyl trifluoroacetate (ETFA) rather than the conventional trifluoroacetic anhydride. The DCH-TFA derivative was readily separated into its *cis* and *trans* isomers using GLC separation techniques. The DCH-TFA derivatives were identified by GLC–MS techniques while the individual geometrical isomers were identified by retention time measurements. The separation of these isomers after trifluoroacetylation is complete and rapid.

Experimental

Apparatus. A Perkin-Elmer 900 gas chromatograph provided with flame ionization detectors (FID) was used for the retention time measurements. This instrument was equipped with a stainless-steel column 6 ft. × 1/8 in. O.D. containing 2 % Versamid 900 on 80–100 mesh acid-washed and silanized Gas-Chrom Q (column I). A Varian 1800 gas chromatograph provided with FID detectors and a Llewellyn separator was coupled to a CEC 21–103 mass spectrometer. This chromatograph was used with a stainless-steel column 6 ft. × 1/8 in. O.D. containing 5 % FFAP on 80–100 mesh acid-washed, DMCS-treated Chromosorb G, (column II).

Preparation of the TFA derivatives. The ETFA was distilled and the fraction boiling between 61–62° was collected. About 5 % of the distillation charge and the initial 5 % of the collected distillate were discarded. The reagent was kept under a nitrogen atmosphere.

In a 25-ml erlenmeyer flask 2.5 ml of the distilled reagent are added to 3 ml of anhydrous ethanol. Two drops of a 0.5 % alcoholic solution of Bromothymol Blue are added to the solution. Ammonia is bubbled through the solution at a very slow rate, until the indicator changes from yellow to a faint blue. This procedure necessitates only a small quantity of ammonia. About 1 ml of an ethanol solution containing

100–1000 μg/ml of the diamine is added. The solution is then heated on a hot plate for 10–15 min, which is necessary for the reaction to proceed to completion rapidly. In this manner any excess ETFA reagent is boiled off. If necessary the solution containing the TFA derivative can now be quantitatively transferred for final dilution with ethanol. This procedure is used for constructing calibration curves. To carry out the reaction with 1–5 g of diamine, it is only necessary to adjust the ETFA quantity to allow for a three-fold excess. The *trans*-DCH was obtained from the Aldrich Co.

Results and discussion

Trifluoroacetylation is usually performed by reacting amines with trifluoroacetic anhydride at −5°. The reagent requires care in handling and the reaction is violent, which complicates matters when making derivatives with such quantities as 1–5 g of HMD. Furthermore, the use of trifluoroacetic anhydride produces trifluoroacetic acid as a reaction by-product; this is highly corrosive and causes damages to metallic ovens and detector components. To overcome these difficulties, ethyl trifluoroacetate was used. ETFA reacts with amines to produce the trifluoroacetamide and ethyl alcohol. The reaction proceeds rapidly at 60–70°, but at room temperature ETFA only reacts very slowly with amines. The quantitative yield of the reaction was studied with two amines: HMD and ε-aminocapronitrile (ε-ACN). The HMD-TFA and ε-ACN-TFA were prepared on the 1-g scale. The purified derivatives were submitted to C, H, N analyses and mass spectra analysis. These TFA derivatives were used to construct the GLC calibration curves for checking the extent of the reaction of HMD and ACN with ETFA. The reaction yields were between 67.2 and 78.3 % for HMD, while for ε-ACN the conversion was between 51.6 and 68.3 %, as shown in Table I. However, when the reagent solution is bubbled with small quantities of ammonia using Bromothymol Blue as the indicator, followed by the addition of the HMD or ε-ACN and heating, the reaction yield is constant and essentially complete at about 98.3–99.0 %. The ammonia probably has the effect of neutralizing traces of trifluoroacetic acid which may be produced by hydrolysis of ETFA while under storage. The traces of trifluoroacetic acid compete with the ester in the reaction with the amines to form the amine salt. Ammonia was chosen as the base since it could be added to the solution as a dry gas. The addition of aqueous basic solutions was avoided so that non-aqueous solutions could be chromatographed.

TABLE I

EFFECT OF AMMONIA ON THE TRIFLUOROACETYLATION YIELDS USING ETHYL TRIFLUOROACETATE

Compound	*Treatment of solution prior to heating*	*Quantity of amine added (μg)*	*Conversion (%)*
HMD	—	154	67.2
HMD	—	362	78.3
HMD	ammonia	154	98.3
HMD	ammonia	362	99.0
ε-ACN	—	268	51.6
ε-ACN	—	740	68.3
ε-ACN	ammonia	268	98.8
ε-ACN	ammonia	740	98.4

The DCH obtained from plant column distillations was treated with TFA. The injection of the DCH-TFA into the GLC apparatus, utilizing column I isothermally at 195°, revealed two peaks, as shown in Fig. 1. An indication that the two peaks might correspond to the two isomers was obtained by trapping a sufficient quantity of the two components in capillary tubes by means of a stream splitter at the end of the column and performing repetitive injections. The IR spectra of the two components were nearly identical. The carbonyl absorption for both components occurred at 5.88 μ, which is in agreement with the solid spectra of alkyl and cyclic trifluoroamides[3].

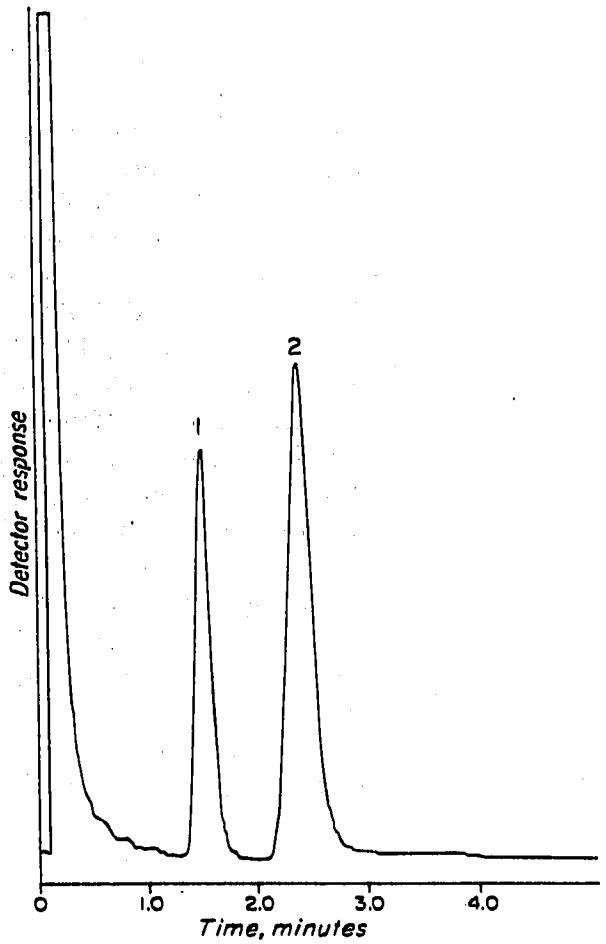

Fig. 1. Chromatogram of the DCH-TFA derivatives. Amount injected, 0.134 μg. 1 = *cis*-DCH-TFA; 2. = *trans*-DCH-TFA. The *trans*/*cis* ratio is 1.91.

Trans- and *cis*-DCH can be prepared in pure form by synthesis from precursors of known steric configuration and utilizing only known stereospecific reactions in the synthesis[4]. The *trans*-DCH obtained commercially was subjected to trifluoroacetylation. This *trans*-DCH-TFA possessed the same retention time as the component having the longer retention time. Thus, the component in Fig. 1 having the shorter retention time was designated as the *cis* isomer while the one having the longer retention time was designated as the *trans* isomer.

The DCH-TFA derivatives were analyzed with column II at a programmed

rate of 10°/min from 110–220°. The column exit was coupled by a splitter to a mass spectrometer. The separation in this column was similar to that shown in Fig. 1. The corresponding mass spectral scans are shown in Figs. 2 and 3 for the *cis*-DCH-TFA and *trans*-DCH-TFA, respectively. The two spectra are identical, showing the same fragmentation pattern. Under electron impact the derivatives show a molecular ion at an *m/e* of 306. A fragment ion of *m/e* 237 corresponding to a loss of a CF_3 is observed which is typical of trifluoroacetamides[5]. A fragment ion at *m/e* of 209 corresponding to the loss of $COCF_3$ is also observed. Proposed structures for other

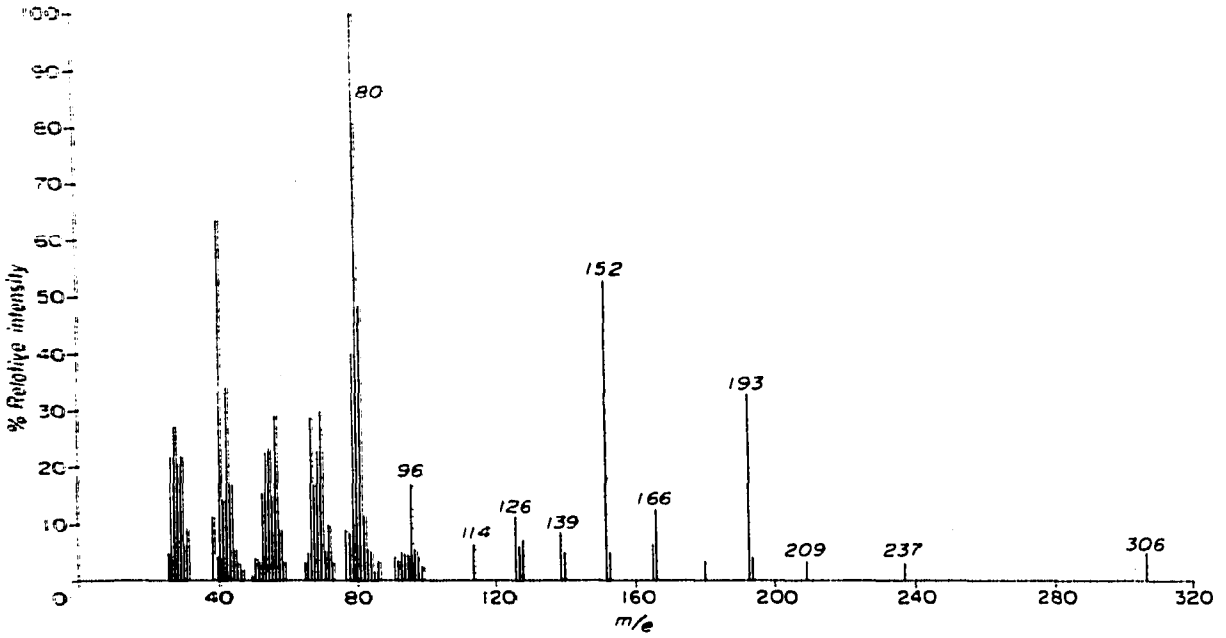

Fig. 2. Mass spectrum of the *cis*-DCH-TFA derivative.

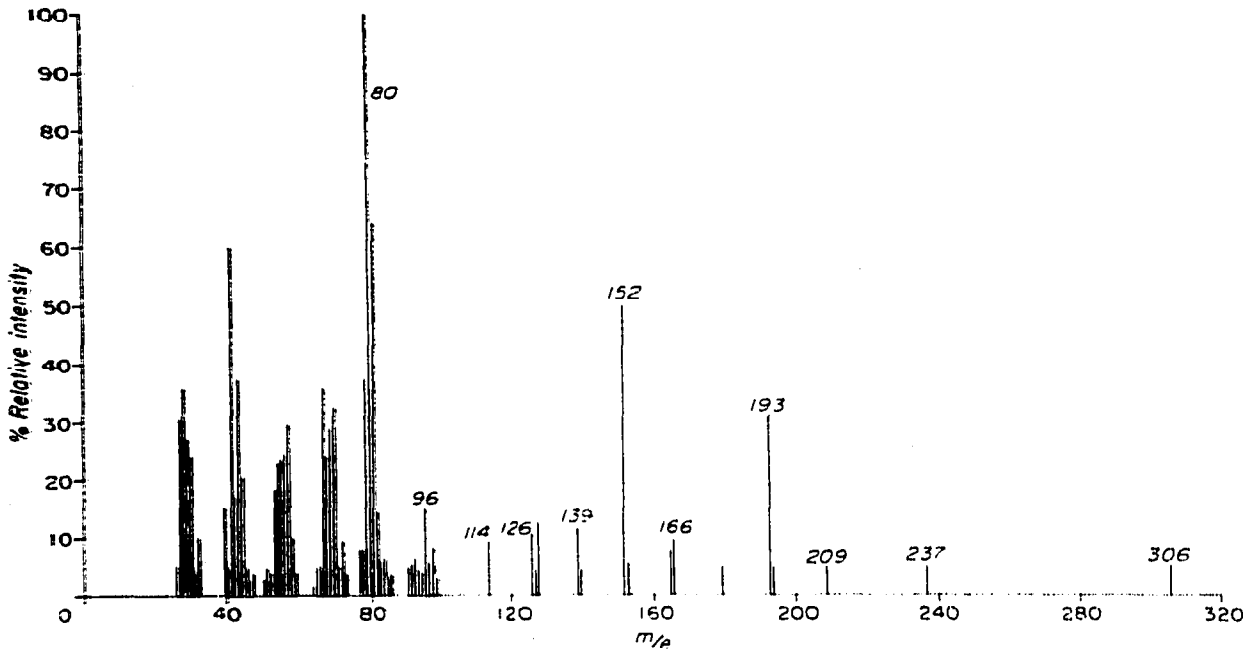

Fig. 3. Mass spectrum of the *trans*-DCH-TFA derivative.

major fragments are as follows: *m/e* 193, corresponding to the loss of $H_2N-COCF_3$; *m/e* 166, corresponding to the loss of $H_2(CF_2)_2$; *m/e* 152 is due to the formation of $(CH_2=CH-CH=NH-COCF_3)^+$ or due to the cyclic structure 2-hydroxy-2-trifluoromethyl-cyclopentene; *m/e* 139 is due to the fragment ion $CH_2=CH-NH-COCF_3$; *m/e* 80, which is the most abundant fragment ion, is due to the pyridyl ion radical.

The mass spectrum indicates the formation of the DCH-TFA and shows that both components have the same structure. The separation of *cis*- and *trans*-DCH via trifluoroacetylation has permitted the determination of the *cis*/*trans* ratio and hence the study of this ratio as a function of the conditions of plant operation during the distillation and purification of HMD. The procedure described here can be used for the determination of DCH in HMD at levels from 100–500 p.p.m. which is not possible by direct chromatography as previously described[2]. A further advantage is gained in that HMD and DCH have very close boiling points and are difficult to separate on conventional columns[2] for diamine analysis. However, once the diamines are converted to their TFA derivatives, they can be easily separated by the columns described.

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