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STRAIN ENERGY MODELING OF SIMPLE AND CROWDED ALIPHATIC KETONES : SPECTROSCOPIC PROPERTIES

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Abstract - Spectroscopic properties of ketones have been correlated with a structure-frequency micro-correlation made possible by dividing the ketone population into sub-populations, $\mathcal{P}_{i,j,\ldots}$. The structure and comportment of those ketones of the population that remain outside the correlations are treated in the discussion. The DARC/PELCO topological treatment is explained and demonstrated : it is based on the notion of ordered populations considered as hyperstructures or formal graphs. The correlations thus obtained, in IR, UV and ^{13}C NMR spectroscopy, are more exhaustive than those obtained with the above-mentioned micro-correlations, and their prediction potential, or "préférence", is very high. Variations in the geometry of compound structures resulting from an abundance of substitutions, as well as their relationship to conformational problems, are shown. A gem-persubstituted β effect associated with a major strain release, leads to major deformations of angles and of interatomic distances.

INTRODUCTION

The structural environment of the carbonyl group influences the spectral characteristics of ketones. Although this fact has long been known, its interpretation is still subject to speculation. Relationships between structure and spectral properties can be approached through isolated cases or via an ordered family of ketones.

The purpose of studying highly substituted ketones, such as tetratertiobutylacetone or triisopropylmethyl-neopentylketone, synthesized in our laboratory, was to verify the hypothesis of an internal strain due largely to repulsions between non-bonded atoms. In fact, we discovered that the situation is somewhat different and that the structures undergo certain important deformations in order to dissipate or redistribute the imposed strain. The real geometry could be considered as resulting from structural deformations of the standard structure because of potential strain. The virtual passage from a standard structure to a real structure would be accompanied by strain release. Such a real structure is said to be "decongested" and its true description is of a topographical nature.

Are the angle and bond modifications observed in highly substituted environments following strain release apt to modify the balance between rotamers? This is the question we asked ourselves during our ketone studies, in which we made use of appropriate spectroscopic treatments as well as extrathermodynamic "structure-property" correlations for our interpretations.

The structures used make it possible to study intragroup interactions developed in alkyl groups, as well as intergroup interactions between the radicals of the sp^2 carbon valence angle.

We approached this difficult area of aliphatic ketones, where the conformational aspect is essential, by supposing the existence of conformational filiations between privileged rotamers of different ketones. The problem with these filiations lies in the assigning of reference conformations, and we shall show how we have sought to assure the validity of our propositions by constantly improving the convergence of deductions based not only on diverse experimental data, but also on various calculations on the existence probability of the rotamers.

In this presentation, our aim is to report on the current state of research, linking present results to the attribution of the real geometries of aliphatic ketones.
This analysis will be based on the continual use of the notion of conformational filiation, as well as on the evaluation of changes in molecular dimensions for certain borderline cases of highly substituted structures. We shall show that the evaluation of interactions in terms of energy is not yet entirely satisfactory, although analyses of tendencies yield interesting

results for structure assignment. The latter are neither complete nor final though reported progress on the coherence of deductions seems satisfactory and most promising.

OUTSTANDING FEATURES IN UV AND IR SPECTROSCOPY OF KETONES

In UV as well as in IR spectroscopy, the influence of structure and solvent on the absorption maximum shift has led to a great number of studies: here, we have considered only the most outstanding of these studies.

$n \rightarrow \pi^*$ absorption band of saturated ketones

The effect of substituents on the absorption band of aliphatic ketones was studied experimentally and rationalized by us in 1954 (1). The absorption band undergoes a strong bathochromic shift (from 35 990 cm^{-1} to 33 650 cm^{-1} in hexane) by increasing substitution from acetone to hexamethylacetone. Each substituent of the molecule contributes to this bathochromic shift by a characteristic increment.

When seeking to extend and develop the relationships between the molecular structure and the energy of the $n \rightarrow \pi^*$ transition, we encountered the difficulty of determining the position of the band with precision, due to the presence of important vibration fine structure for certain aliphatic ketones (2a).

In 1970, our study bearing on a population of 50 aliphatic ketones which was very rich in highly substituted compounds showed the existence of somewhat intense fine structure which, for certain compounds, is analogous to that observed for acetaldehyde or cyclobutanone.

In order to render the analysis of this spectral modulation less subjective, we deemed it necessary to define a fine structure (FS) index, i.e. an index quantitatively describing the intensity of the modulation (Fig. 1). The index scale thus obtained permits situating the importance of the fine structure within the absorption phenomenon and comparing the fine structure of two carbonyl derivatives.

Thus, ditriptylketone $tBu(Me)_2CCOC(Me)_2tBu$: (FS = 10.2 x 10^{-2}) and tetratertiobutylacetone $tBu_2CHCOCHtBu_2$: (FS = 9.4 x 10^{-2}) have a vibrational structure whose intensity is near that of cyclobutanone (FS = 11 x 10^{-2}) and corresponds to a third of that of cyclopentanone (FS = 27.7 x 10^{-2}).

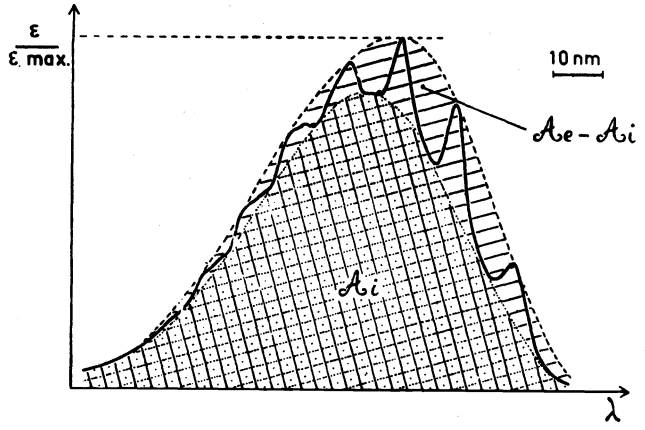


Fig. 1. Definition of the fine structure index FS = $(\mathcal{A}_e - \mathcal{A}_i)/\mathcal{A}_i$

The rules governing the existence of this fine structure are not clearly established. It is observed that the practically inexistent fine structure for acetone tends to become more marked with substitution on the carbons α and β to the carbonyl group. In general, the modulation increases as the hindrance around the carbonyl group also increases; however, there are a certain number of exceptions. The solvent also plays a determining role: the fine structure index is a non-increasing function of the solvating power. However, depending on the nature of the ketones studied, there are several types of comportment with respect to changes in the medium (2b). We especially wish to point out, what, to our knowledge, is the first observation of an intense modulation which resists the increase of the solvating power: $(tBu)(Me)_2CCOC(Me)_2(tBu)$.

The varied character of the modulation with the solvent or structure poses the problem of defining an absorption wave number permitting the comparison of highly modulated spectra

with those bands lacking a fine structure. Locating the maximum of the internal envelope yielded some satisfactory results for our study of the bathochromic shift of the substituents, as well as for our study of the hypsochromic shift of the solvents.

Solvent shift and privileged conformations. We have shown the diversity of the relationships between the hypsochromic shifts of solvents on the $n \rightarrow \pi^*$ transition and the wave number found for a reference solvent (hexane): three different types of comportment are obtained, depending on the hindrance of the two radicals, R and R' (2c) (Fig. 2).

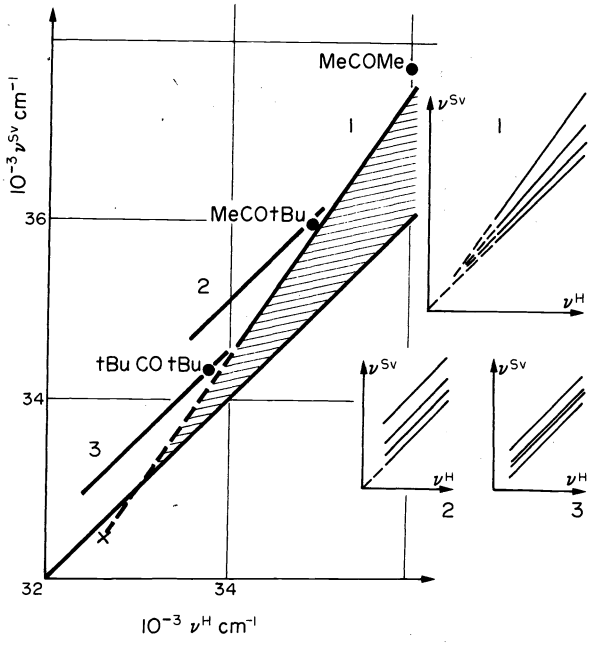
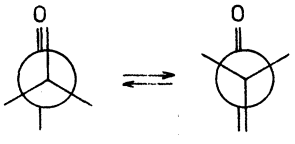


Fig. 2. The two parallel networks and the convergent network of saturated aliphatic ketones RCOR'.

For each of these comportments, straight lines $\nu^{Sv} = f(\nu^{H})$, characterizing the solvents Sv, are organized into networks:
- a convergent network, 1, if both radicals R and R' are only slightly hindered;
- a parallel network, 2, for ketones MeCOR with hindered radical R;
- a parallel network, 3, different from the preceeding network (the amplitude of the solvent effect is weaker) if both radicals, R and R', are hindered.

Comparison of these results with those of the hypsochromic shift of cyclanones having locked environments justified the following conformational interpretation: the carbonyl group of the slightly substituted RCOR' compounds is eclipsed by a C-C or C-H bond of the slightly hindered radical R. In hindered compounds, the carbonyl group would be bisected by the hindered bonds of the radical R (or R'). Thus, tl growing interaction between the carbon atoms of the radical R at β or γ with respect to the carbonyl group and the carbonyl group itself would favor a bisected carbonyl group conformation, or at least one that is sufficiently staggered with respect to the eclipsed carbonyl group (2c).



CO eclipsed CO bisected

Structural effect of the $n \rightarrow \pi^*$ transition and linear free energy relationships. A study in 1963 on a restricted population of slightly hindered ketones (11 ketones RCOR' where R and R' = Me, Et, Pr, iBu) showed us that it is possible to express the influence of environment with a linear free energy relationship when using two structural parameters: $\Delta\nu = -16\ 320\Sigma\sigma^* + 1\ 490\ (n - 6) + 42\ cm^{-1}$. "n" is the number of hydrogens α to the carbonyl group.

However, the slight deviation of "the most highly substituted" ketone, di-isobutylketone, already showed that it would be necessary to use other structural parameters in order to attain a satisfactory correlation (3).

Carbonyl stretching vibrations of ketones

Our recent studies bearing on a vast population of ketones have shown us the interest of the shape of the $\nu_{C=O}$ band in the analysis of the structural effect, as well as in that of solvent effects.

A systematic study has led us to a true typology of $\nu_{C=O}$ bands. It should be pointed that we have split those bands having marked shoulders into two bands of the Lorentzian type (4), using a Dupont de Nemours 310 curve analyzer (5) (Fig. 3).

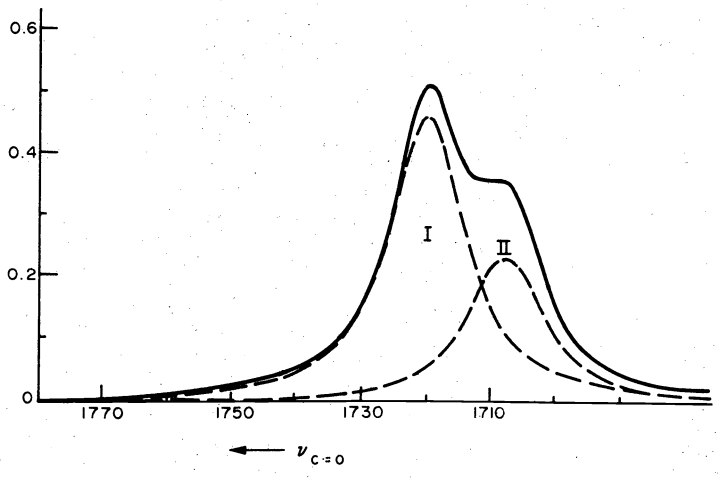


Fig. 3. Shape of the $\nu_{C=O}$ band for neoP-CO-Me in CCl_4

The results show that higher frequency band I corresponds to the only band existing in the gas phase. The relative importance of bands I and II depends on the solvent and varies roughly with Allerhand and Schleyer's solvent parameter, G (6). For example, the area of band II for methylneopentylketone varies from 0% in the gas phase to 55% in $CHBr_3$. In a solvent such as CCl_4, band I is generally preponderant and its frequency corresponds markedly to that of the maximum of the envelope (7); it is this parameter that we have used to analyze the influence of the structural environment.

Ever since 1969, our first studies have allowed us to advance a certain number of results which are summarized in a "topology/$\nu_{C=O}$" relationship and in "reactivity parameter/$\nu_{C=O}$" relationships (8).

"Topology/$\nu_{C=O}$ relationship. The sensitivity to structural effects of the stretching vibration of the carbonyl group of ketones in gas phase is interpreted by a topological analysis of the structural environment, using the DARC/PELCO method which we shall describe in the course of this presentation.

The correlation equation obtained shows that the contributions from the various substituents in positions α and β to the carbonyl group are constant and additive, but that, nevertheless, there are interaction terms between certain positions. These interaction terms express the difference from the strict additivity of contributions, not only within one of the alkyl groups ($tBu(Me)_2C-$), but also between both alkyl groups, on opposite sides of the carbonyl group for bitertiary ketones.

Furthermore, the various contributions from the α substitutions show that the decrease in frequency cannot be attributed only to the inductive effect whose values, which are defined by Taft's polar parameters, σ^*, are proportional to the number of α methyl groups. However, in the gas phase, as well as in the liquid phase, the $\nu_{C=O}$ frequency can be related to the σ^* parameters.

$\nu_{C=O}$ frequency and linear free energy relationship. The $\nu_{C=O}$ frequencies of 41 ketones measured in the liquid state have been correlated with the reactivity parameters (measuring the inductive, steric and hyperconjugation effects) (8a). Several expressions were obtained, which, although contradictory, are, quantitatively equally acceptable.

$$\nu_{C=O}^{liq} = 1720.3 + 124\Sigma\sigma^{*} - 9.4\ (n - 6) - 16.3\ (A_3)_1\ (A_3)_2 \qquad (1)$$

$$\nu_{C=O}^{liq} = 1718 + 5.2\Sigma\sigma^{*} + 2.6\Sigma E_S^{c} - 15.6\ (A_3)_1\ (A_3)_2 \qquad (2)$$

$$\nu_{C=O}^{liq} = 1717.3 + 2.9\Sigma E_S^{c} - 16\ (A_3)_1\ (A_3)_2 \qquad (3)$$

The polar contribution in relationship 2 is considerably reduced and has been eliminated from relationship 3. These three correlations have similar characteristics (in relationship 2, $r = 0.992$ and $\Delta = 1.2\ cm^{-1}$)

Influence of molecular dimensions on the $\nu_{C=O}$ frequency. Bartlett and Stiles (9) have explained the low value of the $\nu_{C=O}$ frequency of two $\alpha\alpha'$ ditertiary ketones (tBu_2CO and TrCOtBu) by the existence of repulsions between the alkyl groups, thus provoking an opening in the $\widehat{C\text{-}CO\text{-}C}$ angle which would produce a variation in force constant $k_{C=O}$, by the hybridization change of the carbonyl carbon.

Afterwards, Zbiden (10) and Schleyer (11) even supposed that the force constant did not vary at all; this boils down to attributing the entire effect to coupling modifications provoked by the angular variation.

Moreover, calculations by Davis et al. (12) show that, without causing the angle to vary, geometrical changes, provoked by rotation of the alkyl groups around the carbonyl, indeed modify the frequency (12 cm^{-1} variation in diethylketone).

PRINCIPLES, CONCEPTS AND METHODS USED FOR THE ANALYSIS OF SPECTROSCOPIC DATA

Our analysis of spectroscopic data is based on the notion of a discrete environment, a fundamental concept of the DARC system, which allows formulating the notion of formal filiation and is the basis of topological correlations. Extrathermodynamic relationships for which we use the polar and steric factors of alkyl radicals, and several procedures for calculating steric energy, have also entered our analysis.

Representation of chemical compounds and compound families within the framework of the DARC system

The DARC (Description, Acquisition, Retrieval, Conception) System, developed since 1963, (13) constitutes a true management information system covering a range extending from the representation of data all the way to computer-aided design. It can be used to process any form or modelled structure by a chromatic graph (G_χ), i.e. a graph whose nodes and edges are symbolically differentiated by a color.

The DARC system is based on the concept of an Environment & which is generated in an ordered and concentric manner. This concept permits the description of chemical formulas as ordered graphs and is essential for locating a formula (or structure) within a series, called a hyperstructure, which is itself represented by a graph whose edges are formal and whose nodes are real. The synchronous generation of a structure and its hyperstructure is a principle which simultaneously creates two graphs: a real one (S) and a formal one (HS).

Generation and description of an environment. A chemical formula is formally assimilated to a chromatic graph whose nodes represent the atoms other than hydrogen, and whose edges represent the bonds between these atoms. The chromaticity of the nodes corresponds to the nature of the atoms, and the chromaticity of the edges to the nature of the bonds. In this graph, we have distinguished two parts: the focus (FO), made up of an atom, a bond, or a group of atoms characterizing a series of compounds; the environment (&), which comprises the remainder of the molecule, and which we have organized concentrically around the focus.

In order to generate an environment (&), it is taken as a target and is constructed in an ordered fashion. This complex ordering is obtained by the propagation over the entire environment of an ordering module, or ELCO (Environment which is Limited Concentric and Ordered), whose amplitude is limited to two rows of atoms.

Once the entire environment is ordered, each site is located by a topological coordinate or total order label which is expressed by A_i or B_{ij} (Fig. 4).

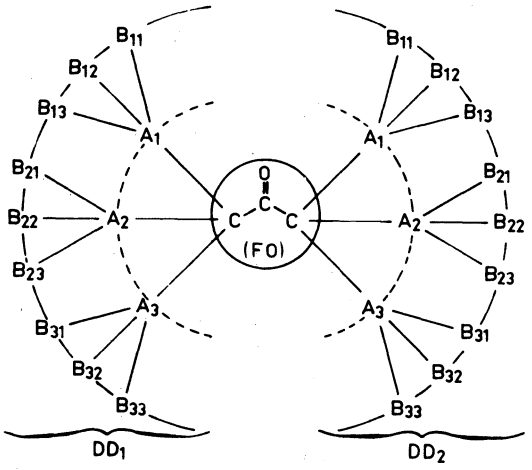


Fig. 4. An ordered and concentric graph of saturated aliphatic ketones. Since our study bears on ketones, the sub-structure common to all the individual members of the population has been chosen as the focus (FO): $\geqq C - CO - C \leqq$. The group having FO as a root, extends itself in two different directions of development: DD_1 and DD_2.

For the description, we consider the graph of existence as the reference graph where each chromatic item of information concerning the multiplicity of the bonds and the nature of the atoms is associated to the index of the site to which it is related. The Descriptor of an Environment which is Limited (DEL) is constituted by the concatenation of the descriptors of each ELCO; each descriptor carries the topological description of the graph of existence (Fig. 5) and the chromatic data.

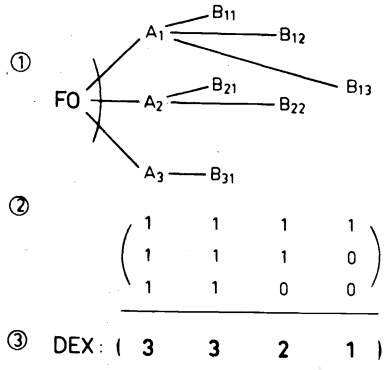


Fig. 5. Total ordering and topological descriptor. The Descriptor of EXistence (DEX) reflects the existence of total ordering labels of the ELCO. It is expressed by the following general formula: $DEX = (\Sigma A_i \ \Sigma B_{i1} \ \Sigma B_{i2} \ \Sigma B_{i3})$.

Synchronism principle and hyperstructure (HS). When a target compound (X) is generated, a particular series of compounds, called a series of anteriologues associated to compound X, is engendered. All the anteriologues of X constitute a family whose members are located with respect to one another by a strict relationship. They constitute a hyperstructure (HS) whose generation is synchronous to the generation of target compound (X) (14).

A hyperstructure can be modelled by a graph whose nodes correspond to the compounds and whose edges correspond to the relationships between these compounds. Figure 6 shows the graph representing the anteriority hyperstructure of hexamethylacetone. We are presently in the process of generating and visually displaying the anteriority hyperstructure of a given target (15). Figure 7 shows the anteriority tree associated to hexatertiobutylacetone ($tBu_3CCOCtBu_3$).

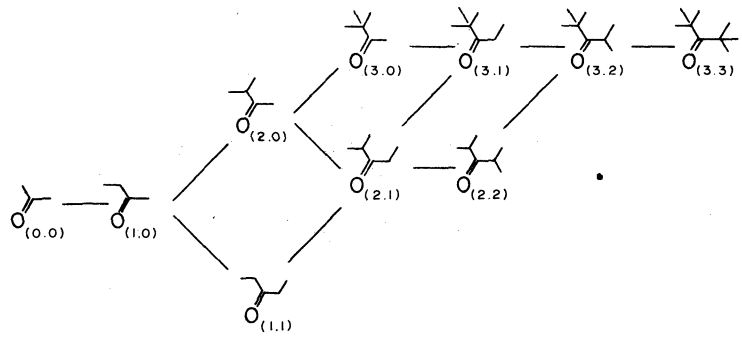


Fig. 6. The anteriority hyperstructure of hexamethylacetone

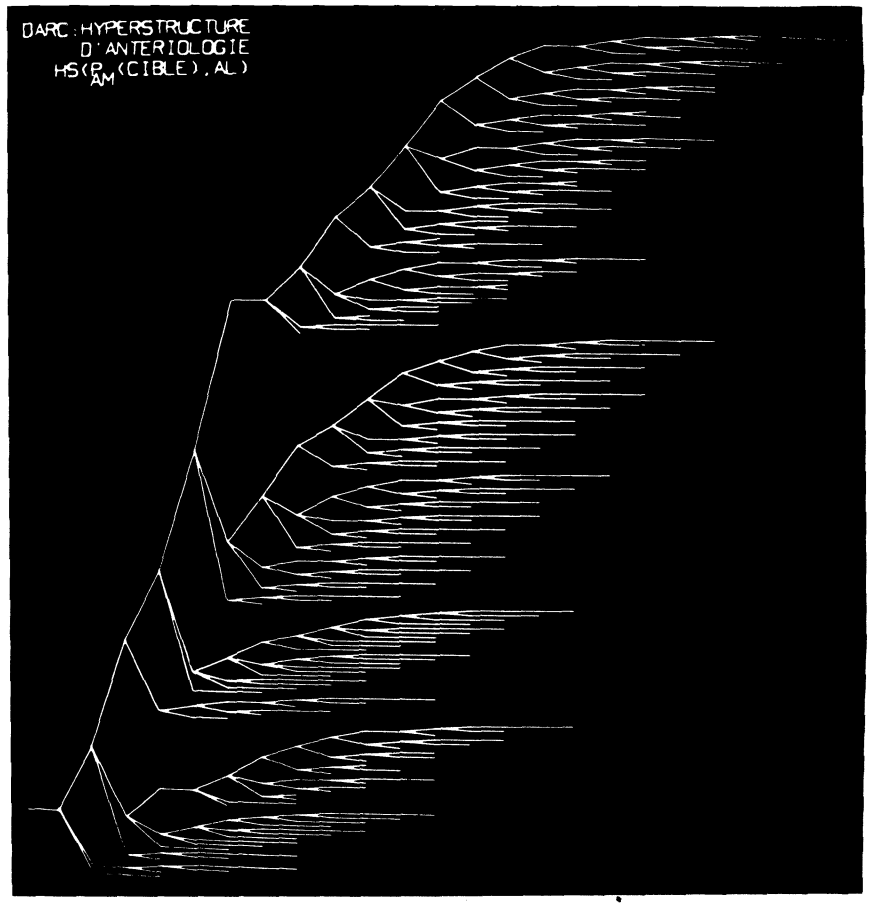


Fig. 7. Generation hyperstructure. The formal generation of 630 ketones whose environment associated to the focus ≧C—CO—C≦ is made up of two rows of atoms at the very most; each node of the graph corresponds to a ketone, from its origin (acetone in the lower-lefthand corner) to the target (hexatertiobutylacetone in the upper-righthand corner); the isomers lie on the same vertical line.

"Structure-Properties" correlation. DARC/PELCO method

In order to approach the problem of structure-comportment correlations, one must have at one's disposal a quantitative variable expressing, in the best possible way, the chemical structure concept. The usual theories use groups or fragments and often imply that "the whole is equal to the sum of the parts". If the properties studied are not as additive as one would wish them to be, we then introduce "constitutive properties corrections" or

interaction increments.

In the DARC system, the correlation problem is approached in a more systematic manner, by considering the contribution of each ordered site to the environment of an active focus (16).

The principle of information generation. A true structural variable, the topological vector $T(\&)$, characterizes the presence or the absence of each ordered site. It permits one to express, in an analytical manner, the principle of an ordered generation of information at the same time as that of the generation of the structure, through the use of the following Topology-Information correlation: $I(\&) = < T(\&) \mid I(m) >$; where $I(m)$ is the characteristic vector of information, resulting from the study of m structures and $I(\&)$ the contribution of the environment. Information $I(X)$, relative to the comportment of structure X, is calculated from information $I(X_o)$ corresponding to the reference structure whose environment reduces to hydrogen atoms: thus, $I(X) = I(X_o) + I(\&)$.

Within the framework of the Topology-Information theory, calculation of I is carried out by various methods, one of which is the PELCO (Perturbation of Environments which are Limited, Concentric and Ordered) method. The information vector I(m) is estimated by the method of least squares from data concerning the m compounds of the relevant population. In effect, a given site in a population may be reached by different generation pathways, which implies that the envirionments anterior to this site will be different according to the pathway followed. This "anterior environment" concept allows the definition of the relevant population.

Correlation search method. The method is made up of three main stages.

Selection of a relevant population. The problem of selection is very important since it conditions the value of the perturbation terms and, thereby, the predictive value of the correlations.

Selection comes into play at two levels; first of all on an overall level, by the following definitions:

Origin: the compound from which it is possible to generate all the individual members of the population
Trace: the graph obtained by uniting the various ordered environments.

Selection then operates on a local level at each site of the trace. In the generation sense, each site is characterized by its minimal and maximal anterior environments; this allows defining a key-population.

Estimation: Topology-Information correlation. The perturbation due to each site is evaluated. The deviations in the strict additivity of the perturbation terms are represented by interactions. The totality of these results can be represented globally and synthetically by a valuated graph (Fig. 8). In the section devoted to "Structure-Spectroscopy" topological correlations, we shall see examples of calculations of properties on the basis of a valuated graph with and without interaction.

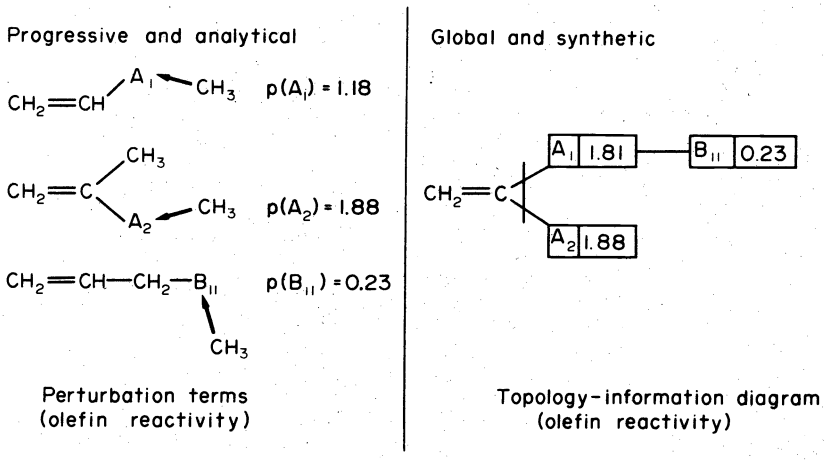


Fig. 8. PELCO method: Presentation of correlation results.

Prediction aptitude. Once the perturbation due to each site of the trace has been determined, it is possible to estimate, by topological interpolation, the comportment of all the compounds included in this trace.

The prediction aptitude, or "proférence", is thus equal to the difference between the number of compounds generated in the trace and the number of compounds in the key-population. The reliability of the proférence depends on the existence or on the possibility of interactions.

Correlation search strategies. There are several possible strategies. We shall briefly review two of them used in our work.

- Strategy with symmetrization of the directions of development: used in a first approximation when one wishes to determine the main tendencies. It is considered a priori that both radicals of the carbonyl group have the same influence: A_1 of DD_1 and DD_2 are thus equally valuated.

- Strategy without symmetrization of the directions of development: used for a fine prediction of properties. Two sites are declared to be equivalent only when the correlation shows their perturbation terms to be extremely near each other, with the difference between them being well below the experimental error.

Polar and steric parameters of alkyl radicals

We did not have the σ^* and E_S parameters of certain alkyl radicals needed to extend the correlations of the $\rho\delta + \delta E_S$ type proposed for spectroscopic data concerning restricted (UV) or average (IR) populations. We thus calculated the missing σ^* values by using a $\mathcal{C}/\sigma^*$ topological correlation (17). New experimental determinations were required for the E_S parameters, before approaching the correlation. The esterification reaction of hindered acids in methanol provided us with a homogeneous scale with a real boundary, $E_S = -7.5$ (18).

Calculation of the steric energy

Here we present mainly the results pertaining to the determination of the most privileged conformation, obtained by using Allinger's version of the empirical potential method (19), that we are presenting. This represents only a part of the in-depth study we are presently carrying out on carbonyl compound conformations (20).

In a refined analysis, the study of the conformational properties of an isolated molecule cannot be limited to determining the most energetically favored conformation. It thus appears to be necessary to determine a surface of conformational energy having as many dimensions as there are parameters that may be easily modified. It is in this manner that we determine preferential zones of stability and forbidden conformational zones.

All of this requires calculating a sufficiently large number of points on the conformational surface, a fact which in itself leads to the choice of a fast calculation method given the size and complexity of the molecules we are interested in.

We thus have recourse to two types of methods:

- Empirical methods, taken from classical mechanics and from statistical thermodynamics. In these methods the total energy is the sum of various additive energetic contributions (torsion energy, interaction energy between non-bonded atoms, participation of hydrogen bonds, contributions from bond lengths and from valence angles,...). These terms are expressed as a function of the ajustable parameters on the basis of experimental information. We have used two versions of this empirical potential method: the Liquori version (21) and the Allinger version (BIGSTRN Program) (19); the second differs from the first, in that a term which stabilizes conformations with the methyl group eclipsing the carbonyl group has been introduced.

- Quantum mechanical methods. We have used the PCILO method (22) (minimization by perturbation (23)) as well as CNDO/2 (24) and INDO (25) methods (minimization by the variation principle) (26).

Nevertheless, the conformational results obtained by any one of these methods always depend on the basic parameters; it is a well-known fact that they are often conflicting on certain important points, as well as with experiment. Thus, for iPr-CH_2-CO-Me, the most stable conformations are: a bisected carbonyl conformation for the PCILO method, a conformation with a C-H bond eclipsing the carbonyl group for the Liquori version, and a conformation where the isopropyl group eclipses the carbonyl group for the Allinger version.

Our efforts were thus directed more towards the analysis of conformational tendencies within a series of compounds, rather than towards the particular results obtained with any one of the methods.

ANALYSIS OF SPECTROSCOPIC DATA

Ultraviolet spectroscopy

σ^*, E'_S/ν^H_i structure-spectroscopy correlation. We have sought to extend the correlation established in 1963, for biprimary ketones, between the σ^* parameters of alkyl radicals R and R' and the position of the maximum of the $n \rightarrow \pi^*$ absorption band. The study reported herein concerns 81 ketones. Figure 9 shows that it is impossible for the entire population to establish a simple link between the σ^* parameters and the maximum of the internal envelope of the absorption band in hexane, ν^H_i (27).

By contrast, we have noticed a tendency towards partitioning depending on the number of substitutions at α and at α' to a carbonyl. The ketones beginning each series are included in $(CH_3)_3CCOC(CH_3)_3$ or FO(3000)(3000). They correspond to the hyperstructure in Fig. 6. Each sub-population is designated by $\mathscr{P}_{i,i'}$, where i and i' are the number of alkyl groups on α and α' which correspond to the number of A and A' sites.

For five of these sub-populations containing about ten points, the correlations carried out by the least-squares method give satisfactory results. The slopes of the straight lines $\nu^H_i = f(\sigma^*)$ are parallel in a first approximation (Fig. 9). However, these sub-populations cannot be brought together in the same correlation by introducing a hyperconjugation term because the deviation for acetone, which is the reference ketone, is not related in a simple way to the number of α and α' substituents.

Taking into account the steric influence within the correlation improves the correlation only to a very slight degree. The δ coefficient of the steric factor E'_S diminishes as the ramification of the ketones increases. This somewhat surprising result leads to attributing a percentage of steric influence on ν^H_i which becomes all the more weaker as the alkyl radicals become more hindered!

iBu-CO-iBu	% σ^* : 83%	% E'_S: 17%
$(iPr)(Me)_2C$-CO-$C(Me)_2iPr$	% σ^* : 98.5%	% E'_S: 1.5%

The ketones which deviate from the correlation when only the σ^* polar factor is considered remain outside of the correlation when the E'_S steric factor is introduced. The ketones present a definite structural analogy; they bear at least one - $CH(iPr)_2$ radical or a radical derived from it by substitution - CH (iPr) (tBu), $-CH(tBu)_2$.

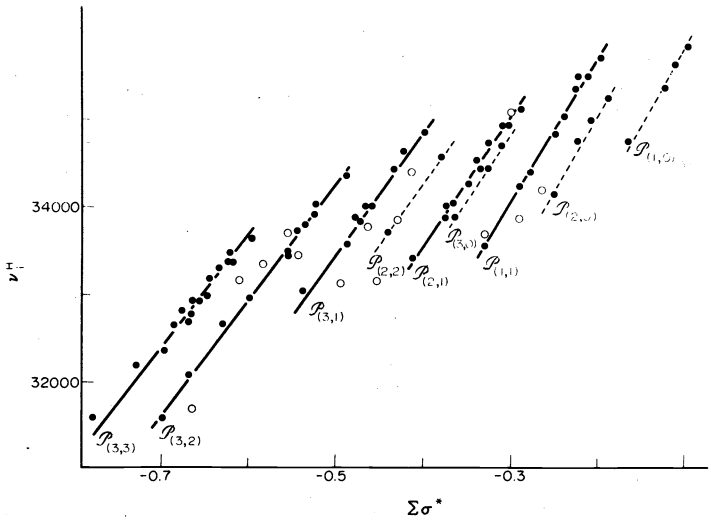


Fig. 9. Parametric correlation σ^*/ν^H_i UV spectra of ketones. Absence of a simple relationship between the σ^* polar parameter and ν^H_i. The ketones have a tendency to fall into a network of parallel straight lines characteristic of the $\mathscr{P}_{i,i'}$ sub-populations (i and i' being the number of alkyl substituents at α and α' of CO).

Topological correlation: $\mathscr{E}/\nu_i^H$. The key-population on which the correlation has been established has 48 ketones. A study of the valuated graph summarizing the totality of the information shows the relative influence of the sites and the presence of interactions. The perturbations arising from each site diminish the wave number of the absorption maximum, whereas the interactions increase it (Fig. 10) (27).

The site whose perturbation term has the highest value is A_3, which corresponds to the 6th substitution at A, i.e. to the bitertiary structures. Sites A_2, A'_2 (corresponding to the secondary radicals 2jkl), B_{13} and B'_{13} (radical neoP: (1111)) also have a very high perturbation value. Thus, in our study of conformational filiations, special attention has been paid to the radicals in which these sites intervene.

The weaker perturbation values of sites B_{31}, B_{32} and B'_{31} indicate an attenuation of the effects; however, the partial overlapping of these sites in the correlation might not permit identifying the presence of possible interactions.

A correlation with three interactions permits accounting for the experimental wave numbers for 25 ketones not included in the key-population, with the experimental wave numbers of 8 ketones being uncorrelatable. This correlation reliably covers 291 compounds, 48 of which have been used to establish the correlation. The proférence is thus 291 - 48 = 243 compounds.

If we introduce two new interactions, $I(B_{22}-B'_{13})$ and $I(B_{23}-B'_{13})$, we account for the experimental wave numbers of five new compounds; the correlation is good (r = 0.998, Ψ = 0.07, Δ = 65) and the perturbation term values are very slightly modified. The range of this new 5-interaction correlation covers 332 compounds.††

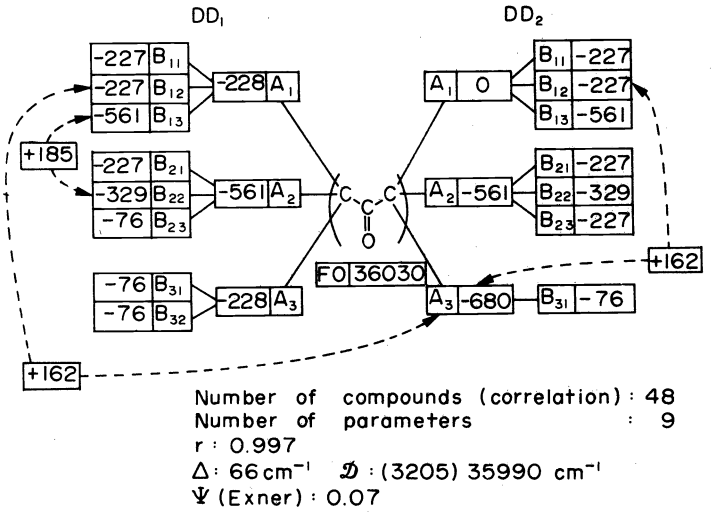


Fig. 10. DARC/PELCO correlation $\mathscr{E}/\nu_i^H$ UV spectra of ketones

Infrared spectroscopy

Seeking linear free energy relationships applied to $\nu_{C=O}^{CCl_4}$. As in UV spectroscopy it is impossible to establish a simple linear relationship between the frequency of the maximum of absorption and the σ^* parameters (Fig. 11) (27).

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† In order to simplify the writing, sites DD_1 are designated by A_i and B_{ij}; sites DD_2 are designated by A'_i and B'_{ij}.

†† Those ketones bearing a $-CH(iPr)_2$ radical or (2220) for DD_2 whose particular comportment would be expressed by other interactions have not been introduced into this correlation.

The same redistribution is found in sub-population $\mathscr{P}_{i,i'}$, but in contrast to what occurs in UV spectroscopy, the parallelism of the straight lines of the correlations is no longer observed. Furthermore, a large number of the ketones deviate from these correlations; aside from some of the bitertiary ketones, those ketones with a particular comportment bear strong structural analogies: they either possess a $-CH(iPr)_2$ radical or one of its derivatives as in UV spectroscopy, or a neopentyl radical $-CH_2tBu$ or its triptyl derivative $-CMe_2tBu$. Introducing a steric term does not render these correlations more significant.

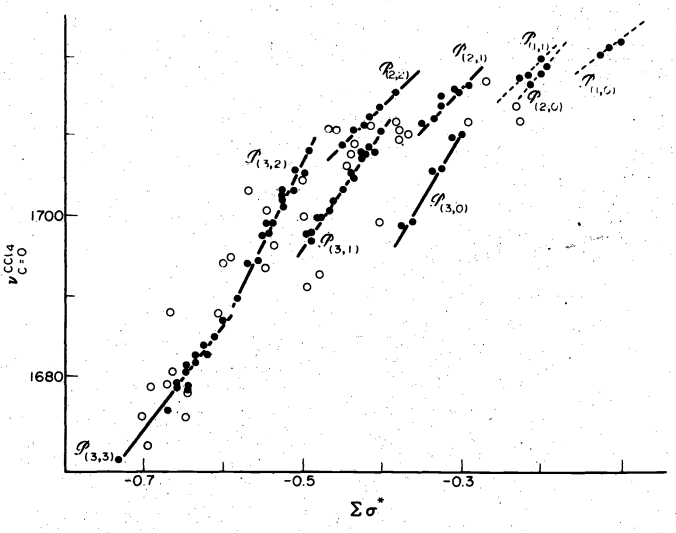

Fig. 11. Parametric correlation $\sigma^*/\nu^{CCl_4}_{C=O}$ IR spectra of ketones

Topological correlation $\mathscr{E}/\nu^{CCl_4}_{C=O}$. The key-population on which the correlation is established consists of 47 ketones. The valuated graph (Fig. 12) shows that the perturbations arising from sites A_i and B_{ij} and from the interaction A_3-B_{13} lessen the $\nu^{CCl_4}_{C=O}$ frequency; the three perturbations corresponding to sites A_1, and to B'_{13} and B'_{31} are an exception to this (27). As in UV spectroscopy, the perturbation arising from site A'_1 is nil; sites A_2 and A'_2 are equivalent as are a certain number of B_{ij} positions. However, in contrast to the results obtained in UV spectroscopy, the perturbations of the A sites increase in the A_1, A_2, A_3 order; the exceptionally important value of A'_3 shows the effect of the 6th substitution at α.† The B_{ij} perturbations which deviate notably from the others, i.e. B_{23}, B_{32}, B'_{13}, B'_{22} and B'_{31}, express respectively the particular comportments of $-CH(tBu)_2$, $-C(iPr)_3$ in DD_1, $-CH_2tBu$, $-CH(iPr)_2$, $-C(Et)_3$ in DD_2 and of their derivatives.

With this correlation we account for frequencies of 42 ketones not included in the key-population, 17 ketones lying outside of the correlation. The excluded ketones are bitertiary, one of whose radicals is triptyl (3111), or tertiary-secondary ketones, whose secondary radical is either derived from neopentyl by substitution (-CH(Me)(tBu) or 2111) (-CH(Et)tBu or 2211), or the radical $-CH(iPr)_2$ or one of its derivatives. The necessary interactions for integrating these compounds to the correlation bring into play sites B_{13} and B'_{13}. The reliable proférence of the correlation is 176 - 47 = 129 compounds.

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† The results of this correlation which concerns solution measurements are complementary to those which we had established in the vapor phase (8c); the deviations between the contributions, in both cases, can be attributed either to the solvent effect, or to the treatment used (e.g., introducing an A_3-A'_3 interaction in order to express the effect of the 6th substitution in symmetrized correlation with $\nu^{gas}_{C=O}$).

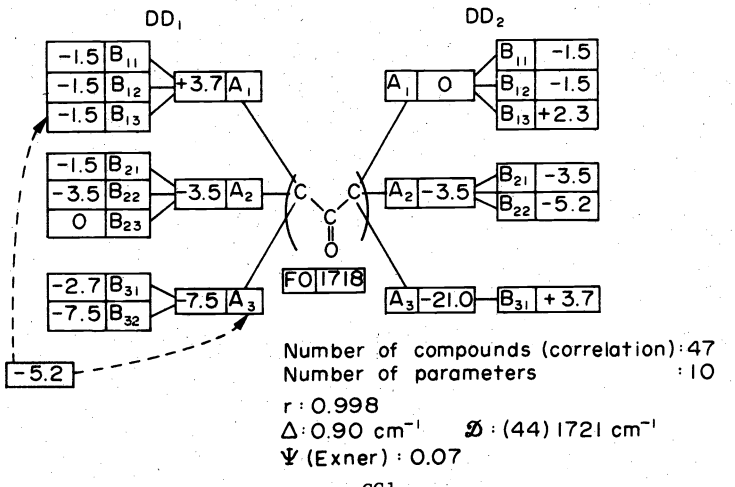

Fig. 12. DARC/PELCO correlation $\mathscr{E}/\nu_{C=O}^{CCl_4}$ IR spectra of ketones

^{13}C Nuclear magnetic resonance and gem-persubstituted β effect

UV and IR spectral observations have shown a particular comportment for structures that are hexasubstituted on the α carbons of the carbonyl group. Confirmation of this comportment was sought by ^{13}C study. In contrast to the previously cited techniques which yield focalized information only on the carbonyl group, ^{13}C resonance permits detecting, at the level of the various sites, the perturbations induced by alkyl substitution. In particular we examined the chemical shifts of the carbon atom of the carbonyl group (28a-b), and those of the sp^3 carbons in the neighborhood of this group (28c).

A $\mathscr{E}$/chemical shift (δ) correlation, corresponding to chemical shifts obtained on pure liquids, was proposed and tested for a population of 53 ketones with a chemical shift variation of 12.8 ppm: for MeCOMe, δ = 12.0 ppm; for iPrCOTr, δ = 24.8 ppm (downfield from external CS_2). The outstanding facts are the attenuation of the A_i perturbations on the heavily ramified C's, the low contribution of the B_{ij} positions, the existence of internal interactions in very ramified groups, such as $C(Me)_2tBu$, and the particular values of A_3'. Thus, the 6th substitution corresponds to an upfield shift of the carbonyl signal: $iPrCOCMe_2tBu$, δ = 24.8 ppm; $tBuCOCMe_2tBu$, δ = 24.2 ppm.

This study is currently underway for the purpose of determining the role played by the internal and external environments in the behavior observed.

The particular role of the 6th α substitution is also detected on the chemical shift of the sp^3 carbons on α of the carbonyl group. Thus, in passing from penta- to hexa- substituted ketones, an important increase (ca. 11 ppm) of the α effect,† and γ downfield effects (1 to 2 ppm) for these carbons, are noted - as opposed to the usual effects detected for less ramified structures. For example, between iPrCOiPr and iPrCOtBu, α effect = 5.9 ppm and shielding γ effect = - 4.9 ppm; between iPrCOtBu and tBuCOtBu, α effect = 11.8 ppm and deshielding γ effect = 1.

All the observations relative to the δ ^{13}C of the carbonyl and of the adjacent sp^3 carbons confirm the IR and UV results, and converge on the remark of a particular comportment of the structures having a hexasubstituted $\geqslant C - C_{sp^2} - C \leqslant$ link (gem-persubstituted β effect); this is in contrast to the monotonic evolution of substitution effects in less ramified molecules (suggesting a breakdown in the conformational filiations).

Spectroscopic results are still too fragmentary to permit a complete characterization of the specific properties of the $\geqslant C - C - C \leqslant$ module on numerous other systems. However, a first verification has been obtained on an analogous population of compounds having the same

† In the $\geqslant C_1-CO-C_2 \leqslant \rightarrow \geqslant C_1-CO-C_2 \leqslant^{Me}_{H}$ substitution, C_1 undergoes a γ effect; and C_2 undergoes an α effect.

$\geqslant C - C_{sp2} - C \leqslant$ module: $H_2C=CRR'$ geminated alkenes, for which a complete comportment analogy with homologous ketones is observed in IR as well as in ^{13}C NMR spectroscopy. For example:

- the 6th A_i substitution leads, for $\delta\ ^{13}C$, to a variation in a sense opposed to that of the effects of the first five A_i substitutions; this is true for both of the ethylenic carbons (29);

a comportment/comportment correlation in IR spectroscopy, concerning the group frequency variation of $\nu_{C=O}/\nu_{C=C}$, shows the important lowering of frequency brought about by the 6th A_i substitution for olefins as well as for ketones (30).

CONFORMATION, GEOMETRY AND STERIC ENERGY†

In order to account for the comportment of certain ketones, we have used calculation methods to test the hypotheses of conformational filiation and their discontinuity, and of changes in molecular dimensions.

Conformational filiations

The DARC/PELCO topological correlations are based on the notion of topological filiations. These correlations lead to a compression of information; in particular, information bearing on the positions of the sites in space is not taken into account.

In order to reach the conformational filiations, topographical correlations must be established, i.e. values must be assigned to perturbations occurring at different positions in 3-D space. To do this, a set of spatial references must be fixed; this set can be chosen using a calculation method, or by analogy with a similar model.

Thus, beginning in 1971, an attempt has been made, in UV spectroscopy, to associate bathochromic contributions to carbon atoms, as a function of their position in space. This has been done by joint use of locked conformations in the alicyclic series and of a physical model (31).

We have used results from energy calculations, in a similar manner, to establish topographical correlations of $\nu^{gas}_{C=O}$ frequencies in IR spectroscopy.

As already indicated (cf. "calculation of the steric energy"), the various methods of calculation (quantum mechanical methods and empirical potential methods) provide divergent results on particular points. However, they all point to the following tendential law (20): the bisection of the carbonyl group is more probable as the compound is more hindered. There is thus a discontinuity in the conformational filiation: the slightly substituted carbonyl group would be eclipsed, whereas the very hindered carbonyl group would be bisected.

This is a tendency; however, it is very difficult to determine precisely the radical for which the inversion occurs, since the energy deviations are weak. With the BIGSTRN program (19), we ascertain (32) that in both of the series tested (tBuCOMe to $tBu(Me)_2CCOMe$ and tBuCOtBu to $tBu(Me)_2CCOtBu$) the staggered conformation becomes favored for the triptyl radical $-C(Me)_2tBu$; this would be in good correspondence with the spectroscopic observations.

We have used these results to establish a topographical correlation of the $\nu^{gas}_{C=O}$ frequencies in infrared spectroscopy. For $CH_3COCH_2CH_3$ we have postulated an eclipsed conformation; for CH_3COCH_2tBu we have postulated two conformations, an eclipsed one and a staggered one, in order to account for the two bands†† obtained for this ketone. We thus attribute a site value to a position in space (Fig. 13) (33).

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† According to Allinger's notation (19), the steric energy corresponds to the sum of the energy terms associated with the deformations of the bond lengths, the valence and torsional angles, and with the interactions between non-bonded atoms.

†† These splittings only appear in solution; however, it is possible to obtain an extrapolated value for the band not existing in the vapor phase by applying Allerhand and Schleyer's relationship: $\nu^{Sv} = \nu^{g} - a\nu^{g}\ G$.

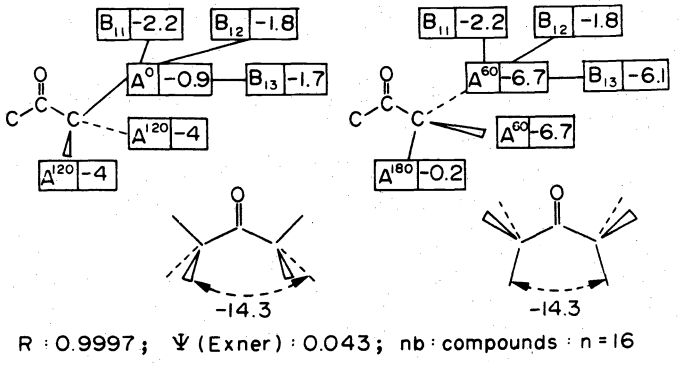
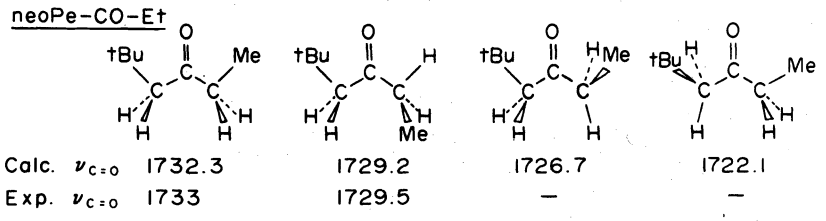


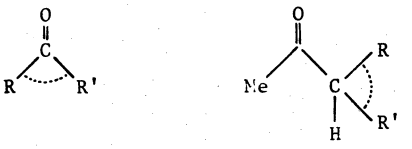
Fig. 13. DARC/PELCO topographical correlation of $\nu_{C=O}^{gas}$ gas phase frequencies

This study constitutes an initial approach which will have to be refined. For example, in this symmetrized treatment, the B positions carried by an A position that is eclipsed (position A^{o}) and by a position that is staggered (position A^{60}) should certainly be distinguished from one another. However, the initial results are encouraging (r = 0.9997; Ψ = 0.043) and, for the ketones where a band-splitting has been performed, we have been able to attribute a conformation to each band.



Changing molecular dimensions

The gem-persubstituted β effect can be interpreted by an important change in molecular geometry. The theoretical calculations indicate a major difference at the sp^2 hybridization ($\widehat{C-CO-C}$ angle) when passing from five α substituents (tBuCOiPr) to six α substituents (tBuCOtBu) (Fig. 14). A noteworthy opening of the $\widehat{C-CH-C}$ angle (deviation from sp^3 hybridization) is also calculated for the passage of MeCOCH(tBu)(iPr) to $MeCOCH(tBu)_2$.



number of neighbors	R	R'		
6			126°	125°
5			120°	121°
4			119°5	119°9

Fig. 14. Gem-persubstituted β effect and changing of molecular dimensions. The 6th substitution provokes a notable change of angle. The calculations are carried out with the help of Allinger's version of the empirical potential method. The PCILO method provides an angle of 132° for tBuCOtBu and an angle of 125° for $MeCOCH(tBu)_2$.

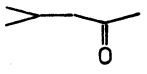
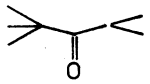
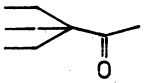
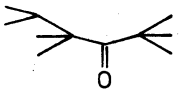
These changes in molecular dimensions correspond to a geometry that is more decongested than the standard geometry, thus leading to a considerable minimization of interactions between non-bonded atoms, at the price of a much more moderate increase in energy contributions resulting from bond lengthenings, and from deviations of angles involving sp^2 and sp^3 hybridized atoms from their classical values.

With the PCILO method, an appreciation of this strain release of the tBuCtBu module is provided by an evaluation of the rotation barriers of a tBu group with respect to the other tBu group in a standard geometry (≃ 30 KC for $(tBu)_2CO$; ≃ 200 KC for $(tBu)_2CH$) and in unstrained geometry (< 10 KC). In hexamethylacetone, the rotation of the tBu groups seems to be practically free (1 KC barrier) in the unstrained geometry (20).

The hypothesis of such a strain release is confirmed by the kinetic results used in the determination of the steric parameters of the highly hindered radicals (18). A residual activity, which would be due to a change of the molecular dimensions, is observed; this is confirmed by the first crystallographic results on hindered acids.†

As with the observations on the conformational filiations, the results from the molecular geometry calculations on the changes in molecular dimensions indicate tendencies, not absolute values. Indeed, energy minimization programs parametrized for simple ketones must be employed with caution in the study of more hindered ketones.

In order to evaluate the reliability which can be granted to the preceeding calculations, we confronted the heats of formation of ketones calculated by energy minimization with those calculated by a polyfocalized DARC/PELCO correlation (34). The results are comparable and near the experimental values whenever these latter are known. The difference becomes more marked (about 1 to 2 Kcal) when the ketone is clearly hindered.

	ΔH°f exp (Kcal/mol)	ΔH°f PELCO	ΔH°f energy minimization
	- 76.60	- 76.46	- 76.81 - 76.36
	- 80.86	- 80.59	- 80.96 - 80.19
	-----	- 79.62	- 79.18 - 79.14
	-----	- 91.78	- 93.38 - 93.24

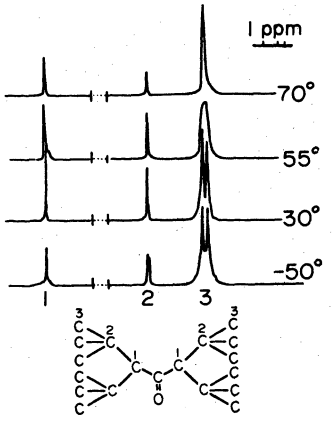
Special molecular dimensions of the gem-di-tBu pattern and its comportment

We have also sought confirmation of molecular mechanics results by comparing molecular dimension data with real data which were measured by crystallography for two hindered molecules bearing the $C(tBu)_2$ pattern: tetra-tertio-butylacetone and ortho-tolyldi-tertio-butylcarbinol.

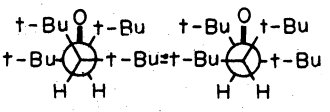
Tetra-tertio-butylacetone: The conformation which is most energetically favored according to calculations (BIGSTRN program) is fairly close to the conformation obtained from the crystallographic data (35). This favored conformation where, for each radical, a tBu group is situated perpendicularly to the carbonyl, is confirmed by both static and thermodynamic ^1H and ^{13}C NMR observations (Fig. 15) (36). Comparing the real with the calculated data shows that the calculation opens the $\widehat{C-C-C}$ angles too much and shortens the C-C bonds. A similar observation is obtained by the PCILO method for the $CH(tBu)_2$ module of the $HCOCH(tBu)_2$ molecule. A shortening of the C-C bond lengths and an increase of the $\widehat{C-C-C}$ bond angles is also observed with respect to the experimental values.

† This work was carried out in collaboration with J. Hospital (Maître de Recherche, CNRS) from the University of Bordeaux I.

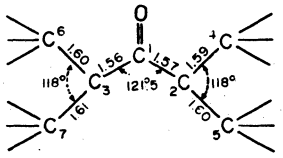
These divergencies, together with the slight difference in energy of the tested conformations, did not permit us to determine whether or not the interconversion of the two equivalent conformations which show up in ^{13}C NMR occurs by a synchronous movement of the "windshield wiper" type.



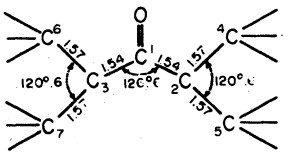
^{13}C NMR spectra
(Solvent $C_6D_5-CD_3$ at 25MHz)



Interconversion equilibrium



Crystallographic data

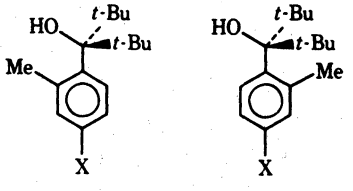


Calculated geometries

Fig. 15. Example of a strained ketone: tetra-tertio-butylacetone; dynamic ^{13}C NMR and conformation. The ^{13}C resonance shows two equivalent privileged conformations whose interconversion is characterized by dynamic NMR. The characteristic geometric elements are: a two-fold symmetry axis passing through the carbonyl group, and a two-by-two equivalence of the tertiobutyl groups bonded to the α carbons. This is coherent with the crystallographic study and the theoretical calculation of the geometry. The exalted values of the valence angle and of the C-C bond lengths of the module $>C<^{tBu}_{tBu}$ (gem-persubstituted β effect) should be noted.

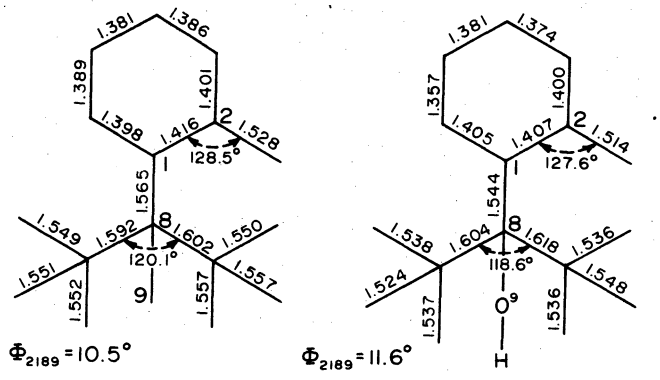
Ortho-tolyldi-tertio-butylcarbinol: If internal strain characterized the influence of a radical, then it is important to follow a hindered "module" during a chemical change.

The chemistry of hexasubstituted ketones allows the transfer of very hindered ketones into other structures, thanks to the easy addition of organolithium compounds. In ortho-tolyldi-tertio-butylcarbinol obtained in this manner from hexamethylacetone, the steric hindrance is such that the rotations around the simple bonds are very hindered. We were thus able to separate easily the syn and anti atropisomers (37).



syn anti

For the calculations, by replacing the hydroxyl function by a methyl group, we obtain a good approximation of the real data; however, the bonds are still rather short and the angles too open (Fig. 16) (38).



Calculated geometries Crystallographic data

Fig. 16. Syn-ortho-tolyldi-tertio-butylcarbinol: structural data

CONCLUSION

Taken alone, the spectral properties of ketones were hard to interpret: however, the overall results considered in terms of progressively established models has led to an improvement in correlating these properties with both the ketone structures and conformations.

The interest that lies in crystallographic structural determinations, a slow but sure means, is not questioned; however, it should be noted that satisfactory results obtained by structure calculation methods are going to permit studying these problems in a faster and more systematic manner, once sufficiently significant "crystallographic data/calculated value" correlations have been obtained. While the parallels drawn in this presentation for geminated and bis-geminated alkyl groups are encouraging, it is nonetheless necessary to envisage improving the molecular mechanics methods by adapting their parameters to the study of hindered ketones. These efforts will be directed towards a surer attribution of certain specific reference conformational assignments from which the conformations and molecular dimensions of numerous other ketones will be deduced by filiation methods.

In short, the power of the methodology, that we have used herein to account for a very large set of data, is based on certain structural assignments of ketones. It should be noted that the optimization of molecular mechanics methods, which we shall undertake, is valid for other types of strained molecules, viz. hydrocarbons and olefins.

Acknowledgment - The author wishes to express his appreciation to his co-workers, whose names appear in the references.

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