

The Captodative Effect

HEINZ G. VIEHE,* ZDENEK JANOUSEK, and ROBERT MERÉNYI

Laboratoire de Chimie Organique, Université de Louvain, B-1348 Louvain-La-Neuve, Belgium

LUCIEN STELLA

Laboratoire de Chimie Organique B Associé au CNRS, LA 109, Université d'Aix-Marseille 3, 13397 Marseille Cedex 13, France

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Some years ago we postulated that the captodative effect, the combined action of an electron-withdrawing (*captor*) and an electron-releasing (*donor*) substituent on a radical center, leads to an enhanced stabilization.¹ It is the goal of this Account to outline the genesis of the concept and to retrace the course of events which have marked its progress from inception to the present day. First, we will describe how the intuitive idea based on the fundamental principles governing the stabilization of radicals and ions led us to formulate the concept. We will then demonstrate that the concept is well founded by emphasizing the most significant experimental evaluations concerning it and especially by describing the mechanistic consequences for homolytic reactions and its applications in selective organic synthesis.

Substituent Effect on Radical Stabilization

Substituent effects in free radical chemistry have been the subject of considerable work and discussion. Being of steric or electronic nature, they influence both the kinetic and thermodynamic radical stabilizations.² Therefore, through their steric effects, substituents can play a significant role in the kinetic stabilization of radicals. It is easily understood that by preventing molecules and other radicals from approaching the radical center, steric effects isolate it from its environment and grant it some persistence. This is the case for di- and tri-*tert*-butylmethyl radicals,³ for example. Thermodynamic stabilization, on the other hand, corresponds to a lowering of the radical energy ground-state. It is, therefore, an intrinsic property that is principally influenced by the ability of the substituents to delocalize the unpaired electron. This can reduce the reactivity by reducing the spin density on the radical center. In general, thermodynamically stabilized radicals are not persistent.² It can be observed, however,

that the combined electronic effects of polar substituents also cause a certain chemical inertia. The remarkable persistences of dicyano(dimethylamino)methyl (1)⁴ and 1-ethyl-4-carbomethoxy-pyridinyl radicals (2)⁵ provide two examples that are, a priori, sur-



prising. How can such a behavior be explained in the cases where, apparently, steric effects do not play a determining role? We tried to find the answer to this question, as well as to other more general questions concerning the fundamental problem of thermodynamic stabilization of polysubstituted radicals.

In parallel with our own work, developed essentially for synthetic application purposes, the captodative effect has been compared in recent years with the combined effect of identical substituents. This Account not only reflects this renewed activity in theoretical and physicochemical studies of polysubstituted radical stabilization but also provides a new perspective on the earlier work in relation to this problem.⁶

With our current understanding of the relationships between structure and reactivity in the homolytic process, it has been well established that free radicals can be thermodynamically stabilized both by electron donors and electron acceptors.⁷ The earliest explanation, and the simplest, is based on the notion of conjugation. It suggests that the substituted radicals are stabilized when and because additional resonance structures can be drawn wherein the unpaired electron is delocalized onto the substituents. Thus, for the α -aminomethyl 3 and the α -cyanomethyl 4 radicals, two mesomeric

Heinz G. Viehe is Professor of Organic Chemistry at the Université de Louvain. After his studies in Braunschweig and Paris he received his Ph.D. with F. Bohmann in 1955 and then did postdoctoral work with R. B. Woodward at Harvard University. His research includes studies of polar effects on multiple bonds, small rings (benzvalene), and mechanistic concepts such as cumulation or σ -delocalization of radical stabilization.

Zdenek Janousek was born in Czechoslovakia but migrated to Belgium in 1969. He received his Ph.D. in 1972 at Louvain. In recent years he has concentrated on topics in free radical chemistry.

Robert Merényi was born in 1926 and studied at the Technical University of Budapest. After an industrial job in Hungary, he joined the European Research Associates at Brussels in 1957. He joined the University of Louvain in 1971 where his main interests have been inorganic chemistry and radical stabilization.

Lucien Stella was born and educated in France, receiving his Ph.D. from the University of Marseille in 1972. Following postdoctoral work (1976-1977) at the University of Louvain he returned to Marseille where he is now a CNRS Research Professor. His research interest concerns the use of radical reactions in synthetic organic chemistry.

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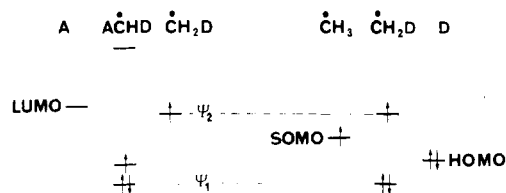
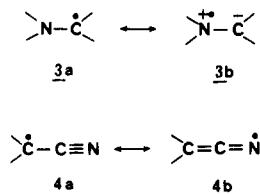


Figure 1. Interactions of a radical orbital (SOMO) with (a) a vacant acceptor orbital, A, and (b) a filled donor orbital, D.

forms **3a,b** and **4a,b** account for the conjugative stabilizing effect of the α -donor and the α -acceptor groups, respectively.



More recently, frontier orbital theory has provided radical stabilization with a representation which emphasizes the relative polar characters of the substituted radicals.⁷ Parts a and b of Figure 1 show the orbital interactions responsible for the stabilization of a radical center by an acceptor A and a donor D, respectively. The interaction between the unperturbed radical SOMO and the acceptor LUMO A results in lowering of the singly occupied orbital of the substituted radical. This accounts for its stabilization as well as for its more electrophilic character. A donor D, on the other hand, stabilizes via a three-electron interaction; the resulting singly occupied orbital ψ_2 is higher in energy than the unperturbed radical SOMO. Consequently, a donor-substituted radical is more nucleophilic than its unsubstituted counterpart.

Even though it is not strictly correct to attribute an intrinsic polar character to a radical without considering the reaction type in which it is involved,⁸ it is possible, to define a relative polarity scale for a homogeneous series of radicals. Thus, the α -aminomethyl radical **3** is more nucleophilic than the methyl radical, which is, in turn, less electrophilic than the α -cyanomethyl radical **4**.

The ability of a substituent to stabilize a cation, an anion, or a polar transition state by direct resonance is now well understood in terms of σ^+ and σ^- .⁹ The intuitive formulation of the concept results from the application of these fundamental ideas to the prediction of substituent effects on the monosubstituted polar radicals **3** and **4**.

The Concept of Captodative Effect

An acceptor substituent (for example cyano) by its nature contributes a stronger stabilization to the nucleophilic radical **3**, and a weaker one to the electrophilic radical **4**, than it contributes to the methyl radical. Conversely, a donor substituent (for example amino) contributes a weaker stabilization to the nucleophilic radical **3**, and a stronger one to the electrophilic radical **4**, than it contributes to the methyl radical. These propositions indicate that pairs of identical

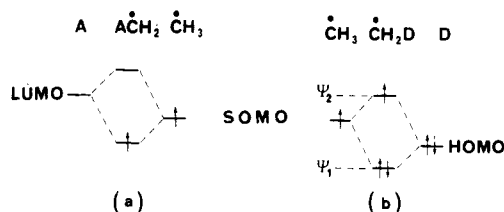
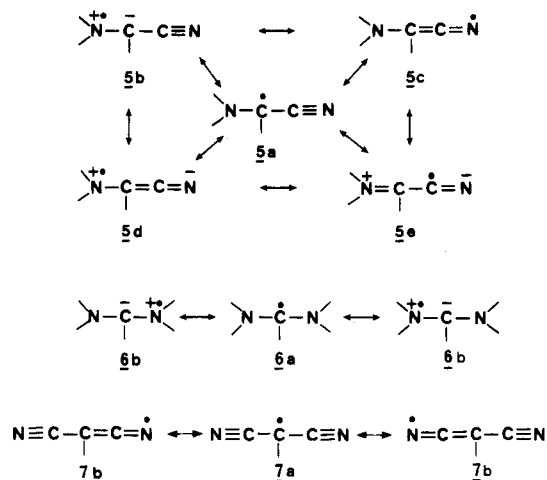


Figure 2. Stepwise perturbational approach of orbital interactions involved in stabilization of a radical center by the captodative substitution.

substituents act on the radicals **6** and **7** in a conflicting manner, while pairs of substituents of opposite polarity act in synergy on the stabilization of the captodative radical **5**.



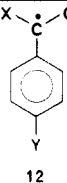
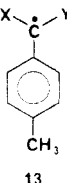
Qualitatively, the concept thus formulated corresponds to the drawing of five resonance structures in the case of the captodative radical **5**, whereas only three are possible in the case of radicals **6** and **7**, which carry two identical substituents. Moreover, the charge separation in the opposite direction to the atom electronegativities in **3b** is a conflicting situation that is enhanced in **6b** by the introduction of a second donor substituent, but which is, in contrast, attenuated in **5b** by the introduction of an acceptor substituent.

This qualitative description of the captodative effect resembles that which can be predicted and visualized with use of a stepwise perturbational approach.^{1b} In terms of frontier orbitals, the stabilizing interactions between a radical and a substituent increase as the orbital energies involved come closer together. It is clear that, in general, when the orbital energies are in the order LUMO A > SOMO > HOMO D (Figure 2), the energy difference between ψ_2 and LUMO A is smaller than that separating the SOMO from the LUMO A. It follows that stabilization by an acceptor A is more effective in the $\dot{\text{A}}\text{CHD}$ captodative radical than in the $\dot{\text{A}}\text{CH}_2$ monosubstituted radical. Furthermore, as the singly occupied orbital of the $\dot{\text{A}}\text{CH}_2$ radical is lower in energy than the methyl radical SOMO, it is closer to the HOMO of the donor substituent D. Stabilization by a donor substituent is, therefore, more significant in the captodative radical $\dot{\text{A}}\text{CHD}$ than in the monosubstituted radical $\dot{\text{C}}\text{H}_2\text{D}$. Thus, in the case of two substituents of opposite polarity A and D, the overall effect on the radical stabilization is greater than the sum of the individual substituent effects. In other words, the two substituents act in unison; they potentialize one another. This is what we call the captodative

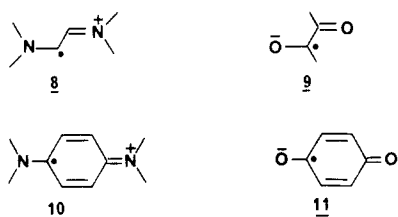
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Table I.
Hyperfine Coupling Constants and Delocalization Parameters in Benzylic Radicals 12 and 13

radical	X	Y	$a_{\text{H}}^{\text{CH}_3}$, G	S^{exptl}	S^{calcd}	ΔS , %	
 12	12a	H	H	17.70	0		
	12b	H	OMe	17.25	0.025		
	12c	H	CN	16.90	9.045		
	12d	CN	H	16.10	0.090		
	12e	CN	CN	15.90	0.102	0.131	-22
	12f	OMe	OMe	15.75	0.110	0.146	-25
	12g	OMe	H	15.50	0.124		
	12h	CN	OMe	14.85	0.161	0.113	+42
	12i	OMe	CN	13.95	0.212	0.163	+30
	 13	13a	H	H	6.53	0	
		13b	OMe	OMe	6.40	0.020	0.0183
13c		H	CN	5.92	0.093		
13d		H	OMe	5.90	0.096		
13e		CN	CN	5.90	0.096	0.177	-46
13f		CN	OMe	4.44	0.320	0.180	+78

effect. The effect is quite general; it appears each time neutral or charged acceptor and donor act simultaneously on a radical center. Their combined action can be produced either directly or through a π system capable of transmitting the substituent effects.¹⁰ Thus, the 1,2-enamine radical cation 8 and the α -diketone radical anion 9 are two typical examples of captodative radical ions. Wurster salts 10 and the hydroquinone radical anion 11 are cyclic vinylogues of 8 and 9, respectively.



Evaluating the Captodative Effect

We have purposely used a qualitative line of reasoning, based on the most basic principles of conjugative interaction or overlap, as a simple introduction to the captodative concept. If the simple argument is true, then any approximate method must confirm it. Foremost among the methods that have been used to evaluate the substituent effects on radical stabilization, electron spin resonance spectroscopy is ideally suited.¹¹ This technique detects free radicals and concerns the ground state of paramagnetic species. Compared with the other methods, this is independent of the substituent effects on the radical precursors or on the decay products. This also discounts any hypotheses on the nature of a postulated transition state wherein the radicals can be more or less developed. At the same time, this technique provides precise information about the delocalization of the unpaired electron.

In the homogeneous series of benzylic radicals 12 (Table I), the freely rotating methyl group provides a suitable probe for the benzylic carbon spin density.¹² The steric interactions between substituents X and Y are nonexistent, and the configurational variations can be considered negligible since the radical planarity is

ensured by the presence of the aromatic nucleus. Therefore, variations in the β -H hyperfine splittings $a_{\text{H}}^{\text{CH}_3}$ should reflect changes in spin delocalization, and an increased spin delocalization should indicate an increased radical stabilization.¹³ An experimental delocalization parameter, $S_{\text{XY}}^{\text{exptl}}$, can be defined (eq 1) for

$$S_{\text{XY}}^{\text{exptl}} = 1 - (a_{\text{XY}}/a_{\text{HH}}) \quad (1)$$

each substituent or substituent pair. For the unsubstituted benzylic radical 12a, $S_{\text{HH}}^{\text{exptl}}$ is zero and the value increases with the stabilizing power of the substituent or substituent pair. The data in Table I clearly indicates that the stabilization contributed by the captodative substitution is greater than those contributed by either two acceptor or two donor substituents.

Furthermore, the value S^{calcd} can be estimated for the disubstituted radicals (eq 2), representing the superim-

$$S_{\text{XY}}^{\text{calcd}} = 1 - (1 - S_{\text{XH}}^{\text{exptl}})(1 - S_{\text{HY}}^{\text{exptl}}) \quad (2)$$

position of the individual substituent effects. These values are greater than the corresponding experimental values in the case of two identical substituents but are, in contrast, smaller than S^{exptl} in the case of captodative radicals. The difference ΔS (eq 3) represents a syner-

$$\Delta S = \frac{S_{\text{XY}}^{\text{exptl}} - S_{\text{XY}}^{\text{calcd}}}{S_{\text{XY}}^{\text{calcd}}} \quad (3)$$

getic substituent effect if positive and an antagonistic one if negative. Although phenylogy attenuates the substituent effect of Y, the variations observed in ΔS certainly are significant. It is obviously verified that the antagonistic or synergetic effects are stronger when X and Y are directly bonded to the radical center¹² such as in benzylic radicals 13. An analogous conclusion is reached following the study of an allylic radical series¹⁴ (Table II). The delocalization parameters derived from the coupling constants a_{H_1} and a_{H_2} emphasize analogous antagonism and synergy in the combined action of two substituents. In addition, the rotational barriers of the substituted allylic radicals reflect the thermodynamic stabilization contributed by the substituents. A comparison of these values shows that the captodative effect exceeds the sum of the individual substituent effects.

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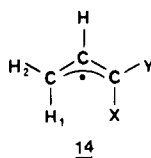
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Table II.
Hyperfine Coupling Constants, Delocalization Parameters, and Rotational Barriers in Allylic Radicals 14



	X	Y	a_{H_1} , G	a_{H_2} , G	S_{exptl}	S_{scaled}	ΔS , %	E_a , kcal/mol
14a	H	H	14.81	13.92	0			15.7
14b	CN	H	13.15	12.42	0.110			10.6
14c	H	CN	13.05	12.20	0.121			9.8
14d	MeO	H	13.64	13.18	0.067			14.7
14e	H	MeO	13.11	13.07	0.089			14.3
14f	CN	CN	12.16	11.30	0.184	0.218	-16	9.6
14g	MeO	MeO	14.91	14.35	-0.018	0.150	-112	12
14h	MeO	CN	10.77	10.34	0.267	0.180	+48	6.0
14i	CN	MeO	10.89	10.09	0.267	0.189	+41	6.1

Stabilization energies of polysubstituted radicals have been estimated in recent years by various physico-chemical and theoretical methods. The studies relating to carbon-carbon bond homolysis of hexasubstituted ethanes,^{15a-e} cis-trans isomerization of tetrasubstituted ethylenes^{15f} and cyclopropanes,^{15g-i} and thermolysis of azo compounds,^{15j} as well as theoretical calculations,^{15k-m} all converge on the fact that the action of a captodative couple is more stabilizing than the actions of the corresponding dicaptor or didonor pairs.

The captodative effect appears to be general, not only in the stabilization of monoradicals but also in that of the 1,1-biradicals (carbene triplet states),¹⁶ 1,2-biradicals (transition state for cis-trans isomerization of ethylenes),^{15f} 1,3-biradicals (transition state for cis-trans isomerization of cyclopropanes),^{15g-i} and other 1, ω -diradicals.¹⁷

Mechanistic Consequences of the Captodative Effect

Whatever may be the exact magnitude of the captodative effect, which obviously depends on each of the partners in the couple considered, a synergetic contribution to radical stabilization can, under thermodynamic control, promote the formation of captodative radicals and influence the product distribution and yield of reactions where these radicals are intermediates.

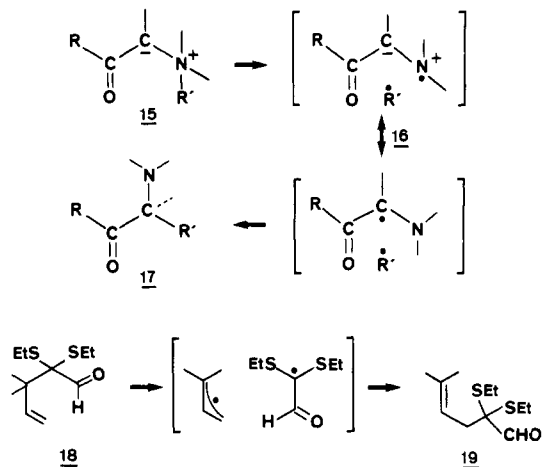
A σ bond linking an atom, or group of atoms, to a captodatively substituted center is activated toward homolysis. This *proradical* property is clearly illustrated by the rearrangement reactions involving radical pairs. Thus, the *meso-dl* interconversion of the captodative radical dimers takes place at relatively low temperatures.^{15d,e} The weak dissociation enthalpy of the dimers reflects the importance of the σ bond energy

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lowering.¹⁸ Thus, the dimers of 1,3-bis (captodative) allyl radicals homolyze already around room temperature.^{18b} The {1,2}- or {1,3}-type rearrangements also take place with remarkable ease if the radicals involved carry captodative substitution. Ammonium ylides 15 rearrange to tertiary amines 17, whereby radical pairs 16 may intervene.¹⁹ The compound 18 undergoes a thermal 1,3 shift to its isomer 19. The strongly positive activation entropy and the lack of any significant solvent effect are consistent with the homolytic cleavage to an intermediate pair of stabilized radicals.²⁰



The transition state of C-H abstractions being polar, other radicals than the captodative ones may be formed under kinetic control. The initially formed radicals would then undergo a fast hydrogen transfer reaction which generates a thermodynamically favored captodative radicals.²¹

The captodative effect such as in 37 appears also in the weakening of π bonds. The captodative substitution draws together the olefin frontier orbitals (with respect to ethylene, simultaneous increase of the HOMO and decrease of the LUMO energies).^{1b} Consequently,

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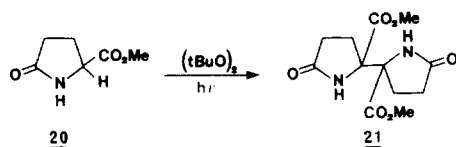
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radical addition and cycloaddition reactions are favored thermodynamically and even kinetically;²² the captodative olefins can be considered as *radicophiles*.^{1b} The LUMO lowering of captodative olefins also results in good dienophilic properties.

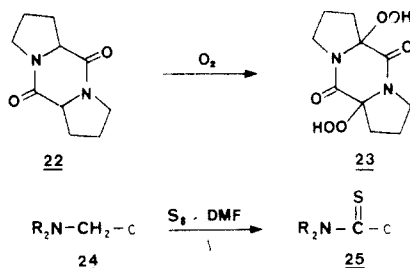
Finally, by stabilizing the radical, the captodative effect favors homolytic reactions of lowest activation energies (dimerization or coupling) to the detriment of other reactions such as addition (polymerization), hydrogen abstraction, dismutation. A mechanistic study shows that the captodative radicals dimerize without noticeable energy barrier.²³ Many attractive synthetic applications result from this set of properties, some of which are illustrated in the next section of this Account.

Synthetic Applications of the Captodative Effect

The dehydromers of captodative compounds can be obtained very selectively and in good yields.²⁴ The captodative centers can be used to interlink numerous derivatives (α -amino esters or nitriles, α -alkoxy esters or nitriles, etc...). The reaction of methyl pyroglutamate (20) with *tert*-butyloxy radicals illustrates the possibility



of bond forming between two tertiary carbon atoms.²⁵ With various oxidizing agents such as oxygen, sulfur, and halogens, the selective functionalization of captodative methylene or methyne groups can be easily performed. Piperazinedione (22) reacts regioselectively with oxygen, thereby forming the double hydroperoxide 23.²⁶ If the donor is an amino group, compounds 24



react smoothly with sulfur; this thionation represents a useful entry to captor-substituted thioamides 25.²⁷ Halogenating agents such as Cl_2 , Br_2 , NBS, NCS, and SO_2Cl_2 lead selectively to captodative halo compounds²⁸ which have been applied for alkylations of olefinic²⁹ and aromatic³⁰ derivatives.

When the amide chlorides are activated by an electron-withdrawing group, their covalent form 26 un-

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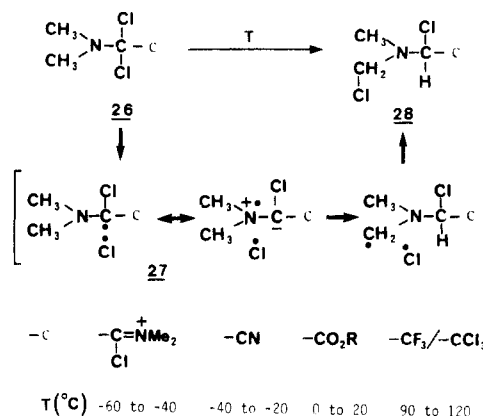
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dergoes an unprecedented internal, nonionic, redox reaction, leading to the bis-electrophilic synthon 28.³¹

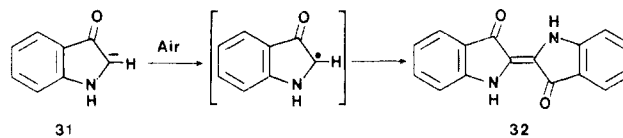


Its ease depends on the strength of the acceptor group. Although details of the mechanism remain open, there is evidence for facile homolysis of C-Cl bonds when the carbon carries captodative substitution.^{28,32}

Benzylic captodative anions can readily take up oxygen from the air. Thus, donor-substituted benzylic cyanides 29 produce, in a basic medium, the corre-



sponding amides, esters, and thio esters while benzylic cyanide itself remains unaffected.³³ Since captodative carbanions tend to be destabilized depending on the electron-donating group, they are readily oxidized through a single electron transfer (SET) process,³⁴ leading to captodative radicals. From the many examples known to date, the classical synthesis of indigo 32 is particularly enlightening because air is sufficient as oxidant.³⁵ Captodative radical intermediates may occur



in nucleophilic substitutions where they arise through a SET process. When the anion deriving from 29 ($d = \text{NMe}_2$) is reacted with a chiral secondary alkyl bromide, a partial racemization takes place. This side reaction can be suppressed by adding a radical inhibitor.³⁶

Strongly nucleophilic captodative anions 33 and 35 react with unprecedented ease with *tert*-butyl iodide.^{37,38}

(31) (a) Huys, F.; Merényi, R.; Janousek, Z.; Stella, L.; Viehe, H. G. *Angew. Chem., Int. Ed. Engl.* 1979, 18, 615. (b) Janousek, Z.; Huys, F.; René, L.; Masquelier, M.; Stella, L.; Merényi, R.; Viehe, H. G. *Ibid.* 1979, 18, 616. (c) Rover-Kevers, M.; Vertommen, L.; Huys, F.; Merényi, R.; Janousek, Z.; Viehe, H. G. *Ibid.* 1981, 20, 1023.

(32) Singh, H.; Tedder, J. M. *J. Chem. Soc., Chem. Commun.* 1980, 1095.

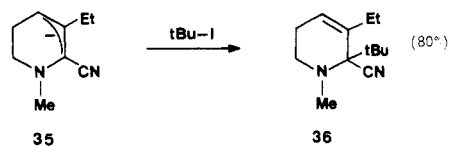
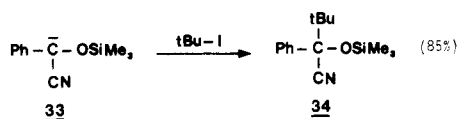
(33) (a) Stella, L. unpublished results. (b) Aurich, H. G. *Tetrahedron Lett.* 1964, 657.

(34) Chanon, M.; Tobe, M. L. *Angew. Chem., Int. Ed. Engl.* 1982, 21, 1.

(35) Russel, G. A.; Kaupp, G. *J. Am. Chem. Soc.* 1969, 91, 3851.

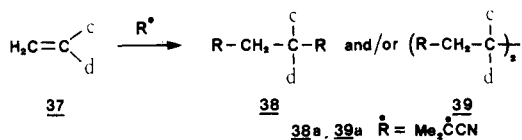
(36) Chauffaille, J.; Hebert, E.; Welvert, Z. *J. Chem. Soc., Perkin Trans. 2* 1982, 1645.

(37) (a) Deuchert, K.; Hertenstein, V.; Hünig, S. *Synthesis* 1973, 777. (b) Deuchert, K.; Hertenstein, U.; Hünig, S.; Wehner, G. *Chem. Ber.* 1979, 112, 2045.

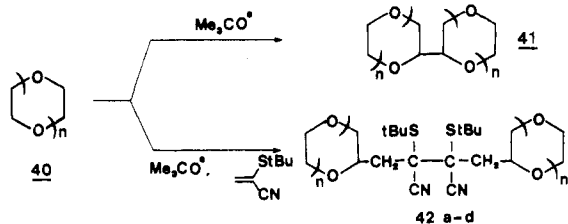


This finding does not fit the classical S_N1 or S_N2 patterns. A SET process apparently leads to the incursion of energetically favorable captodative radicals; their dimers accompany the substitution products. Intimate radical pairs deriving from **35** have been proposed.³⁸

Original reactions can also be accessed through homolytic additions to captodative olefins **37**.^{1a,39} The thermodynamic stabilization of the captodative radical adduct permits the selective formation of double adducts **38** or adduct dimers **39** without side reactions.



Thus, addition of isobutyronitrile radical (IBN) to various captodative olefins **37** takes place on preparative scale leading to double adducts **38a** and adduct dimers **39a**, whereas acryl esters, acrylonitrile, methylene malonate, and the like, lead to polymerization.^{1a} IBN radical leads mostly to double adducts **38a** because the corresponding adduct dimers reversibly dissociate to radicals which are irreversibly scavenged by IBN radical. The study has been extended to a host of radicals ranging from strongly electrophilic ones, like *tert*-butoxy, to nucleophilic species, e.g., acyl and α -amino-methyl radicals.³⁹ In all cases, good yields of adduct dimers **39** are obtained. This new reaction is complementary to dehydrodimerization since four carbon atoms are inserted between two substrate molecules. This is illustrated in the case of crown ethers **40**,⁴⁰ which can be selectively transformed to either dehydro dimers **41** or bridged dehydro dimers **42a-d** ($n = 1, 3, 4, 5$).

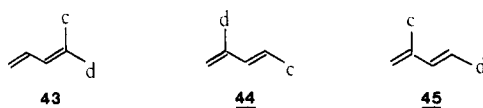


Captodative dienes **43**, **44**, and **45** are better radical traps than captodative olefins since allylic resonance joins the captodative effect in stabilizing the corresponding radical adducts. They usually form mixtures of diadducts and adduct dimers which renders them less attractive from purely preparative standpoint.^{41,42}

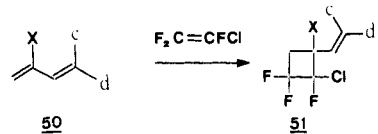
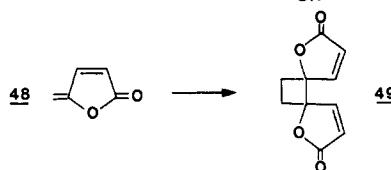
(38) Grierson, D.; Urrea, M.; Husson, H. P. *J. Chem. Soc., Chem. Commun.* 1983, 891.

(39) (a) Mignani, S.; Beaujean, M.; Janousek, Z.; Merényi, R.; Viehe H. G. *Tetrahedron* 1981, 37 (Suppl. 1), 111. (b) Mignani, S.; Janousek, Z.; Merényi, R.; Viehe, H. G.; Riga, J.; Verbist, J. *Tetrahedron Lett.* 1984, 25, 1571. (c) Mignani, S.; Merényi, R.; Janousek, Z.; Viehe, H. G. *Bull. Soc. Chim. Belg.* 1984, 93, 991.

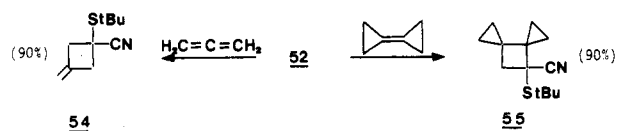
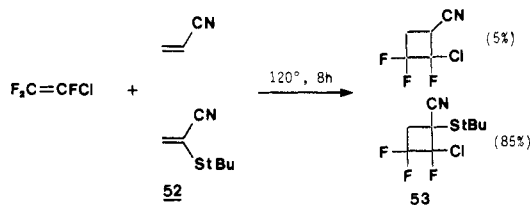
(40) Beaujean, M.; Mignani, S.; Merényi, R.; Janousek, Z.; Viehe, H. G.; Kirch, M.; Lehn, J. M. *Tetrahedron* 1984, 40, 4395.



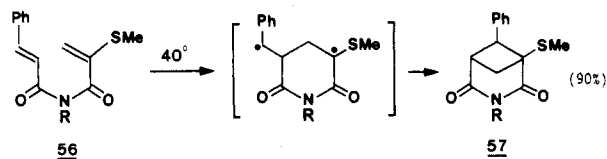
The long-known spontaneous head-to-head cyclo-dimerizations of α -(alkylthio)acrylonitriles (**46**)⁴³ and of the naturally occurring protoanemonine (**48**)⁴⁴ are typical of captodative olefins and dienes; apparently, such reactions are favored because of intermediate-stabilized captodative 1,4-biradicals. Trifluorochloroethylene forms (2 + 2) adducts with various captodative olefins and dienes.^{41,42,45,46} Dienes **50** react at the less substituted double bond.^{41a}



Competition experiments reveal that α -(*tert*-butylthio)acrylonitrile (**52**) reacts faster than acrylonitrile.⁴⁵



The regiospecific cycloaddition of **52** to allene⁴⁷ and dicyclopopylidene⁴⁸ warrants further study in this field. The thermal intramolecular (2 + 2) cycloaddition of the captodative olefin **56** has been reported to occur with exceptional ease.⁴⁹ Aldonitrone **58** undergoes a regio-



(41) Stevenart-De Mesmaeker, N. Ph. D. Thesis, Louvain-la-Neuve, 1983.

(42) Vandeveld, O. Ph. D. Thesis, Louvain-la-Neuve, 1984.

(43) Gundermann, K. D.; Röhl, E. *Liebigs Ann. Chem.* 1974, 1661.

(44) Moriarty, R. M.; Romain, C. R.; Karle, I. L.; Karle, J. *J. Am. Chem. Soc.* 1965, 87, 3521.

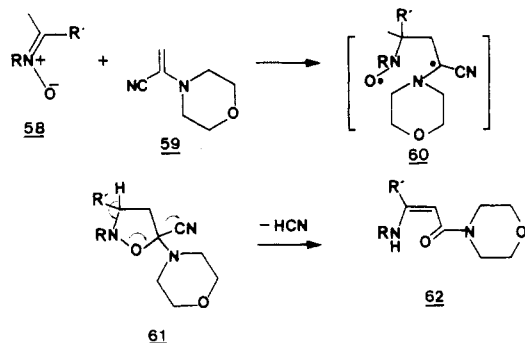
(45) (a) De Cock, C. Ph. D. work, Louvain-la-Neuve, 1983. (b) De Cock, C.; Piettre, S.; Lahousse, F.; Janousek, Z.; Merényi, R.; Viehe, H. G., submitted for publication in *Tetrahedron*.

(46) Groutars, P.; Ghosez, A.; Viehe, H. G.; unpublished results.

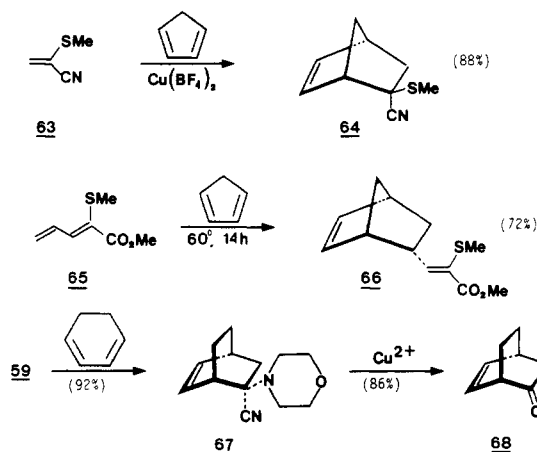
(47) Motte, G. Ph. D. work, Louvain-la-Neuve, 1983.

(48) De Meijere, A.; Gallez, V.; Viehe, H. G., to be submitted for publication.

pecific (3 + 2) cycloaddition to α -morpholinoacrylonitrile (59) whereby the stabilized biradical 60 may be the intermediate. The oxazolidines 61 cannot be isolated, as they undergo an eliminative ring-opening to push-pull amides 62.⁵⁰ The versatile α -(tert-butylthio)acrylonitrile (52) can even act as the π -4 component in (3 + 2) cycloadditions with electron-poor dienophiles, e.g., *N*-phenylmaleic imide, maleic anhydride, and acetylenedicarboxylate.⁵¹



Finally, captodative olefins and dienes react cleanly as π -2 components in Diels-Alder reactions.⁵² The α -(methylthio)acrylonitrile (63) exhibits more dienophilic character than acrylonitrile or α -chloroacrylonitrile.^{52c} The captodative dienes, e.g., 65, react at the less substituted double bond with unactivated dienes.^{52c} The cycloadducts (e.g., 67) of α -morpholinoacrylonitrile (59) are easily transformed to the corresponding ketones 68. Thus, this captodative olefin constitutes a new ketene equivalent.^{52b} Owing to the numerous possi-



bilities offered by variations of the captodative substitution and by their further transformations, the new concept provides a general approach for organic synthesis of polyfunctional compounds via radicals, especially in the field of selective reduction and oxidation, substitution, addition, and cycloaddition reactions.

Outlook

Although much work still remains to be done, the captodative substituent effect now emerges as theoretically and experimentally well-founded. The captodative concept has proven to be useful in explaining many phenomena and in stimulating synthetic work. The applications are anticipated to reach beyond chemistry to all fields where unpaired electrons are occurring, last but not least in life processes.

We gratefully acknowledge the valuable contribution of numerous co-workers whose names appear on the articles quoted in this Account. We are particularly indebted to Professors H. G. Aurich, Sir Derek Barton, R. Louw, G. Leroy, R. Sustmann, and Lord Tedder for valuable discussions. Acknowledgment is also made to SPPS Grant 79/84-13 for financial support of this research.

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Competitive Binding of Nucleofugal Anions in Carbocationic-like Processes

NIKOLAI S. ZEFIROV* and ANATOLY S. KOZ'MIN

Department of Chemistry, Moscow State University, 117234 Moscow, U.S.S.R.

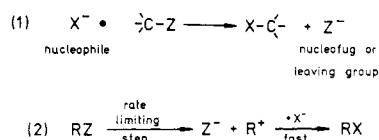
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The concept of *nucleophilicity* has been a cornerstone of organic chemistry ever since the early investigations of Ingold and co-workers.¹ The definition of *nucleophilic reactions* forms an important conceptual

Nikolai S. Zefirov is a Corresponding Member of the Academy of Sciences, USSR, Chairman of the Organic Chemistry Section of the All-Union Mendeleev Chemical Society, and Professor and Head of Laboratory of the Department of Chemistry of Moscow State University. He was born in Yaroslavl in 1935 and studied chemistry at Moscow State University, where he received the Candidate degree (1981) and Doctor habil. Degree (1986). Among his research interests are conformational analysis, addition reactions, synthesis of cage compounds, and application of computers in organic chemistry.

Anatoly S. Koz'min is Senior Scientist of the Department of Chemistry of Moscow State University, where he received his Candidate Degree (1971) and Doctor habil. Degree (1984). His major research interests concern the chemistry of cage compounds and electrophilic additions.

basis. For many years they were the favorites of physical organic chemists. In his classical work Ingold clearly defined a series of reaction mechanisms with two limiting cases of S_N2 (eq 1) and S_N1 (eq 2) type.



Equation 1 clearly demonstrates that nucleophiles and nucleofuges are basically species of the same sort.

(1) C. K. Ingold "Structure and Mechanism in Organic Chemistry", 2nd ed., Cornell University Press, Ithaca, N.Y., 1969, Chapter 7.