

Homolytic Cleavage Energies of R–H Bonds Centered on Carbon Atoms of High Electronegativity: First General Observations of *O*-type Variation on C–H BDEs and the Implication for the Governing Factors Leading to the Distinct *O/S* Patterns of Radical Substituent Effects

Jin-Pei Cheng,* Bo Liu, Yongyu Zhao,† Zhong Wen, and Yongkai Sun‡

Contribution from the Department of Chemistry, Nankai University, Tianjin 300071, China

Received November 24, 1999. Revised Manuscript Received July 12, 2000

Abstract: A systematic investigation of the methylene C–H bond dissociation energies (BDEs) of the onium-substituted toluene series (**1–6**) and of the adjacent electron-pulling group-substituted acetophenone and fluorene series (**7** and **8**) (Chart 1) was carried out using a modified electrochemical method (eq 1) incorporating the pK_a 's measured in DMSO solution. This provided the first opportunity to examine the stabilization effect of substituents on carbon radicals (or C–H bonds) of varying degrees of electron deficiency. The relative BDE (Δ BDE) values estimated for these substrates within a family showed that for most systems, the adjacent or remote electron-withdrawing groups (EWGs) were found to strengthen the benzylic (or methylene) C–H bonds (i.e., the *O*-type), which is in sharp contrast to the universally observed C–H bond-weakening effect of EWGs (i.e., the *S*-type) in the literature. This general phenomenon reveals that it is the apparent electronegativity of the methylene carbon, rather than the nonbonded electron pair as suggested in the literature, that governs the direction of radical substituent effects.

Introduction

Chemical and many biological phenomena are recognized as bond reorganization processes in which the energetics of bond scission and formation, as well as that of the relevant transition state and intermediates, are key issues. They have attracted considerable interests in the past¹ and continue to be investigated in both theoretical and experimental aspects.² In this connection the most fundamental problem is the quantitative measurement of bond dissociation energy (BDE) of covalent bonds in various oxidation states, because these are used to analyze the reaction characteristics and properties of the reactive intermediates.

* To whom correspondence should be addressed. Phone: 86-22-23505098. Fax: 86-22-23500035. E-mail: jpcheng@nankai.edu.cn.

† Current address: Department of Chemistry, Northwestern University, Evanston, IL 60208.

‡ Current address: Department of Chemistry, Washington University, St. Louis, MO 63130.

(1) (a) McMillen, D. F.; Golden, D. M. *Annu. Rev. Phys. Chem.* **1982**, *33*, 493 and references therein. (b) Benson, S. W. *Thermodynamic Kinetics*, 2nd ed., John Wiley & Sons: New York, 1976. (c) Gutman, D. *Acc. Chem. Res.* **1993**, *26*, 287. (d) Arnett, E. M.; Amarnath, K.; Harvey, N. G.; Cheng, J.-P. *Science* **1990**, *247*, 423. (e) Wayner, D. D. M.; Parker, V. D. *Acc. Chem. Res.* **1993**, *26*, 510. (f) Bordwell, F. G.; Zhang, X.-M. *Acc. Chem. Res.* **1993**, *26*, 510.

(2) For representative recent works, see: (a) Trujillo, H. A.; Casado, C. M.; Ruiz, J.; Astruc, D. *J. Am. Chem. Soc.* **1999**, *121*, 5674. (b) Barckholtz, C.; Barckholtz, T. A.; Hadad, C. *J. Am. Chem. Soc.* **1999**, *121*, 491. (c) Laarhoven, L. J. J.; Mulder, P.; Wayner, D. D. M. *Acc. Chem. Res.* **1999**, *32*, 2, 342. (d) Pratt, D. A.; Wright, J. S.; Ingold, K. U. *J. Am. Chem. Soc.* **1999**, *121*, 4877. (e) Anne, A.; Fraoua, S.; Grass, V.; Moiroux, J.; Savéant, J.-M. *J. Am. Chem. Soc.* **1998**, *120*, 2951. (f) Brocks, J. J.; Beckhaus, H.-D.; Beckwith, A. L. J.; Rüchardt, C. *J. Org. Chem.* **1998**, *63*, 1935. (g) Deng, H.; Kebarle, P. *J. Am. Chem. Soc.* **1998**, *120*, 2925. (h) Zhao, Y.; Bordwell, F. G.; Cheng, J.-P.; Wang, D. *J. Am. Chem. Soc.* **1997**, *119*, 9125. (i) Cioslowski, J.; Liu, G.; Moncrieff, D. *J. Am. Chem. Soc.* **1997**, *119*, 11452. (j) Mayer, P. M.; Glukhovtsev, M. N.; Gauld, J. W.; Radom, L. *J. Am. Chem. Soc.* **1997**, *119*, 9, 12889. (k) Wayner, D. D. M.; Clark, K. B.; Rauk, A.; Yu, D.; Armstrong, D. A. *J. Am. Chem. Soc.* **1997**, *119*, 8925.

Among dissociation processes, the free energy of R–H bond heterolysis, as represented by the classical term pK_a , is the most investigated one³ and for which have been found in recent years many new applications to resolve substantive problems.^{2a,4} Studies of the equally important R–H bond homolysis energies have been mostly limited to small molecules for a long time,^{1,2} however, owing to complications from the likely concurrence of secondary bond scissions in bulky organic molecules in gas-phase determinations. For example, attempts to repeat a BDE of 75 kcal/mol (henceforth abbreviated as kcal) for the $\text{Ph}_3\text{C}-\text{H}$ bond⁵ reported earlier have encountered enormous difficulties over decades until recently when a BDE of 81 kcal, as determined by an indirect thermodynamic approach,⁴ⁱ was reported as the more reasonable value.⁶ In recent years, the solution-phase BDE methodology has been developed via

(3) (a) Bordwell, F. G. *Acc. Chem. Res.* **1988**, *21*, 456 and references therein. (b) Ritchie, C. D. *Solute Solvent Interactions*; Coetzee, J. F., Ritchie, C. D., Eds.; Marcel Dekker: New York, 1969, Chapter 4. (c) Kolthoff, I. M.; Chantooni, J. K., Jr.; Bhowmik, S. *J. Am. Chem. Soc.* **1968**, *90*, 23. (d) Streitwieser, A., Jr.; Juaristi, E.; Nebenzahl, L. L. *Comprehensive Carbanion Chemistry*; Bunzel, E., Durst, T., Eds.; Elsevier: Amsterdam, 1980, Chapter 7. (e) Thiele, G.; Streitwieser, A., Jr. *J. Am. Chem. Soc.* **1994**, *116*, 446.

(4) (a) Parker, V. D.; Handoo, K. L.; Roness, F.; Tilset, M. *J. Am. Chem. Soc.* **1991**, *113*, 7493. (b) Tilset, M.; Parker, V. D. *J. Am. Chem. Soc.* **1989**, *111*, 6711. (c) Cheng, J.-P.; Handoo, K. L.; Parker, V. D. *J. Am. Chem. Soc.* **1993**, *115*, 2655. (d) Parker, V. D. *J. Am. Chem. Soc.* **1992**, *114*, 7458. (e) Griller, D.; Simoes, J. A. M.; Mulder, P.; Sim, B. A.; Wayner, D. D. M. *J. Am. Chem. Soc.* **1989**, *111*, 7892. (f) Sim, B. A.; Milne, P. H.; Griller, D.; Wayner, D. D. M. *J. Am. Chem. Soc.* **1990**, *112*, 6635. (g) Zhang, X.-M.; Bordwell, F. G. *J. Am. Chem. Soc.* **1994**, *116*, 4251. (h) Bordwell, F. G.; Bausch, M. J. *J. Am. Chem. Soc.* **1986**, *108*, 1979, 2473. (i) Bordwell, F. G.; Cheng, J.-P.; Harrelson, J. A. *J. Am. Chem. Soc.* **1988**, *110*, 1229, 2867. (j) Cheng, J.-P.; Lu, Y.; Zhu, X.; Mu, L. *J. Org. Chem.* **1998**, *63*, 6108.

(5) Swarc, M. *Proc. R. Soc. London, Ser. A* **1951**, *207*, 5.

(6) Bordwell, F. G.; Cheng, J.-P.; Ji, G.-Z.; Satish, A. V.; Zhang, X.-M. *J. Am. Chem. Soc.* **1991**, *113*, 9790.

various approaches by Bordwell,⁶ Parker,^{4b,d} Wayner,^{2c} Arnett,⁷ and this group.⁸ These methods are most useful for the BDE measurement of relatively bulky molecules and, therefore, constitute reliable counterparts to the well-established gas-phase techniques.^{1a} Indeed, for substrates whose BDEs were measurable in both phases, the values obtained in solution were generally found to agree very well with those from the gas-phase^{4d,6,9} determinations, provided certain cautions are exercised; that is, for solvation-sensitive compounds, such as phenols, the solution data are best discussed as relative values because of complex effects arising from differential solvation.¹⁰

The relative R–H bond dissociation energy (Δ BDE) is widely practiced to represent the stabilization energy of the corresponding radical R• (i.e., RSE); that is, a stronger R–H bond generates a less stable R•. In the mid-60s, Walter proposed an *O/S* radical classification on the basis of the stability expressed by an equilibrium study of homolysis.¹¹ Because carbon radicals have been widely found to be stabilized by both EDGs and electron withdrawing groups (EWGs), they were designated as the class *S* (for same) type. Alternatively, heteroatom radicals Y• (such as R₂N• and RO•) were classified as the Class *O* (for opposite) type; i.e., being stabilized by EDGs but destabilized by EWGs. The common feature of heteroatoms (O, N, S, etc.) to bear a nonbonded lone electron pair was then taken as the structural criterion for distinguishing *O*-type radicals from *S*-type radicals.¹¹ Note that the latter lacks a nonbonded electron pair. This *O/S* radical concept, although it has not been widely applied, has nevertheless been extensively supported by the currently known σ° constant scales¹² and by many BDE studies. These investigations show that Y• (O•, N•, S•, etc.) radicals are, indeed, almost entirely of the *O*-type,^{2h,9,13,14} whereas the C• radicals are universally of the *S*-type,^{1a,15,16} with only one distinct exception, that is, the C–H bond in CHF₃ is *strengthened* by the electron-withdrawing fluorine atom by 1.5 kcal, as compared to the C–H bond in CH₄ (106.3 versus 104.8 kcal).¹⁷

The fact that the radicals showing *O*-type behavior are centered either at a carbon atom of induced high electronega-

(7) (a) Arnett, E. M.; Amarnath, K.; Harvey, N. G.; Cheng, J.-P. *J. Am. Chem. Soc.* **1990**, *112*, 344. (b) Arnett, E. M.; Amarnath, K.; Harvey, N. G.; Cheng, J.-P. *Science* **1990**, *247*, 423.

(8) Cheng, J.-P.; Zhao, Y.; Huan, Z. *Sci. China, Ser. B: Chem. (Engl. Ed.)* **1995**, *38*, 1417.

(9) Lind, J.; Shen, X.; Erikson, T. E.; Merényi, G. *J. Am. Chem. Soc.* **1990**, *112*, 479.

(10) Wayner, D. D. M.; Luszyk, E.; Page, D.; Ingold, K. U.; Mulder, P.; Laarhoven, L. J. J.; Aldrich, H. S. *J. Am. Chem. Soc.* **1995**, *117*, 4858.

(11) Walter, R. I. *J. Am. Chem. Soc.* **1966**, *88*, 1923, 1930.

(12) (a) Dust, J. M.; Arnold, D. R. *J. Am. Chem. Soc.* **1983**, *105*, 1221 and references therein. (b) Jiang, X.-K. *Acc. Chem. Soc.* **1997**, *30*, 283 and references therein.

(13) (a) Berkowitz, J.; Ellison, G. B.; Gutman, D. *J. Phys. Chem.* **1994**, *98*, 2744. (b) Bordwell, F. G.; Zhang, X.-M.; Cheng, J.-P. *J. Org. Chem.* **1993**, *58*, 6410. (c) Bordwell, F. G.; Cheng, J.-P. *J. Am. Chem. Soc.* **1991**, *113*, 1736. (d) Bordwell, F. G.; Zhang, X.-M.; Cheng, J.-P. *J. Org. Chem.* **1991**, *56*, 3216. (e) Brinck, T.; Haeblerlein, M.; Jonsson, M. *J. Am. Chem. Soc.* **1997**, *119*, 4239. (f) Wu, Y.-D.; Lai, D.-K. W. *J. Org. Chem.* **1996**, *61*, 7904. (g) Bordwell, F. G.; Harrelson, J. A., Jr.; Lynch, T. Y. *J. Org. Chem.* **1990**, *55*, 3337. (h) Bordwell, F. G.; Zhang, X.-M.; Satish, A. V.; Cheng, J.-P. *J. Am. Chem. Soc.* **1994**, *116*, 6605.

(14) (a) Cheng, J.-P.; Xian, M.; Wang, K.; Zhu, X.; Yin, Z.; Wang, P. *J. Am. Chem. Soc.* **1998**, *120*, 10266. (b) Cheng, J.-P.; Liu, B.; Zhao, Y.; Zhang, X. *J. Org. Chem.* **1998**, *63*, 7072. (c) Cheng, J.-P.; Zhao, Y. *Tetrahedron* **1993**, *49*, 5267. (d) Cheng, J.-P.; Lu, Y.; Liu, B.; Zhao, Y.; Wang, D.; Sun, Y.; Mi, J. *Sci. China, Ser. B: Chem. (Engl. Ed.)* **1998**, *41*, 215.

(15) (a) Pryor, N. A. *Frontiers of Free Radical Chemistry*; Academic Press: New York, 1980. (b) Viehe, H. G.; Janousek, Z.; Merényi, R. *Substituent Effects in Radical Chemistry*; NATO ASI Series; D. Reidel Publishing Co.: Dordrecht, The Netherlands, 1986.

(16) (a) Bordwell, F. G.; Cheng, J.-P.; Bausch, M. J. *J. Am. Chem. Soc.* **1988**, *110*, 2867, 2872. (b) Bordwell, F. G.; Cheng, J.-P.; Seyedrezai, S. E.; Wilson, C. A. *J. Am. Chem. Soc.* **1988**, *110*, 8178. (c) Zhang, X.-M.; Bordwell, F. G.; Bares, J. E.; Cheng, J.-P. *J. Org. Chem.* **1993**, *58*, 3051.

tivity (such as F₃C•), or at a heteroatom of intrinsically high electronegativity (such as O•, N•, or S•) gives rise to a fundamental question: which is the ultimate factor, the electronegativity or the nonbonded electron pair, that governs the direction (i.e., the *O* or *S* pattern) of radical substituent effect? In this regard, knowledge of the BDEs of the methylene C–H bond centered at the highly electronegative carbon would be very desirable. Unfortunately, these classes of substrates have not been systematically investigated and not much is available in the literature in terms of their substituent effects.

In a recent study by this group,⁸ we observed a number of intriguing “anomalies” that have led us to this study. For the benzyl carbon carrying an adjacent electron-pulling cyano group, as in phenylacetonitrile, strong *para* EWGs such as CN, CF₃, and CO₂Me were observed to *strengthen* the benzylic C–H bond. Furthermore, in the case of *p*-G-C₆H₄CH(CN)CO₂Et, which has two electron-withdrawing groups attached to the benzyl carbon, the C–H bond is *strengthened* by all *para* EWGs. These results are obviously not in accordance with Walter’s *S*-definition for carbon radicals¹¹ and also with the σ° scales in indirect comparisons.¹² These results directly disagree with the general observation of weaker C–H bonds by all remote substituents, as shown by many BDE determinations on record (vide infra). This suggests that the apparent electronegativity of the C- or Y-center may play a critical role in switching the pattern of substitution effects on benzyl BDEs.

To examine the generality of the critical electronegativity issue, we carried out an investigation of the remote, as well as the adjacent, substitution effects on benzyl C–H BDEs possessing high electronegative carbon centers. Chart 1 shows the type of compound series examined in this study. These substrates were synthesized for the study of their equilibrium acidities.¹⁸ In this report we discuss the substituent effects on the BDEs that lead us to identify the factor governing the shifts at the border area of the *S/O* radical pattern. In a separate paper we have applied theoretical calculations to study the BDEs of these compound series; this is in the process of submission.

Results and Discussion

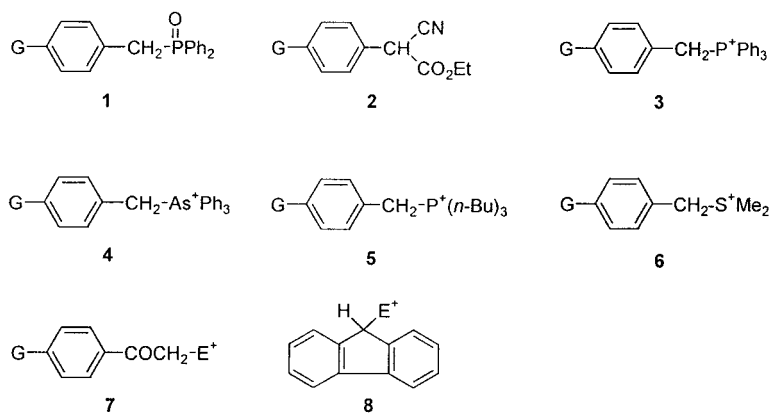
In the present work, the homolytic C–H bond dissociation energies were determined according to eq 1, the revised form¹⁹ of Bordwell’s approach.⁴ⁱ The C–H equilibrium acidity p*K*_a was measured in DMSO by the “overlapping indicator method”,^{3a} and oxidation potentials of the corresponding carbanions [*E*_{ox}(C[−]), versus Fc⁺/Fc] in DMSO by cyclic voltametry (CV). The stepwise derivation of this equation and the description of the terms therein were outlined previously⁸ and are also given in the Supporting Information. The *E*_{ox}(C[−]) used in eq 1 was an irreversible value, and the error margin thus introduced in the final BDEs was in the acceptable range of ~1.5 kcal. This value was estimated on the basis of comparisons of irreversible and reversible oxidation potentials of structurally similar carbanions.²⁰ In view of the well-behaved cyclic voltammograms, the electrode irreversibility of the ylidic carbanions should be comparable in size; thus, the error margin for Δ BDEs is believed

(17) Afeefy, H. Y.; Liebman, J. F.; Stein, S. E. Neutral Thermochemical Data. In *NIST Chemistry Webbook*; Mallard, W. G., Linstrom, P. J., Eds.; NIST Standard Reference Database No.69; National Institute of Standards and Technology: Gaithersburg, MD, March 1998; <http://webbook.nist.gov>.

(18) Cheng, J.-P.; Liu, B.; Zhao, Y.; Sun, Y.; Zhang, X.; Lu, Y. *J. Org. Chem.* **1999**, *64*, 604.

(19) The original BDE equation⁴ⁱ was scrupulously revised with necessary corrections of two errantly used literature data (see descriptions in ref 8). The final form (eq 1) is similar, however, to those of Bordwell⁶ and Parker^{4b,d} with only marginal differences (0.3 and 0.2 kcal/mol, respectively) in the constant term.

Chart 1



G = H (a), Me (b), MeO (c), CF₃ (d), CO₂Me (e), CN (f), NO₂ (g)

E⁺ = Ph₃P⁺ (A), (n-Bu)₃P⁺ (B), Ph₃As⁺ (C), Me₂S⁺ (D), (n-Bu)₂S⁺ (E), Me₂Se⁺ (F), (n-Bu)₂Te⁺ (G)

counterion: Br⁻

to be much smaller, probably in the range of ≤ 0.5 kcal.²³ Because the BDEs in this work are used in a relative sense within the similarly substituted families, the overall results should not alter the main perspective of the forthcoming discussion.

$$\text{BDE (kcal/mol)} = 1.364 \text{ p}K_a + 23.06 E_{\text{ox}}(\text{C}^-) + 73.6 \quad (1)$$

To facilitate the discussion, it is necessary to present some representative indices of structural effects on BDEs (i.e., ΔBDE values) and on radical stabilities (σ_s^*) that have been reported in the literature for comparison (Table 1). These literature data indicate, at least qualitatively, that both EDGs and EWGs at either the adjacent or remote positions can reduce the C–H bond strength (or stabilize the carbon radical), showing a typical class *S* behavior, regardless of whether the system is of a σ -type or a π -type.

Effect of Adjacent Electron-Pulling Groups on C–H BDEs. The methylene C–H bond-homolysis energies of the compounds bearing an adjacent electron-pulling group (**1a–6a**, **7**, and **8**; Chart 1) were investigated. In Table 2, the BDEs calculated from eq 1 are tabulated.

A cursory inspection of the ΔBDE data in Table 2 reveals that most of the positively charged adjacent electron-pulling groups are, indeed found to strengthen the C–H bonds, which is in contrast to the general *S*-type phenomenon seen from the literature data in Table 1. Comparisons of the ΔBDE data between toluene and acetophenone derivatives indicate that such a bond-strengthening effect by the adjacent electron-pulling group could be enhanced for acetophenone derivatives where there already preexists a strongly electron-pulling carbonyl

(20) The irreversible oxidation potentials (CV) of some ylide anions, namely, PhCH₂⁻P⁺Ph₃ and PhCH₂⁻N⁺Me₃,^{13b,21} were found to agree within 50 mV (1.15 kcal) with the corresponding reversible potentials obtained by fast-scan CV.²² Similarly, the reversible E_{ox} 's of a number of delocalized carbanions by the second-harmonic AC voltametry (SHACV) reported by Arnett also agree within 50 mV with the irreversible potentials measured by CV as reported by Bordwell.^{7a}

(21) Bordwell, F. G.; Zhang, X.-M.; Alnajjar, M. S. *J. Am. Chem. Soc.* **1992**, *114*, 7623.

(22) Zhang, X.-M.; Fry, A. J.; Bordwell, F. G. *J. Org. Chem.* **1996**, *61*, 4101.

(23) This was based in part on the measured uncertainties in $\text{p}K_a$ (± 0.1) and E_{ox} (± 0.005 V).

Table 1. Relative Bond Dissociation Energies (ΔBDEs) and Radical Substituent Constants in the Literature^a

substituent	ΔBDE			$10 \times \sigma_{\alpha}^*$ ^h	σ_{β}^* ⁱ
	(G-CH ₂ -H) ^b	(<i>p</i> -G-C ₆ H ₄ CH ₂ -H) ^c	(9-G-Fl-H) ^e		
G = H	0	0	0	0	0
Me ₂ N	-21	-2.2	-10.7	0.34	0.23
MeO	-12	-1.1	-7.0		0.47
Ph	-16 ^c		-5.9		
<i>t</i> -Bu	-5.1			0.36	0.26
Me	-4.2 ^c	-0.4	-4.5	0.15	0.15
F	-5.1	-0.2		-0.11	-0.02
Cl	-4.2	-0.2		0.17	0.22
CF ₃	1.6	0		0.01	-0.01
MeCO	-11	-1.2	-2.5	0.66	0.54
PhCO	-12 ^d			0.64	
PhSO ₂	-6 ^e		2.1	0.26	
CN	-12	-0.9	-5.7	0.43	0.42
NO ₂	-7 ^e	-1.0			0.36

^a ΔBDEs are in kcal/mol. ^b From ref 1a except otherwise noted. ^c Reference 17. ^d Reference 24. ^e Reference 21. ^f Reference 25. ^g Reference 1f. ^h Reference 12a. ⁱ Reference 12b.

group. For instance, the strengthening effects of Ph₃P⁺ and ⁿBu₃P⁺ on the methylene C–H bond in the toluene series (0.2 and 0.6 kcal, respectively) are both significantly increased; to 3.5 and 4.2 kcal, respectively; in the acetophenone series. These results, as well as other allied comparisons in Table 2, imply that the apparent electronegativity of the methylene carbon is very likely the key factor that governs the overall patterns of substituent effects on the BDE variation. As stated in the literature,^{8,14c,28} an electron-pulling group usually plays a dual role in affecting radical stabilities. Although it stabilizes the spin by resonance delocalization, it also destabilizes the radical center by electron induction. The balance of these two effects is, conceivably, related to the apparent electronegativity of the methylene carbon atom. If this atom is highly electron-

(24) Pasto, D. J. *J. Am. Chem. Soc.* **1988**, *110*, 8164.

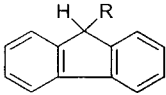
(25) Wu, Y.-D.; Wong, C.-L.; Chan, K. W. K.; Ji, G.-Z.; Jiang, X.-K. *J. Org. Chem.* **1996**, *61*, 746.

(26) (a) Zhang, X.-M.; Bordwell, F. G.; Puy, M. V. D.; Fried, H. E. *J. Org. Chem.* **1993**, *58*, 3060. (b) Zhang, X.-M.; Bordwell, F. G. *J. Am. Chem. Soc.* **1994**, *116*, 968.

(27) Bordwell, F. G.; Cheng, J.-P.; Bausch, M. J.; Bares, J. E. *J. Phys. Org. Chem.* **1988**, *1*, 209.

(28) Bordwell, F. G.; Harrelson, J. A., Jr.; Zhang, X.-M. *J. Org. Chem.* **1991**, *56*, 4448.

Table 2. Homolytic C–H Bond Dissociation Energies of α -Substituted Toluenes, Fluorenes, and Acetophenones^a

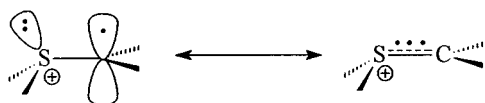
substrate (R-H)		pK_a^b	$E_{ox}(C)^g$	BDE ^h (kcal/mol)	ΔBDE^i (kcal/mol)	reference
PhCHR ₁ R ₂						
R ₁ = H,	R ₂ = H			88.6	(0)	15a
	CN	21.9 ^c	-0.929	82.1	-6.5	8, 27
	CN	8.0	-0.181	80.3	-8.3	8
	P(O)Ph ₂	27.5	-1.004	88.0	-0.6	This work
	P ⁺ Ph ₃	17.6	-0.385	88.7 ^j	0.1	This work
	P ⁺ Bu ⁿ ₃	21.9	-0.620	89.2	0.6	This work
	N ⁺ Me ₃	31.9 ^d	-1.143	90.8	2.2	26
	As ⁺ Ph ₃	22.7	-0.558	91.7	3.1	This work
	S ⁺ Bu ⁿ ₂	18.9	-0.667	84.0	-4.6	This work
	Se ⁺ Bu ⁿ ₂	23.5	-0.724	89.0	0.4	This work
	Te ⁺ Bu ⁿ ₂	23.8	-0.705	89.8	1.2	This work
PhCOCH ₂ -R (7)						
	R = H	24.7 ^c		93.0	(0)	6
	P ⁺ Ph ₃	6.0 ^c	0.639	96.5	+3.5	26
	P ⁺ Bu ⁿ ₃	10.1	0.425	97.2	+4.2	This work
	N ⁺ Me ₃	14.6 ^d	0.141	96.8	+3.8	16b
	As ⁺ Ph ₃	8.6	0.450	95.7	+2.7	This work
	S ⁺ Bu ⁿ ₂	8.4	0.423	94.8	+1.8	This work
	Se ⁺ Me ₂	11.1	0.399	97.9	+4.9	This work
	Te ⁺ Bu ⁿ ₂	11.2	0.358	97.1	+4.1	This work
						
	R = H	22.6 ^c		79.5	(0)	4i
	CN	8.3 ^c	-0.448	73.8	-5.7	4h
	CO ₂ Me	10.35 ^c	-0.492	75.6	-3.9	4h
	P ⁺ Ph ₃	6.6 ^c	-0.044	81.6	+2.1	26
	P ⁺ Bu ⁿ ₃	10.7	-0.229	83.0	+3.5	This work
	N ⁺ Me ₃	17.8 ^d	-0.563	84.9	+5.4	26
	As ⁺ Ph ₃	9.8	-0.191	82.6	+3.1	This work
	S ⁺ Me ₂	6.5	-0.215	77.6	-1.9	This work
	Se ⁺ Me ₂	10.2 ^f	-0.384	78.7	-0.8	This work
	Te ⁺ Bu ⁿ ₂	10.4	-0.455	77.3	-2.2	This work

^a In kcal/mol at 25 °C. For onium salts, the counterion is Br⁻. ^b Measured in Me₂SO at 25 °C, as reported in the preceding paper of this group,¹⁸ except otherwise noted. ^c From ref 3a. ^d From ref 26a. ^e From ref 26b. ^f Due to severe absorption overlap in direct pK_a measurement, this value was estimated by parallel comparisons of related pK_a data. Estimated uncertainty, <0.2 pK unit. ^g Irreversible oxidation potentials (in volts) of carbanions measured in DMSO by CV at Pt electrode taking ferrocenium/ferrocene redox couple as the internal reference (see Experimental Section). ^h Calculated from pK_a and anion oxidation potential by eq 1. ⁱ Lit. 26b. BDE, 88.3 kcal. ^j $\Delta BDE = BDE(\alpha\text{-substituted}) - BDE(\text{parent}) = -RSE$ (radical stabilization energy).

demanding, as in the cases for the phenacyl radical of the present work and the phenoxy radical in the literature,^{13c} the inductive-

destabilizing effect of an EWG could become large enough to dominate its resonance-stabilizing effect. As shown in Tables

Chart 2



1 and 2, only if the C–H bonds do not have an external electronegativity enhancement, such as those of methane, toluene, and the fluorene series (Table 1), would it allow a chance for both EDG and EWG to exert a bond-weakening effect. The fact that all adjacent strong electron-withdrawing groups universally increased the methylene C–H BDE of acetophenones (Table 2) further demonstrated the importance of electronegativity enhancement to cause a switch in the directions of substituent effects.

The effect of adjacent 9-electron-pulling groups on the BDE of fluorenes in Table 2 merits some comments. For “normal” adjacent EWG substituents, CN and CO₂Me, the Δ BDE values are negative, which agrees with the general observations in the literature on the BDE variation pattern for “regular” (i.e., without induced electronegativity enhancement) C–H bonds (cf. the BDE data in Table 1). Very strong electron-pulling groups, such as positively charged onium cations of the Group VB elements (i.e., N⁺, P⁺, or As⁺), exert a bond-strengthening effect, whereas those of the Group VIB elements (i.e., R₂S⁺, R₂Se⁺, or R₂Te⁺) exhibit a weakening effect. Although the strengthening effect has already been rationalized in the foregoing discussion, the weakening effect (i.e., radical-stabilizing) of the chalcogenide onium group, such as R₂S⁺, requires a consideration of its special bonding situation. Clearly, the radical-stabilizing effect of the R₂S⁺ group must be associated with the lone-pair electrons of the sulfur atom, which can stabilize the radical center by forming a three-electron bond shown in Chart 2.²⁹ This type of radical stabilization has been suggested to account for the enhanced captodative radical stabilizing effects.³⁰ The relatively small radical-stabilizing effect of R₂S⁺ on the fluorenyl radical (1.9 kcal), as compared to that on the benzyl radical (4.6 kcal), is probably due to a combination of steric inhibition of three-electron overlapping and saturation effects. The small radical-destabilizing effect of Bu₂S⁺ on the phenacyl radical may be mainly the result of its enhanced inductive destabilizing effect (vide supra). Similarly, the effects of the other two chalcogenide onium groups, R₂Se⁺ and R₂Te⁺, can also be understood by the same arguments on the basis of a combined outcome of inductive, steric, and three-electron-bonding effects, with a consideration of the differences of their structural progressions (i.e., longer C–M bond, more dispersed lone-pair electrons, etc.). In this respect, the importance of the electron-demanding property (i.e., electronegativity) of the radical center in controlling the direction and magnitude of substituent effects is revealed.

In connection with the role of electronegativity of the radical center, it would be helpful to compare the present observations with those in the literature regarding the effect of an adjacent electron-pulling group on the Y–H bonds centered at the atom which is intrinsically of high electronegativity. As shown in Table 3, the Δ BDE data of the representative N–H (Y = N) systems show that the adjacent electron-pulling groups do strengthen the N–H bond in anilines, although they are not so strong in electron-pulling as those onium groups in Table 2.

Table 3. N–H BDEs in Adjacently Substituted Anilines and Amines in the Literature ^a

substrate	pK _a	E _{ox} (N ^{•-})	BDE	Δ BDE	reference
MeNH ₂			99.9	0	1a
MeNHCOMe	25.9	-0.217	103.9	4.0	13g
PhNH ₂	30.6	-0.992	92.5	0	13b
PhNHPO(OEt) ₂	18.4	-0.174	94.7	2.2	14d
PhNHSO ₂ Ph	11.9	0.161	93.6	1.1	14c
PhNHCOPh	18.8	-0.085	97.3	4.8	14c
PhNHCONMe ₂	21.2	-0.435	92.7	0.2	14a
PhNHCOMe	21.5	-0.159	99.3	6.8	14c
PhNHCOCF ₃	12.6	0.384	99.6	7.1	16c

^a BDEs are in kcal/mol. Electrode potentials are in volts vs Fc^{+/•}/Fc. All data are taken from the literature as cited. The pK_a and E_{ox}(N^{•-}) were measured in DMSO.

This supports the hypothesis that the patterns of substituent effect are related to the electronic nature of the bond-breaking site.

Effects of Remote Substituents on C–H Bonds of Electronegative Carbon. The benzyl C–H BDEs of six series of toluene derivatives (1–6) carrying various electron-pulling groups at the benzyl carbon were investigated with respect to the *para* substituent effects. The thermodynamic pK_a's (measured in previous work¹⁸), the carbanion oxidation potentials [E_{ox}(C^{•-})], and the BDEs calculated according to eq 1 are summarized in Table 4; some relevant data from early works are also listed.

It is noted from Table 4 that for toluene series 1–6, all *para* EDGs give a negative Δ BDE, whereas all *para* EWGs give a positive Δ BDE; namely, showing a bond-weakening effect by *p*-EDG and a bond-strengthening effect by *p*-EWG. These results are not what one would normally expect, on the basis of the reported benzylic C–H BDEs in the literature (vide supra). The cause of this distinct phenomenon, in analogy to the situation for the C–H systems with an adjacent substituent (Table 2), is, again, believed to be related to the enhanced electronegativity of the benzylic carbon atom as a result of the adjacent electron-pulling group.

To understand the crucial role of the electronegativity of the benzylic carbon, we have to invoke a consideration of the electrostatic interactions between the substituent and the site of the reaction within the system. For a homolytic process, it is conceivable that a highly electron-deficient radical center (such as the benzylic carbon of high electronegativity that is induced by a strong adjacent electron-pulling group) would be stabilized electrostatically by a *para* EDG but destabilized by a *para* EWG. It means that the polarized benzylic C–H bond is expected to be weakened by a *p*-EDG but strengthened by a *p*-EWG simply because of their opposing effect on the stability of the corresponding C[•] radical. It should be pointed out that the radical stability is not the only factor controlling the C–H BDE. A fuller understanding of the bond-breaking energetics should involve a consideration of the substituent effect on the stability of the substrate (i.e., the ground-state energy level), as well.³¹ Previous calculations have concluded that such an effect is, indeed, minor in comparison to the effect of the same substituent on the stability of its corresponding radical, especially where a C–H bond breaking is considered.^{2d,15f,25} As Ingold et al.^{2d} recently stated: “The effect of Y substituents on 4-YC₆H₄CH₂-H BDE must be attributed mainly (or entirely) to the greater ability of Y to delocalize the unpaired electron relative to a hydrogen atom.” All of these give credence to the use of relative BDEs

(29) Cheng, J.-P.; Liu, B.; Zhang, X. *J. Org. Chem.* **1998**, *63*, 7574.

(30) (a) Viehe, H. G.; Merényi, R.; Stella, L.; Janousek, Z. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 917. (b) Viehe, H. G.; Janousek, Z.; Merényi, R.; Stella, L. *Acc. Chem. Res.* **1985**, *18*, 148.

(31) (a) Nau, W. M.; Harrer, H. M.; Adam, W. *J. Am. Chem. Soc.* **1994**, *116*, 10972. (b) Nau, W. M. *J. Org. Chem.* **1996**, *61*, 8312. (c) Welle, F. M.; Beckhaus, H.-D.; Ruchardt, R. *J. Org. Chem.* **1997**, *62*, 552.

Table 4. Homolytic C–H Bond Dissociation Energies (BDEs) of *Para*-Substituted Toluene Derivatives^a

Substrate	pK_a^b	$E_{ox}(C^-)^c$	BDE ^d	ΔBDE^e
<i>p</i> -G-C ₆ H ₄ CH ₂ P(O)Ph ₂ (1)				
G = OMe	29.2	-1.158	86.7	-1.3
Me	28.0	-1.051	87.6	-0.4
H	27.5	-1.004	88.0	0
CF ₃	23.6	-0.739	88.8	0.8
NO ₂	17.7	-0.274	91.4	3.4
<i>p</i> -G-C ₆ H ₄ CH(CN)CO ₂ Et ^f (2)				
G = OMe	9.4	-0.351	78.3	-2.0
Me	9.2	-0.267	80.0	-0.3
H	8.0	-0.181	80.3	0
F	7.8	-0.172	80.3	0
Cl	7.3	-0.120	80.8	0.5
CO ₂ Me	5.9	0.015	82.0	1.7
CF ₃	5.8	0.028	82.2	1.9
CN	5.3	0.101	83.2	2.9
<i>p</i> -G-C ₆ H ₄ CH ₂ P ⁺ Ph ₃ (3)				
G = Me	18.0	-0.457	87.6	-1.0
H	17.6	-0.385	88.7	0
CF ₃	14.6	-0.152	90.0	1.3
CO ₂ Me	14.2	-0.166	89.1	0.4
CN	13.4	-0.092	89.8	1.1
NO ₂	11.4	0.038	90.2	1.5
<i>p</i> -G-C ₆ H ₄ CH ₂ As ⁺ Ph ₃ (4)				
G = Me	23.8	-0.630	91.5	-0.2
H	22.7	-0.558	91.7	0
CF ₃	18.4	-0.290	92.0	0.3
CO ₂ Me	18.2	-0.276	92.1	0.4
CN	17.7	-0.221	92.7	1.0
NO ₂	16.1	-0.062	94.1	2.4
<i>p</i> -G-C ₆ H ₄ CH ₂ P ⁺ Bu ₃ ^g (5)				
G = Me	23.1	-0.694	89.1	-0.1
H	21.9	-0.620	89.2	0
CF ₃	18.9	-0.370	90.8	1.6
CO ₂ Me	17.9	-0.358	89.8	0.6
CN	17.5	-0.292	90.7	1.5
NO ₂	15.0	-0.127	91.2	2.0
<i>p</i> -G-C ₆ H ₄ CH ₂ S ⁺ Me ₂ (6)				
G = Me	23.6	-0.701	82.5	-0.6
H	23.1	-0.642	83.1	0
CN	14.6	-0.324	86.0	2.9
CO ₂ Me	14.6	-0.378	84.8	1.7
NO ₂	13.6	-0.004	92.0	8.9

^a BDEs are in kcal/mol, obtained at 25 °C in this work, except as noted. All substrates were synthesized in the early work of this laboratory¹⁸ (see Experimental Section). The counterion of oniums is Br⁻. ^b See footnote *b* in Table 2. ^c See footnote *g* in Table 2. ^d Derived from eq 1; in kcal/mol. ^e See footnote *j* in Table 2. ^f See ref 8 of this group. ^g See ref 14b of this group.

for the present discussion of substituent effect on benzylic carbon radical stabilization.³²

Substituent Effects on Radical Thermodynamic Stability: The Class *O* Concept. As stated above, the ΔBDE value should be a reasonably good model serving as the quantitative guide for radical stabilization energies (RSE) induced by substitution. This forms the basis for the present discussion of the directions of radical substituent effects.

From the ΔBDE data in Table 4, one can see a general phenomenon that as the methylene carbon of the benzylic radical

(32) Our recent DFT calculations (at the B3LYP/6-31G* level) of the C–H BDEs in *para*-substituted phenylacetone nitriles also indicated that the substituent effect on the ground-state energy (G. E.) of the parent molecules is, indeed, a minor factor in the BDE variations of the benzylic C–H bonds. This paper was recently submitted to *J. Am. Chem. Soc.*

becomes sufficiently electron-demanding by connecting to a strong electron-pulling group, the thermodynamic stability of such a radical increases with a *para*-EDG substitution but decreases with a *para*-EWG substitution. Radicals featuring this *opposite* substituent effect, according to the description in the Introduction, should belong to the so-called class *O* radical. These broad observations of the opposing substituent effects with the benzylic radical series **1–6** clearly indicate the necessity of modifying the previous structural criterion for *O*-type radicals; that is, to bear a nonbonded electron pair on the center atom.¹¹ The ample experimental evidence collected in the present work allows us to propose that *it must be the electron-demanding property (i.e., apparent electronegativity) of the radical center, rather than the existence of a nonbonded electron pair, that plays the critical role in controlling the directions of radical substituent effects.*

In conclusion, we have in the present work defined a new concept for the class *O* carbon radical that takes into account the apparent electronegativity of the central atom. This is believed to provide a general (though yet qualitative) criterion for assessing the direction of the substituent effect on radical thermodynamic stabilities. The intriguing findings that EWGs can usually strengthen the benzylic C–H bonds (or destabilize the carbon radicals) are rationalized in terms of the enhanced electronegativity of the center atom, which, in turn, warrants further experimental and theoretical investigations.

Experimental Section

Materials. All the substrates studied (**1–8**, see Tables 2 and 4) were prepared in this laboratory following literature procedures and were already reported in the preceding paper.¹⁸ The supporting electrolyte tetra-*n*-butylammonium hexafluorophosphate (ⁿBu₄NPF₆, Aldrich) was recrystallized from dichloromethane and vacuum-dried at 110 °C for 10 h before use. The purification of dimethyl sulfoxide solvent and the preparation of potassium dimethyl sulfoxide ($CH_3SOCH_2^- \cdot K^+$) were carried out according to the standard procedures in the literature.³³

Electrochemical Measurement. Cyclic voltammograms were recorded on a BAS-100B electrochemical analyzer equipped with a three-electrode assembly. Oxidation potentials of carbanions (~1.5 mM, generated in situ by reaction of substrate with dimethyl sulfoxide in DMSO) were measured in 0.1 M ⁿBu₄NPF₆-DMSO solution under argon at 23 °C as previously described.^{8,14c} The working electrode was a Pt disk ($\phi = 1$ mm). The reference electrode was a AgNO₃/Ag (0.1 M) couple. The counterelectrode was a Pt wire. The scan rate was 100 mV/s. The reported potentials were all referenced to the ferrocenium/ferrocene (Fc⁺/Fc) redox couple, which was taken as the internal standard. The reproducibility was generally ≤ 5 mV.

Acknowledgment. This work was made possible by grants from the Natural Science Foundation of China (nos. 2939 2006, and 29472053) and the Ministry of Education of China to whom the authors want to express their sincere gratitude. J.-P.C. thanks Profs. Fred Bordwell and Ned Arnett for their generous support with instruments and chemicals.

Supporting Information Available: Information concerning the revised BDE method. This material is available free of charge via the Internet at <http://pubs.acs.org>.

JA994120M

(33) Matthews, W. S.; Bares, J. E.; Bartmess, J. E.; Bordwell, F. G.; Cornforth, F. D.; Drucker, G. E.; Margolin, Z.; McCallum, R. J.; McCollum, G. J.; Vanier, N. R. *J. Am. Chem. Soc.* **1975**, *97*, 7006.