# Thermochemical Stability of α-Amino-α-carbonylmethyl Radicals and Their Resonance As Measured by ESR

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ESR spectra of the captodative α-amino-α-carbonylmethyl radicals **8** have been recorded. No coalescence temperature for the rotation of the two NMe groups was found at temperatures below the decomposition temperature of the radicals. From known coalescence temperatures and rotational barriers of substituted methyl radicals the rotational barrier of $\geq 17$ kcal mol$^{-1}$ was estimated for the ·C−N bond in the radicals **8**. Enthalpies $\Delta H_{diss}$ and entropies $\Delta S_{diss}$ of the homolytic dissociation of **7a,c,d** into **8a,c,d** have been obtained from equilibrium measurements by ESR. By correcting for substituent interaction enthalpies in **7** (steric and geminal), a radical stabilization enthalpy RSE $= -20.7 \pm 1.0$ kcal mol$^{-1}$ was obtained for **8**. By addition of the known RSEs of dialkylamino- and carbonyl groups, a RSE $= -9.9$ kcal mol$^{-1}$ is predicted for **8**. The difference between the experimental and predicted values of 10.8 kcal mol$^{-1}$ is attributed to a synergistic captodative substituent effect. A linear correlation between the radical stabilization enthalpies of the radicals **8** and of other mono- and disubstituted alkyl radicals and their ESR $a$H$_\alpha$ coupling constants was found. According to this correlation the reduction of $a$H$_\alpha$ by 1 G corresponds to an increase in RSE of 1.57 kcal mol$^{-1}$. The large resonance of the captodative α-amino-α-carbonylmethyl radicals **3**, expressed by their high RSE, their small $a$H$_\alpha$ coupling constant, and their high rotational barrier, can be rationalized by a strong interaction between the α-amino and the α-carbonyl groups similar to that in amides and expressed in the resonance structures **6**.

## Introduction

During our investigation of substituent effects on the strength of C−C bonds[1,2] we have used thermochemical data and kinetic measurements of C−C bond-cleavage reactions to determine the stability of radicals with various α-substituents. The radical stabilization enthalpy RSE[3] obtained in this way is a thermochemical notion, which expresses the difference in stability of a pure hydrocabon radical **1** (A, B, C = H, alkyl) and the corresponding substituted radical **2** (A, B = H, alkyl; S = functional group).

If the radical stabilization enthalpy RSE is mainly due to resonance stabilization, i.e., delocalization of the single electron by a substituent S in **2**, then a relationship between RSEs and spin densities at the central carbon atom of radicals **2** as obtained from ESR coupling

constants is expected.[4] Attempts to test this in a limited range of substituted benzyl radicals[5] or with calculated RSEs[6] have been made previously.
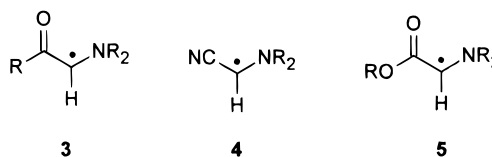
It was recently shown by *kinetic measurements*[7] that α-amino-α-carbonylmethyl radicals **3** are of exceptional thermodynamic stability and, accordingly, have a high RSE of about $-17.6$ kcal mol$^{-1}$, which is 9.7 kcal mol$^{-1}$ higher than expected on the basis of an additive-stabilizing effect by the amino and carbonyl groups.

Radicals **3** and the corresponding α-amino-α-cyanomethyl radicals[1] **4** and α-amino-α-(ethoxycarbonyl)-methyl radicals[8] **5** together with a cyclic radical of the same type[3d] are the first radicals for which quantitative thermochemical evidence for a synergistic captodative stabilization has been presented.[9] The synergistic captodative stabilization of these radicals is well rationalized by *homo-amide-resonance* as expressed by **6a** and **6b**.

[⊗] Abstract published in *Advance ACS Abstracts,* January 15, 1997.
(1) Previous communication: Welle, F. M.; Verevkin, S. P.; Beckhaus, H.-D.; Rüchardt, C. *Liebigs Ann.* **1997,** 155−163.
(2) Rüchardt, C.; Beckhaus, H.-D. *Top. Curr. Chem.* **1985,** *130,* 1−22.
(3) RSE has to be distinguished from the difference in bond energy ΔBDE between substituted C−C bonds and the corresponding C−C bonds in hydrocarbons because the RSEs have been corrected for substituent interactions in the radical precursor but not the ΔBDEs. For a discussion see: (a) Rüchardt, C. *Angew. Chem.* **1970,** *82,* 845−888; *Angew. Chem., Int. Ed. Engl.* **1970,** *9,* 830. (b) Nicholas, A. M. de P.; Arnold, D. R. *Can. J. Chem.* **1984,** *62,* 1850−1859. (c) Clark, K. B.; Wayner, D. D. M. *J. Am. Chem. Soc.* **1991,** *113,* 9363−9365. (d) Clark, K. B.; Wayner, D. D. M.; Demirdij, S. H.; Koch, T. H. *J. Am. Chem. Soc.* **1993,** *115,* 2447−2453. (e) Jackson, R. A. *Tetrahedron* **1991,** *47,* 6777−6786.

(4) (a) Fischer, H. *Z. Naturforsch.* **1964,** *19a,* 866−887. (b) Fischer, H. *Z. Naturforsch.* **1965,** *20a,* 428−432.
(5) Suryan, M. M.; Stein, S. E. *J. Phys. Chem.* **1989,** *93,* 7362−7365.
(6) Nicholas, A. M. de P.; Arnold, D. R. *Can. J. Chem.* **1986,** *64,* 270−276. The correlation between RSE and the $a$H$_\alpha$ coupling constant was expressed by the linear equation: RSE (kcal mol$^{-1}$) $= -34.7$ ($\pm$ 0.7) $+ 1.37$ ($\pm$ 0.05) $a$H$_\alpha$; $r = 0.997$.
(7) Welle, F.; Verevkin, S. P.; Keller, M.; Beckhaus, H.-D.; Rüchardt, C. *Chem. Ber.* **1994,** *127,* 697−710.
(8) (a) Schulze, R.; Beckhaus, H.-D.; Rüchardt, C. *Chem. Ber.* **1993,** *126,* 1031−1038. (b) Schulze, R.; Beckhaus, H.-D.; Rüchardt, C. *J. Prakt. Chem.* **1990,** *332,* 325−330.
(9) For a discussion of the captodative effect see: Sustmann, R.; Korth, H.-G. *Adv. Phys. Org. Chem.* **1990,** *26,* 131−178.
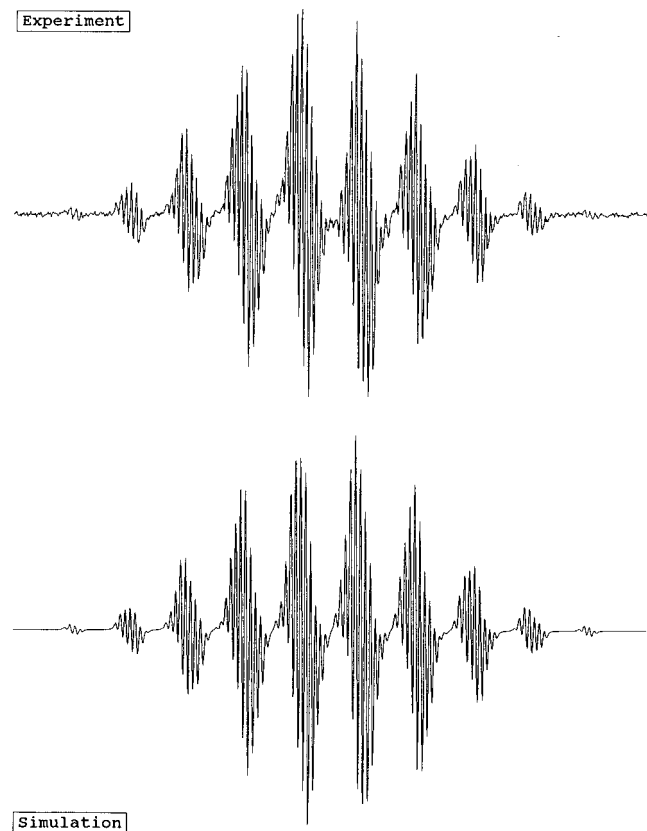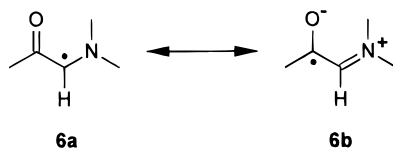
Experiment



Simulation

**Figure 1.** ESR spectrum of **8a** in diphenyl ether at 140 °C and its simulation (for parameters see Table 1).

These radicals, therefore, seemed particularly suited for testing the proposed relationship between RSE and spin density.



**6a** **6b**

### Results and Discussion

**ESR Spectra.** We generated the α-amino-α-carbonylmethyl radicals **8** by thermal dissociation of the dimers **7** in solution in the cavity of an ESR spectrometer. In this way, we detected[7] the ESR spectra of α-amino-α-carbonylmethyl radicals, for which only one example was mentioned previously in a footnote in the literature.[3d]



**7** **8**
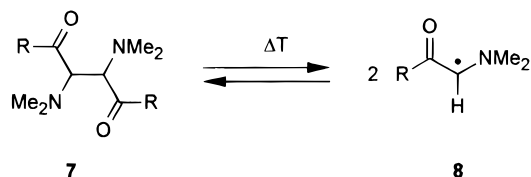
**a** R = PH, **b** R = [D$_5$]Ph, **c** R = 4-MeO-Ph, **d** = *t*Bu

Figure 1 shows the ESR spectrum of the radical **8a** in diphenyl ether at 140 °C.[7] Rigorous analysis of this spectrum by simulation showed our previous qualitative analysis[7] to be incorrect. The previous analysis of the ESR spectra of **8a** was based on the assumption of a low barrier to rotation around the •C−N bond, which would make the two *N*-methyl groups magnetically equivalent. But our recent results, especially the ESR spectra of the

**Table 1. ESR Coupling Constants[a] of the α-Amino-α-Carbonylmethyl Radicals 8**

| | $a$H$_\alpha$ | $a$N | $a$CH$_3$ | $a$CH$_3$ | $a$H$_{ortho}$ | $a$H$_{meta}$ | $a$H$_{para}$ | $a$H$_{tbut}$ |
|---|---|---|---|---|---|---|---|---|
| **8a** | 8.21 | 7.50 | 7.50 | 6.30 | 0.60 | 0.10 | 0.64 | |
| **8b** | 8.25 | 7.66 | 7.58 | 6.46 | 0.6[b] | 0.1[b] | 0.6[b] | |
| **8c** | 8.48 | 7.50 | 7.52 | 6.30 | 0.61 | 0.10 | | |
| **8d** | 9.21 | 7.68 | 7.81 | 6.35 | | | | 0.11 |

[a] In Gauss. [b] Calculated from the experimental deuterium coupling constants ($a$D$_{ortho}$ = 0.09, $a$D$_{meta}$ = 0.02, $a$D$_{para}$ = 0.09) using $g_N(D)/g_N(H) = 0.1535$.
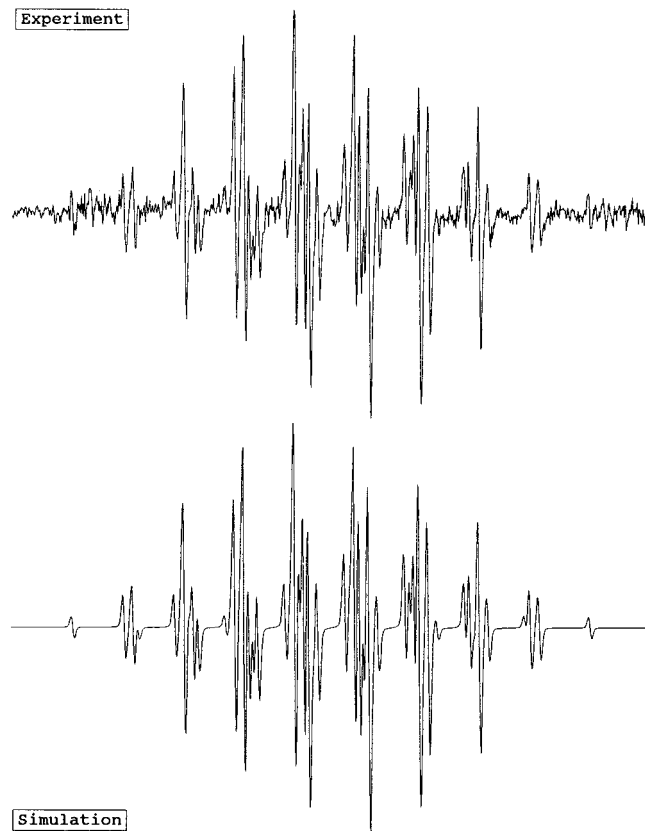
Experiment



Simulation

**Figure 2.** ESR spectrum of **8b** in diphenyl ether at 113 °C and its simulation (for parameters see Table 1).

radicals **8b** and **8d**, showed clearly that the two methyl groups have different coupling constants. Therefore, an appreciable rotational barrier exists that makes the two methyl groups magnetically nonequivalent. Table 1 contains the coupling constants for the radicals **8a−d**, which were obtained from the optimized simulation of the spectra (Figures 1−4). We also obtained the same ESR spectrum of the radical **8a** as shown in Figure 1 in benzonitrile and in the even more polar solvent *N*-methylacetamide. The polarity of the solvent, apparently, has no effect on the magnitude of the coupling constants.

Figures 2−4 show the ESR spectra of the radicals **8b−d**, respectively. The coupling constants of the aromatic deuterium atoms of **8b** were smaller than 0.1 G, which simplified the ESR spectrum and allowed a more reliable analysis of the coupling pattern of **8b**. The simplification of the spectrum of the radicals **8d** is caused by replacement of the phenyl group by a *tert*-butyl group (Figure 3). The protons of the *tert*-butyl group have coupling constants of only ca 0.1 G. The coupling constants of the α-amino-α-carbonylmethyl radicals **8**, which were determined from the spectra in Figure 1−4 by simulation, are recorded in Table 1.
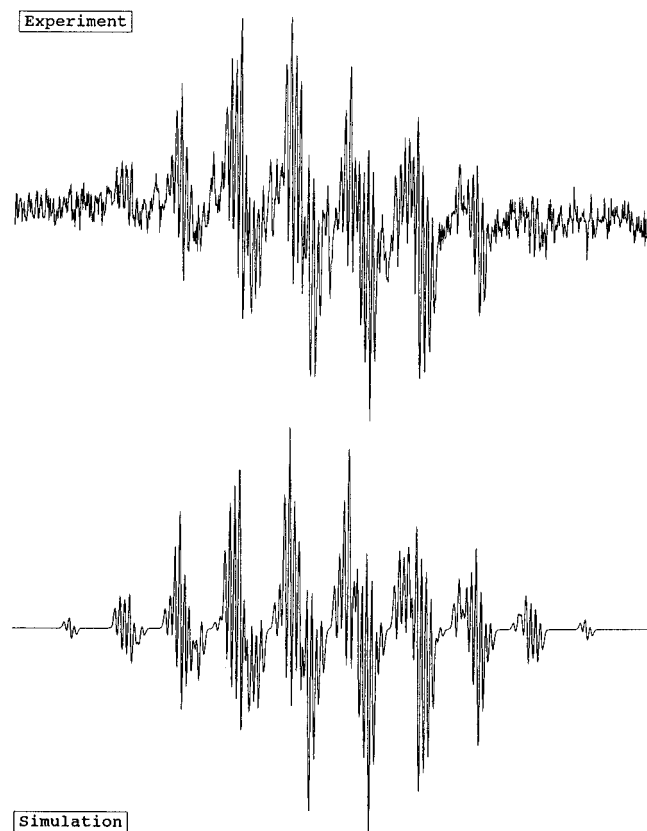
**Figure 3.** ESR spectrum of **8c** in diphenyl ether at 113 °C and its simulation (for parameters see Table 1).

The exceptionally small $aH_\alpha$ coupling constants of the aminocarbonylmethyl radicals **8a**−**d** are remarkable. This points to a small spin density at the radical center caused by a strong delocalization of the single electron in these radicals. The replacement of the phenyl group in **8a** or **8b** by a *tert*-butyl group in **8d** and, accordingly, the loss of the delocalization by the phenyl ring raises the $aH_\alpha$ coupling constant in **8d** by 1 G. The $aH_\alpha$ coupling constant in **8c** is moderately increased by comparison with **8a** (or **8b**) due to the electron-donating effect of the *p*-methoxy substituent in the phenyl group. This same substituent, apparently, changes the coupling constant $aH_{ortho}$ (see Table 1) even less.

**Bond Dissociation Enthalpies.** The equilibrium constants of C−C bond dissociations were determined, and from their temperature dependence the dissociation enthalpies $\Delta H_{diss}$ and the dissociation entropies $\Delta S_{diss}$ for the homolytic bond cleavage reactions of **7** were obtained. The absolute concentrations of **8** were determined from the intensity of the ESR signals at various temperatures (Table 2). The dissociation parameters of **7a** were previously published[7] together with equilibrium measurements in more polar solvents. It was shown there that the polarity of the solvent has no effect on the homolytic bond dissociation.

The small dissociation entropies $\Delta S_{diss}$ of **7** (Table 2) are remarkable and are in contrast to other equilibrium measurements.[10] The restricted internal rotation about

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(10) (a) Zamkanei, M.; Kaiser, J. H.; Birkhofer, H.; Beckhaus, H.-D.; Rüchardt, C. *Chem. Ber.* **1983**, *116*, 3216−3234. The dissociation parameters of, e.g., 2,3-dimethoxy-2,3-diphenylsuccinonitrile into α-cyano-α-methoxybenzyl radicals are as follows: $\Delta H_{diss} = 35.8 \pm 0.4$ kcal mol⁻¹ and $\Delta S_{diss} = 31.1 \pm 0.8$ cal mol⁻¹ K⁻¹. (b) For a collection of data see: Welle, F. M. Dissertation, University of Freiburg, Germany, 1996.
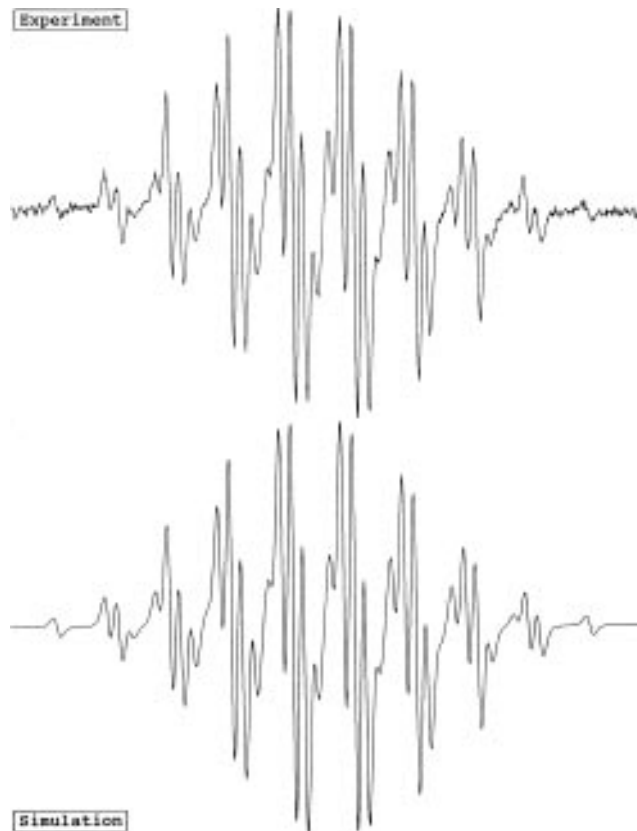


**Figure 4.** ESR spectrum of **8d** in diphenyl ether at 156 °C and its simulation (for parameters see Table 1).

**Table 2. Dissociation Parameters of the Homolytic Bond Cleavage Reaction of 7 from Radical-Dimer Equilibrium Measurements**[a]

| solvent (temp range (°C)) | $\Delta H_{diss}$ (kcal mol⁻¹) | $\Delta S_{diss}$ (cal mol⁻¹ K⁻¹) | $\Delta G_{diss}$[b] (kcal mol⁻¹) |
|---|---|---|---|
| **7a** diphenyl ether (71−124) | $24.7 \pm 0.3$[c] | $22.1 \pm 0.8$[c] | $16.5 \pm 0.3$[c] |
| **7c** diphenyl ether (88−163) | $20.3 \pm 0.4$ | $9.6 \pm 1.1$ | $16.7 \pm 0.4$ |
| **7d** diphenyl ether (95−169) | $19.6 \pm 0.3$ | $1.2 \pm 0.6$ | $19.2 \pm 0.3$ |

[a] Before the measurements the solutions of pure *meso*-diastereomers were heated to ca. 90 °C until the equilibrium mixture of *meso*/DL was reached. The ratios ∼30:70 show that the stability of the diastereomers is closely similar. [b] Extrapolated to 100 °C. *meso*/DL mixture. [c] Reference 7.

the •C−N bond in the radicals **8** (see below) by comparison with the radical precursor molecules **7** decreases the overall entropy of the dissociation process.

**Radical Stabilization Enthalpies.** In order to deduce the radical stabilization enthalpies RSE (**8**) from the equilibria of C−C bond dissociation we have to consider the influence of the substituents R on the stability of the reactants and their steric effect on the dissociation process.[2] The release of strain during dissociation ($D_S$) was taken as the difference of the strain enthalpies $H_S$ of the dimer R−R and of the corresponding two monomer molecules R−H. $D_S = H_S(RR) - 2H_S(RH)$. $H_s$ was calculated by using the MM2 force field.[2] The $D_S$ values obtained in this way (Table 3) are rather small. Steric effects on the thermolysis of tetraalkylethanes, the corresponding type of hydrocarbons, were measured previously[11] and were expressed in a linear correlation between $\Delta H^\ddagger$ and $D_S$ (eq 1).

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(11) Hellmann, G.; Hellmann, S.; Beckhaus, H.-D.; Rüchardt, C. *Chem. Ber.* **1982**, *115*, 3364−3383.

**Table 3. Radical Stabilization Enthalpies RSE of 8 from Equilibrium of C−C Bond Dissociation (in kcal mol⁻¹)**

|   | $\Delta H_{diss}(7)^a$ | $D_S(7)^b$ | $\Delta H^{\ddagger}$ (alkane)$^c$ | $\Delta$BDE(C-C) | RSE(8)$^d$ |
|---|---|---|---|---|---|
| **a** | 24.7 | 5.9 | 69.3 | 22.3 | 19.6 |
| **c** | 20.3 | 7.1 | 68.8 | 24.1 | 21.4 |
| **d** | 19.6 | 8.7 | 67.2 | 23.8 | 21.1 |

$^a$ From Table 2. $^b$ Release of strain enthalpy. $^c$ Activation enthalpy of a reference alkane of similar strain enthalpy $D_S$ (from eq 1). $^d$ Mean value 20.7 ± 1.0 kcal mol⁻¹.

$$\Delta H^{\ddagger}(\text{alkane}) =$$
$$73.8\ (\pm\ 2.6) - 0.76\ (\pm\ 0.08)D_S\ (\text{kcal mol}^{-1})\quad(1)$$

The difference $\Delta$BDE(C−C) in $\Delta H$ between the unsubstituted reference alkane and the experimental value of **7** corresponds to the substituent effect on the homolytic C−C bond dissociation $\Delta$BDE (eq 2).[2] In order to account

$$\Delta\text{BDE(C−C)} = {}^1\!/_2[\Delta H^{\ddagger}(\text{alkane},\ D_S = x) -$$
$$\Delta H_{diss}(\textbf{7},\ D_S = x)]\ (\text{kcal mol}^{-1})\quad(2)$$

$$\text{RSE} = \Delta\text{BDE(C−C)} - \Delta H_g\ (\text{kcal mol}^{-1})\quad(3)$$

for the effect of the substituents on the stability of the radical precursor molecules the geminal interaction ($\Delta H_g$ = 2.67 kcal mol⁻¹) of the amino and the carbonyl group, which we have deduced previously from thermochemical measurements,[7] must be substracted (eq 3). $\Delta H_g$ is defined as the influence of one or more substituents on the heat of formation, i.e., on the thermochemical increments[12] of the carbon to which the substituents are attached. Table 3 contains the RSEs of the radicals **8** deduced from the equilibrium between **8** and **7**.

The mean value of RSE(**8**), 20.7 ± 1.0 kcal mol⁻¹ (Table 3), is about 3 kcal mol⁻¹ higher than in our previous work,[7] which was based on kinetic and not on equilibrium measurements. This deviation is probably a systematic error in the kinetic measurements by a scavenger procedure using galvinoxyl and may be due to slow scavenging of the radicals **8** by the bulky persistent radical galvinoxyl. It was shown previously that captodative-substituted radicals are not kinetically stabilized.[13,14]

The synergistic substituent effect $H_{syn}$ (captodative effect) was calculated from the RSEs (see Table 5) of the *mono*substituted α-amino- and α-carbonylmethyl radicals by eq 4 to be 10.8 kcal mol⁻¹. The synergistic substituent

$$H_{syn} = \text{RSE}(\textbf{cd}) - [\text{RSE}(\textbf{c}) + \text{RSE}(\textbf{d})]\quad(4)$$

effect of the title radicals **8** is, therefore, larger than $H_{syn}$ of the α-amino-α-cyanomethyl radicals **4** (6.2 kcal mol⁻¹)[1] and α-amino-α-(ethoxycarbonyl)methyl radicals **5** (6.8 kcal mol⁻¹)[8] due to the stronger electron-acceptor power of CO vs CN or COOR.

Theoretical investigations have been published by the groups of Leroy[15] and of Pasto.[16] Both calculated the RSEs of disubstituted methyl radicals with computa-

tional methods on the basis of isodesmic reactions. Therefore, a quantitative comparison of our experimental results with the calculated RSEs of Leroy and Pasto is not possible. But the results of Leroy and Pasto are in qualitative agreement with our experimental results. In both cases the highest RSEs were calculated for the geminal substitution by an amino and a carbonyl group at the radical center, and in comparison to the monosubstituted radicals a synergistic stabilization was found for aminocarbonylmethyl radicals. Leroy and Pasto also found, in agreement with our work, that an amino-capto substitution pattern resulted always in a higher RSE than a hydroxy-capto substitution. Another experimental investigation to determine the RSE of α-amino-α-carbonyl radicals was done by the group of Bordwell.[17] Bordwell's methyl-based RSEs, which are based on $\Delta$BDEs solely, are also in good agreement with our results; e.g., they also found the largest RSE for α-amino-α-carbonyl radicals.

**Rotational Barrier.** We tried to determine the rotational barrier of the •C−N bond of the radical **8d** by recording the change in its ESR spectrum at various temperatures between 138 and 235 °C. At the highest applied temperature (235 °C) we could detect the ESR signal of the radical **8d** only for a few minutes, and no signal was obtained at higher temperatures. There was no change in the ESR spectra of **8d** between 138 and 235 °C. Therefore, no free rotation of the dimethylamino group occurs even at 235 °C. The comparison of this result with rotational barriers of radicals deduced from exchange-broadening effects in their ESR spectra as described in the literature (Table 4) allows an estimate of the lower limit of the rotational barrier in the α-amino-α-carbonylmethyl radicals **8** of at least 17 kcal mol⁻¹. In the transition state for the rotation of a •C−N bond, most of the conjugation between the amino group and the rest of the molecule should be lost. In particular, the contribution of the synergistic stabilization due to homo-amide-resonance is inhibited, and accordingly, the RSE of the perpendicular radicals **9b** must be decreased. It follows that the height of the rotational barrier is an indicator of this special conjugative stabilization of the radical.[18] Because the RSE of **9a** was found to be −20.7 kcal mol⁻¹ and in **9b** mainly the carbonyl resonance is left a rotational barrier of ≥17 kcal mol⁻¹ in Table 4 seems resonable.



(12) Rakus, K.; Verevkin, S. P.; Peng, W.-H.; Beckhaus, H.-D.; Rüchardt, C. *Liebigs Ann.* **1995**, 2059−2067.

(13) Korth, H.-G.; Sustmann, R.; Merenyi, R.; Viehe, H. G. *J. Chem. Soc. Perkin Trans. 2* **1983**, 67−74.
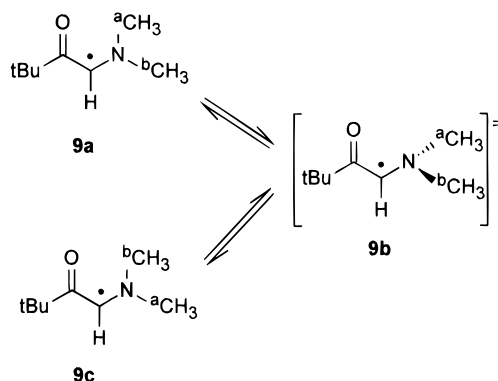
(14) Birkhofer, H.; Beckhaus, H.-D.; Rüchardt, C. In *Substituent effects in Radical Chemistry*; Viehe, H. G.; Janousek, Z.; Merenyi, R., Eds.; NATO ASI Series C 189; Reidel Publishing Company: Dordecht, 1986, p 199.

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(18) Korth, H.-G.; Trill, H.; Sustmann, R. *J. Am. Chem. Soc.* **1981**, *103*, 4483−4489.

**Table 4. Rotational Barriers of Substituted Methyl Radicals ·CHXY**

| X | Y | $E_a$ (kcal mol$^{-1}$)[a] | $T_c$[b] (°C) | ref |
|---|---|---|---|---|
| NH$_2$ | Me | 7.6 ± 0.4 | ca. −13 | 19 |
| MeCO | H | 9.4 ± 0.5 | 52 | 20 |
| NH$_2$ | C≡CH | 10.5 ± 1.2 | ca. 30 | 21 |
| NH$_2$ | CN | 11 ± 2 | ca. 60 | 22 |
| NH$_2$ | COOtBu | 14.9 ± 1.2 | ca. 200 | 23 |
| NMe$_2$ | COtBu | >17 | >235 | c |

[a] Rotational barrier. [b] Coalescence temperature. [c] This work.

**Table 5. Radical Stabilization Enthalpies RSE of Substituted Alkyl Radicals ·CHXY and the Corresponding $a$H$_\alpha$ Coupling Constants**

| | X | Y | RSE[a] (kcal mol$^{-1}$) | $a$H$_\alpha$ (G) |
|---|---|---|---|---|
| 1 | C | C | ≡ 0 | 21.94[25] |
| 2 | C | COOR | −2.8[2,26] | 20.3[27] |
| 3 | C | CN | −3.4[2,28] | 20.3[27] |
| 4 | C | NR$_2$ | (−3.9[7,29])[b] | 13.65[30] |
| 5 | C | OR | (−5.9[2,31])[b] | 13.7[32] |
| 6 | C | CO | −6.0[26] | 18.8[25] |
| 7 | CN | CN | −6.4[28,33] | 19.6[34] |
| 8 | CN | OR | −6.8[10a,31] | 17.4[35] |
| 9 | CO | CO | −8.1[36] | 17.9[34] |
| 10 | C | Ph | −8.4[2,37] | 16.3[32] |
| 11 | | allyl | −12.6[38] | 14.4[39] |
| 12 | Ph | Ph | −12.9[40] | 14.7[41] |
| 13 | CN | NR$_2$ | −12.9[1] | 14.9[22] |
| 14 | COOR | NR$_2$ | −14.4[8,42] | 11.8[42] |
| 15 | 10,10-dimethyl-9-hydroanthryl | | −15.2[43] | 13.4[38b] |
| 16 | | fluorenyl | −16.0[40] | 13.9[41] |
| 17 | | xanthyl | −18.1[43] | 12.7[38b] |
| 18 | CO | NR$_2$ | −20.7[c] | 8.5[c] |

[a] For the definition see eq 3; frequently in the references only the values not corrected for the substituent effects on the reactants are found. [b] See text. [c] This work.

Nonhebel, Walton, et al.[19] found a linear correlation between the C−H bond dissociation enthalpies $\Delta H_f°$(XYCH−H) of some substituted methanes and the rotational barriers in the radicals ·CHXY. From this correlation and from the C−H bond dissociation enthalpy of α-amino-α-carbonylmethanes[7] (76.8 kcal mol$^{-1}$) a rotational barrier of 27 kcal mol$^{-1}$ may be calculated for **8**. However, the top of the barrier corresponds to the perpendicular structure **9b** where the conjugation with the carbonyl group is retained. Therefore the rotational barrier of 27 kcal mol$^{-1}$ estimated from the Nonhebel− Walton correlation must be reduced by the RSE of an α-carbonylalkyl radical (−6.0 kcal mol$^{-1}$, Table 5). In this way, a barrier of ca. 21 kcal mol$^{-1}$ results for the rotation about the ·C−N bond in **8** in agreement with our estimate above.

**Correlation of the Radical Stabilization and the Coupling Constants.** The influence of delocalization of the single electron on the coupling constants turns out to be a general and almost quantitative one as predicted previously.[4] It becomes obvious in the correlation between the $a$H$_\alpha$ coupling constants of mono- and disubstituted radicals ·CHXY (Table 5) and their radical stabilization enthalpies RSE in Figure 5. All RSEs were determined by our group from activation enthalpies $\Delta H^{\ddagger}$ and/or dissociation enthalpies $\Delta H_{diss}$ of the homolytic bond cleavage reaction and their comparison with the corresponding dissociation enthalpies of alkanes of similar strain enthalpies. In all cases, the substituent effects on the reactants were eliminated in the manner discussed above (eq 3). This linear correlation can be expressed
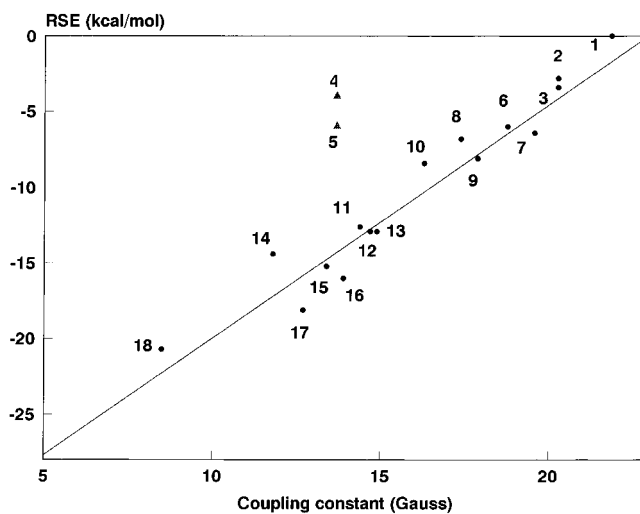


**Figure 5.** Correlation between the $a$H$_\alpha$ coupling constants of the ESR spectra of substituted alkyl radicals ·CHXY and the radical stabilization enthalpy RSE (for the numbers see Table 5).

by eq 5. Furthermore, the coefficients of the equation

$$\text{RSE (kcal mol}^{-1}) = -35.5 \ (\pm 1.7) + 1.57 \ (\pm 0.11)a\text{H}_\alpha; \quad r = 0.9400 \quad (5)$$

found by Arnold et al.[6] for a series of conjugated hydrocarbon radicals do not differ significantly. Stein et al.[5] found for a limited range of benzyl radicals that a change of 1 G in the benzylic coupling constant corresponds to 1.8 kcal mol$^{-1}$ change in the bond strength.

The correlation shows that a higher RSE leads to a smaller spin density at the radical center and therefore to a smaller $a$H$_\alpha$ coupling constant in the radicals. But the aminomethyl radical and the methoxymethyl radical (Table 5, entries 4 and 5, respectively) deviate from the correlation, because the heterosubstituted methoxy- and aminomethyl radicals are not planar.[30,32] Bent radical centers decrease the magnitude of the $a$H$_\alpha$ coupling constants, which cannot, therefore, be taken as a measure of the spin density at the radical center.[44] The small $a$H$_\alpha$ coupling constants in the methoxy- and aminomethyl radicals are, therefore, mainly a structure effect rather than a resonance effect. It is remarkable that the calculated $a$H$_\alpha$ coupling constant of ca. 19 Gauss[45] (INDO) of a hypothetical planar aminomethyl radical gave a better fit in our linear correlation (Figure 5). Presumably, the captodative substitution pattern of aminocarbonylmethyl radicals **8a−d** prefers a planar radical center, because the greatest possible delocalization of the single electron can be realized by the homoamide resonance (**6a,b**). All other radicals including planar radicals with twisted phenyl rings like the diphenylmethyl radicals (Table 5, entry 12) show the same good fit in the correlation. The observation of linear correlations is always satisfying, but there is no necessity for nature to prefer these over possible nonlinear correlations. Therefore, a slight curvature, which could give an even better correlation in Figure 5, is not unacceptable.

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## Conclusions

From the combination of kinetic and equilibrium data for C−C bond cleavage reactions, which generate the captodative radicals **3−5**, were obtained C−C bond dissociation enthalpies. By correction for steric acceleration and for substituent interaction enthalpies in the reactants radical stabilization enthalpies RSE were calculated (Table 5). They compare favorably with values that Leroy et al. and Pasto et al. derived from ab initio calculations. They are also in accord with the rotational barrier estimated from the ESR spectra for the radical **3**.

When the RSEs, obtained in this work, together with the RSEs for mono- and disubstituted radicals, which were obtained previously, are plotted vs the ESR coupling constants $a\mathrm{H}_\alpha$ a linear correlation is obtained (Figure 5). The reduction of the $a\mathrm{H}_\alpha$ coupling constants by 1 G corresponds to 1.57 kcal mol$^{-1}$ RSE. The result, that a synergistic stabilization is only found for α-amino-capto-substituted radicals **3−5**, is rationalized by the homo-amide resonance expressed in **6**.

## Experimental Section

**General Methods.** The analytical instruments employed have been described in a previous paper.[1]

***meso*-2,3-Bis(dimethylamino)-1,4-diphenylbutane-1,4-dione (*meso*-7a).** The synthesis was described previously:[7] mp 154−158 °C dec; $^1$H NMR $\delta$ 2.25 ppm (s, 12H, Me), 4.96 (s, 2H, CH), 7.45−7.61 (m, 6H, *m*-, *p*-Ph H), 8.00−8.08 (m, 4H, *o*-Ph H); $^{13}$C NMR $\delta$ 42.24 (NMe$_2$), 63.63 (CH), 128.38 (C-3), 128.78 (C-2), 133.04 (C-4), 139.02 (C-1), 197.50 (CO); EIMS $m/e$ 324 (M$^+$, <5), 219 (<5), 162 (M$^+$/2, 100), 114 (18), 105 (18), 77 (15), 58 (13), 42 (11). Anal. Calcd for C$_{20}$H$_{24}$N$_2$O$_2$: C, 74.05; H, 7.46; N, 8.63. Found: C, 73.99; H, 7.40; N, 8.56.

***meso*-2,3-Bis(dimethylamino)-1,4-di[D$_5$]phenylbutane-1,4-dione (*meso*-7b).** Dimethylamine (3.2 g, 71 mmol) was condensed in a reaction flask, and 30 mL of benzene was added. *trans*-1,4-Di[D$_5$]phenylbut-2-ene-1,4-dione (2.46 g, 10.0 mmol) was added followed by a solution of 2.53 g (10.0 mmol) of iodine in 25 mL of benzene. After 5 d the dimethylamine hydroiodide was filtered, and the solvent was removed. The residue was triturated with methanol, and the precipitate was isolated (0.77 g, 23%): mp 133 °C; $^1$H NMR $\delta$ 2.28 (s, 12H, NMe$_2$), 4.97 (s, 2H, CH); $^{13}$C NMR $\delta$ 135.17 (CH), 189.35 (CO). Anal. Calcd for C$_{20}$H$_{14}$D$_{10}$N$_2$O$_2$: C, 71.82; H/D, 10.25; N, 8.37. Found: C, 71.43; H, 4.13; N, 8.45.

***meso*-2,3-Bis(dimethylamino)-1,4-(4-methoxyphenyl)-butane-1,4-dione (*meso*-7c).** Dimethylamine (1.4 g, 31 mmol) was condensed in a reaction flask. Fifteen mL of benzene and then a solution of 1.46 g (5.75 mmol) of iodine in 20 mL of benzene were added, followed by 1.70 g (5.74 mmol) of 1,4-bis(4-methoxyphenyl)but-2-ene-1,4-dione. After 12 h, the dimethylamine hydroiodide was filtered, and the solvent was removed. The residue was recrystallized from dimethoxy-ethane (1.43 g, 65%): mp 128−132 °C; $^1$H NMR $\delta$ 2.26 (s, 12H, NMe$_2$), 3.90 (s, 6H, OMe), 4.93 (s, 2H, C*H*), 7.00 (d, $J$ = 8 Hz, 4H, *m*-Ph H), 8.06 (d, $J$ = 8, 4H, *o*-Ph H); $^{13}$C NMR $\delta$ 42.36 (NMe$_2$), 55.57 (OMe), 63.24 (CH), 113.99 (C-3), 130.83 (C-2), 132.25 (C-4), 163.61 (C-1), 181.08 (CO). Anal. Calcd for C$_{22}$H$_{28}$N$_2$O$_4$: C, 68.73; H, 7.34; N, 7.29. Found: C, 68.95; H, 7.40; N, 6.47.

***meso*-4,5-Bis(dimethylamino)-2,2,7,7-tetramethyloctane-3,6-dione (*meso*-7d).** Dimethylamine (2.5 g, 55.4 mmol) was condensed in a reaction flask, and 10 mL of benzene was added. Then, a solution of 1.17 g (4.61 mmol) of iodine in 25 mL of benzene and 0.90 g (4.59 mmol) of *trans*-2,2,7,7-tetramethyloct-4-ene-3,6-dione were added. After 4 d, the dimethylamine hydroiodide was filtered, and the solvent was removed. The residue was recrystallized from dimethoxy-ethane (420 mg, 32%): mp 106−108 °C; $^1$H NMR $\delta$ 1.12 (s, 18H, CMe$_3$), 2.26 (s, 12H, NMe$_2$), 4.14 (s, 2H, CH); $^{13}$C NMR

$\delta$ 26.59 (Me), 42.15 (NMe$_2$), 43.69 (CMe$_3$), 63.77 (CH), 213.78 (CO). Anal. Calcd for C$_{16}$H$_{32}$N$_2$O$_2$: C, 67.56; H, 11.34; N, 9.85. Found: C, 67.28; H, 11.49; N, 9.62.

***trans*-1,4-Di[D$_5$]phenylbut-2-ene-1,4-dione.** Fumaroyl chloride (8.41 g, 55.0 mmol) was dropped to a mixture of 10.28 g (122 mmol) of [D$_6$]benzene and 16.30 g (112 mmol) of aluminum trichloride in 60 mL of dichloromethane. After 1 h, the mixture was hydrolyzed, extracted with CH$_2$Cl$_2$, and dried (Na$_2$SO$_4$). The solvent was removed, and the solid residue was recrystallized from methanol (6.40 g, 47%): mp 137 °C; $^1$H NMR $\delta$ 8.02 (s, 2H, CH).

***trans*-1,4-Bis(4-methoxyphenyl)but-2-ene-1,4-dione** was prepared according to literature procedures:[46] mp 155−161 °C; $^1$H NMR $\delta$ 3.92 (s, 6H, OMe), 7.00 (d, $J$ = 8 Hz, 4H, *m*-Ph H), 8.04 (s, 2H, CH), 8.10 (d, $J$ = 8 Hz, 4H, *o*-Ph H).

***trans*-2,2,7,7-Tetramethyloct-4-ene-3,6-dione** was prepared according to literature procedures:[47] mp 95 °C; $^1$H NMR $\delta$ 1.20 (s, 18H, *t*-Bu), 7.43 (s, 2H, CH); $^{13}$C NMR $\delta$ 25.86 ppm (Me), 43.76 (CMe$_3$), 133.20 (CH), 204.52 (CO).

**ESR Spectra.** The radicals **8** were generated by homolytic bond dissociation of the dimers **7** in the cavity of the ESR spectrometer. A solution of **7** in diphenyl ether in an ESR tube were deoxygenated, placed in the cavity of the ESR spectrometer, and heated with a warmed gas flow. Recording conditions of the radical **8a**: $c$(**7a**), 179 mM; temperature, 140 °C; frequency, 9.31 GHz; centerfield, 3330 G; modulation, 0.2 G; time constant, 1 s; sweeptime, 3000 s; sweepwidth, 80 G; signal gain, 5 × 10$^5$; microwave power, 4 mW; simulation, (s = $^1/_2$, 1H, 8.21 G), (s = 1, 1N, 7.50 G), (s = $^1/_2$, 3H, 7.50 G), (s = $^1/_2$, 3H, 6.30 G), (s = $^1/_2$, 2H, 0.60 G), (s = $^1/_2$, 2H, 0.10 G), (s = $^1/_2$, 1H, 0.64 G); line width 0.19; line shape 100. **8b**: $c$(**7b**), 150 mM; temperature, 113 °C; frequency, 9.31 GHz; centerfield, 3324 G; modulation, 0.32 G; time constant, 0.5 s; sweeptime, 1000 s; sweepwidth, 80 G; signal gain, 6.3 × 10$^6$; microwave power, 4 mW; simulation, (s = $^1/_2$, 1H, 8.25 G), (s = 1, 1N, 7.66 G), (s = $^1/_2$, 3H, 7.58 G), (s = $^1/_2$, 3H, 6.46 G), (s = $^1/_2$, 2H, 0.09 G), (s = $^1/_2$, 1H, 0.09 G); line width, 0.18; line shape, 50. **8c**: $c$(**7c**), 153 mM; temperature, 113 °C; frequency, 9.34 GHz; centerfield, 3325 G; modulation, 0.25 G; time constant, 0.5 s; sweeptime, 3000 s; sweepwidth, 80 G; signal gain, 3.2 × 10$^6$; microwave power, 4 mW; simulation, (s = $^1/_2$, 1H, 8.48 G), (s = 1, 1N, 7.50 G), (s = $^1/_2$, 3H, 7.52 G), (s = $^1/_2$, 3H, 6.30 G), (s = $^1/_2$, 2H, 0.61 G), (s = $^1/_2$, 2H, 0.1 G); line width, 0.20; line shape, 74. **8d**: $c$(**7d**), 176 mM; temperature, 156 °C; frequency, 9.31 GHz; centerfield, 3325 G; modulation, 0.32 G; time constant, 0.5 s; sweeptime, 750 s; sweepwidth, 80 G; signal gain, 6.3 × 10$^5$; microwave power, 4 mW; simulation, (s = $^1/_2$, 1H, 9.21 G), (s = 1, 1N, 7.68 G), (s = $^1/_2$, 3H, 7.81 G), (s = $^1/_2$, 3H, 6.35 G), (s = $^1/_2$, 9H, 0.11 G); line width, 0.49; line shape, 71.

**Equilibrium Measurements.** Solutions of *meso*-**7** in diphenyl ether ($c$(**7c**) = 135 mM, $c$(**7d**) = 274 mM) were carefully deoxygenated, filled in ESR-tubes ($\varnothing$ 2.5 mm), and heated for at least 30 min to the mid temperature of the measurements for steric equilibration. It was then placed in one part of the ESR double cavity and heated with a warmed gas flow. In the second, unheated part of the cavity was placed a standard ("strong pitch"). In order to prevent internal fluctuations all intensities of the ESR signals were referred to this standard. The concentrations of the radicals **8** were deduced by measuring the peak to peak height of the over-modulated ESR signals (2 G) at each temperature. The expansion of the solvent was taken into account. The absolute concentrations $c$(**8**) were obtained from the peak to peak height in comparison to the intensity of a solution of the persistent diphenylpicrylhydrazyl (DPPH) of a known concentration, detected by the UV−vis extinction at 519 nm ($\epsilon$ 14 150 L mol$^{-1}$ K$^{-1}$).[48] It was shown that the peak to peak heights of the

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radicals **8** were proportional to the signal areas, which were obtained by double integration of the ESR spectra. The radical concentrations, which were deduced from the temperature-increasing series, were in the margin of error equal to those of the temperature-decreasing series, so that the equilibrium between the radicals and the dimers was reached in each case.

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**Table 6. Equilibrium Constants $K_{diss}$ of 7c−d from Radical−Dimer−Equilibrium Measurements**

| compd (solvent) | $T$ (°C) | $K_{diss}{}^a$ (mol L$^{-1}$) | compd (solvent) | T (°C) | $K_{diss}{}^a$ (mol L$^{-1}$) |
|---|---|---|---|---|---|
| **7c**[b] (diphenyl ether) | 88.3 | $4.99 \times 10^{-11}$ | **7d**[b] (diphenyl ether) | 94.5 | $4.18 \times 10^{-12}$ |
| | 94.5 | $1.04 \times 10^{-10}$ | | 100.8 | $6.60 \times 10^{-12}$ |
| | 100.8 | $1.76 \times 10^{-10}$ | | 107.0 | $9.52 \times 10^{-12}$ |
| | 107.0 | $2.78 \times 10^{-10}$ | | 113.2 | $1.41 \times 10^{-11}$ |
| | 113.2 | $4.73 \times 10^{-10}$ | | 119.4 | $2.60 \times 10^{-11}$ |
| | 119.4 | $6.69 \times 10^{-10}$ | | 125.6 | $3.56 \times 10^{-11}$ |
| | 125.6 | $1.06 \times 10^{-9}$ | | 131.9 | $4.85 \times 10^{-11}$ |
| | 131.9 | $1.41 \times 10^{-9}$ | | 138.1 | $7.08 \times 10^{-11}$ |
| | 138.1 | $2.07 \times 10^{-9}$ | | 144.3 | $1.11 \times 10^{-10}$ |
| | 144.3 | $2.85 \times 10^{-9}$ | | 150.5 | $1.38 \times 10^{-10}$ |
| | 150.5 | $4.03 \times 10^{-9}$ | | 156.7 | $1.98 \times 10^{-10}$ |
| | 156.7 | $5.16 \times 10^{-9}$ | | 162.9 | $2.81 \times 10^{-10}$ |
| | 162.9 | $7.69 \times 10^{-9}$ | | 169.2 | $3.54 \times 10^{-10}$ |

*a* Eq 6. *b* See footnote[a] of Table 2.

Table 6 contains the equilibrium constants $K_{diss}$ (eq 6) of **7c**−**d**. $K_{diss}$ of **7a** were published previously.[7] $\Delta H_{diss}$ and $\Delta S_{diss}$ were deduced from a linear correlation between ln $K_{diss}$ versus $T^{-1}$ (eq 7).

$$K_{diss} = c(\mathbf{8})^2/c(\mathbf{7}) - {}^1/_2 c(\mathbf{8}) \qquad (6)$$

$$\ln K_{diss} = \Delta H_{diss}/RT - \Delta S_{diss}/R \qquad (7)$$

**Force Field Calculations.** The calculations have been made using the MM2 program[49] for the global minimum of each structure. The strain enthalpies $H_s$ are calculated from SE by defining $H_s \equiv 0$ for the parent compound (dimethylamino)propanone (SE = 4.97 kcal/mol).

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