

Crystallographic Studies of Dehydrohalogenation in Solid *meso*-Dibromobutane Derivatives.

III. Conformational Analyses and the Stereo Course of the Reaction

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The dibromobutane molecules described in this series undergo double dehydrobromination yielding the corresponding 1,3-butadienes. In all these cases except one (*meso*- β,β' -dibromoadiponitrile) the reaction is strictly topochemical in the sense that the configurations of the products correlate directly with the conformations of the molecules in the crystal. From these results it is also clear that an *anti* elimination-type mechanism operates under the conditions of gas/solid reaction. Conformational analyses of these molecules show that the observed molecular conformations are determined mainly by intramolecular forces and that the non-topochemical behaviour of β,β' -dibromoadiponitrile results from a pre-reaction equilibrium of conformers. The possible effects of the packing arrangement on the reaction rate are discussed.

Introduction

The crystallographic studies of parts I and II (Rabinovich & Shakked, 1977, 1978) have prepared the ground for a discussion of the double dehydrohalogenation of solid *meso*-dihalogenobutanes by gaseous ammonia or amines, which we have briefly described there.

It is our purpose to show that the dominant factor that controls the course of these reactions and dictates the stereochemistry of the products is the molecular conformation of the starting compounds.

The importance of conformationally controlled reactions in the solid rests on the fact that, in general, the molecule adopts a unique conformation in the crystal, compared to a complex mixture of conformers in the dispersed phase. Thus, in principle, the correlation between the geometries of the starting compounds and the end products may become straightforward in the solid and can therefore yield information about the reaction mechanisms. Indeed, all the dibromobutane derivatives described in parts I and II undergo double dehydrohalogenation yielding the corresponding 1,3-butadienes. In all these cases, except for *meso*- β,β' -dibromoadiponitrile, the reaction is strictly topochemical in the sense that the configurations of the products correlate directly with the conformations of the starting molecules in the crystal. In other words, the chemical transformation involves minimal spatial rearrangement of the reacting molecule.

Here we discuss the conformational aspects of these molecules and the stereo course of the reaction in terms

of the correlation between the initial conformations and the configurations of the products.

Discussion

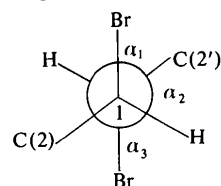
Molecular conformation

The molecular conformation of the butane skeleton is conveniently displayed by the Newman projections along C(1)–C(1') and C(1)–C(2) (Table 1, Fig. 1).

The maximum separation of the Br atoms and the bulky groups attached to C(1) and C(1') is achieved by virtue of the molecular centre of symmetry so that both

Table 1. Torsion angles ($^{\circ}$) about C(1)–C(1')

Newman projection along C(1)–C(1')



	(I)	(II)	(IIIa)	(IIIb)	(IV)	(V)
α_1	59.0	59.7	59.5	57.9	59.3	58.2
α_2	57.8	56.1	49.8	55.5	50.1	52.5
α_3	63.2	64.1	70.7	66.6	70.6	69.3

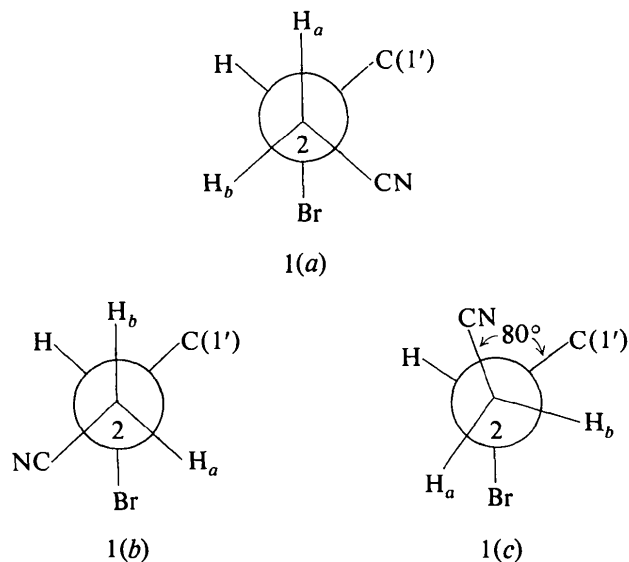
- (I) *meso*- β,β' -Dibromoadiponitrile.
 (II) (*RSRS*)- α,α' -Dimethyl- β,β' -dibromoadiponitrile.
 (IIIa) (IIIb) (*RRSS*)- α,α' -Dimethyl- β,β' -dibromoadiponitrile.
 (IV) Dimethyl (*RSRS*)- α,α' -dimethyl- β,β' -dibromoadipate.
 (V) Dimethyl (*RRSS*)- α,α' -dimethyl- β,β' -dibromoadipate.

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steric and dipolar repulsions are at a minimum (Eliel, Allinger, Argyal & Morrison, 1965; Eliel, 1962). The Newman projections along C(1)–C(2) show the expected staggered conformation (Fig. 1). However, this arrangement is not determined by the 1...4 non-bonded interactions between the atoms attached to C(1) on the one hand and those attached to C(2) on the other, but rather by the 1...5 interactions of the latter with the substituents at C(1'). In the observed arrangement the H_α atom attached to C_α is antiperiplanar to the Br atom attached to C(1), and hence makes a short 1...5 contact (2.7–2.8 Å) with Br'. Any other staggered orientation where a non-hydrogen group [–CH₃, –C≡N or –C(=O)–OCH₃] is antiperiplanar to Br will lead to too short a contact with Br' which can be relaxed only by a considerable deviation from perfect staggering. In cases where only one H_α exists, the relative orientations of the non-hydrogen substituents are determined by the molecular configuration (*RSRS* or *RRSS*). In (I) where two H_α atoms exist (H_a, H_b), one would expect two similarly stabilized conformations where the nitrile group is either *gauche* or *trans* oriented to C(1)–C(1').

To verify our qualitative arguments regarding the most stable conformation along C(1)–C(2) we have calculated the energy variation (ΔE) of the isolated molecule as a function of the rotation angle (ϕ) about C(1)–C(2), using as a model the observed molecular geometry. The calculations included only non-bonded and torsional energy contributions. The potential functions used were those given for saturated molecules by Warshel & Karplus (1972). The parameters for the non-bonded potential involving Br atoms were taken from Kawaguchi, Takashina, Tanaka & Watanabe (1972). The non-bonded parameters of the other atoms and the torsional parameters were taken from Warshel & Karplus (1972).

The results of the analysis of (I) are presented in Fig. 2 (dotted curve). The three energy minima correspond to the Newman conformations:



As expected from our qualitative arguments, conformations 1(a) and 1(b) are nearly equally stabilized. Conformation 1(c) deviates considerably from perfect staggering (by nearly 20°) in order to relax the interaction of the nitrile group with Br', and is energetically higher by 1 kcal mol⁻¹ than 1(a) or 1(b).

The preference of 1(a) over 1(b) in the crystal probably results from packing considerations. It is noteworthy that spectroscopic measurements of 2-chloro- and 2-bromopropionitrile (Klaboe & Grundnes, 1968) have shown that these compounds crystallize as *gauche* conformers, although the preferred conformation in the gaseous phase is *trans*.

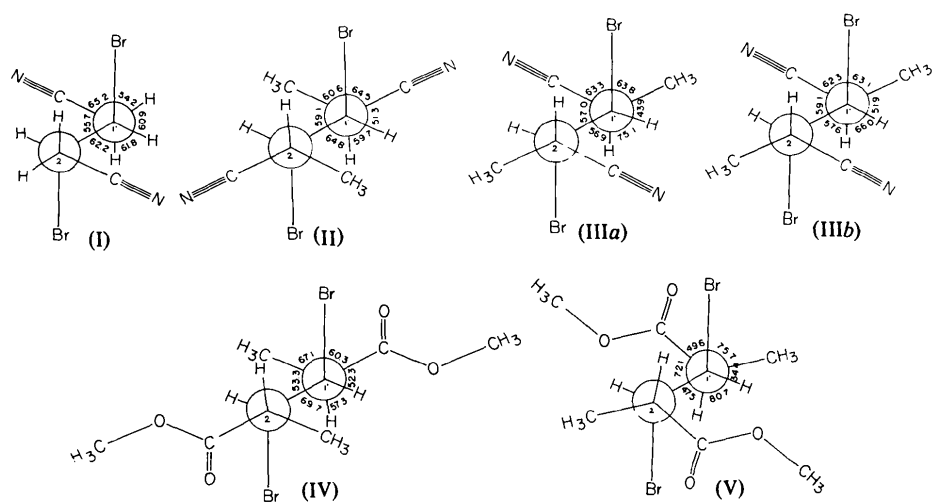
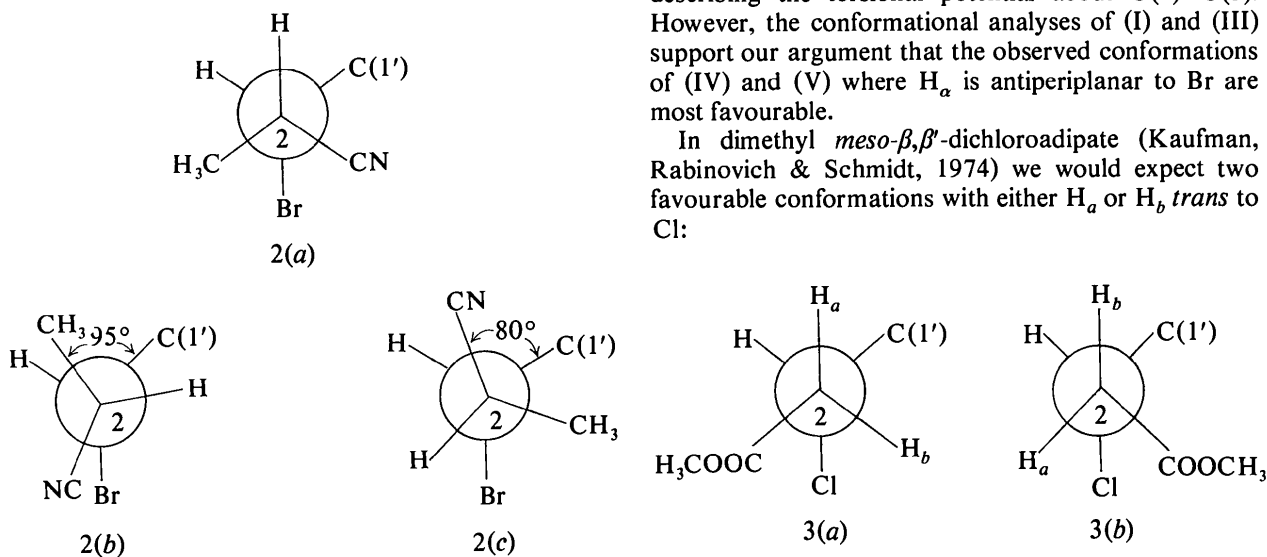


Fig. 1. Newman projections along C(1)–C(2).

The replacement of one H atom (H_b) in (I) by a methyl group leads to considerable changes in the energy pattern, as shown by the conformational analysis of (III) in Fig. 2 (full line). The three energy minima in this case correspond to the conformations:



The observed conformation 2(a) is more stable than 2(b) and 2(c) by 4 and 2 kcal mol⁻¹ respectively. 2(b) and 2(c) deviate considerably from a perfect staggered arrangement, the effect being larger in 2(b) because of the bulkier nature of the methyl compared to the nitrile group in the interaction with Br'.

The conformational analyses of the esters (IV) and (V) are more complex, since the rotation about C(1)–C(2) must be accompanied by a rotation about C(2)–C(3) in order to avoid strong steric repulsions of

the methoxycarbonyl group with the β -substituents. Such rotation destroys the observed stable synplanar arrangement of the α -methyl group with respect to the methoxycarbonyl group (see discussion in part I). The intramolecular potential surface of the esters was not calculated owing to the lack of appropriate parameters describing the torsional potential about C(2)–C(3). However, the conformational analyses of (I) and (III) support our argument that the observed conformations of (IV) and (V) where H_a is antiperiplanar to Br are most favourable.

In dimethyl *meso*- β,β' -dichloroadipate (Kaufman, Rabinovich & Schmidt, 1974) we would expect two favourable conformations with either H_a or H_b *trans* to Cl:

In this molecule the methoxycarbonyl group has an approximate synplanar arrangement with C(1)–C(2). However, the energy barrier for rotation, about C(2)–C(3) in this case, seems to be lower than that in (IV) and (V) as indicated by the observed rotation of 24° from a perfect coplanar arrangement. Preserving the observed arrangement about C(2)–C(3), we obtained, by similar calculations, two minimum-energy conformations as predicted [3(a), 3(b)]. The observed conformation 3(a) is stabilized by nearly 2 kcal mol⁻¹ with respect to 3(b). These results are also supported by NMR studies showing that 3(a) is preferentially populated in solution (Lahav, 1977).

The crystallization of only one of two equally stable conformers may be attributed to packing considerations, as shown by (I). However, once a conformer is selected, the effects of crystal forces on its molecular conformation seem to be rather small as displayed by the observed conformations in the two crystalline modifications [(IIIa), (IIIb)]. The significant differences between equivalent torsion angles involving non-hydrogen atoms are within 2° (Fig. 1, Table 1). Therefore, we may conclude that significant deviations from the ideal staggered arrangement in the present aliphatic systems result mainly from the various intramolecular non-bonded interactions. This argument is substantiated by theoretical studies of linear alkanes (Warshel & Lifson, 1970) showing that the minimum-energy conformations of the free molecules are essentially the same as those in the crystal.

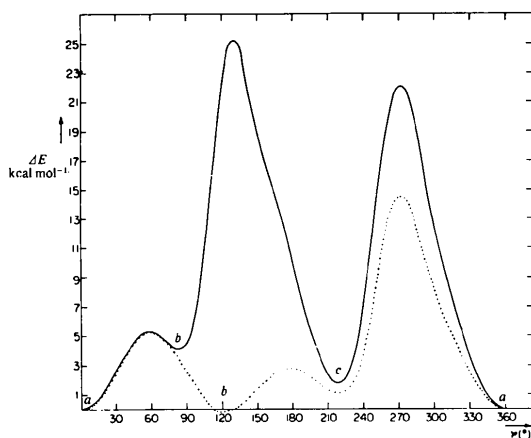
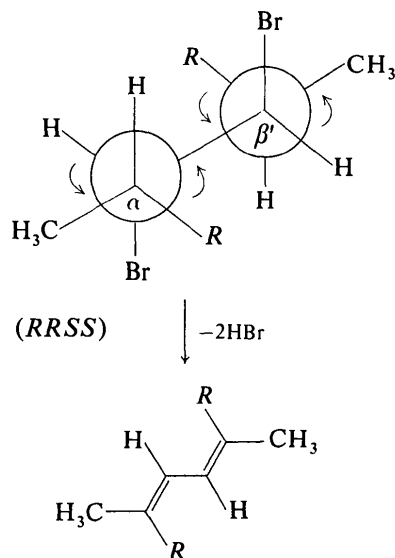
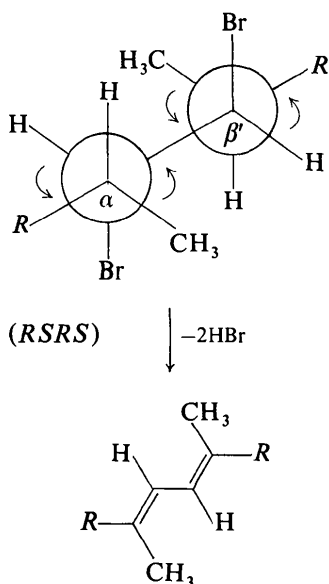


Fig. 2. The energy variation of (I) (dotted line) and (III) (full line) as a function of rotation about C(1)–C(2).

The observed deviations from perfect staggering along C(1)–C(2) are larger than those along C(1)–C(1') since the torsion angles about C(1)–C(1') are determined solely by the related bond angles because of the centrosymmetric arrangement. The largest deviations are observed in (V); all the torsion angles about C(1)–C(2) deviate by more than 10° from the ideal staggered value of 60° (Fig. 1). As discussed earlier (Rabinovich & Shakked, 1977), the preferred synplanar arrangement of the α -methyl group with the methoxycarbonyl group leads to a close 1...5 contact between O(2) and C(1'). The observed equilibrium distance of 3.02 Å between these atoms is achieved by the angle opening (114.7°) of C(1)–C(2)–C(3) and by a rotation of nearly 10° about C(1)–C(2) from the staggered orientation.

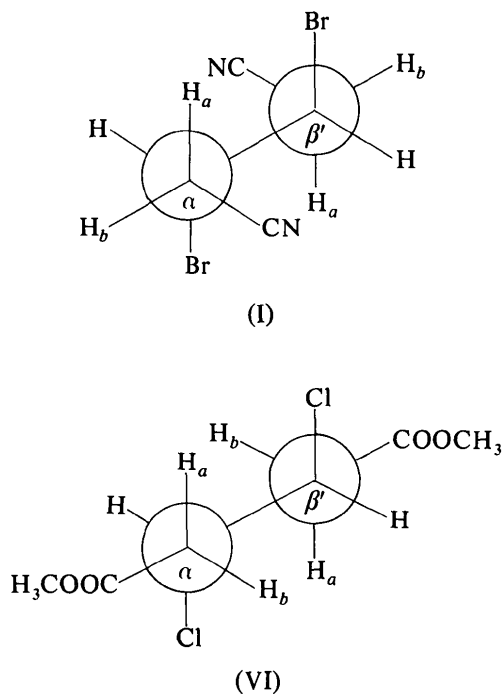
The course of the double-elimination reaction

The correlation between the conformation of the starting molecules and the configuration of the dienic products may best be deduced from the Newman projections of the molecules along C_α – C_β [C(2)–C(1)]. First, we shall consider the α,α' -dimethyl derivatives [(II), (IIIa), (IIIb), (IV), (V)] where only one H atom is available for elimination at each C_α atom. In all these compounds the single H_α is antiperiplanar to the Br atom owing to the intramolecular forces discussed earlier. Assuming an *anti* elimination-type mechanism involving minimal adjustment to sp^2 hybridization, one would expect the formation of the corresponding *trans,trans*-butadiene from the (*RSRS*) molecules [(II), (IV)] and the *cis,cis*-butadiene from the (*RRSS*) molecules [(IIIa,b), (V)]:



These expectations are in accord with the experimental results (parts I, II) and demonstrate that the steric course of the elimination (*anti*-type mechanism) and the configuration of the products are controlled by the conformation of the starting molecules, under the heterogeneous conditions of gas/solid reaction.

The course of the elimination reaction in molecules containing two H_α atoms may be more complex. In the nitrile (I) and the ester (VI), one of the H atoms (H_a) is antiperiplanar to the Br atom whereas the other (H_b) is *gauche*-oriented:

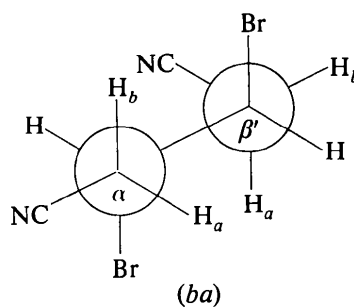
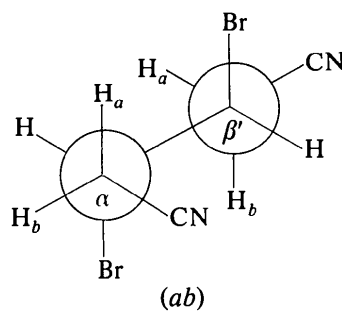
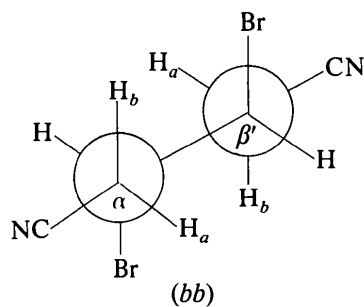
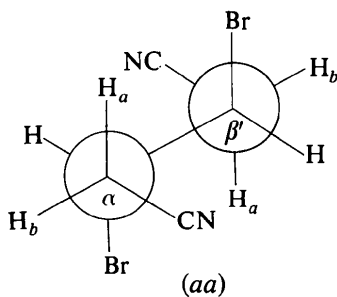


The results obtained from the α,α' -dimethyl molecules have shown that the *anti* elimination course operates in the nitriles as well as in the esters. Assuming a similar mechanism for (I) and (VI) one would expect the formation of the corresponding dinitrile of *cis,cis*-butadiene from (I) and the diester of *trans,trans*-butadiene from (VI). These expectations are in accordance with the stereospecific elimination (Friedman, Lahav & Schmidt, 1974) of (VI) but not with that of (I). As mentioned in part I, the latter yields three isomers (*cis,cis*-, *cis,trans*- and *trans,trans*-muconodinitrile) in the approximate ratio of 2:5:3.

Regarding the observed stability of *cis,cis*-muconodinitrile under the conditions of the reaction (no conversion from the *cis,cis* isomer to the other isomers was detected) and the fact that treatment of α,α' -tetra-deuterated (I) with gaseous NH_3 does not lead to deuterium exchange during the reaction (Lahav, 1977), it is reasonable to assume that the formation of *cis,trans* and *trans,trans* isomers in (I) results from internal rotation about $\text{C}_\alpha\text{--C}_\beta$ prior to elimination. The conformational analysis of the isolated molecule (Fig. 2) shows that conformers 1(a) and 1(b) are similarly stabilized and the conversion from 1(a) to 1(b) involves an energy barrier of nearly 5 kcal mol⁻¹. Such rotations are highly unlikely in the ordered matrix because of crystal forces. However, at specific sites (e.g. surfaces, dislocations) where the reaction is believed to initiate (Desvergne & Thomas, 1973), the molecules can undergo considerable loosening and under the reaction conditions (e.g. the thermal energy evolved in the reaction) may acquire sufficient energy to overcome the potential barrier involved in these internal rotations.

In this context conformational studies of succinonitrile in the plastic crystal phase by several methods [dielectric relaxation (Williams & Smyth, 1962), NMR (Powles, Begum & Norris, 1969), and Raman spectra (Fontanie, Longueville & Wallart, 1971)] have shown orientational freedom of this molecule resulting from a combination of inter- and intramolecular rotations along the four triad axes of the cubic unit cell. This process is believed (Powles, Begum & Norris, 1969) to involve an activation energy of 6 kcal mol⁻¹.

Since the rotations about the two equivalent $\text{C}_\alpha\text{--C}_\beta$ bonds are independent owing to their large separation, the following conformations are almost equally stable:



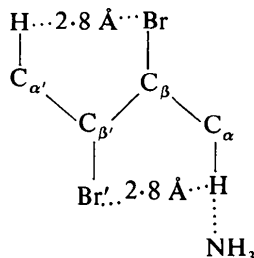
Double elimination of HBr controlled by an *anti*-type mechanism will lead to the formation of the following isomers: *cis,cis*-muconodinitrile from (aa); *trans,trans*-muconodinitrile from (bb); *cis,trans*-muconodinitrile from (ab) and (ba) [see (2), (3) and (4), part II]. The observed ratio of 2:3:5 showing a preferred formation of the *trans* over the *cis* double bond probably results from different rates of elimination in (a) and (b).

The stereospecific elimination of the ester (VI) indicates that the conversion from the observed conformation 3(a) to conformation 3(b) does not occur under the reaction conditions. As discussed previously, the rotation about $\text{C}_\alpha\text{--C}_\beta$ [$\text{C}(1)\text{--C}(2)$] in the ester must be accompanied by an additional rotation about $\text{C}_\alpha\text{--C}(\text{O})$ to avoid strong steric repulsions of the methoxycarbonyl group with the β substituents. Although the potential barrier for rotation about $\text{C}_\alpha\text{--C}(\text{O})$ is not known, its lower limit may be estimated as 2 kcal mol⁻¹ which is the maximum decrease in non-bonded energy obtained by rotating the methoxycarbonyl group ($\sim 60^\circ$) from the observed synplanar arrangement. Subsequent rotation about $\text{C}_\alpha\text{--C}_\beta$ from 3(a) to 3(b) involves an additional

potential barrier of nearly 7 kcal mol⁻¹. The greater barrier for internal rotation in (VI) compared to (I) and the larger interference of neighbouring molecules with the motion of the bulkier methoxycarbonyl group compared to that of a nitrile group explain the different behaviour of these compounds in the elimination reaction.

Although the *anti* steric course is generally preferred owing to stereoelectronic requirements (Depuy, Thurn & Morris, 1962; Banthrope, Hughes & Ingold, 1960) we still need to understand how such a mechanism proceeds in the solid state as the formation of the NH₄⁺ ion on one side of the molecule and the departure of halide ion from the other (charge separation) without the aid of a solvation process (which exists in solution) seems rather unlikely. However, the following energetically feasible mechanism, controlled by an *anti* elimination course, may be envisaged in such systems.

By virtue of the relatively short distance between H_α and Br_{β'} (~2.8 Å), the NH₄⁺ ion formed at C_{α'}, behaving as a strong Lewis acid, may induce the elimination of the Br atom attached to C_{β'}, whereas the unsolvated Br⁻ anion formed at C_β may serve as a strong base capable of eliminating the H attached to C_α. The proximity of the oppositely charged ions leads to their subsequent and rapid interaction to form NH₄Br and HBr:



If the double elimination occurs almost simultaneously by two molecules of NH₃, this process may be even faster.

The possible effects of the packing arrangement on the rate of dehydrohalogenation in polymorphic crystals

As mentioned in part II, the two crystalline forms [(IIIa), (IIIb)] of (*RRSS*)- α,α' -dimethyl- β,β' -dibromo-adiponitrile show different rates of dehydrohalogenation; the elimination in (IIIa) is faster than in (IIIb). The possible effects of the molecular packing on the various processes which may be involved in such gas/solid reactions are discussed below.

Diffusion of gas into the crystal. The induction period, prior to reaction, which is often observed in gas/solid reactions (Hadjoudis, Kariv & Schmidt, 1972) and the influence of crystal defects in increasing the reaction rate (Hadjoudis *et al.*, 1972; Desvergne & Thomas, 1973) suggest that the gas diffuses to certain

nucleation sites (*e.g.* dislocations, impurities) in the crystal where the reaction initiates and propagates therefrom into the bulk of the crystal.

Different packing arrangements may lead to different rates of diffusion and the process is expected to be faster in the less dense crystalline form where the crystal forces which oppose such diffusion are usually weaker. This argument seems to hold in the present case since the density of (IIIa) is less than that of (IIIb) (Table 1, part II) and the intermolecular forces in the former are weaker as indicated by the larger values of the thermal vibrations at room temperature. The different rates of gas/solid bromination in polymorphic forms of mesaconic acid (Hadjoudis *et al.*, 1972) were also attributed to different rates of bromine diffusion resulting from different molecular packing modes.

Surface reaction. Recent studies of gas/solid reactions at microscopic level (Desvergne & Thomas, 1973; Miller, Curtin & Paul, 1971, 1972; Lin, Paul & Curtin, 1974) show that such heterogeneous reactions may proceed at the crystal surface and the rate-limiting process is the loosening of the product layer which permits access of the gas to the next layer. The marked anisotropy of the reaction between the gas (NH₃) and the crystal faces in these cases demonstrates the influence of the molecular packing on the reaction rates in different directions. The anisotropic behaviour is interpreted by the authors in terms of the accessibility of the reacting groups to the diffusing gas molecules at the different crystal faces. Anisotropic propagation of the reaction front from a nucleation site has also been observed in thermally induced rearrangements (Byrn, Curtin & Paul, 1972).

The packing arrangements of (IIIa) and (IIIb) show the accessibility of the H_α atoms (the potentially reacting atoms) at the various molecular planes (Figs. 7 and 8, part II). The groups of atoms which would most likely block the access of NH₃ to the H_α atoms are the methyl, nitrile and C_β groups. A favourable arrangement which permits easy access of NH₃ to H_α is displayed by the molecular packing of (IIIa). The molecules are arranged in layers which are perpendicular to **b**. The molecules in the layer are related by translations along **a** and **c**. The C_α-H bonds protrude nearly vertically out of the layer whereas the other groups attached to C_α are oriented backwards. In this manner the interference of the α groups and the neighbouring molecules in the layer with the approaching NH₃ molecules is relatively small. The initial elimination of one H_α atom involving the formation of NH₄⁺ and Br⁻ species induces the elimination of the second H_α (as discussed previously) on the one hand and the loosening of the molecule from the crystalline layer on the other. The rate of the latter process depends on the crystal forces which have been shown to be weaker in (IIIa) than in (IIIb). The partial unpacking of the layer permits further access of NH₃ to

the next molecular layer. The accessibility of the H_{α} atoms at any molecular layer of (IIIb) is much less than that of (IIIa) and may also explain the slower rate of dehydrohalogenation in this crystalline modification.

Conclusions

The solid-state reactions discussed in this series exhibit the advantage and potentialities of the study of chemical reactions involving the solid state. The defined molecular geometry at $t = 0$ is of great help in understanding the steric course of the reaction and in predicting the configuration of the product. Thus, it is clear that an *anti* elimination-type mechanism operates under the conditions of gas/solid reactions and that by applying the topochemical principle (Schmidt, 1971) the course of the reaction and the configuration of the products can be predicted with a reasonable degree of certainty. In exceptional cases (*e.g.* dihaloadiponitrile) the somewhat unexpected results could be explained by the lower stability of the molecular conformation at the reaction sites during the initial stages of the reaction. The knowledge of intra- and intermolecular forces which determine the relative stability of the possible conformers enables the design of appropriate molecular systems (*e.g.* bulky substituents inhibiting free rotations about C—C single bonds) in order to perform stereospecific reactions in the solid. Such quantitative stereospecific reactions provide a powerful tool for the study of the possible courses of the reaction.

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