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Design of low-energy barrier intramolecular rearrangements by fitting stereoelectronic requirements of reaction paths

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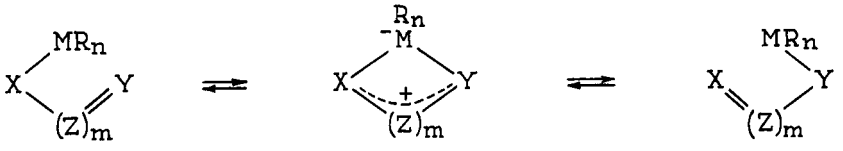
Abstract - A general approach to molecular design of structurally non-rigid compounds capable of fast and reversible intramolecular rearrangements due to migration of the C,N,P,As,S,Se,Te - centered groups has been developed. High frequencies of migration amounting to 10^7 s^{-1} at ambient temperature are achieved by adjusting the initial structure of the rearranged compound to the steric requirements of reaction paths and transition state or intermediate structures for nucleophilic substitution at the central atom of a migratory group through low-energy barrier conformational or polytopal interconversions.

INTRODUCTION

Intramolecular rearrangements play a remarkable role in organic chemistry, representing key steps of many important reactions. Hence, an understanding of the origin of the factors governing steric courses and heights of the energy barriers of these rearrangements is necessary for a deliberate design of particular reactions. Within the last several years work in our laboratory was directed towards the study of compounds susceptible to fast and reversible rearrangements (1) caused by migration within a molecule of bulky groups formed by nonmetallic elements to the right of carbon in the Periodic Table



(1a) (1c) (1b) (1)

X, Y = O, S, NR

Z = CH, CR, N. $(Z)_m$ = Carbo or heterocycle

MR_n = C(O)R, Aryl, Hetaryl, NO, NO_2, PR_2, $^+PR_3$, $P(O)R_2$, AsR_2, SR, S(O)R, SO_2R, TeR

Whereas the rearrangements of this type with hydrogen atom or organometallic fragments have been known for a long time, it was only in the seventies that first examples of the intramolecular displacements of carbon and phosphorus - centered groups, occurring on the tautomeric energy scale (2),were documented, for comprehensive reviews see (Refs.1,2).

$$\Delta G^{\circ}_{25} < 5 \text{ kcal mol}^{-1}$$
$$\Delta G^{\ddagger}_{25} < 25 \text{ kcal mol}^{-1} \quad (2)$$

While the first inequality characterizes the degree of reversibility of reaction, the second one allows the differentiation of the tautomeric interconversions from slower rearrangements in which the life time of isomers is long enough to make their preparative isolation possible at ambient temperature. The requirement of reversibility can obviously be met in the case of degenerate rearrangements. Rather more complicated is the problem of adjusting a molecule to the energy barrier limits.

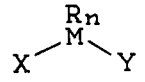
We have suggested (Refs. 1-3) that in order to be capable of fast intramolecular rearrangements the molecule, in its ground state, must be rigidly fixed in a structure similar in its geometrical characteristics to those of the transition state of the reaction, or display a high conformational (polytopal) flexibility permitting it to take on such a structure without overcoming significant energy barriers. In case these conditions are met, the rearrangement frequencies can be strongly affected by a proper selection of the substituents attached to the central atom of a migrant. A close connection of this approach to the molecular design of fluxional compounds with the Pauling seminal transition state

stabilization theory of enzymic reactions (Ref.4) may be traced. According to this theory advanced fourty years ago, binding enzyme to substrate leads to a strained configuration of the latter molecule, which becomes similar in its geometry to that of the activated complex of a catalyzed reaction. While in enzymic reactions a total or partial compensation for the energy losses due to the strain of a substrate is provided by the binding energy of the enzyme - substrate complex, smaller but appreciable stabilizing intramolecular interactions between the approaching functionalities contribute to the relief of strain in reactive conformations of the rearranged molecules.

Since the intramolecular reactivity often achieves the highest limits of the enzymic reaction rates and even rivals them (Refs.5,6), a special attention has been paid to studying its sources. A variety of use-ful rules and concepts such as entropy and stereopopulation control, orbital steering, propinquity and spatiotemporal hypotheses have been evolved and their scope and limitations critically reviewed (Refs.6 - 8). While differing from one another in their terms and emphases, they are common in reflecting in their essence a general principle of steric fitness of initial and transition state structures of fast intramolecular reactions. In the following, the progress report on consistent application of this principle to the design of rapid, mainly degenerate, sigmatropic rearrangements of the type (1) is presented.

OUTLINE

To promote fast displacement of the MR_n groups between the nucleophilic centers in compounds (1), a suitable molecular chain (Z_m) adjusted to the steric demands of transition state structures for nucleophilic substitution at nonmetallic atoms M has to be furnished. There are two principal structural types of reaction site for both concerted and addition - elimination reaction mechanisms differing in the alignment of entering and leaving groups relative to the central atom of the migratory moiety. Both qualitative (VSEPR, frontier MO) models and quantum mechanical calculations of reaction paths performed at various levels of approximation indicate angular approach (2) of the attacking nucleophile to the first-row sp^2- hybridized electrophilic centers at intermediate and reactive distances. By contrast, a linear alignment (3) of making and breaking bonds, which may be realized in trigonal - bipyramidal, bisphenoidal and T-shaped transition state or intermediate structures, is characteristic of the second and lower - row migrants. The axial bonds in these are elongated by 0.2 - 0.3 A as compared with the standard M-X, M-Y bonds.

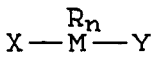


(2)

(XMY) = 90 - 130°

l_{XY} = 2.3 - 2.8 Å

MR_n = C(O)R,Aryl, NO, NO_2

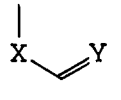


(3)

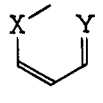
(XMY) = 90°

l_{XY} = 3.5 - 4.5 Å

MR_n = CR_3,PR_2,$^+PR_3$, $P(O)R_2$, SR,S(O)R,SO_2R



(4) j=3



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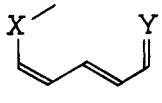
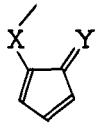
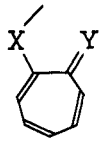


(8) j = 7

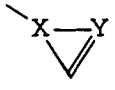


(6) j=7

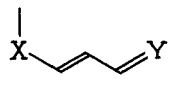


(7) j=9

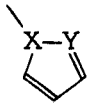
Some of the appropriate molecular fragments which, being attached to the above placed migrant, can form conjugated non-charged molecules prone to fast 1,j - sigmatropic rearrangements, are given by generalized formulaes (4) - (8). The simplest, though preparatively not easily accessible molecular structure (8), suitable for the occurrence of fast displacement of the type (3) migrants, is that ensuring the possibility of 1,7- migration. Structures (9) - (12) exemplify the molecular frameworks that do not satisfy the steric requirements of compounds capable of intramolecular rearrangements of the main - group element migrants.



(9)



(10)



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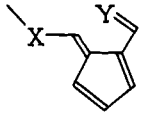
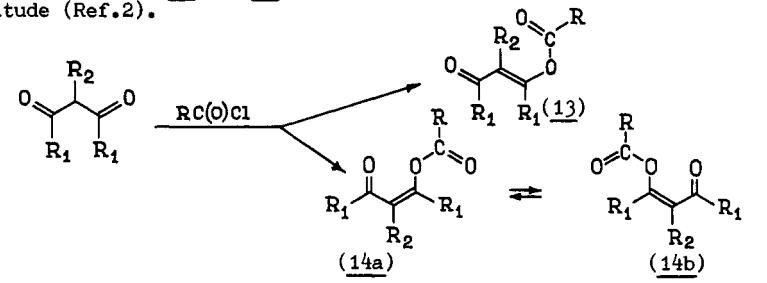
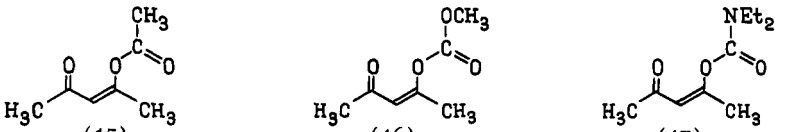


(12)

ACYL GROUP MIGRATION

It was, indeed, found that only Z-isomers of O-acylenols of 1,3-diketones (14) obtained upon acylation of 1,3-diketones or their salts in a mixture with E-isomers (13) readily undergo intramolecular O,O' - acyl transfers (Ref.9). E-Isomers pertaining to the unreactive structural type (10) do not show such a fluxionality. The frequencies of the acyl migration are only slightly affected by the solvent polarity but depend strongly on the substitution in the migrant. This is illustrated by an excerpt of kinetical data on degenerate rearrangement of compounds (15) - (17) which span the range of six orders of the rate constant magnitude (Ref.2).





	(15)	(16)	(17)
k_{25}, s^{-1}	35	$3 \cdot 10^{-1}$	$6.5 \cdot 10^{-5}$
$\Delta G^{\ddagger}_{25}$, kcal mol^{-1}	15.3	18.1	23.1

The propensity to fast rearrangements, which Z-acylenols (14) display, stems from a close correspondence of their reaction site structure attained in the s-cis conformation (21) to the steric requirements of the optimal reaction path for nucleophilic addition to the carbonyl function. The important coordinates for this reaction path are specified by the angles θ and φ whose preferred values were determined by means of ab initio calculations (Ref.10), mapping the reaction path by crystal structures (REf.11) or using various qualitative (Ref.12) or semiquantitative (Ref.13) approaches (Fig. 1).

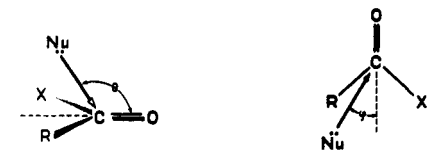


Fig. 1. The θ and φ trajectories for a nucleophilic attack at carbonyl group

Fig. 2 allows a comparison of the optimal directionality for the sterically unhindered approach of a nucleophile to carbonyl group (Fig. 1) with the reaction site geometries in the sequence of compounds (18) - (22). These were calculated using the semiempirical AM1 method (Ref.14) for the conformations resulted from rotations about the - X - C(O)R bonds which bring the reacting centers together and place them into the proper steric position.

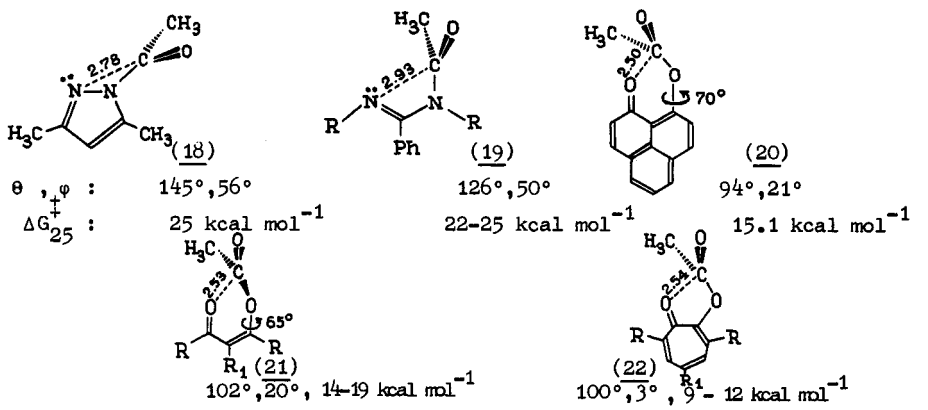


Fig. 2. The AM1 calculated reaction site geometries of O-,N- acylated compounds to be compared with the optimal θ and φ trajectories (Fig. 1) and the energy barriers of O,O'- and N,N'-migration as determined by dynamic NMR studies (Refs.1,3)

The energy required for such a conformational adjustment does not exceed 7 - 8 kcal mol^{-1}, whereas the relative energies of conformations (18) - (22) with respect to their ground state ones are as low as 1 - 4 kcal mol^{-1}. This suggests that no significant energy consumption is necessary for the molecules to be conformationally tuned to a propagation of the intramolecular rearrangement. Molecular structures of some of tropolone and phenalenone O-acyl derivatives in crystal shown in Fig. 3 exhibit a coupling of C(ring)-O and O-C(O) rotations which provides a simultaneous optimization of both θ and φ trajectories.

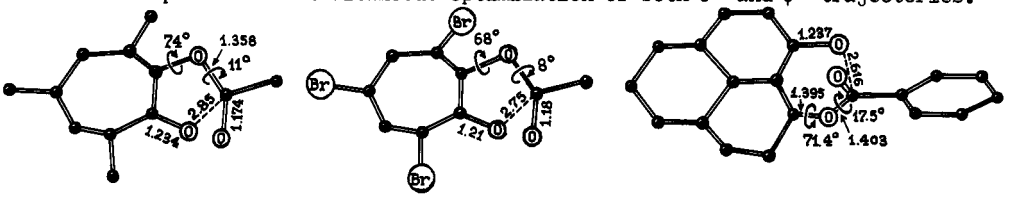


Fig. 3. Stereoprojections of molecular structures of 2-acetoxy-3,5,7-trimethyltropone, 2-acetoxy-3,5,7-tribromotropone and 9-benzoyloxy-phenalenone according to the data of X-ray studies (Refs.15,16).

The closer is an adjustment of the reaction site to the optimal θ and φ directionalities, the lower are the energy barriers against the acyl transfers within the molecule(Fig. 2). This correlation implies that the distortion of molecular frameworks into the structures bearing the reacting functions in the immediate vicinity of the transition state geometry represents the main component of a magnitude of the total energy barrier of intramolecular rearrangement.

Amongst the compounds considered, the best steric conditions, which internal rotations may provide, are found in tropolone derivatives (22), see also Fig. 3. The O...C(O)R distances in these are close enough to those found in ab initio calculations (Ref.17) of the transition state structures for additions of neutral nucleophiles to carbonyl compounds. A subtle additional distortion of the conformationally adjusted molecules (22) is required to fit them to the transition state structures for the O,O' - migration. Extremely rapid intramolecular acyl shifts were, indeed, observed in ^{1}H and ^{13}C NMR spectra of O-acyloxy-tropones. In the case of trifluoroacetyl derivative the frequency of O,O' - migration is so high that it can not be frozen on the NMR time scale even at temperature of a solution as low as -120°C. Table 1 contains results of kinetic investigations of the degenerate rearrangements (22a) ⇌ (22b) by dynamic NMR method.

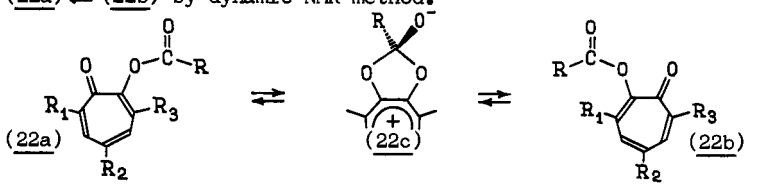


TABLE 1. Kinetic parameters of O,O' - migration of acyl groups in (22). Solvents : CH_2Cl_2, $CDCl_3$,C_6H_5Cl (Refs.3, 18)

C(O)R	R_1	R_2	R_3	k_{25},s^{-1}	$\Delta H^{\ddagger}$, kcal/mol	$\Delta S^{\ddagger}$, e.u.	$\Delta G^{\ddagger}_{25}$,kcal/mol
CH_3 [a]	H	H	H	2.4×10^{5}	10.1±0.4	0.0±0.9	10.1
OCH_3	H	H	H	2.1×10^{3}	13.8±0.5	-0.3±1.3	13.9
$N(CH_3)_2$	H	H	H	2.1×10^{-2}	19.6±0.5	-0.4±1.2	19.7
CH_3	CH_3	CH_3	CH_3	1.2×10^{6}	9.2±0.2	0.0±1.1	9.2
OCH_3	CH_3	CH_3	CH_3	5.6×10^{4}	11.0±0.2	0.1±1.2	11.0
OCH_3	Br	Br	Br	22	15.6±0.2	0.0±0.6	15.6
CH_3	CH_2Ph	H	CH_2Ph	3.1×10^{6}	8.3±0.5	-1.1±1.6	8.6
OCH_3	CH_2Ph	H	CH_2Ph	9.7×10^{3}	12.0±0.3	-0.1±0.7	12.0
$N(CH_3)_2$	CH_2Ph	H	CH_2Ph	3.8×10^{-1}	18.0±0.3	0.0±1.0	18.0
CF_3	CH_2Ph	H	CH_2Ph	$> 5 \times 10^{7}$	-	-	< 7.0

[a] From the data of Ref.19

Fig. 4 shows temperature - variable ^{1}H NMR spectra of compound (22,R=NMe_2,R_1=R_3=CH_2Ph,R_2=H), which display the sequence of conformational processes preceding the O,O' - transfer of the acyl group. Diastereotopic behavior of one of the methylene groups indicates acoplanar ground state conformation of the molecule. With raising the temperature of solution, rotation about the C-O bonds becomes faster resulting in the averaging of the methylene AB spectral pattern. At higher temperature, an acceleration of the amide rotation manifests itself in broadening and coalescence of N-methyl peaks. Through these rotations the molecule is adjusted to the s-cis conformation (22), in which the intramolecular transfer of acyl group can occur.

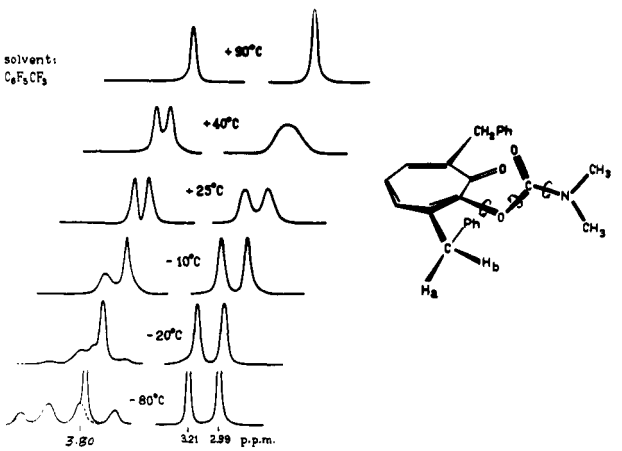


Fig. 4. Variable-temperature ^1H NMR spectra of compound (22, $R_1=R_2=CH_2Ph, R_2=H$) in $C_6F_5CF_3$ - $CDCl_3$ solution. The following kinetic parameters were calculated by total ^{3}line-shape analysis of the spectra. C(ring)-O, O-C(O) rotations : k_{25}= 2.2 10^3 s^{-1}, $\Delta G^{\ddagger}_{25}$ = 12.9 kcal mol^{-1}; amide rotation : k_{25}= 20 s^{-1}, ΔG_{25}= 15.7 kcal mol^{-1}. For kinetic parameters of O,O'-migration see Table 1.

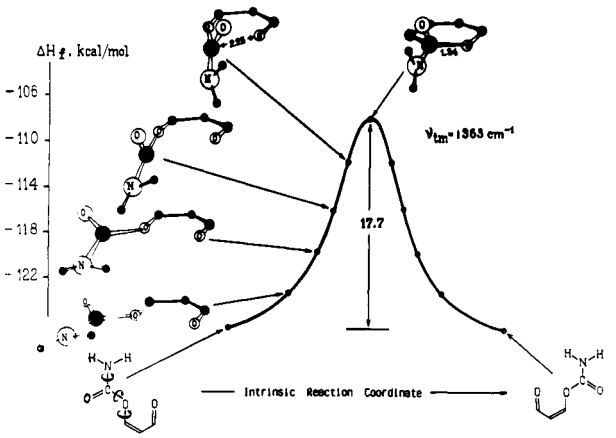


Fig. 5. Energy profile of degenerate rearrangement due to carbamoyl O,O'-migration in cis-enol malondialdehyde derivative calculated by MINDO/3 method

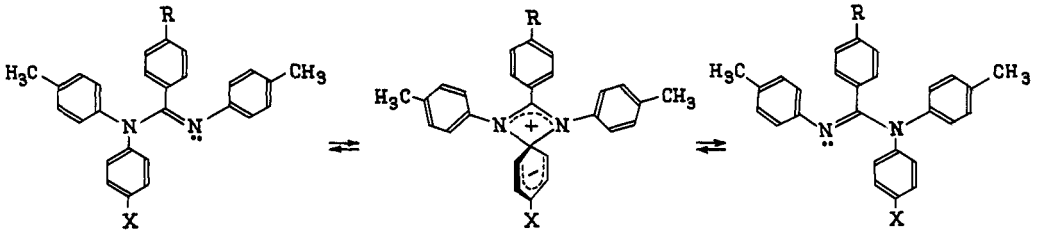
In general, the conformational and group transfer stages of the rearrangements (1) are strongly coupled. It is seen from the structural changes occurring in the course of carbamoyl O,O'-migration in cis-enol malondialdehyde derivative pictured in Fig. 5. A propagation of the rearrangement along the intrinsic reaction coordinate, i.e. the steepest descent path from the saddle point to the nearest energy minimum (ref.20), is shown by the snapshot sequence of momentary structures. The very late transition state structure, which might rather conform to that expected for a probable tetrahedral intermediate, is predicted.

The turn of the carbonyl group of migrating moiety to the plane orthogonal to the rest of the molecule as well as the twisting around the C-N bond are displayed by the structure shown in Fig. 5 in a vicinity of the transition state. Noteworthy is that the twisting is predicted no to be combined with the appreciable pyramidalization of the amino group. This may be explained by taking into account a recent conclusion about the trend in charge density redistribution affected by a pyramidalization of amino groups in amides (Ref.21). Contrary to expectations, it has been found that this distortion leads to an increase in the π and total electron population of the carbonyl carbon. It may be, therefore,suggested that pyramidalization of the amino group in compound shown in Fig. 5 would lower the electrophilicity of the carbamoyl carbon and thus diminish a migrating aptitude of the acyl group.

ARYL GROUP MIGRATION

The steric courses of nucleophilic addition to the sp^2-hybridized carbonyl and aromatic carbons are similar. Thus, it should be expected that when acyl groups in molecular systems, analogous to those considered above,i.e. (4) - (7), are substituted by aryl groups activated with electron-withdrawing substituents, it will lead to tautomeric carbonotropic compounds, in which rapid migration of these groups occurs.

The validity of this conclusion was supported by the discovery of a sufficiently fast intramolecular 2,4,6-trinitrophenyl group migration in amidine derivatives (23) (Ref.22). Some examples of fluxional compounds in this series are given below.

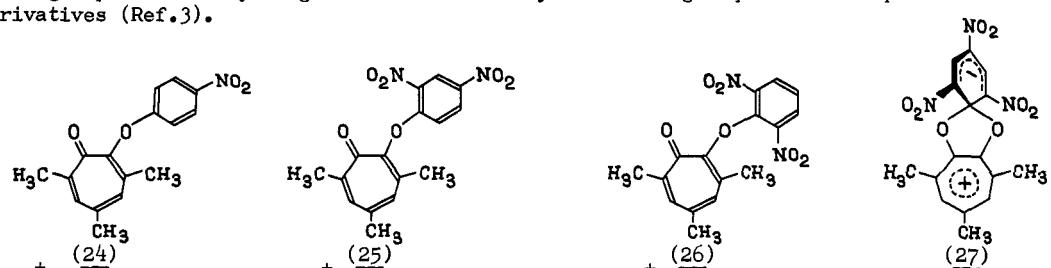


(23a) (23c) (23b)

X	R	k_{25}, s^{-1}	$\Delta H^{\ddagger}$, kcal mol^{-1}	$\Delta S^{\ddagger}$, e.u.	$\Delta G^{\ddagger}$, kcal mol^{-1}
2,4-$(NO_2)_2$	H	$1.9 \cdot 10^{-6}$	25.2	0.2	25.1
2,4,6-$(NO_2)_3$	H	$7 \cdot 10^{-1}$	16.3	-4.4	17.6
2,4,6-$(NO_2)_3$	NO_2	$8 \cdot 10^{-2}$	17.3	-5.5	18.9
2,4,6-$(NO_2)_3$	OCH_3	2	15.7	-4.3	17.0
2,4,6-$(SO_2CF_3)_3$	H	22	4.2	-38.3	15.6

It was found that only the presence of three nitro or trifluoromethylsulfonyl groups in the aryl moiety warrants its rapid N,N'-migration. Removing one of these substituents decrease the rate constant of the rearrangement by approximately six orders of magnitude. The C-aryl substituent delocalizing positive charge in (23c) is necessary the rearrangement to proceed on the NMR time scale. In similar formamidine derivatives the aryl migration is completely frozen. Electron-releasing substituents in the C-aryl group accelerate N,N'-migration. All these peculiarities are characteristic of aromatic nucleophilic substitution. Ground state conformations of amidines (23) are fitted to the steric course of this reaction, which is evidenced by X-ray structural investigation(a turn of the migrating aryl on 116° about the C-N bond, θ =133°) (Ref. 23) as well as dipole moment and Kerr constant measurements (ref.24).

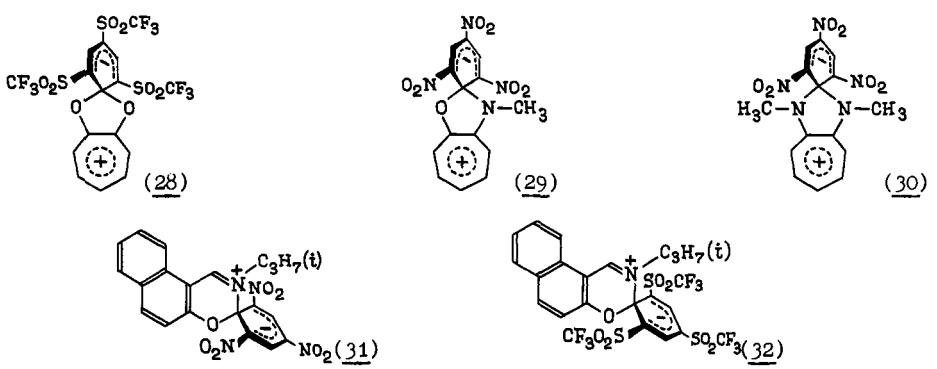
The same trend towards facilitating intramolecular rearrangements by a larger number of nitro groups in the aryl migrant was revealed by a following sequence of tropolone derivatives (Ref.3).



(24) (25) (26) (27)

$\Delta G^{\ddagger}_{25} > 27$ kcal/mol $\Delta G^{\ddagger}_{25} = 11.7$ kcal/mol $\Delta G^{\ddagger}_{25} < 7$ kcal/mol $\Delta G^{\circ} > 5$ kcal/mol

The O,O'-migration of 2,6-dinitrophenyl group in solution of compound (26) is so fast that both ^{1}H and ^{13}C NMR spectra are averaged even at -100°C. An assignment of the ground state structure of (26) to the aryl ether or to the symmetric dipolar spiro-σ -complex isomeric forms was made on the basis of electronic absorption spectra, which unequivocally witnessed preferability of the former structure. However, in the case of the trinitrophenyl derivative (27) clear evidence in favour of dipolar spiro-σ -complex structure was obtained by means of various spectral methods and the X-ray structural investigation as well. The compounds (27) - (32) represent stable, easily isolable dipolar spiro-σ -complexes, whose structure was proved by the X-ray studies (Refs.1,25). These are deeply coloured (λ_{max} = 480-540 nm) compounds possessing high values of dipole moment (5-6 D).



(28) (29) (30)

(31) (32)

A sequence of crystal structures of aryloxytropone derivatives, shown in Fig. 6, clarifies the peculiar-ities of the reaction path connecting the initial s-trans conformation with the dipolar spiro-σ -complex which, depending on substituents in migrating aryl group,represents either the final or the intermediate product. The structures A - D are arranged in the decreasing order of both the $C_1...O$ distance and the angle φ , parallel to that in which the energy barriers of the intramolecular aryl group transfer diminish. The s-cis conformation (φ = 0°), best sterically fitted to the aryl migration step of the rearrangement, was found in compounds C, D. A very strong attractive interaction between the bond-forming centers in these compounds manifests itself in significant shortening of the $C_1...O$ distances. In both compounds these are about 0.5 A shorter than the van der Waals C...O contact (Ref.26), whereas the breaking C(aryl) - O bonds remain virtually unstretched, thus indicating a very early transition state structure for the formation of a dipolar spiro-σ -complex.

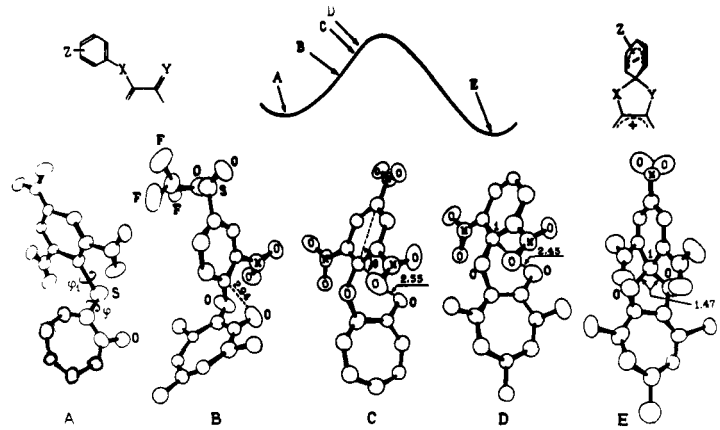


Fig. 6. Structural mapping of the reaction path of the intramolecular transfer of activated aryl groups in the tropolone derivatives. The following structural parameters and rate constant values of 0,0'-migration (CH_2Cl_2, 25°C) were obtained (Ref.2): A (φ =170°, $k < 10^{-6}$ s^{-1}) ; B (φ =77°, θ =129°, $k=10^{3}$ s^{-1}); C(φ=10°,θ =111°, $k > 10^{7}$ s^{-1}); D (φ =2°,θ =107°,$k > 10^{7}$ s^{-1}) ; E - C_{2v}-spiro-σ -complex structure (27).

The 0,0'-migration in solutions of compounds C,D (Fig. 6) occurs with the extremely high frequency, but it completely frozen in solid, as evidenced by the CPMAS ^{13}C NMR spectrum of compound C, shown in Fig. 7. An inequivalence of C_1,C_2 and other pairs of tropolone ring and methyl carbons, whose signals are averaged in solution, is unaffected over the temperature range of 25° - 100°C.

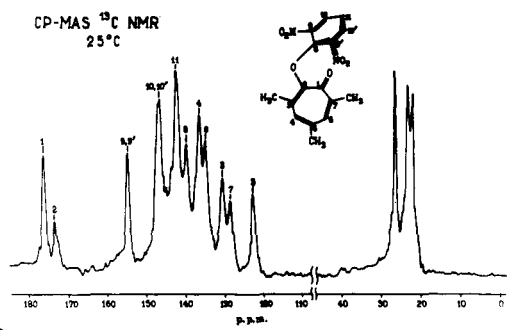


Fig. 7. CPMAS ^{13}C NMR spectrum of 2-(2',6'-dinitrophenoxy)-3,5,7-trimethyl tropone at 25°C, 2-ms cross-polarization time, 2.6-s repetition time, 3.1-μs ^{1}H - 90° pulses, 19294 scans on the average.

INTRAMOLECULAR DISPLACEMENT OF ANCHORED GROUP 5,6 ELEMENT-CENTRED MIGRANTS

A linear alignment of the forming and breaking bonds in trigonal bipyramid-derived transition state or energy-rich intermediate structures (3) can be achieved in tridentate ligands (33)-(35) containing built-in P,S-centered migrants (Refs. 28,29). These are shown in Fig. 8. An assignment of (33c) to the transition state structure of the concerted rearrangement or to the stable intermediate, which is referred to as "frozen" transition state (Ref.28), depends on the strength of the three-center four-electron bonds forming by the central atom X. The situation is completely similar to the above-considered case of dipolar spiro-σ -complexes. The high frequencies of intramolecular oscillations of the anchored main-group element

migrants, which Fig. 8 exemplifies, may be achieved not only in the case of ions[a], but also in similarly designed non-charged species (Ref. 30). This is illustrated by the example of a very fast scrambling of the ^{125}Te - ^{15}N bonds in a conformationally flexible o,o'-diformyl diphenyltelluride N,N'-diphenyldiimine (36). X-ray structural investigation evidences the T-shaped tricoordinate tellurium structure of compound (36) with the only sufficiently strong fractional Te..N bond, which is about 1 A shorter than the Te..N van der Waals contact, though 0.5 A longer than than covalent Te-N bond (Fig. 9). In solution ^{125}Te NMR spectrum of the ^{15}N-isotopomer of (36) is represented by a triplet signal, which is consisted with either its existence in a stable tellurane (12-Te-4) form (36c) or a dynamical equilibrium of two 10-Te-3 structures (36a)⇋(36b) rapidly interchanging positions of nitrogens relative to tellurium within the molecule. The latter possibility has been proved by that the the ^{1}J (^{125}Te-^{15}N) coupling constant observed is equal to half the value found for it in compounds with the rigid Te-N bonds (Refs.30,31).

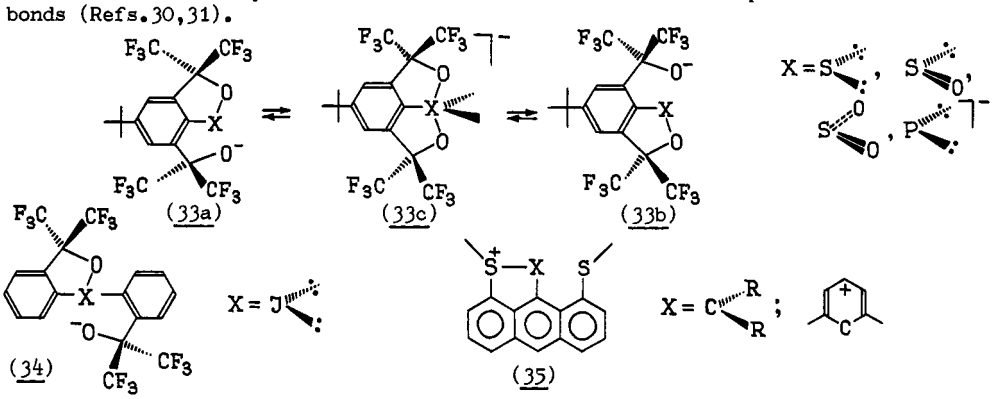


Fig. 8. Tridentate ligands ensuring linear arrangement (3) of forming and breaking bonds of the C,P,S-centered migrants through their anchoring to molecular frameworks (Refs.28,29).

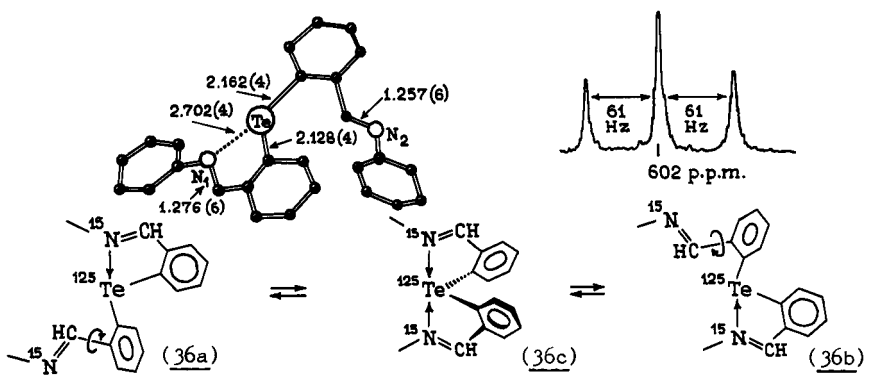


Fig. 9. X-ray crystal structure and ^{125}Te NMR spectrum ($CDCl_3$,25°C) of ^{15}N-isotopomer of compound (36), 98% enrichment in (Ref.30).

The spectral pattern, shown in Fig. 9, closely resembles that observed for the proton signal in its $^{15}N...H$ - ^{15}N environment in porphynes, oxalamidines and related compounds exhibiting fast intramolecular proton shifts along the hydrogen bond between the two nitrogens. Such a migration gives rise to a triplet form of the proton signal in ^{1}H NMR spectrum with the line components separated by 1/2 ^{1}J (^{15}N-H) intervals (Ref.32). The (36a ⇌ 36b) exchange process continues being fast on the NMR time scale even at the temperature of solution lowered to -70°C, at which no detected perceptible broadening of the spectral lines has been observed.

ADDITION-REARRANGEMENT-ELIMINATION MECHANISM

We have investigated another complementary possibility of the occurrence of intramolecular migration of P,S,As - centered groups in structural environments not suitable for a linear alignment of forming and breaking bonds. Such a possibility appears thanks to the stepwise reaction mechanism of nucleophilic substitution predicted by Westheimer (Ref.33). We found that it can readily be realized in the case of degenerate intramolecular rearrangements (1). The necessary condition for axial approach of the attacking nucleophile and departure of the leaving group from the axial position in trigonal bipyramid-derived transition structures can be met if the initial axial attack leads to the formation of an intermediate capable of a low-energy barrier polytopal rearrangement. The result of this rearrangement has to be the interchange of positions of the entering axial and the leaving equatorial groups. The departure of the leaving group proceeds then from the axial position in accordance with the requirement of the principle of microscopic reversibility.

[a] In fact, the interconversion (33a)⇋(33b) is one of the steps of experimentally observed base-catalyzed rearrangement of corresponding alcohols (Ref.29).

An important obligatory condition for such an addition-rearrangement-elimination (AdRE) mechanism to operate is the existence of at least one extra reaction valleys on the potential energy surface of reaction, complementary to the minimal energy reaction path (MERP) for nucleophile addition. The energy-richer, though sufficiently long-lived intermediate should be formed by approaching nucleophile to the attacking center along the less favorable pathway.

It was indeed shown by calculations performed at various levels of approximation (CNDO/2, MINDO/3, MNDO) that, apart from the MERP, there do exist such additional reaction channels through which nucleophile can approach to the P,S-centered groups. The total number of the reaction trajectories is equal to that of the ligands attached to the central atom, with the MERP trajectory being collinear with the bond formed by the most electronegative ligand, the trajectory second in energy - with the bond formed by the ligand next in electronegativity and so forth (Refs. 34,35). Two representative examples are given in Fig. 10.

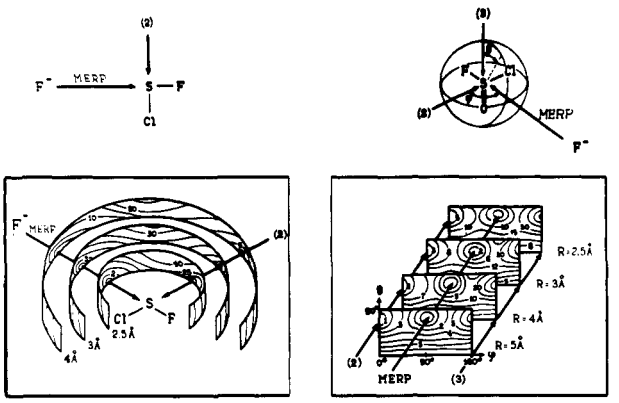
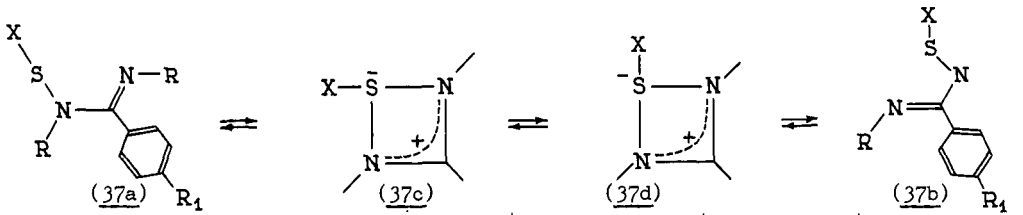


Fig. 10. Sections of the potential energy surfaces for addition of fluoride-anion to model sulfide and sulphoxide as calculated by CNDO/2 method. In the former case two reaction trajectories for the approach of the nucleophile lead to the formation of two isomeric T-shaped sulfuranides $SClF_2^-$. In the latter case, three reaction trajectories, each collinear with one of the S-X bonds, exist giving rise to three isomeric bisphenoidal sulfuranoxides $SClF_2O^-$. The energy preferable structures are those bearing both most electronegative atoms,i.e. fluorines, in the axial position.

In the case of the F^- + SClF reaction, the isoenergy curves are given on the cylindrical surfaces spaced at different distances between the interacting centers. It is seen from the Fig. 10, that in accordance with the polarity rule (Ref. 36) the preferable direction of the attacking nucleophile approach is that which affords the formation of a T-shaped tricoordinate sulfur anion with linear F-S-F arrangement. No reaction valley exist for the bisectral approach of the F^-, yet the second, though less energy favorable, reaction channel appears when the attacking anion comes from the rear of less electronegative chlorine. The T-shaped adduct is subject to low-energy barrier polytopal rearrangement by in-plane motion of chlorine from axial to equatorial position (Refs.34,37). This places the substituted fluorine into axial posion required for its departure. These three stages model the AdRE mechanism of rearrangements (1) which were found to readily occur in the case of arenesulfenyl amidine derivatives (37). The strong electron-withdrawing substituent X has to be attached to the sulfur in order to facilitate an alternative back-side approach to it and to delocalize the negative charge at the forming tricoordinate sulfur center. The intramolecular character of the rearrangements has been proved by cross-experiments. A brief selection of kinetical data available for the (37a) (37b) rearrangement (Refs.1,2,38) is given below.



X	R_1	k_{25}, s^{-1}	$\Delta H^{\ddagger}$, kcal/mol	$\Delta S^{\ddagger}$, e.u.	$\Delta G^{\ddagger}_{25}$, kcal/mol
CCl_3	H	$2\cdot10^{-2}$	13.6±0.6	-20.1±1.1	19.6
$2,4\text{-}C_6H_3(NO_2)_2$	4-OCH_3	$2\cdot10^{-2}$	15.4±0.5	-14.8±1.4	19.8
- " -	H	$6\cdot10^{-2}$	15.0±0.6	-13.6±1.2	19.0
- " -	4-Br	$1.2\cdot10^{-1}$	13.3±0.5	-18.5±1.4	18.8
- " -	4-NO_2	3.1	9.8±0.3	-23.2±0.9	16.7

High negative values of $\Delta S^{\ddagger}$ are consisted with the multistep mechanism of 1,3-migration of the arenesulfenyl groups in (37). The formation of the T-shaped intermediate, similar to (37c,d), is sterically inhibited in the case of the three-membered cycle. For this reason, the pyrazole derivative (38) is not susceptible to tautomeric migration of arenesulfonyl group even when heated in solution to 200°.

Fig. 11 features an energy profile common to the whole variety of degenerate intramolecular rearrangements governed by AdRE mechanism. Apart from the sulfenyl group, sulfinyl, phosphinyl, phosphonio, phosphoryl, phosphoranyl and some other groups were found to display high migration aptitude in sterically constrained amidine systems (Refs. 39-43). With the exception of the phosphoranyl group, other migrants form intermediates whose structure is derived on the basis of the fluxional trigonal bipyramidal bond framework. This implies that the most feasible ligand permutation mode, i.e. Berry-pseudorotation, can operate at the key-stage of reaction. Its energy barrier is strongly affected by apicophilicities of the substituents at the central atom. Since the energy barrier of polytopal rearrangement contributes to the total energy barrier for a group transfer reaction (Fig. 11), a proper selection of the substituents is important for fitting the rearranged molecule to the tautomeric energy scale (2).

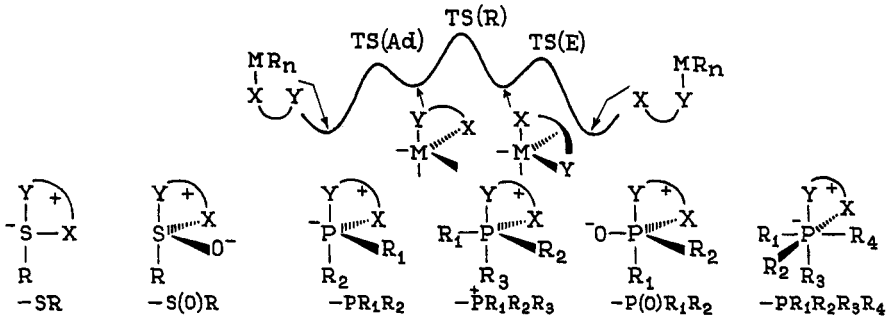
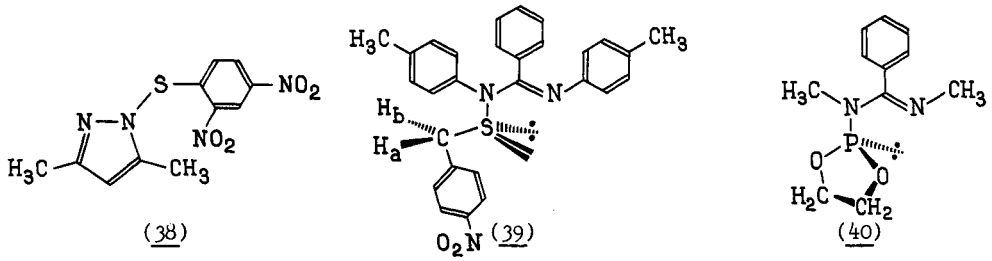


Fig. 11. The energy profile of the degenerate (X=Y) rearrangement due to $X \rightleftharpoons Y$ displacement of group 5,6 element-centered migrants according to the AdRE mechanistic scheme. At the bottom of the Figure, the structural types of intermediates belonged to the local minima of the energy curve and capable of low-energy barrier polytopal interconversion are presented.

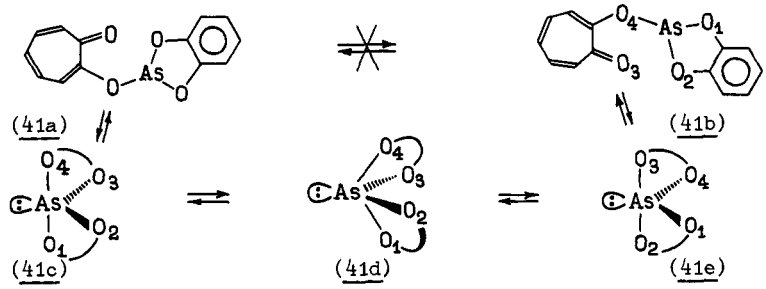
An expected stereochemical outcome of the AdRE rearrangement (1) is retention of configuration at the central atom of the migrating group (Refs.1,44). The truth of this prediction has been proved by results of the dynamic NMR studies of various amidine derivatives bearing P,S-centered migrants with prochiral groups. These were found to retain a diastereotopic behaviour at the temperature of their solutions higher than that at which the fairly fast migration occurs.



T_c(PhCN)=124°, $k_{25}=3\ 10^{-3}\ s^{-1}$; $T_c(C_6D_{12})$=23°, $k_{40}=12\ s^{-1}$,
$\Delta H^{\ddagger}$=16.0 kcal/mol, $\Delta S^{\ddagger}$= -14.3 e.u. $\Delta H^{\ddagger}$=13.3 kcal/mol, $\Delta S^{\ddagger}$= -12.6 e.u.
$\Delta G^{\ddagger}_{25}$ = 20.4 kcal/mol $\Delta G^{\ddagger}_{23}$=17.0 kcal/mol (Ref.41)

In the case of compound (40), the ^{1}H-^{31}P spin-coupling of N-methyl protons is not disturbed up to 40°, thus indicating the intramolecular character of the phosphinyl migration. Only at the solution temperature rising above 80° the intermolecular route of the rearrangement becomes dominant. The ^{1}H-^{31}P spin-coupling disappears and an inversion of configuration at phosphorus manifests itself in the averaging ($AA'BB'X \rightleftharpoons A_4X$) methylene spectral pattern.

While making the central atom of migrating moiety heavier, a substantial acceleration of intramolecular displacements is achieved. Such is the case of very fast arsinyl group migration found in (2'-tropolonyl)-1,3,2-benzodioxaarsole (41) (Ref.45). The ^{13}C NMR spectrum of compound (41) is averaged (only seven signals) in solution even at -70°.[6] The frequency of arsinyl migration at this temperature was estimated to be higher than 10^6 s^{-1} and therefore, $\Delta G^{\ddagger}_{-70} < 6.5$ kcal/mol.



The origin of such a low energy barrier in a molecule that does not meet steric requirements (3) of concerted rearrangement of the arsinyl migrant is made clear by the results of an X-ray investigation of the molecular structure of compound (41), which are shown in Fig. 12.

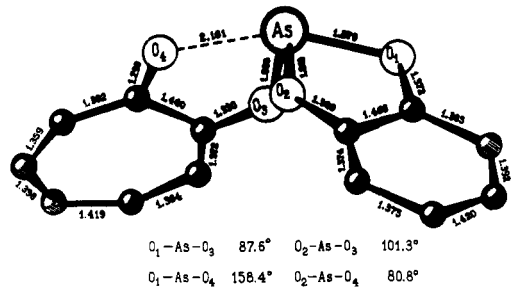


Fig. 12. The molecular structure of 2-tropolonyl-1,3,2-benzodioxaarsole (41) from X-ray structural data (Ref. 45)

Although the distance As...O_4 is longer that the length of the covalent As-O bond, it is 1.2 Å shorter than the van der Waals contact (3.4 A). This indicates a very strong attractive interaction between these centers in the ground state conformation of (41), which is very close to a pyramidally distorted bisphenoid with an inner nucleophile O_4 entering into an axial position. The conformation is thus well adjusted to the steric course of the AdRE rearrangement, because the square-pyramidal structures serve as transition states for the Berry-pseudorotation of bisphenoidal species (refs. 46,47).

It is worthwhile to arrange main-group element migrants in the order according to their migratory aptitudes regardless of the particular mechanism which the intramolecular rearrangement (1) follows. Abundant experimental data for such a comparison are found in the series of benzamidine and tropolone derivatives. Though variation of substituents at the migrating center may lead to shifts in the migrant position in the sequence below, it gives a clear impression of how the origin and coordination number of the central atom influence the rates of migration. These vary from more than 10^6 s^{-1} for the groups on the left side of the sequence to less than 10^{-8} s^{-1} for the groups on the right, thus spanning the frequency range of more than 14 orders of magnitude.

$$As(-OC_6H_4O-) > {}^{+}AsPh_3 > Ge(CH_3)_3 > Si(CH_3)_3 > {}^{+}PPh_3 > C_6H_2(NO_2)_3 > SC_6H_2(NO_2)_3 > S(O)R > {}^{+}SPh_2 > PF_3Ph > P(-OCH_2CH_2O-) > P(NR)(OR')_2 > PPh_2 > NO > C(O)CH_3 > NO_2 > SO_2Ar >> Alk$$

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