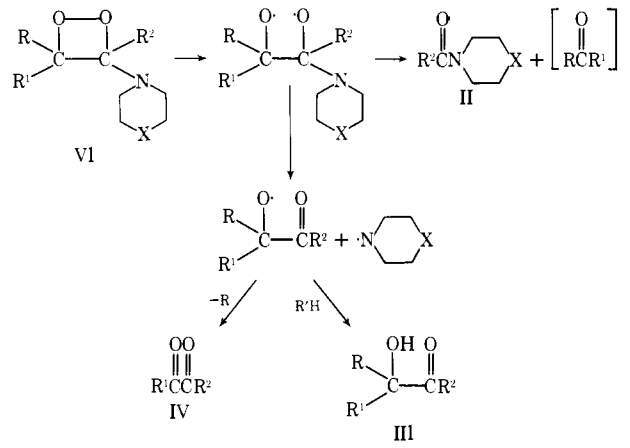
Table I. Substituent Effects for the Cleavage of C–N and C–C Bonds in Oxygenation of Enamines I (at 20°)

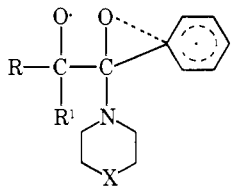
Substituent				Relative yield, %	
R	R^1	R^2	X	C–C cleavage	C–N cleavage
Me	Me	H	O	100	0
Et	Et	H	O	100	0
H	Me	Et	O	69	31
H	Me	Et	CH_2	78	22
Me	Me	*i*-Pr	O	95	5
H	Ph	CH_2Ph	O	95	5
Me	Me	Ph	O	68	32
Me	Me	Ph	CH_2	49	51
H	Me	Ph	O	29	71

cleavage can be classified into two categories: (1) a hydrogen atom on the β-carbon and (2) a phenyl group on the α-carbon. Another example of the first case has been observed quite recently by Wasserman and Terao[13] when *N*-(1-cycloalkenyl)morpholines were photooxygenated, and the authors postulate for the mechanism of C–N cleavage, a β-elimination from the intermediate dioxetane induced by the presence of base. Formation of the C–N cleavage products observed in the reaction of Id and Ie might be explained by the same mechanism, since the photooxygenations in the present work were carried out in basic solvent (pyridine).

However, β-elimination mechanism could not be applied to the C–N cleavage in the photooxygenation of enamines of the second category, especially Ib and Ic which bear no hydrogen atom on their β-carbon. This C–N cleavage can be best explained in terms of a biradical mechanism, in which the O–O bond is completely broken followed by C–N bond cleavage to give a nitrogen center radical and a keto alkoxy radical. The keto alkoxy radical either abstracts a hydrogen to give III or undergoes unimolecular fragmentation by scission of the C–C bond or H-atom abstraction by another radical to give IV. 1,2-Dioxetane can collapse through two modes: (1) a concerted fission of O–O and



C–C bonds forming two carbonyl group[7] and (2) two-step homolysis involving a biradical process.[10] The phenyl substituent would assist homolysis of a O–O bond by participating as seen in the decomposition of benzoyl peroxide,[14] and the biradical thus formed could undergo cleavage of C–C and C–N bonds competitively.



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(4) Cleavage of the C–C bond of a biradical produced through homolysis of an O–O bond of 1,2-dioxetane is so highly exothermic that one of two carbonyl compounds produced may be in the excited state.[7] Thus, the net exothermicity of the C–C bond fission may be small. Now, about 10 kcal/mol difference in average bond energy between C–C and C–N bonds may be apparently sufficient to make the C–N bond fission competitive with the C–C bond fission process.
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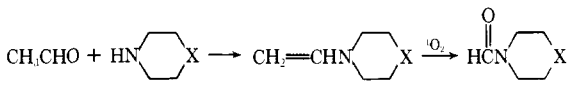
(11) Under the reaction conditions, an acetaldehyde formed in C–C bond cleavage reacts with morpholine to give enamine, which reacts with singlet oxygen to give *N*-formylmorpholine (V). Intermediate enamine is unstable under the reaction conditions.



(12) The enamines Ic–Id were not stable under the reaction conditions, and unidentified non-volatile compounds are also formed. However, the products II, III, and V are only formed in the presence of sensitizer, light, and oxygen.
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Wataru Ando*
Department of Chemistry, The University of Tsukuba Niiharigun, Ibaraki 300-31, Japan

Takeo Saiki, Toshihiko Migita
Department of Chemistry, Gunma University Kiryu, Gunma 376, Japan

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Suggested Method for Multiple Comparisons of Treatment Means

Sir:

Often chemical data consists of *nk* observations; as shown in Table I for each of *n* "blocks" (molecules, etc.) there is one "observation" (experimental or theoretical result) for each of *k* "treatments" (method of calculation, etc.). The basic task is to test the hypothesis that there are no treatment differences, and, if the hypothesis is rejected, multiple comparisons of the treatments are required.

Due to major developments in the past few decades, nonparametric statistics may be employed to perform this basic task. These methods offer the following advantages: (1) they forgo the assumption that the populations under consideration are normal, (2) they are often easier to apply than normal theory counterparts, and (3) they have a high efficiency when the populations are not normal and are only slightly less efficient for normal populations than the normal theory counterparts.[1] In cases of data subject to systematic error these advantages are compelling.

In statistics the basic task as cited above is a two way analysis of variance with multiple comparisons, and the objective of this paper is to point out the utility of doing this analysis nonparametrically using the Friedman S-test and Friedman rank sums.[2]

In Table I the observations within a given block are not independent, but are associated in some way. The Friedman *S* statistic tests the null hypothesis

Table I. Organization of Data for Friedman S Test

Blocks	Treatments 1	2	...	k
1	x_{11}	x_{12}	...	x_{1k}
2	x_{21}	x_{22}	...	x_{2k}
...				
n	x_{n1}	x_{n2}	...	x_{nk}

$$H_0: \tau_1 = \tau_2 = \ldots = \tau_k \quad (1)$$

against the alternate hypothesis that not all the τ's are equal, where τ_i is the sample mean for the ith treatment. This is equivalent to testing whether the treatments all come from the same continuous population (i.e., whether there are no differences among the treatments).

The nonparametric procedure uses information only on the order of the observations and does not use the values of the observations as such, so no assumptions need be made concerning the distributions of the observations from each treatment. In particular, the k observations in each block are ranked, where a rank of 1 is assigned to the smallest observation and k to the largest. The following notation is used for the rank sums:

$$R_j = \sum_{i=1}^{n} r_{ij} \quad (2)$$

where r_{ij} is the rank of x_{ij} in the ranking of $x_{i1}, x_{i2}, \ldots, x_{ik}$.

The Friedman S statistic is computed as follows:

$$S = (12/[nk(k+1)]) \sum_{j=1}^{k} R_j^2 - 3n(k+1) \quad (3)$$

At the α level of significance,

$$\text{reject } H_0 \text{ if } S \geq s(\alpha,k,n) \quad (4)$$

$$\text{accept } H_0 \text{ if } S < s(\alpha,k,n)$$

where the constant $s(\alpha,k,n)$ is available in tables.[1]

If the null hypothesis is rejected, which means the treatments are not all equivalent, multiple comparisons can be carried out to determine which treatments differ. At the α error rate, the uth and vth treatments differ (i.e., $\tau_u \neq \tau_v$) if

$$|R_u - R_v| \geq r(\alpha,k,n) \quad (5)$$

where $r(\alpha,k,n)$ is available in tables.[1]

For large n the S statistic has an asymptotic χ^2_{k-1} distribution when H_0 is true, so in this case $\chi^2(k-1,\alpha)$ replaces $s(\alpha,k,n)$ in eq 4. Also for large n, $r(\alpha,k,n)$ in eq 5 is related to the studentized range $q(\alpha,k,\infty)$, which is also available in tables.[1] In this case eq 5 becomes

$$|R_u - R_v| > q(\alpha,k,\infty)(nk(k+1)/12)^{1/2} \quad (6)$$

As an example of the application of the statistics to a small sample consider the recent rotational barrier calculations of Alston, Shillady, and Trindle[3] (AST) whose results appear here as Table II. The calculations of AST involve the semiempirical natural orbital methods CNDO-NO and INDO-NO, and in this example we will gauge the accuracy with respect to experiment of barriers obtained by these methods relative to the CNDO, INDO, and ab initio results also reported by AST.

The statistics are performed to a 80% confidence level so the task at hand is that specified in the first paragraph where α, the error rate, is 0.20.

In Table II the absolute values of differences between experimental and calculated barriers are listed, and the differences are ranked for each molecule.

From the sum of ranks, R, the Friedman S statistic in eq 3 equals 10.4, where $n = k = 5$. This statistic exceeds the constant $s(\alpha,k,n)$, which from the tables of ref 1 is approximately 6. From eq 4 we reject the null hypothesis (H_0, eq 1), so indeed, to an 80% confidence, there is a difference among the treatments.

For $n = k = 5$ the approximation given in eq 6 reproduces well the accurate least significant difference, $r(\alpha,k,n)$, for the small α values reported in the tables of ref 1. Thus eq 6 is accurate for larger α, and for $\alpha = 0.20$ the least significant difference is 10.7.

The statistics indicate that CNDO/2-NO has a mean deviation smaller than CNDO/2 or INDO, but not necessarily smaller than the ab initio mean. Furthermore, the analysis can not distinguish the INDO-NO mean from the CNDO/2-NO mean, so the apparent difference in the means could be due to chance.

After presenting their data AST observed that "the CNDO/2-NO method gives slightly better agreement than the ab initio methods . . . ; the INDO-NO option is not as satisfactory using standard parameters."[4] This point of view is supported by the order of rank sums in Table II, but from the analysis we view the differences in R values for these three treatments as statistically insignificant at the 80% confidence level.

It is interesting to note that the statistics also show that the ab initio mean is smaller than that of CNDO/2, but the data can not distinguish it from the INDO mean. Evidently more data are required to determine whether ab initio methods give a smaller mean deviation for rotational barriers than even the simple INDO method. Here the lack of cases where both good ab initio and experimental values of rotational barriers are available is clearly a limiting factor.

In the example just completed note that (i) the samples were drawn from a completely unknown population and (ii) one block of data (that of formic acid) has enormous errors relative to the other blocks. As these statistical calculations require merely ranked data rather than the values of the observations themselves, item (i) is not a problem, and the data block in item (ii) does not assume a perverse weight relative to the other blocks.

Another advantage of using ranked data rather than the values of the observations themselves is that the algebra involved is trivial; only 30 min with a hand calculator was required to do the analysis of variance with multiple compari-

Table II. Rotational Barriers (kcal/mol)[a,b]

Compound	CNDO/2	CNDO/2-NO	INDO	INDO-NO	Ab initio
Formic acid (cis-90°)	4.654 (8.746;5)	6.780 (6.620;3)	6.057 (7.343;4)	9.719 (3.681;2)	13.0 (0.4;1)
Acetaldehyde (H ecl. O-H ecl. H)	0.743 (0.417;4)	0.980 (0.180;2)	0.728 (0.432;5)	0.876 (0.284;3)	1.09 (0.07;1)
Propene (ecl.-stag.)	1.199 (0.781;5)	1.507 (0.473;1)	1.234 (0.746;4)	1.373 (0.607;2)	1.25 (0.73;3)
trans-Fluoropropene (ecl.-stag.)	1.270 (0.930;5)	1.715 (0.485;2)	1.353 (0.847;3)	1.727 (0.473;1)	1.34 (0.86;4)
cis-Fluoropropene (ecl.-stag.)	1.071 (0.011;3)	1.053 (0.007;1)	1.043 (0.017;4)	1.431 (0.371;5)	1.07 (0.01;2)
τ^c	2.177	1.553	1.877	1.083	0.41
R^d	22	9	20	13	11

[a] Reference 2, Table IV. [b] In brackets is the deviation of experimental and calculated barrier followed by Friedman rank. The deviations are ranked from smallest to largest. [c] Mean deviation. [d] Sum of Friedman ranks. A small value of R could indicate an accurate treatment.

sons for the above example.

In view of the advantages of nonparametric statistics illustrated in this paper, we recommend this procedure for consideration.

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Stuart M. Rothstein
Department of Chemistry, Brock University
St. Catharines, Ontario L2S 3A1 Canada
Received April 15, 1975

Carbon-13 Chemical Shift Anisotropy Relaxation in Organic Compounds

Sir:

In the last few years numerous studies of ^{13}C spin–lattice relaxation times (T_1's) have shown that these investigations can yield valuable information about molecular dynamics in liquid systems.[1,2] The various applications for these measurements require that all contributing relaxation mechanisms must be identified. For carbon-13 nuclei, relaxation occurs by four processes:

$$R_1^{obsd} = R_1^{DD} + R_1^{SR} + R_1^{SC} + R_1^{CSA} \quad (1)$$

In eq 1, R_1^{obsd} is the observed relaxation rate ($\equiv 1/T_1$). The R_1 terms refer to *d*ipole–*d*ipole, *s*pin–*r*otation, *sc*alar, and *c*hemical *s*hift *a*nisotropy contributions. For essentially all carbons in large molecules and for protonated carbons in small molecules the dipole–dipole term generally has been shown to be predominant.[2a-c]

It has often been assumed that relaxation due to chemical shift anisotropy and modulated scalar coupling affords a negligible contribution to R_1^{obsd} and that R_1^{SR} is the only process that can co pete with efficient dipole–dipole relaxation.[1,2b] In this co munication we present results for representative organi compounds showing that the CSA mechanism has bee underestimated as a contributing term for unsaturated ca ons not having directly attached hydrogens.

Relaxation thr gh the anisotropic chemical shift can be separated unamb uously because R_1^{CSA} is proportional to the square of the static magnetic field. Within the extreme narrowing limit this could be written as[1b]

$$R_1^{CSA} \equiv 1/T_1^{CSA} = (\gamma_C^2 H_0^2/5)(\sigma_{12}^2 + \sigma_{23}^2 + \sigma_{31}^2)\tau_{eff} \quad (2)$$

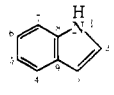
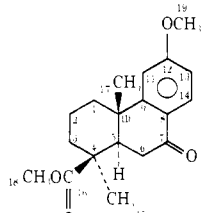
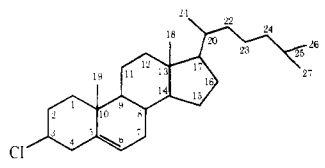
where the σ_{ij} terms represent the anisotropic magnitudes, $\sigma_i\sigma_j/3$, of the three principal terms of the diagonalized shielding tensor σ. An approximation that is often made is that σ is axially symmetric. Then eq 2 reduces to

$$1/T_1^{CSA} = (2/15)\gamma_C^2\Delta\sigma^2 H_0^2\tau_{eff} \quad (3)$$

where $\Delta\sigma$ is the difference of the chemical shielding parallel and perpendicular to the axis of the shift tensor ($\sigma_\parallel - \sigma_\perp$).

Although it has been pointed out theoretically that anisotropic chemical shielding could provide significant relaxa-

Table I. ^{13}C Spin Lattice Relaxation Times (T_1's) and Nuclear Overhauser Effects (NOE's) Measured at 38° at High and Low Fields

	Carbons	67.9 MHz[b]		22.6 MHz[c]	
		T_1 (sec)	NOE (η)	T_1 (sec)	NOE (η)
 I[a]	2	5.8	2.0	5.5	2.0
	3	5.8	1.9	6.4	2.0
	4	5.8	2.0	5.6	2.0
	5	5.3	1.8	5.4	2.0
	6	5.8	1.9	6.4	2.0
	7	5.8	1.9	5.4	2.0
	8	49	1.1	83	1.6
	9	47	1.0	85	1.5
 II[d]	1, 2, 6[e]	1.0 ± 0.05	1.9 ± 0.1	1.1 ± 0.2	1.9
	3	0.83	2.0	. . .[e]	. .[f]
	11, 14, 5[e]	1.8 ± 0.1	1.9 ± 0.1	1.9 ± 0.2	2.0
	13	1.34	2.0	1.5	2.0
	4	16.2	2.0	16.0	1.9
	10	13.8	2.0	15.0	1.9
	7	18.0	0.9	34.5	1.8
	8	25.0	0.8	48.0	1.7
	9	18.0	0.9	29.0	1.9
	12	22.0	1.1	33.0	1.8
	16	27.0	1.0	48.0	1.8
 III[g]	1, 2, 4, 7, 15, 16, 11, 12[e]	0.37 ± 0.03	1.9 ± 0.15	0.39 ± 0.06	1.9 ± 0.2
	3, 6, 8, 9, 17[e]	0.70 ± 0.10	1.9 ± 0.15	0.70 ± 0.16	1.9 ± 0.2
	10, 13[e]	4.2 ± 0.10	1.9 ± 0.15	4.5 ± 0.20	1.9 ± 0.2
	5	3.2	0.8	5.6	1.6

[a] Indole (4 *M*) in acetone-d_6; degassed by three freeze–pump–thaw cycles. [b] T_1's and NOE's have internal estimated errors less than 10%. Several separate runs for each sample produced deviations less than 5–10%. The T_1 measurements were performed using the fast inversion–recovery sequence (see ref.10)(FIRFT) and/or the unmodified IRFT sequence. [c] T_1's are accurate to 5–15%, and the accuracy of the NOE's is 5% (compd I), 15% (compd II), and 10% (compd III). [d] Me–OMe–Podocarpate (0.8 *M*) in acetone-d_6; degassed by three freeze–pump–thaw cycles. [e] The stated values represent the range observed for all carbons in the group. [f] C-3 not well resolved at 22.6 MHz. [g] Cholesteryl chloride (1 *M*) in benzene-d_6, undegassed.