

most importantly, by setting the length of the burst of decoupling irradiation at $(J)^{-1}$ s for sequence C, the total sequence time prior to acquisition is the same for sequences A to C. This is not possible with the proton-flip method. Unavoidable inhomogeneity in the $\pi[C]$ pulse leads to phase errors,^{4,8} which are different from one resonance to the next but are the same for each resonance in the three A to C spectra (same sequence time) and are cancelled when combination of the three spectra results in resonance subtraction. If different sequence times were used, the phase errors would differ in the three spectra and could not be cancelled. In subspectral generation the cancellation of unwanted signals is the prime requirement.

Four scans were averaged separately for sequences A, B, and D and eight scans for sequence C, repetitively. This permits the use of phase cycling and the repetition compensates for drifts in spectrometer parameters. The sequence A data was Fourier transformed and manually phase corrected. This phase correction can then be used for B and C but not for the D spectra. The spectra were then combined as previously described^{4,6,7}: $[A-B]$ yields a CH_3/CH subspectrum, $[A+B]$ a CH_2/q subspectrum,^{3/2} $[A+B-C]$ a CH_2 subspectrum, $^{3/2}(C^{-1}/_3[A+B])$ a q subspectrum; $^{3/2}(D-x[A-B])$ a CH subspectrum. The experimental parameter, x (in our case, 0.04), depends on the spectrometer probe geometry.⁷ The $^{3/2}$ fractions are used to keep the resonance intensities the same for all spectra. Much of this procedure may be automated. An accurate CH_3 subspectrum cannot be generated because the A and B phase errors differ from the D phase errors.

The ristocetin subspectra are shown in Figure 1. The phase and intensity errors in the subspectra result from inhomogeneous pulses over the wide spectral width, but unambiguous assignments are given. When this data was combined with more accurate intensity data (reverse-gated 1H decoupled spectrum, i.e., no NOE, recycle time 3 s) we concluded that ristocetin had the following carbon-type composition: $(q-C)_{30\pm 1}(CH)_{56\pm 2}(CH_2)_{6\pm 1}(CH_3)_4$. The actual numbers of carbons of each type, as determined by extensive structural studies,⁹⁻¹¹ and a ^{13}C study¹¹ (using almost all existing applicable assignment techniques, excepting that given in the present work) are 29, 57, 5, and 4, respectively. The ambiguities associated with the numbers in the present work arise from difficulties in assessing the intensities of overlapping signals and could be resolved by a more careful reverse-gated experiment (e.g., longer recycle time).

The aromatic region can be studied as described in Figure 1, or for spectra with a substantial gap between the aromatic and aliphatic spectrum regions, it is preferable to study the two regions in separate experiments, enabling

the use of smaller spectrum widths and thus more accurate pulses. In the latter case it is only necessary to use sequences A and B for the aromatic region and the $(J)^{-1}$ times are set by assuming $J = 170$ Hz.

Unlike previous subspectral studies on the ^{13}C aliphatic region, the three methods combined in sequences A to D are reasonably tolerant of divergence from the compromise J value assumed, and $J = 135$ Hz is a good compromise. This may need to be increased in some cases, for example to 140 Hz for compounds with monohalogenated groups. The method will not be accurate for groups with two electronegative substituents, but signals from such groups will usually be obvious as they will partly occur in two or more of the subspectra. Signals from groups with divergent J values can be further studied by repeating some or all of the sequences on a narrower spectrum width assuming a new J value.

The method requires about 5 times more accumulation time than a normal decoupled spectrum, which compares favorably with the less useful SFORD method. The spectra in Figure 1 represent a first attempt, on this complex molecule, of a method devised using simpler compounds. Its successful application here should ensure its use by organic chemists as an adjunct to traditional NMR techniques.

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Influence of an α -Cyano Function on Charge Delocalization in the Benzyl Cation. Relationship between Inductive Destabilization and Conjugative Stabilization by the Cyano Group

Summary: The solvolytic behavior of a series of substituted acetophenone cyanohydrin methanesulfonates has been studied in 2,2,2-trifluoroethanol. A ρ value of -6.70 was observed when the rate data was evaluated vs. Brown's σ^+ values.

Sir: As part of the extensive activity which currently exists in the investigation of the influence of strongly electron-withdrawing substituents on the formation of carbocation intermediates,¹⁻³ we have studied the effect of the α -cyano

(7) Bendall, M. R.; Pegg, D. T.; Doddrell, D. M. *J. Chem. Soc., Chem. Commun.*, in press. Bendall, M. R.; Pegg, D. T.; Doddrell, D. M. *J. Magn. Reson.*, submitted for publication. The $(\pi/2)[\pm y]$ proton pulse for EPT signifies phase alternation of this pulse for alternate transients, which must be subtracted as for INEPT.^{2,3} For good nulling of CH_2 and CH_3 resonances, this pulse must be homogeneous and accurately set. The $\pi/2$ proton pulse length can be accurately set by nulling the CH_2 resonances of a sample of a known compound such as cholesterol. CH_2 groups give positive or negative resonances, depending on whether this pulse is too short or too long, respectively. CH_3 groups give small positive resonances because of inhomogeneity of this pulse, hence the experimental x parameter. x is a constant for a particular spectrometer probe, it is small for modern probes of good design, and for some probes it is negligible.

(8) An inhomogeneous π pulse leaves a component of a magnetization vector unrefocused. The phase of this component depends on the total free precession time and the chemical shift off-resonance.³

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(10) Kalman, J. R.; Williams, D. H. *J. Am. Chem. Soc.* 1980, 102, 897.

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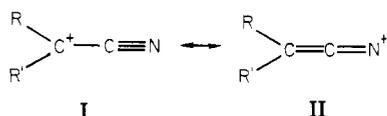
(1) (a) Allen, A. D.; Jansen, M. P.; Koshy, K. M.; Mangru, N. N.; Tidwell, T. T. *J. Am. Chem. Soc.* 1982, 104, 207. Jansen, M. P.; Koshy, K. M.; Mangru, N. N.; Tidwell, T. T. *Ibid.* 1981, 103, 3863. Koshy, K. M.; Roy, D.; Tidwell, T. T. *Ibid.* 1979, 101, 357. Koshy, K. M.; Tidwell, T. T. *Ibid.* 1980, 102, 1216. (b) Liu, K.-T.; Sheu, C.-F. *Tetrahedron Lett.* 1980, 21, 4091. Liu, K.-T.; Kuo, M.-Y.; Shu, C.-F. *J. Am. Chem. Soc.* 1982, 104, 211. (c) Gassman, P. G.; Harrington, C. K., unpublished results; see Harrington, C. K. Ph.D. Thesis, The Ohio State University, Columbus, OH, 1976; *Diss. Abstr. B.* 1976, 37, 2248.

Table I. Yields Obtained in the Syntheses of 2, 3, and/or 4 from Substituted Acetophenones (1)

compd	X	% yield of 2		% yield of 3 and/or 4	
		compd	yield	compd	yield
1a	4-NO ₂	2a	89 ^a	3a	40
1b	4-CN	2b	95 ^a	3b	44
1c	4-CF ₃	2c	73	3c	75
1d	3-CF ₃	2d	81	3d	51
1e	3-Cl	2e	90	3e	56 ^a
1f	3-CH ₂ F	2f	95	3f	87 ^a
				4f	30 ^b
1g	H	2g	91 ^a	4g	20 ^b
1h	4-CH ₃	2h	97 ^a	4h	24 ^b

^aCompounds 3e and 3f were extremely reactive and decomposed on standing. ^bThe yields of bromides were low due to various side reactions and due to extreme difficulties in purification.

group.² We have found that substrates, which tend to have charge localized on a single carbon, place extensive electron demand on an α -cyano moiety and that this results in a considerable degree of charge delocalization to nitrogen. This is represented by resonance structures I and II. For



systems when R and R' are unable to provide resonance stabilization, hydrogen/ α -cyano rate ratios are approximately 10³.^{2a,b} When charge can be delocalized by R and R', the hydrogen/ α -cyano rate ratios range up to 10⁶.^{2a,e} It would appear that while a relationship does exist between inductive destabilization and conjugative stabilization for the α -cyano group, this relationship is not linear.^{2e} In view of these observations, it was of considerable interest to study the effect of the α -cyano group on an extensively delocalized carbocation, where the inductive influence should predominate. We now report our studies of α -cyanobenzyl cations.

Treatment of a series of substituted acetophenones (1) with trimethylsilyl cyanide, followed by removal of the trimethylsilyl protecting group with 3 N hydrochloric acid gave the corresponding α -hydroxy- α -methylbenzeneacetonitriles⁴ (acetophenone cyanohydrins, 2) as listed in Table I.⁴⁻⁷ These cyanohydrins were either converted into methanesulfonates, 3, or, in those cases where the methanesulfonates were too reactive, into bromides, 4. For α -hydroxy- α -methyl-3-(fluoromethyl)benzeneacetonitrile both the methanesulfonate and the bromide were prepared in order to have a pair of crossover compounds which would allow a methanesulfonate/bromide rate ratio to be determined in the same solvent for our substrate.

Solvolyses of the methanesulfonates, 3a-f, and of the

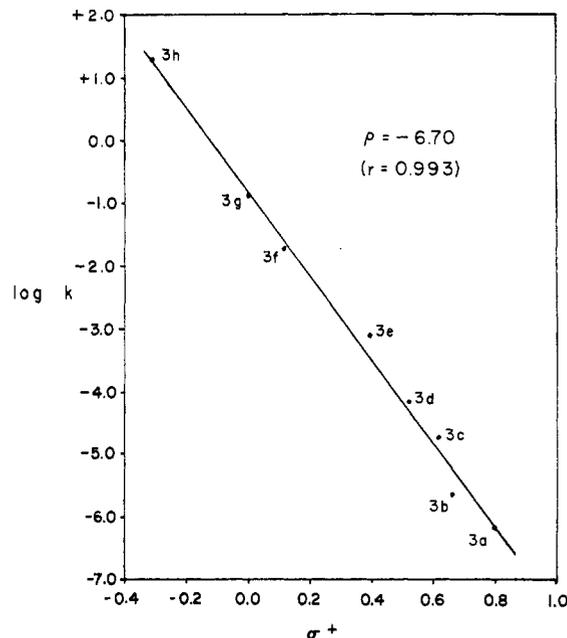
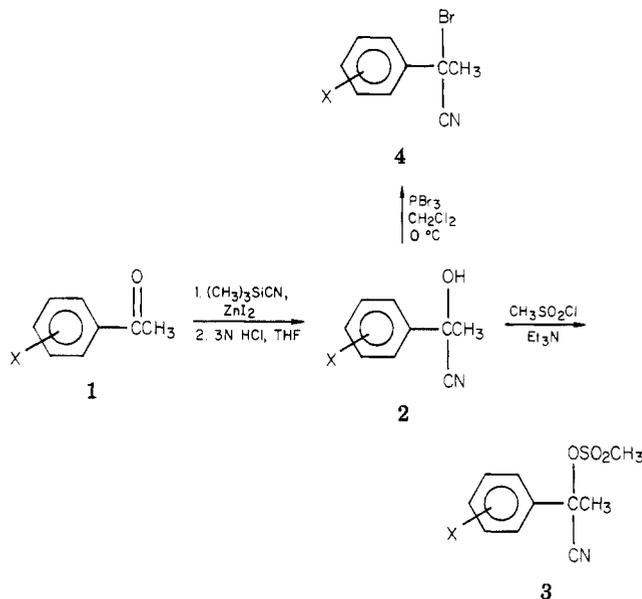


Figure 1. Plot of $\log k$ for the 2,2,2-trifluoroethanolysis of α -hydroxy- α -methylbenzeneacetonitrile methanesulfonates vs. Brown's σ^+ values for the aryl substituents.

bromides, 4f-h, were carried out in anhydrous 2,2,2-trifluoroethanol⁸ buffered with 2,6-lutidine. The rates, which were obtained conductometrically, showed excellent pseudo-first-order kinetics through 3-5 half-lives. The rates are listed in Table II. From the rate data for 3f and 4f, a methanesulfonate/bromide rate ratio of 8.01×10^4 was determined. This was used to calculate the rates for 3g and 3h. As shown in Figure 1, a reasonable plot of $\log k$ vs. Brown's σ^+ values was obtained. This gave a ρ value of -6.70. Our ρ value of -6.70 can be compared to related values for the generation of other benzylic cations. In their classic paper, Brown and Okamoto observed a ρ value of -4.54 for the solvolysis of *tert*-cumyl chlorides in 90% aqueous acetone.⁹ For α -methylbenzyl chlorides in the same solvent, a ρ value of -4.95 was obtained.¹⁰ Liu and

(8) 2,2,2-Trifluoroethanol was chosen as solvent because of its strong ionizing power ($\gamma = 1.80$) and low nucleophilicity.

(9) Brown, H. C.; Okamoto, Y. *J. Am. Chem. Soc.* 1958, 80, 4979.

(10) Tsuno, Y.; Kusuyama, Y.; Sawada, M.; Fujii, T.; Yukawa, Y. *Bull. Chem. Soc. Jpn.* 1975, 48, 3337.

(2) (a) Gassman, P. G.; Talley, J. J. *J. Am. Chem. Soc.* 1980, 102, 1214, 4138. (b) Gassman, P. G.; Saito, K.; Talley, J. J. *Ibid.* 1980, 102, 7613. (c) Dixon, D. A.; Charlier, P. A.; Gassman, P. G. *Ibid.* 1980, 102, 3957. (d) Gassman, P. G.; Saito, K. *Tetrahedron Lett.* 1981, 22, 1311. (e) Gassman, P. G.; Talley, J. J. *Ibid.* 1981, 22, 5253.

(3) (a) Creary, X. *J. Org. Chem.* 1979, 44, 3938. (b) Creary, X. *J. Am. Chem. Soc.* 1981, 103, 2463.

(4) Gassman, P. G.; Talley, J. J. *Tetrahedron Lett.* 1978, 3773.

(5) In all cases, detailed spectral data were consistent with the assigned structures. Satisfactory elemental analyses and/or exact mass molecular weights were obtained on all new compounds.

(6) 3-(Fluoromethyl)acetophenone was prepared by the addition of 3-(fluoromethyl)phenyllithium⁷ to acetaldehyde followed by oxidation of the secondary alcohol to the ketone with pyridinium dichromate. The σ^+ value for the 3-fluoromethyl group has been established as +0.104.⁷

(7) Gassman, P. G.; Guggenheim, T. L., submitted for publication.

Table II. Rates of Solvolysis of Methanesulfonates and Bromides Derived from α -Hydroxy- α -methylbenzeneacetonitriles in 2,2,2-Trifluoroethanol Buffered with 2,6-Lutidine

compd	temp (± 0.05 °C), °C	rate, s ⁻¹	ΔH^\ddagger , kcal/mol	ΔS^\ddagger , eu
3a	80.00	$(2.22 \pm 0.03) \times 10^{-4}$	22.0 \pm 0.3	-13.2 \pm 1.7
	90.00	$(5.65 \pm 0.06) \times 10^{-4}$		
	100.00	$(1.28 \pm 0.02) \times 10^{-3}$		
	25.00 ^a	6.00×10^{-7}		
3b	55.00	$(6.72 \pm 0.17) \times 10^{-5}$	21.5 \pm 0.6	-12.2 \pm 1.7
	70.00	$(3.35 \pm 0.04) \times 10^{-4}$		
	85.00	$(1.16 \pm 0.01) \times 10^{-3}$		
	25.00 ^a	2.25×10^{-6}		
3c	45.00	$(1.72 \pm 0.04) \times 10^{-4}$	20.2 \pm 0.2	-12.3 \pm 0.6
	60.00	$(7.92 \pm 0.08) \times 10^{-4}$		
	75.00	$(2.96 \pm 0.02) \times 10^{-3}$		
	25.00 ^a	1.87×10^{-5}		
3d	30.00	$(1.22 \pm 0.05) \times 10^{-4}$	19.9 \pm 0.5	-10.8 \pm 1.6
	45.00	$(6.85 \pm 0.20) \times 10^{-4}$		
	60.00	$(2.60 \pm 0.06) \times 10^{-3}$		
	25.00 ^a	7.03×10^{-5}		
3e	10.00	$(1.22 \pm 0.09) \times 10^{-4}$	20.4 \pm 0.6	-4.0 \pm 2.1
	25.00	$(9.34 \pm 0.10) \times 10^{-4}$		
	40.00	$(4.37 \pm 0.15) \times 10^{-3}$		
	25.00 ^a	8.25×10^{-4}		
3f	-9.90	$(3.68 \pm 0.10) \times 10^{-4}$	17.0 \pm 0.2	-9.6 \pm 0.7
	0.00	$(1.20 \pm 0.01) \times 10^{-3}$		
	10.00	$(3.86 \pm 0.01) \times 10^{-3}$		
	25.00 ^a	1.80×10^{-2}		
4f	95.00	$(2.15 \pm 0.02) \times 10^{-4}$	20.7 \pm 0.2	-19.6 \pm 0.4
	110.00	$(6.80 \pm 0.04) \times 10^{-4}$		
	125.00	$(1.95 \pm 0.01) \times 10^{-3}$		
	25.00 ^a	2.25×10^{-7}		
4g	70.00	$(1.53 \pm 0.01) \times 10^{-4}$	19.9 \pm 0.2	-18.2 \pm 0.6
	80.00	$(3.58 \pm 0.02) \times 10^{-4}$		
	90.00	$(7.10 \pm 0.20) \times 10^{-4}$		
	25.00 ^a	1.58×10^{-6}		
3g	25.00 ^{a,b}	1.27×10^{-1}	14.5 \pm 0.4	-26.4 \pm 1.2
4h	25.00	$(2.47 \pm 0.09) \times 10^{-4}$		
	40.00	$(7.91 \pm 0.19) \times 10^{-4}$		
	55.00	$(2.56 \pm 0.13) \times 10^{-3}$		
3h	25.00 ^{a,b}	2.39×10^{-4}		
		1.91×10^1		

^a Extrapolated from other temperatures. ^b Extrapolated from the rate of the corresponding bromide using the rate ratio of 3f/4f (8.01×10^4) as the extrapolation factor.

co-workers have recently reported $\rho = -6.85$ for the solvolysis of 1-aryl-1-(trifluoromethyl)ethyl tosylates in 80% aqueous ethanol,^{1b} over the same range of substituents as was used in our study. Thus, a reasonably direct comparison of the trifluoromethyl and cyano groups is possible. Since σ_{para}^+ values for trifluoromethyl and cyano are 0.61 and 0.66, respectively, the ρ values measured by Liu and in the present study compare quite well.¹¹ On the basis of comparing *only* the ρ values it might be concluded that there is little resonance contribution as represented by 5.

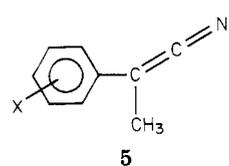
Although the ρ values would appear to rule out a major role of 5, a direct rate comparison of 3g with 1-phenyl-1-(trifluoromethyl)ethyl *p*-toluenesulfonate^{1a,b} indicated that the cyano substituted system is ca. 2×10^3 faster than the trifluoromethyl-substituted system. Since the cyano group is more electron withdrawing than the trifluoromethyl group, this rate comparison would appear to be incompatible with the complete lack of charge delocalization onto the cyano group.¹³

This apparent anomaly between the reaction parameter,

(11) It should be noted that ρ values increase slightly with decreased solvent polarity.^{9,12} Thus, our value of $\rho = -6.70$ would be expected to increase in magnitude when extrapolated to 80% aqueous ethanol.

(12) Kondo, Y.; Matsui, T.; Tokura, N. *Bull. Chem. Soc. Jpn.* 1969, 42, 1037.

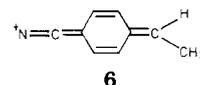
(13) Similarly, comparison of 1-phenethyl bromide (extrapolated from the chloride)¹⁴ with 4g resulted in a hydrogen/ α -cyano rate ratio of ca. 6×10^3 . This value is in line with those for systems which have either maximum delocalization by the cyano moiety or very little delocalization of charge into the cyano group.^{2a}



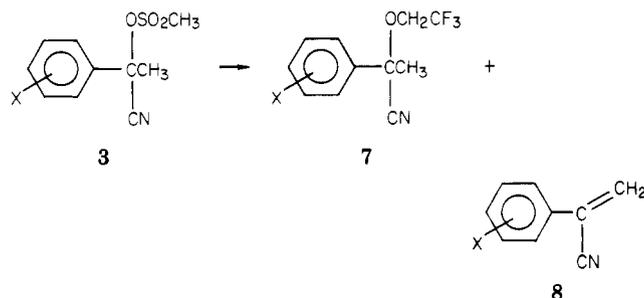
ρ , and the absolute rate constant is similar to that observed for another system^{2e} for which it was postulated that when "the charge is so effectively delocalized, both the inductive and conjugative effects of the α -cyano group decrease significantly". In the present example, conjugative stabilization by the cyano moiety would appear to be much less than that in most previously studied examples.^{2a-d,15} The linearity of the $\rho\sigma^+$ plot requires that the involvement by 5 be linearly related to the inductive effect of the α -cyano moiety.¹⁶

(14) We thank a referee for bringing this literature and the resulting comparison to our attention. The value, obtained under conditions suitable for extrapolation, was reported by Shiner, V. J., Jr.; Dowd, W.; Fisher, R. D.; Hartshorn, S. R.; Kessick, M. A.; Milakofsky, L.; Rapp, M. W. *J. Am. Chem. Soc.* 1969, 91, 4838.

(15) Because of the close comparison of the data for the α -trifluoromethyl and α -cyano groups on the benzyl cation and the similar comparison of ρ_{para}^+ for these two groups, one could postulate that, to the



extent that 5 is a resonance contributor in our system, 6 may contribute to the stability of *p*-cyanobenzyl cations.



Comparison of this study with our earlier work on simple, nonconjugated, α -cyano-substituted cations reveals that a large range of resonance contributions by the α -cyano group to incipient cationic centers exists.² As might be expected, the balance between inductive destabilization and resonance stabilization by the α -cyano moiety appears to be a function of the electron demand of the incipient cationic center.^{2e}

Product studies showed that 7 and 8 were formed as primary products in the 2,2,2-trifluoroethanolysis of 3. In general, the yields of 7 decreased and the yields of 8 increased as X became more electron withdrawing. While 7 was stable to the reaction conditions, 8 slowly dimerized when X was hydrogen or methyl.¹⁷

(16) Recent studies by Olah of substituted benzophenone cyanohydrins in superacid solutions at -78°C indicate that such a linear balance exists. However, it is difficult to ascertain the exact extent to which ^{15}N NMR shifts are a measure of the amount of positive charge on nitrogen. Olah, G. A.; Prakash, G. K. S.; Arvanghi, M. *J. Am. Chem. Soc.* **1980**, *102*, 6640. Olah, G. A.; Arvanghi, M.; Prakash, G. K. S. *Ibid.* **1982**, *104*, 1628.

The formation of 8 as a substantial product prompted us to question whether a concerted elimination process was possible. Solvolysis of α -hydroxy- α -(methyl- d_3)-4-nitrobenzeneacetonitrile methanesulfonate at 90.00°C gave a rate of $(3.63 \pm 0.05) \times 10^{-4} \text{ s}^{-1}$. Comparison with the rate for 3a at 90.00°C gave $k_{\text{CH}_3}/k_{\text{CD}_3} = 1.56$. We believe that this value argues against 8 being formed in a concerted elimination.

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Registry No. 1a, 100-19-6; 1b, 1443-80-7; 1c, 709-63-7; 1d, 349-76-8; 1e, 99-02-5; 1f, 82026-75-3; 1g, 98-86-2; 1h, 122-00-9; 2a, 69813-77-0; 2b, 69813-76-9; 2c, 82026-76-4; 2d, 82026-77-5; 2e, 82026-78-6; 2f, 82026-79-7; 2g, 20102-12-9; 2h, 69813-74-7; 3a, 82026-80-0; 3b, 82026-81-1; 3c, 82026-82-2; 3d, 82026-83-3; 3e, 82026-84-4; 3f, 82026-85-5; 3g, 82026-86-6; 3h, 82026-87-7; 4f, 82026-88-8; 4g, 82026-89-9; 4h, 82026-90-2.

(17) Dimers of substituted styrenes have previously been isolated: Newey, H. A.; Erickson, J. G. *J. Am. Chem. Soc.* **1950**, *72*, 5645. Grasselli, R. K.; Burrington, J. D.; Suresh, D. D.; Friedrich, M. S.; Hazle, M. A. S. *J. Catal.* **1981**, *68*, 109.

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