Structural features in epoxy networks from *N*-diglycidyl epoxies and amines: 1. Dominant intramolecular cyclization reaction in the reactions of *N,N*-diglycidylaniline with aniline and substituted anilines

P. Johncock and G. F. Tudgey
Royal Aerospace Establishment, Farnborough, Hants GU14 6TD, UK

and A. V. Cunliffe and R. K. Morrell
Royal Armaments Research and Development Establishment, Waltham Abbey, Essex EN9 1AX, UK
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The reactions of *N,N*-diglycidylaniline with aniline, 2,6-dimethylaniline, 2,6-dichloroaniline, 2,4,6-trichloroaniline, 3-trifluoromethylaniline and 3,5-bis(trifluoromethyl)aniline were investigated. The formation of similar amounts of the *cis* (equatorial/equatorial dihydroxy arrangement) and *trans* (axial/equatorial dihydroxy arrangement) isomers of the eight-membered 3,7-dihydroxy-perhydro-1,5-diazocine ring was the predominant intramolecular cyclization reaction. Steric effects were more important than polar effects in determining the extent of cyclization to the extent that the combined yields of *cis* and *trans* isomers was increased from ≈15% with aniline to ≈45% with 2,6-dimethylaniline. Conformational structural assignments were made on the basis of ^{1}H and ^{13}C nuclear magnetic resonance spectroscopy and infrared spectroscopy at high dilution.

(Keywords: *N,N*-diglycidylaniline; aniline and substituted anilines; intramolecular reactions; n.m.r.; i.r. spectroscopy)

INTRODUCTION

The occurrence of intramolecular cyclization reactions during the cure of an epoxy system is important because of their effect on the rheology of cure and on the crosslink density of the resultant network. Such reactions to give morpholine and perhydro-1,5-diazocine rings have been considered to play a significant part in the cure of *N,N*-diglycidyl epoxies with amines. Direct recognition of such structural elements has been attempted, but the results cannot be regarded as conclusive: in a CP/MAS ^{13}C nuclear magnetic resonance (n.m.r.) analysis[1] of the thermoset from bis[*N,N*-bis(2,3-epoxypropyl)-4-aminophenyl]methane (TGDDM) and 4,4′-diaminodiphenylsulphone, absorptions in the expected regions within a complex pattern were assigned to primary alcohol and ether groups from which the presence of morpholine rings was inferred; in similar n.m.r. studies, absorptions were also specifically assigned to morpholine rings[2] and from deconvoluted spectra[3] to both morpholine and 1,5-diazocine rings. Other evidence is indirect. Dusek and co-workers[4] found that for *N,N*-diglycidylaniline (DGA) or TGDDM cured with 4,4′-diaminodiphenylmethane in solvent, the critical molar ratio of amine to epoxy (with amine in excess) required to prevent gel formation decreased with increasing dilution, behaviour consistent with the occurrence of intramolecular cyclization. In contrast, 2,2-bis[4-(2,3-epoxypropoxy)phenyl]propane, which cannot undergo such intramolecular reactions with amines, provided a gel factor which was independent of concentration. Morgan and Mones[5], from infrared (i.r.) data, concluded that reactions between epoxide and secondary amine or secondary alcohol were a factor of 10 slower than reaction with primary amine groups, and that the reaction with secondary alcohol was dominant in the later stages of cure: on the basis of molecular modelling and reaction probability studies, it was considered that ≈75% of the reaction with secondary amines and secondary alcohols occurred intramolecularly.

Spectroscopic recognition of cyclic structures within a polymer network clearly requires good data for model compounds, and investigations in this area have recently been reported. In the reactions of *N*-diglycidyl systems with amines, intramolecular cyclization to give morpholine (II), perhydro-1,4-oxazepine (III), perhydro-1,5-diazocine (IV) and perhydro-1,4-diazepine (V) ring systems can occur in addition to the intermolecular reaction to give chain product (VI) as shown in *Figure 1*. Available evidence suggests that the reaction between epoxide and secondary alcohol only occurs in the absence of a competing reaction with secondary amine. Matejka *et al.*[6] isolated a product from the reaction between DGA and *N*-methylaniline which, from mass spectral evidence, was considered to be the seven-membered cyclic com-

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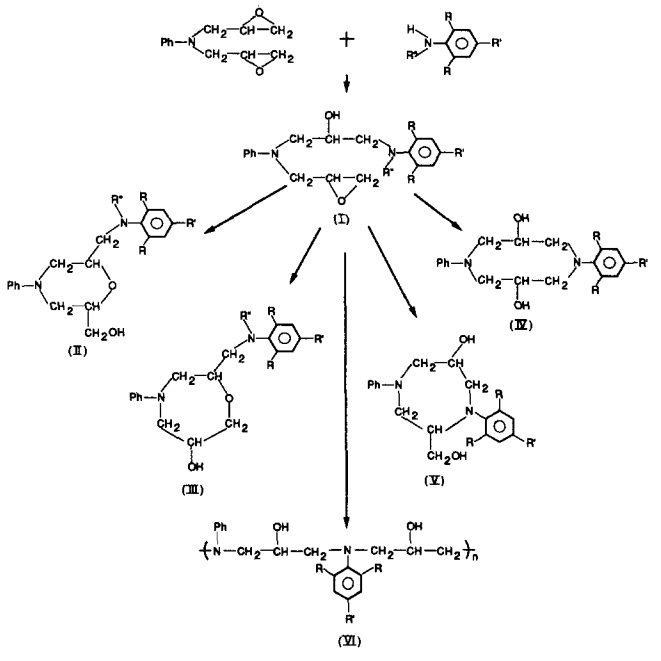


Figure 1 Competing processes in the reactions between DGA and aniline or substituted anilines

pound (III; R,R′ = H, R″ = CH_3): another suspected cyclic compound was not isolated. Attias *et al.*[7] examined this reaction using *N*-ethylaniline and, on the basis of gel permeation chromatography (g.p.c.), high performance liquid chromatography (h.p.l.c.) and ^{13}C n.m.r. evidence, concluded that both the six- and seven-membered ring compounds (II; R,R′ = H, R″ = C_2H_5) and (III; R,R′ = H, R″ = C_2H_5) were formed each as a pair of h.p.l.c.-resolved isomers. Note that these authors also observed the consumption of epoxy groups by another process which involved an intramolecular reaction of the *N*-glycidyl group with the adjacent aromatic ring to form a tetrahydroquinoline ring system. The formation of both six- and seven-membered rings is as might be expected since, although nucleophilic attack of amines on epoxides usually occurs at the least hindered carbon atom[8], Baldwin's rules for ring closure[9], which are based on stereochemical considerations, predict that in a six- *versus* seven-membered ring forming situation, the former is favoured. Evidence in support of this was recently provided by Buriks and Lovett[10] for the base-induced reactions of (2,3-epoxypropyl)(2-hydroxyethyl)alkylamines, which predominantly gave the corresponding morpholine derivatives; however, (2,3-epoxypropyl)(2-hydroxyethyl)dialkylammonium chlorides gave about equal amounts of the corresponding six- and seven-membered rings. Baldwin does not consider a competitive seven- *versus* eight-ring forming situation (e.g. formation of (V) *versus* (IV)), but does predict that in such a situation the formation of a seven-membered ring is a favoured process. However, only eight-membered rings have been identified so far. Dusek and co-worker[6,11] isolated a crystalline isomer of (IV: R,R′ = H) and other workers[12] have reported both isomers for the compound: ^1H and ^{13}C n.m.r.[11,12] together with infrared[11] spectroscopy were used in an attempt to determine their structural conformations but the assignments are inconclusive.

As a more realistic model of a competitive situation in which secondary amine and secondary alcohol compete for epoxide, which might, for example, occur in the later stages of cure, we have examined the reactions of DGA with- aniline and with substituted anilines to determine to what extent the course of the reactions might be influenced by steric and electronic factors. Thus it was considered that the reactions of the secondary amine group in (I; R″ = H) to give perhydro-1,5-diazocine (IV) and perhydro-1,4-diazepine (V) rings might be discouraged by the steric effects of *ortho* substituents and by the polar deactivating effects of electronegative substituents to the extent that the reactions of the secondary alcohol group to give morpholine (II) and perhydro-1,4-oxazepine (III) rings might become dominant.

This paper is confined to a detailed consideration of the structures of the dominant cyclic products formed in these reactions using n.m.r. spectroscopy together with i.r. spectroscopy at high dilution as a probe for intramolecular hydrogen bonding. In a subsequent paper[20], the use of n.m.r. to identify the minor cyclic products, and to characterize the structural features of the polymeric product formed in these reactions will be reported. The question of analysing the TGDDM/DDS network structure from its solid-state n.m.r. spectra on the basis of well defined model compound data will also be addressed at that time.

EXPERIMENTAL

Materials

DGA, b.p. 110–111°C (0.13 mm) was prepared by a procedure described in the literature[13] and had, by analysis[14], an epoxy equivalent of 104 (theoretical, 107). Aniline was purified by distillation. The substituted anilines were obtained from Aldrich Chemicals and were used as supplied.

Instrumentation

For analytical h.p.l.c. a Waters ALC/g.p.c. 244 chromatograph was used. For reverse phase operation (h.p.l.c./r.p.), it was equipped with a 25 × 0.49 cm Spherisorb 50DS2 column and the flow rate was 2 ml min^{-1}. For gel permeation chromatography (g.p.c.) a 100 Å* + 500 Å Ultrastyragel column combination (each 30 × 0.78 cm) was used with a flow rate of 1 ml min^{-1}. Detection was by ultraviolet (u.v.) at 280 nm and the data were recorded with a Spectra Physics SP4100 computing integrator.

Poly(oxypropylene)glycol standards from Waters were used for molecular weight calibration. For preparative h.p.l.c., a Waters Prep LC/System 500 with a refractometer detector and fitted with either a 30 × 5.7 cm PrePak 500 silica cartridge for normal phase (h.p.l.c./n.p.) or PrePak 500/C18 cartridge for h.p.l.c./r.p. was used with an eluent flow rate of 150 ml min^{-1}. H.p.l.c. grade dichloromethane from May and Baker, and tetrahydrofuran (THF) from Rathburn Chemicals were used as supplied but, for preparative work, the latter was freshly distilled. Collected fractions were freed of solvent by rotary evaporation under reduced pressure, and then dried at 50°C (0.001 mm) before being sublimed in a Buchi GKR-50 sublimator at 150–180°C (0.1 mm) depending on the volatility of the compound. The purities

*1 Å = 10^{-1} nm

of the products quoted in the text are based on non-calibrated peak areas.

Glass transition temperatures (T_g) and melting points (T_m) were determined under nitrogen by differential scanning calorimetry (d.s.c.) with a DuPont 9900 or a 1090 thermal analyser at a heating rate of 10°C min^{-1}.

I.r. spectra were recorded with a Perkin–Elmer 1750 *FT*i.r. spectrometer for 0.002 M solutions using a 2 cm cell. The solvents were analytical grade benzene (from M&B) or CCl_4 (from BDH), which had been dried over molecular sieve (4 Å).

The mass spectra of the perhydro-1,5-diazocines were measured with a Finnegan 1020 automated GC/MS system.

^1H and ^{13}C n.m.r. spectra were recorded at 300.13 and 75.47 MHz, respectively, on a Bruker MSL-300 superconducting multinuclear n.m.r. spectrometer. Proton spectra were recorded on ≈5% solutions, using either $CDCl_3$ or acetone-D_6 as solvent, in a 5 mm proton–carbon dual probe. Carbon spectra were measured on ≈20% solutions in the same solvents, using either the same 5 mm probe or a 10 mm broadband multinuclear probe. Carbon spectra were recorded with broadband proton decoupling, typically with 256 scans. All spectra were recorded at ambient probe temperature (≈20°C). The proton spectra were fitted to obtain values of the chemical shifts and spin–spin coupling constants using the PANIC spin simulation software supplied by Bruker as part of the MSL software package.

DGA and aniline

A solution of DGA (32.5 g, 0.159 mol) and aniline (14.8 g, 0.159 mol) was degassed in a Carius tube, which was then sealed and heated at 100°C for 18 h, then at 150°C for 5 h, and finally at 176°C for 18 h. The product solidified to a friable glass on cooling. The h.p.l.c./r.p. trace (*Figure 2a*, 50–90% THF in water with a 20 min linear gradient) of the product was dominated by two early peaks and a broad, much later peak. G.p.c. with THF as eluent (*Figure 2b*) showed a clean resolution of the high (M_n = 700–4000 by polyoxypropylene) and low molecular weight fractions. Sublimation of ≈10 g quantities at 180–200°C (0.05 mm) with a repeat treatment of the combined sublimates gave sublimate (3.5 g) which contained ≈80% of the two early components. These were isolated by preparative h.p.l.c./n.p. with CH_2Cl_2 containing 5% THF as eluent.

The first component, a white powder, was 99% pure (IVt; R,R′ = H) (0.68 g), T_m = 132°C (the sample when quench-cooled after melting gave a T_g = 46°C but no melting exotherm). Elemental analysis for $C_{18}H_{22}N_2O_2$: calculated C, 72.5; H, 7.4; N, 9.4%; found, C, 72.2; H, 7.5; N, 9.6%.

The second component, a white powder, was 99% pure (IVc; R,R′ = H) (0.86 g), T_m = 218°C (the exotherm was reproducible when the sample was quench-cooled after melting). A m.p. of 193–196°C was reported[6] for this compound.

H.p.l.c./r.p. with pure internal standards showed that 5% of (IVt; R,R′ = H) and 8% of (IVc; R,R′ = H) had been formed.

DGA and 2,6-dimethylaniline

A solution of DGA (10.1 g, 0.049 mol) and 2,6-dimethylaniline (5.96 g, 0.049 mol) were heated under argon at 160°C for 18 h. The molten product gave a friable glass on cooling. H.p.l.c./r.p. with 40–90% THF in water as eluent and a 20 min linear gradient showed (see *Figure 2c*) two dominant early peaks and a mixture of these (7.8 g) was obtained by preparative h.p.l.c./r.p. with 45% THF in water as the eluent. Further resolution by preparative h.p.l.c./n.p. with CH_2Cl_2 as eluent afforded the two components.

The first component, a white powder, was 98% pure (IVt; R = CH_3, R′ = H) (2.5 g). It showed no T_m by d.s.c., and the T_g for a sample which was quench-cooled after melting was 49°C. Elemental analysis for $C_{20}H_{26}N_2O_2$: calculated, C, 73.6; H, 8.0; N, 8.6%; found, C, 73.4; H, 7.9; N, 8.5%.

The second component, a white powder, was 98% pure (IVc; R = CH_3, R′ = H) (2.3 g). It gave no T_m by d.s.c. and a sample which was quench-cooled after melting had a T_g of 72°C. Elemental analysis for $C_{20}H_{26}N_2O_2$: calculated, C, 73.6; H, 8.0; N, 8.6%; found, C, 73.5; H, 8.2; N, 8.5%.

H.p.l.c./r.p. with pure internal standards showed that 21% of (IVt; R = CH_3, R′ = H) and 22% of (IVc; R = CH_3, R′ = H) had been formed and that 2% of the 2,6-dimethylaniline was unconsumed.

DGA and 2,6-dichloroaniline

DGA (9.98 g, 0.049 mol) and 2,6-dichloroaniline (7.89 g, 0.049 mol) were heated under argon at 180°C, but h.p.l.c./r.p. (40–90% THF in water with a 20 min linear gradient) showed little reaction after 6 h; however, a reaction occurred at 200°C and there was little difference in the product composition after 7 and 12 h. The molten product cooled to a friable glass. The h.p.l.c. trace (see *Figure 2d*) was dominated by two components. These were isolated from 5 g of the crude product by preparative h.p.l.c./n.p. with CH_2Cl_2 containing 4% THF as eluent.

The first component, a white powder, was 87% pure (IVt; R = Cl, R′ = H) (0.57 g) which contained an unidentified major impurity (8%) of very similar retention time.

The second component, a white powder, was 94% pure (IVc; R = Cl, R′ = H) (0.63 g). The compound showed no T_m by d.s.c. and a sample quench-cooled after melting gave a T_g of 69°C. Elemental analysis for $C_{18}H_{20}Cl_2N_2O_2$: calculated, C, 53.8; H, 4.7; Cl, 26.7; N, 7.0%; found, C, 54.0; H, 4.7; Cl, 26.5; N, 7.0%.

H.p.l.c./r.p. with the separated isomers as standards showed that each had been formed in ≈17% yield and that 5% of the 2,6-dichloroaniline was unconsumed.

DGA and 2,4,6-trichloroaniline

DGA (8.94 g, 0.044 mol) and 2,4,6-trichloroaniline (8.57 g, 0.044 mol) were degassed in a Carius tube, which was then sealed and heated at 200°C for 24 h to give on cooling a friable glass. The h.p.l.c. trace is given in *Figure 2e*. A trial experiment, which had been monitored by h.p.l.c./r.p. (50–90% THF in water with a 20 min linear gradient), had shown from non-calibrated peak areas that after 3 h the reaction components included DGA (52%), 2,4,6-trichloroaniline (33%), the two perhydro-1,5-diazocines (IVc; R,R′ = Cl) and (IVt; R,R′ = Cl) (each <0.5%) and a component (7%) considered to be their precursor (I; R,R′ = Cl, R″ = H). After 8 h, these values were 27, 6, 5, 25 and 11%, respectively; and, after 24 h,

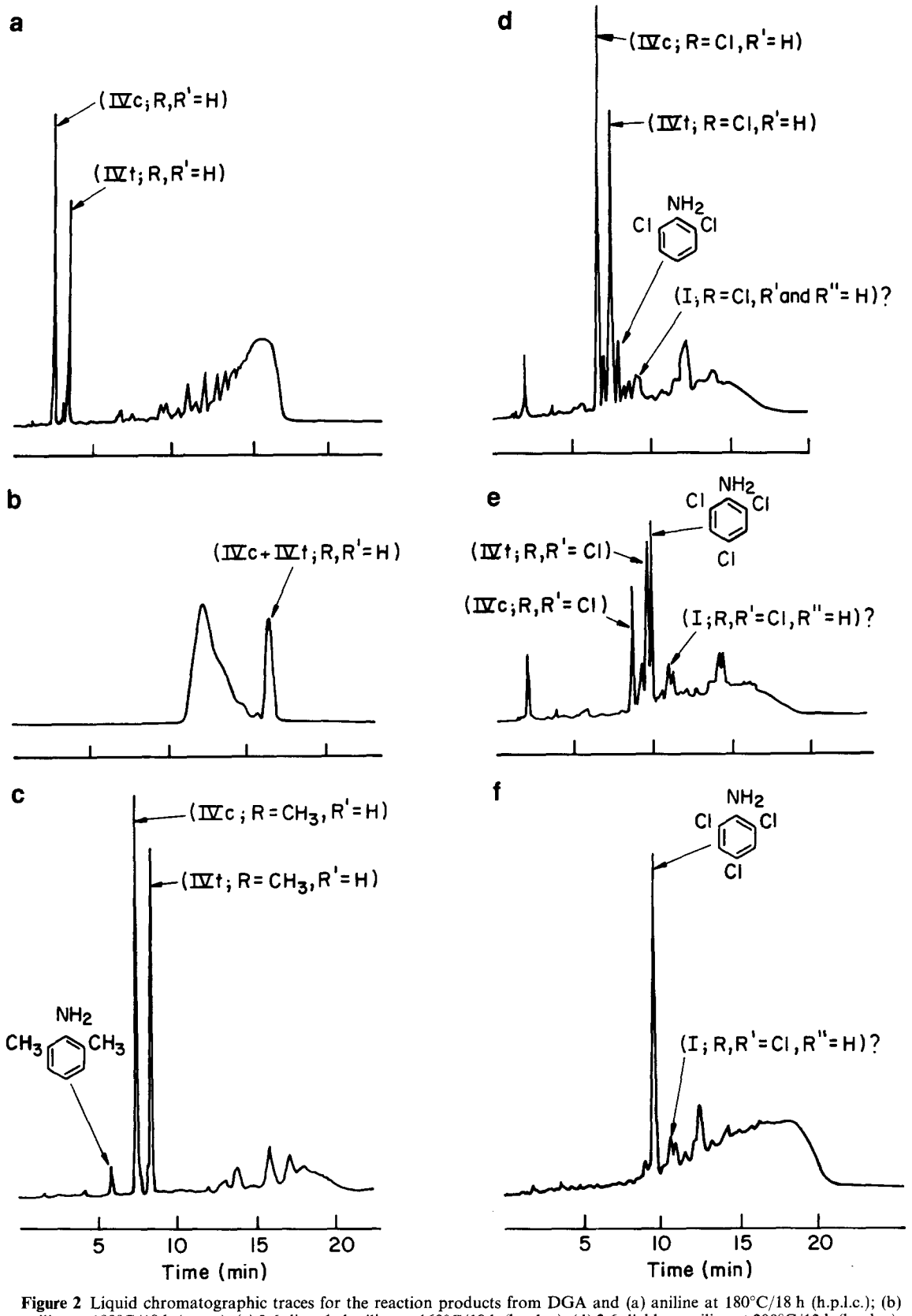


Figure 2 Liquid chromatographic traces for the reaction products from DGA and (a) aniline at 180°C/18 h (h.p.l.c.); (b) aniline at 180°C/18 h (g.p.c.); (c) 2,6-dimethylaniline at 160°C/18 h (h.p.l.c.); (d) 2,6-dichloroaniline at 200°C/12 h (h.p.l.c.); (e) 2,4,6-trichloroaniline at 200°C/24 h (h.p.l.c.); and (f) 2,4,6-trichloroaniline at 230°C/18 h (h.p.l.c.)

0, 7, 7, 10 and 2%, respectively. Crude product (12 g) was partially resolved by preparative h.p.l.c./r.p. with 70% THF/30% water as eluent to give a fraction (3.4 g) which was mainly a mixture of 2,4,6-trichloroaniline and the two perhydro-1,5-diazocine isomers. Resolution of these components by preparative h.p.l.c./n.p. with CH_2Cl_2 containing THF (5%) as eluent allowed these assignments to be confirmed.

The first component was 99% pure 2,4,6-trichloroaniline (0.96 g), which had an i.r. spectrum identical to that of the authentic compound.

The second component, a white powder, was 83% pure

(IVt; R,R′ = Cl) (0.42 g), which contained a major unidentified impurity (14%).

The third component, a white powder, was 96% pure (IVc; R,R′ = Cl) (0.98 g). It gave no T_m by d.s.c. and a sample which was quench-cooled after melting had a T_g of 76°C. Elemental analysis for $C_{18}H_{19}Cl_3N_2O_2$: calculated, C, 58.9; H, 5.4; Cl, 19.3; N, 7.6%; found, C, 58.6; H, 5.5; Cl, 19.2; N, 7.6%.

H.p.l.c./r.p. with the above purified components as standards showed that the two perhydro-1,5-diazocine isomers were each formed in ≈11% yield and that 37% of 2,4,6-trichloroaniline was unconsumed.

DGA with meta*-trifluoromethyl substituted anilines*

DGA (≈0.0005 mol) and the corresponding stoichiometric amount of aniline, 3-trifluoromethylaniline and 3,5-bis(trifluoromethyl)aniline were heated at 150°C for 21 h and then at 180°C for 5 h in sealed tubes with prior degassing. Examination of the products, which were soluble in THF, by h.p.l.c./r.p. (50–90% THF in water with a 20 min linear gradient) showed that the amounts (based on non-calibrated peak areas) of the corresponding *cis*- and *trans*-3,7-dihydroxy-perhydro-1,5-diazocines were 9 and 7%, respectively, with aniline, 13 and 9% with 3-trifluoromethylaniline, and 12 and 9% with 3,5-bis(trifluoromethyl)aniline. G.p.c. with THF as eluent showed that, with increasing trifluoromethyl content, the complexity of the trace increased, which reflected the less advanced state of the polymerization reaction. The perhydro-1,5-diazocine content, which was based on the low molecular weight peak assigned to these compounds, agreed well with h.p.l.c. for the reactions with aniline (17%) and 3-trifluoromethylaniline (23%), but the value for the reaction with 3,5-bis(trifluoromethyl)aniline (27%) was somewhat high, presumably because of non-resolution from some other low molecular weight material.

RESULTS AND DISCUSSION

Intramolecular cyclization products in the reaction of DGA with aniline and some substituted anilines

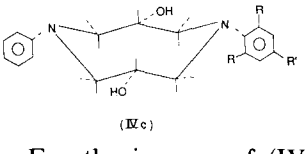
The stoichiometric reactions of DGA with aniline, 2,6-dimethylaniline, 2,6-dichloroaniline and 2,4,6-trichloroaniline were investigated without solvent at temperatures from 160 to 200°C, depending on the system. The corresponding h.p.l.c. traces are given in *Figures 2a* and *c–e*, and clearly show a common feature of a characteristic pair of early peaks. In the reactions with aniline, and with 2,6-dimethylaniline, these components are well separated from the remaining product of higher retention time. The g.p.c. trace for the reaction with aniline is shown in *Figure 2b*, and the areas of the low and high molecular weight fractions correspond closely to those of the two early h.p.l.c. components and that of higher retention time product, respectively. In these two reactions, none of the aniline and only 2% of the 2,6-dimethylaniline remained unconsumed. The reactions with the less reactive chloroanilines required more forcing conditions. With 2,6-dichloroaniline, of which 5% remained unconsumed, the early pair of peaks is much less well separated from other product. In the reaction with 2,4,6-trichloroaniline, the DGA was completely consumed after 24 h at 200°C, but a large amount of the chloroaniline (37%) remained. In an attempt to force the reaction by using a higher reaction temperature of 230°C, h.p.l.c. (*Figure 2f*) showed that only trace quantities of the two early components remained, with much unconsumed 2,4,6-trichloroaniline.

Other workers have carried out the reaction between DGA and aniline in bulk[6] at 100°C, and in toluene[6,11,12] at ≈140°C. It is apparent from their h.p.l.c. data[6] that their reaction was less complete and much more complex than we obtained for a more advanced reaction. This enabled us to use a relatively easy separation procedure (sublimation followed by simple preparative h.p.l.c.) for the isolation of the two components. Both of these compounds have been isolated by other workers and identified as perhydro-1,5-diazocine isomers, and crown configurations were assigned, but the actual conformational assignments were not rigorous: one isomer is highly crystalline and can be readily separated from a solution of the crude product[6,11,12]; the other required a selective extraction procedure[12]. As will be seen later, we agree with the conformational assignment (IVc; R,R′ = H) for the highly crystalline isomer but not with the conformational assignment for the other isomer. The highly crystalline nature of the first eluted isomer was confirmed by d.s.c., which showed that full crystallinity was recovered when the isomer was quench-cooled from above its melting point. Although the other isomer was isolated as a crystalline solid, it was amorphous after being similarly quench-cooled, and gave a good T_g by d.s.c. The corresponding products, formed in the reactions of DGA with the substituted anilines, were isolated by preparative h.p.l.c.: these were all amorphous solids and quenched samples gave well defined T_gs by d.s.c.

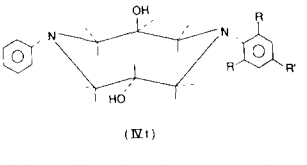
Before discussing the significance of the product distribution, it is desirable to establish the structure of the main reaction products. This was done by n.m.r., i.r. and mass spectrometries.

Structure by n.m.r. spectroscopy

The ^1H and ^{13}C spectra for the two products isolated from the DGA/aniline reaction are shown in *Figures 3* and *4*, respectively. The ^{13}C chemical shifts for the aromatic and aliphatic regions are given for the four pairs of products in *Tables 1* and *2*, the ^1H shifts in *Tables 3* and *4*, and the aliphatic ^1H–^1H coupling constants in *Table 5*. It is readily apparent from the ^{13}C n.m.r. data that each system produces a pair of eight-membered ring isomers. The nature of these isomers is most readily apparent from the detailed analysis of their ^1H n.m.r. spectra. It will be shown that each pair of isomers consists of a *cis*-dihydroxy structure (IVc) with both hydroxyl groups in equatorial positions, and a *trans*-dihydroxy isomer (IVt) with the hydroxyl groups in an axial/equatorial arrangement.

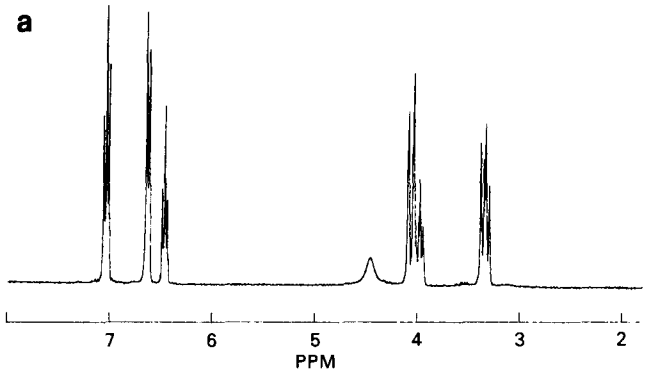


(IVc)



(IVt)

For the isomers of (IV; R,R′ = H) obtained in the reaction involving aniline, there is a most striking difference between their aliphatic n.m.r. parameters. The highly crystalline isomer is characterized by a very large chemical shift difference between the geminal protons of the $-CH_2N-$ group which is so pronounced that one of the protons occurs close to and to low field of the methine $-CH(OH)-$ proton, rather than on the



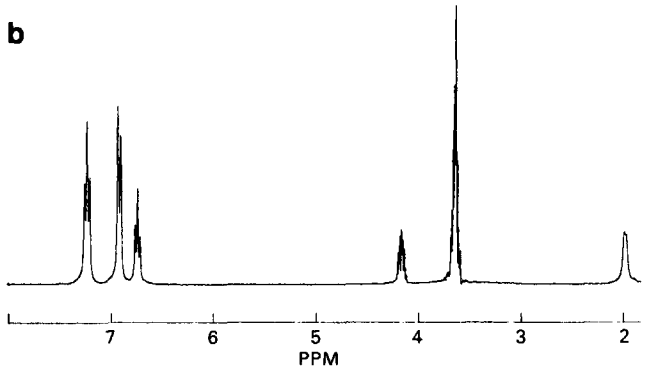
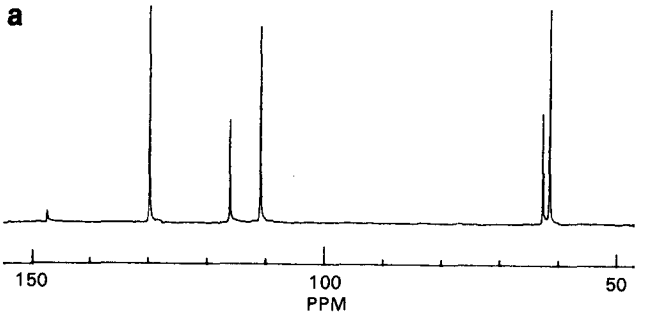


Figure 3 300 MHz proton spectra of (a) (IVc; R,R′ = H) and (b) (IVt; R,R′ = H)



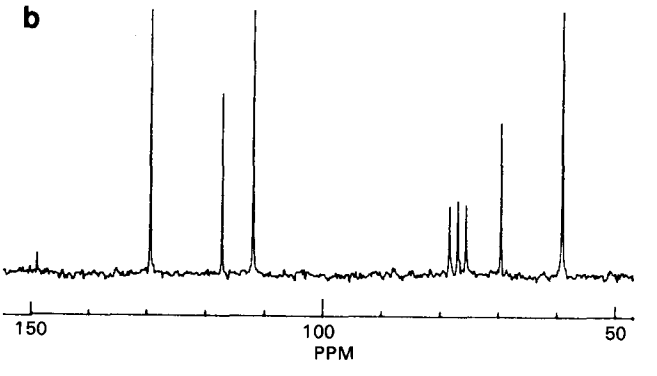
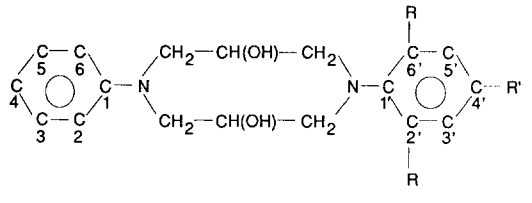


Figure 4 75.47 MHz ^{13}C n.m.r. spectra of (a) (IVc; R,R′ = H) and (b) (IVt; R,R′ = H)

Table 1 Aromatic carbon chemical shifts (ppm) for (IVc) and (IVt) in $CDCl_3$ at 20°C except where R,R′ = H when acetone-D_6 was used

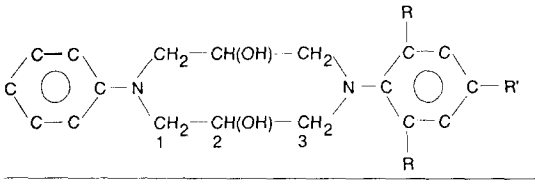


Compound	1	2,6	3,5	4	1′	2′,6′	3′,5′	4′
(IVc)								
R = H	147.6	111.0	129.9	116.2	147.6	111.0	129.8	116.2
R′ = H								
R = Cl	148.2	111.7	129.4	116.5	148.4	136.8	129.8	127.7
R′ = H						136.3	129.3	
R = Cl	147.2	111.6	129.4	116.6	148.0	137.4	129.4	134.5
R′ = Cl						137.0	129.2	
R = Me	147.4	111.0	129.5	116.2	152.4	137.7	129.8	125.9
R′ = H						136.6	128.7	
(IVt)								
R = H	149.1	112.1	129.5	117.3	149.1	112.1	129.5	117.3
R′ = H								
R = Cl	149.2	110.7	129.4	116.8	149.3	136.4	129.2	127.5
R′ = H								
R = Cl	149.1	111.9	129.4	116.9	148.1	136.9	129.4	132.4
R′ = Cl								
R = Me	149.2	112.0	129.5	116.8	152.8	136.4	129.3	125.9
R′ = H								

expected high field side. In contrast, the other isomer shows normal behaviour with very similar shifts for the $-CH_2N-$ protons appreciably to high field of the methine $-CH(OH)-$ proton. Similarly, the ^{13}C n.m.r. spectra of the highly crystalline isomer show very similar shifts for the $-CH_2N-$ and $-CH(OH)-$ carbons, rather than the expected large difference in shifts which is found in the other isomer and in the analogous linear $-NCH_2CH(OH)CH_2N-$ grouping[1,3,12]. In addition, the highly crystalline isomer is characterized by a large

$-NCH_2CH(OH)CH_2N-$ grouping[1,3,12]. In addition, the highly crystalline isomer is characterized by a large difference in the three-bond coupling constants between the methine $-CH(OH)-$ proton and the two $-CH_2N-$ protons ($^3J_{1ax,2}$, $^3J_{1eq,2}$).

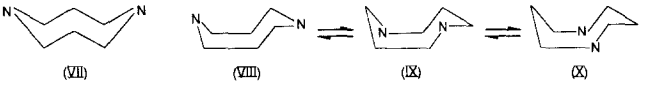
Table 2 Aliphatic ring carbon chemical shifts (ppm) for (IVc) and (IVt) in $CDCl_3$ at 20°C except for R,R′ = H when acetone-D_6 was used



Compound	1	2	3	Methyl
(IVc)				
R = H	61.5	62.6	61.5	
R′ = H				
R = Cl	63.2	68.2	57.9	
R′ = H				
R = Cl	63.2	68.0	58.1	
R′ = Cl				
R = Me	67.0	67.0	59.7	19.0
R′ = H				18.9
(IVt)				
R = H	59.3	69.8	59.3	
R′ = H				
R = Cl	58.0	69.6	65.0	
R′ = H				
R = Cl	58.1	69.6	64.9	
R′ = Cl				
R = Me	57.4	70.0	64.7	19.3
R′ = H				

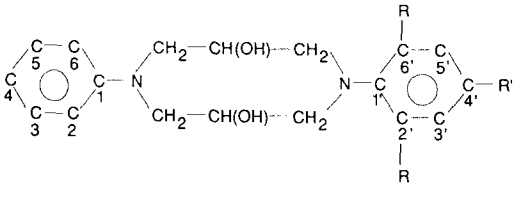
difference in the three-bond coupling constants between the methine $-CH(OH)-$ proton and the two $-CH_2N-$ protons ($^3J_{1ax,2}$, $^3J_{1eq,2}$).

These factors indicate that the molecule has a symmetrical structure with the hydroxyl groups occupying equatorial sites in accordance with the conclusions of Grenier-Loustalot and Grenier[12], and it is accordingly assigned as the *cis*-dihydroxyl isomer. The large shift difference between the $-CH_2N-$ protons H_{1ax} and H_{1eq} arises because they occupy their positions exclusively, and do not show averaged chemical shifts by conformer interconversion. The axial and equatorial proton assignments are, of course, based on the vicinal coupling constants to H_2. According to Anet and Anet[15], eight-membered rings can show a number of conformations of similar energy and, whereas the boat–chair form is predominant in cyclo-octane itself, the crown family of conformations may become important or even dominant in substituted cyclo-octanes and other eight-membered rings. The phenyl groups would be expected to occupy and retain strain-free equatorial positions since, as occurs with piperidine[16], nitrogen inversion will presumably occur much faster than ring inversion. In fact, Courtauld models clearly showed the difficulties of accommodating axially disposed phenyl groups. Undistorted Courtauld models of both the crown (VII) and boat–chair (VIII) conformations with the hydroxyl groups in axial or equatorial positions and the phenyl or substituted phenyl groups in equatorial positions could be assembled.



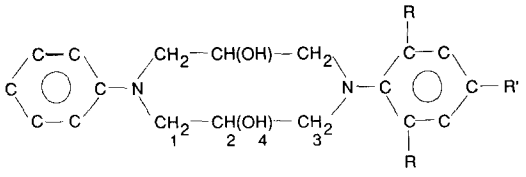
(VII) (VIII) (IX) (X)

Table 3 Aromatic ring proton chemical shifts (ppm) for (IVc) and (IVt) in $CDCl_3$ at 20°C except where R,R′ = H when acetone-D_6 was used



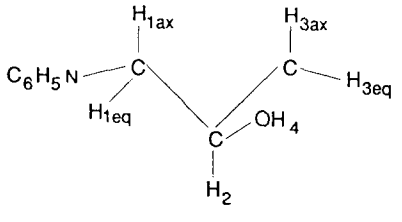
Compound	$H_{2,6}$	$H_{3,5}$	H_4	$H_{2',6'}$	$H_{3',5'}$	$H_{4'}$
(IVc)						
R = H	6.63	7.03	6.47	6.63	7.03	6.47
R′ = H						
R = Cl	6.90	7.25	6.70		7.20	7.05
R′ = H					7.30	
R = Cl	6.84	7.25	6.72		7.28	
R′ = Cl					7.34	
R = Me	6.75	7.23	6.69		6.85	6.92
R′ = H					6.84	
(IVt)						
R = H	6.89	7.21	6.72	6.89	7.21	6.72
R′ = H						
R = Cl	7.01	7.24	6.72		7.29	7.03
R′ = H						
R = Cl	6.93	7.22	6.72		7.30	
R′ = Cl						
R = Me	7.00	7.25	6.65		7.05	7.05
R′ = H						

Table 4 Aliphatic ring proton chemical shifts (ppm) for (IVc) and (IVt) in $CDCl_3$ at 20°C except where R,R′ = H when acetone-D_6 was used



Compound	H_{1ax}	H_{1eq}	H_2	H_{3ax}	H_{3eq}	H_4	Methyl
(IVc)							
R = H	3.34	4.04	3.97	3.34	4.04	4.34	
R′ = H							
R = Cl	3.12	3.51	4.03	3.71	3.81	2.50	
R′ = H							
R = Cl	3.18	3.46	4.05	3.62	3.86	2.13	
R′ = Cl							
R = Me	3.21	4.07	4.00	3.14	3.33	1.87	2.26
R′ = H							1.83
(IVt)							
R = H	3.60	3.65	4.15	3.60	3.65	2.03	
R′ = H							
R = Cl	3.60	3.72	4.06	3.37	3.42	2.43	
R′ = H							
R = Cl	3.66	3.72	4.02	3.32	3.39	2.46	
R′ = Cl							
R = Me	3.55	3.65	4.00	3.25	3.35	2.00	2.25
R′ = H							

Table 5 Aliphatic proton–proton coupling constants (H_z) for (IVc) and (IVt) in $CDCl_3$ at 20°C except where R,R′ = H when acetone-D_6 was used



Compound	$^2J_{1ax,1eq}$	$^3J_{1ax,2}$	$^3J_{1eq,2}$	$^3J_{2,3ax}$	$^3J_{2,3eq}$	$^2J_{3ax,3eq}$	$^3J_{2,4}$
(IVc)							
R = H	−14.5	10.0	2.7	10.0	2.7	−14.5	5.0
R′ = H							
R = Cl	−14.3	6.8	2.8	7.4	2.7	−14.7	4.9
R′ = H							
R = Cl	−14.3	7.1	2.9	8.2	2.9	−14.6	4.9
R′ = Cl							
R = Me	−14.1	9.2	2.6	9.9	2.9	−14.9	3.3
R′ = H							
(IVt)							
R = H	−14.7	6.2	4.1	6.2	4.1	−14.7	5.7
R′ = H							
R = Cl	−14.4	6.9	3.5	6.5	4.0	−14.7	7.3
R′ = H							
R = Cl	−14.6	6.5	3.4	6.5	3.3	−14.8	8.0
R′ = Cl							
R = Me	−14.1	7.3	2.9	6.9	3.5	−14.5	6.6
R′ = H							

The crown isomer with *cis* equatorial hydroxyl groups is, of course, symmetrical and the asymmetrical boat–chair form (VIII) can rapidly interconvert by pseudo-rotation[17] through intermediates such as (IX) and (X) to give an overall symmetry on the n.m.r. scale. Although such a process does not completely average the substituent positions, a substituent does experience both axial and equatorial situations and, as a consequence, intramolecular hydrogen bonding between the axial hydroxyl and the ring nitrogen would be detected by i.r. spectroscopy at high dilution.

As will be discussed later, the i.r. data, which is in accord with model predictions, support our conclusions that the n.m.r. data are best explained by a single symmetrical crown or a stretched crown conformation, and the highly crystalline isomer is accordingly assigned the structure (IVc; R,R′ = H). The preference for a single symmetrical conformation would account for the highly crystalline character of the *cis* isomer in contrast to the much lower tendency of the other isomer to crystallize. This second isomer is assigned the *trans*-dihydroxy structure (IVt; R,R′ = H) with the hydroxyl groups in an axial/equatorial arrangement, which is not in agreement with the axial/axial arrangement proposed by Grenier-Loustalot and Grenier[12]. Its n.m.r. parameters are much more normal, being similar to those of linear analogues. The very close chemical shifts of the $-CH_2N-$ protons and the equivalence of the two sides of the ring as regards n.m.r. parameters are readily explained in terms of interconversion of two conformations on the n.m.r. time scale with its associated exchange of axial and equatorial positions.

The pairs of isomers obtained from the other reaction systems also show clear differences in their n.m.r. spectra, but these are not as marked as for the aniline-derived system. In particular, the *cis* isomers (always eluted first in h.p.l.c. analysis) do not show such characteristic spectra, being more like those of the *trans* isomers. However, when all of the spectra are considered together, each of the series shows strong similarities, and the assignment of the *cis* and *trans* isomers is unambiguous and agrees with i.r. data to be discussed later.

The *trans*-dihydroxy isomers with substituted phenyl rings show proton spectra which are closely related to that for the aniline derived *trans*-dihydroxy isomer. The methine protons (H_2) all appear at about 4.0 ppm, and a pair of strongly coupled geminal protons with very similar chemical shifts close to 3.65 ppm are assigned to the two H_1 protons closer to the unsubstituted phenyl ring. The other geminal (H_3) protons appear close to 3.3 ppm and their chemical shift differences are also very small for the 2,4-dichlorophenyl and the 2,4,6-trichlorophenyl derivatives, although slightly larger for the 2,6-dimethylphenyl derivative.

The spectra of the chloro-substituted *cis* isomers are not so unusual: they still show larger differences between pairs of protons attached to the same carbon than the *trans* isomers, but not so large as for the aniline-derived isomers, and show geminal pairs grouped at about 3.2–3.5 and 3.6–3.9 ppm, and the methine $-CH(OH)-$ protons at $\approx$4.05 ppm. However, the dimethyl-substituted *cis* isomer still shows a very large chemical shift difference between the two H_1 protons so that the equatorial proton lies to low field of the methine (H_2) proton, but the shift difference between the other two geminal protons (H_3) is much smaller. As will be discussed later, for the chloro compounds, hydrogen bonding occurs with the chlorine atoms. The methyl-substituted compound is not, of course, affected in this way. This behaviour suggests that for the methyl-substituted *cis* isomer, the conformation near the unsubstituted phenyl ring is similar to that for the aniline-derived isomer but that the conformation near the substituted phenyl ring is somewhat different. The eight-membered rings for the chloro *cis* systems seem to be more generally distorted.

The ring distortion presumably arises from the strong interactions introduced by the *ortho* substituents together with a greater tendency of eight-membered rings to distort compared with, for example, cyclohexane rings[15]. There is direct evidence for strong interactions involving the substituted aromatic ring in these *cis* systems. Thus, whereas all aromatic rings in the *trans* isomers, and the unsubstituted rings in the *cis* isomers, are symmetrical about the carbon 1–carbon 6 axis, the substituted rings in the *cis* isomers all show different chemical shifts for the $C_{2'}$, $C_{6'}$ and $C_{3'}$, $C_{5'}$ carbon pairs and the $H_{3'}$, $H_{5'}$ proton pairs. Moreover, the dimethyl substituted isomer shows two methyl carbons, and very different chemical shifts (1.83 and 2.26 ppm) for the methyl protons. Finally, the chemical shifts are quite unlike the normal ones for aniline derivatives and indicate practically no conjugative effect of the nitrogen on the aromatic ring shifts. This is supported by the Courtauld models, which show least distortion when the aromatic rings are at right-angles to the plane of the aliphatic ring.

The two isomers, which are found in roughly equal amounts for all the reactions studied, arise from the inherent asymmetry of the *N*-diglycidyl unit. Since each diglycidyl unit is asymmetric, two such units attached to a nitrogen atom can give rise to a diastereoisomeric pair, which can sometimes be observed as splittings in the ^{13}C n.m.r. spectra[12,15]. The reaction of the two diastereoisomers leads directly to the two isomers postulated. This doubling of the structures due to isomerism is likely to occur for many of the reaction products in *N*-diglycidyl/amine systems, and greatly complicates the n.m.r. spectra. Note that the chemical shift differences between the isomers is very large, and it is clearly not possible to assign a single shift for a particular chemically distinct unit (e.g. a CHOH unit). In particular, this casts some doubt on the interpretation of solid state ^{13}C n.m.r. spectra, which usually assign single resonances to most chemical types, although the presence of two eight-membered ring isomers has been recognized previously[3,12]. Thus the extra complexity due to isomerism makes the interpretation of poorly resolved solid state spectra, which consist of complicated mixtures of resonances, even more difficult. This aspect will be considered in more detail in a subsequent paper[20].

Hydrogen bonding in 3,7-dihydroxy-perhydro-1,5-diazocines by i.r. spectroscopy

Courtauld models showed that the equatorial hydroxyl groups in the *cis* isomers of the crown conformation could not undergo any intramolecular hydrogen bonding either with themselves or with adjacent nitrogen, whereas the axial hydroxyl group present in the *trans* isomers could form a hydrogen bond with a nearby nitrogen atom. Further, with the chloro derivatives, it was apparent that intramolecular hydrogen bonding could occur between an aromatic *ortho* chlorine atom and either an axial or

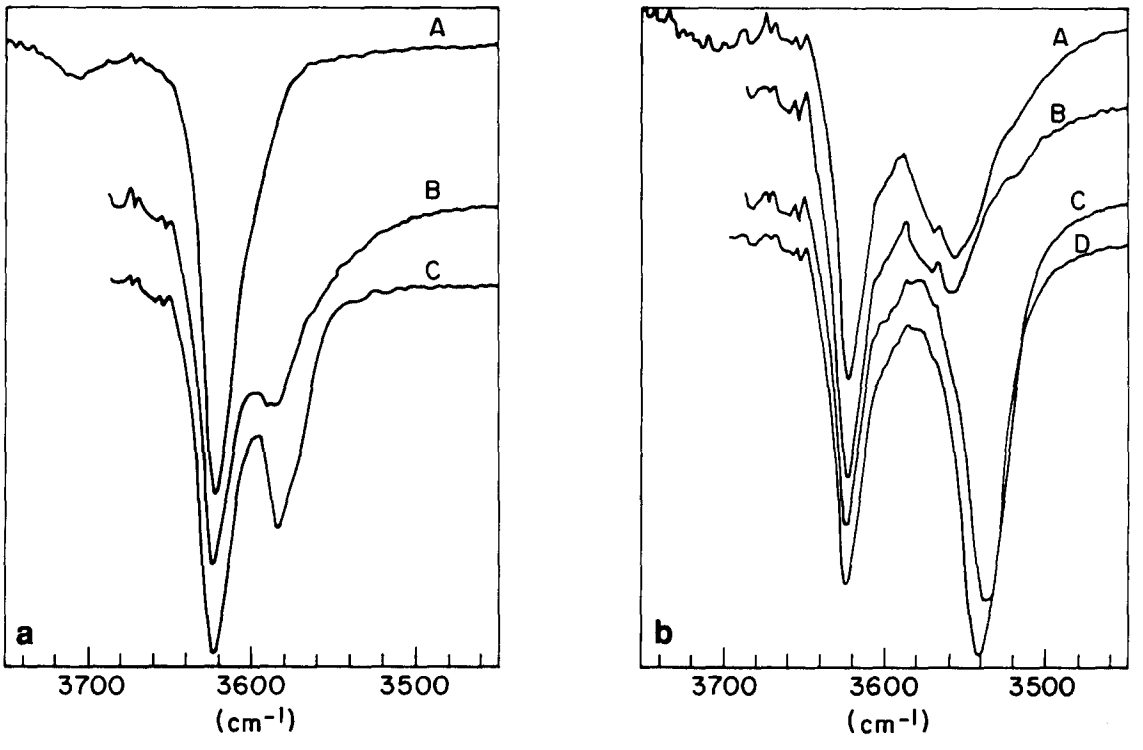


Figure 5 (a) Infrared spectra in CCl_4 (0.002 M) of: A, (IVc; R = CH_3, R′ = H); B, (IVt; R = CH_3, R′ = H); C, (IVt; R,R′ = H). (b) Spectra of: A, (IVc; R = Cl, R′ = H); B, (IVc; R,R′ = Cl); C, (IVt; R = Cl, R′ = H); D, (IVt; R,R′ = Cl)

indeed with an equatorially sited hydroxyl group. The observed spectra in carbon tetrachloride at high dilution (0.002 M) were fully in accord with the predictions from these models. It has already been mentioned that pseudorotation of boat–chair conformers would involve transposition of equatorial hydroxyl groups to axial sites and that intramolecular hydrogen bonding with nitrogen could then occur. This is not compatible with the observed spectra. Further, it was not possible to assemble a model of conformer (X) containing a substituted aromatic ring because of steric factors. Unfortunately, these predictions could not be tested with the highly crystalline *cis* isomer (IVc; R,R′ = H) which, unlike the other isomers, was insoluble in carbon tetrachloride. It was adequately soluble in benzene but, as found with the analogous methyl-substituted *cis* isomer (IVc; R′ = H, R = CH_3), the absorptions of free and hydrogen bonded hydroxyl groups overlapped in this solvent. In carbon tetrachloride, this methyl substituted *cis* isomer showed (*Figure 5a*, trace A) only a sharp free hydroxyl absorption at 3621 cm^{-1}, whereas the *trans* dihydroxy isomers (IVt; R,R′ = H) and (IVt; R′ = H, R = CH_3) showed (traces C and B), in addition to the free hydroxyl absorption at 3622 cm^{-1}, intramolecular hydrogen bonding due to axial hydroxyl/ring nitrogen interaction as a sharp peak at 3584 cm^{-1} for the former and a doublet for the latter at 3592 and 3586 cm^{-1}, the higher frequency presumably being associated with the less basic nitrogen atom attached to the methyl substituted ring. The spectra for the chlorine substituted derivatives are given in *Figure 5b*. The *cis* and *trans* isomers of the two compounds had very similar spectra. The *cis* isomers showed (traces A and B), in addition to the free hydroxyl absorption at 3622 cm^{-1}, fairly weak intramolecular hydrogen bonded absorptions at about 3570 and 3560 cm^{-1}, which are attributed to hydrogen bonding between the equatorial hydroxyl group and adjacent aromatic chlorine substituents. The *trans* isomers also each showed (traces C and D), besides the free hydroxyl absorption at 3622 cm^{-1}, a strong hydrogen bonded absorption involving nitrogen at $\approx$3540 cm^{-1}, which partly enveloped the weaker absorptions involving chlorine on its higher frequency side.

Mass spectra of the 3,7-dihydroxy-perhydro-1,5-diazocines

There was little difference in the spectra of the aniline-derived *cis* (IVc; R,R′ = H) and *trans* (IVt; R,R′ = H) isomers and prominent peaks were generally in agreement with those already reported[6] for the former isomer and concordant with the structure. However, additional prominent peaks were observed at $m/e = 174$ $[PhN(CH_2CHO)\overset{+}{C}H{=}CH\overset{+}{C}H_2]$, 146 $[Ph\overset{+}{N}(=CH_2)CH_2CH{=}CH_2]$, 106 $[Ph\overset{+}{N}(=CH_2)H]$, 104, 93 and 91. The phenyl substituted derivatives all gave parent ions and prominent peaks corresponding to the same breakdown pattern.

Some general comments

The analytical data presented clearly show that the only major cyclic products formed in the reactions of DGA with aniline and the aforementioned substituted anilines were *cis* (IVc) and *trans* (IVt) isomers of the eight-membered perhydro-1,5-diazocine ring. The respective yields of these isomers, as determined by quantitative h.p.l.c., were 8 and 5%, where R and R′ are hydrogen, 22 and 21% where R is methyl and R′ is hydrogen, both 17% where R is chlorine and R′ is hydrogen, and both 11% where R and R′ are chlorine; the corresponding amounts of unconsumed amines were

0, 2, 5 and 37%, respectively. The n.m.r. peak intensities agreed well with the relative amounts of the *cis* and *trans* isomers. It was apparent from the h.p.l.c. traces that only very small amounts of the corresponding morpholines (II) and perhydro-1,4-oxazepines (III), which would have appeared as sharp early peaks, could have been formed in these reactions. This, of course, could be a result of either their formation in very low yield, or a consequence of their further reaction with epoxide. This aspect will be considered in a subsequent paper[20]. Note that, during the h.p.l.c. monitoring of the reactions involving 2,6-dichloroaniline and 2,4,6-trichloroaniline, a peak attributed to (I; R″ = H, R = Cl, R′ = H or Cl), precursor to the eight-membered rings, never developed to any large extent. In addition to these reaction systems, the reactions of DGA at 180°C with the deactivated amines, 3-trifluoromethylaniline and 3,5-bis(trifluoromethyl)-aniline, for which steric factors should play little part, were also examined but in much less detail: h.p.l.c. analysis, based on non-calibrated peak areas, showed that the *meta* substituted group effected only a very slight increase in the concentration of the corresponding *cis*- (9–12%) and *trans*- (7–9%) perhydro-1,5-diazocines; the DGA and the anilines were completely consumed in these reactions but, as expected, the deactivating trifluoromethyl groups decreased the extent to which the reaction had advanced.

It is evident from this investigation of the effect of substituents on the course of the reaction between DGA and aromatic amines that steric effects play a much more significant role than electronic effects in determining the reaction pattern. The objective of trying to reduce the reactivity of the secondary aromatic amine sterically by introducing substituents *ortho* to the amino group and thus to encourage reactions of the secondary alcohol group with epoxide to give morpholine (II) and perhydro-1,5-oxazepine (III) rings was not realized, even though Courtauld models indicated that such rings were less subject to distortion than the eight-membered rings (IV). Indeed, somewhat unexpectedly, the steric effects actually encouraged the formation of the eight-membered ring. The presence of a large amount (37%) of unconsumed 2,4,6-trichloroaniline was unexpected, especially since Matejka and Dusek[18] have recently reported that the second epoxy group of DGA is more reactive than the first (factor of 2.2) in its reaction with aniline. Thus, for the highly deactivated trichloroaniline, a high yielding initial two-step reaction involving primary amine might have been reasonably expected:

$$C_6H_5NGl_2 \xrightarrow{ArNH_2} C_6H_5N(Gl)CH_2CH(OH)CH_2NHAr$$
$$\xrightarrow{ArNH_2} C_6H_5N[CH_2CH(OH)CH_2NHAr]_2$$

Clearly, the intramolecular reaction involving secondary amine and epoxide to give (IV; R,R′ = Cl) was dominant to such an extent that only a small amount of the suspected ring precursor remained. This behaviour is, of course, contrary to that which occurs in a competitive non-cyclic forming situation[19], and presumably reflects a powerful contribution from the pre-exponential factor for the ring forming reaction.

This paper has been essentially confined to a consideration of the predominant low molecular weight cyclic products formed in the reactions of DGA with aniline and substituted anilines, and a detailed analysis of their structure. The recognition by n.m.r. of other structural features, both cyclic and linear, in these and other *N*-glycidyl based systems will be discussed in a subsequent paper[20].

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