Factors Affecting the Stability and Equilibria of Free Radicals. 14.[1] Unexpected Spin Densities in 1-(Trifluoroacetyl)-2,2-diarylhydrazyl Revealed by ^{15}N Labeling

Ursula Bologa and Alexandru T. Balaban*

Department of Organic Chemistry, Polytechnic Institute, 76206 Bucharest, Roumania

Nicoleta Grecu and Nicolae Negoita

Institute of Nuclear and Engineering Physics, Bucharest, Roumania

Miron T. Caproiu

Center of Organic Chemistry—ICECHIM, 78100 Bucharest, Roumania

Robert I. Walter*

Department of Chemistry, University of Illinois at Chicago, Chicago, Illinois 60680

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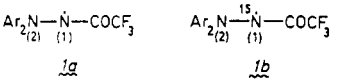
1-(Trifluoroacetyl)-2,2-bis(3,5-di-*tert*-butylphenyl)hydrazyl and its congener labeled at the dicoordinated 1-nitrogen atom with ^{15}N were prepared. ESR spectra of solutions of both compounds were recorded and hyperfine coupling constants determined by optimizing simulated spectra. Unlike all other 1,2,2-triarylhydrazyls which have been investigated, the hyperfine coupling constant for the dicoordinated nitrogen is lower (0.7 mT) than that for the tricoordinated nitrogen (1.0 mT) in this free radical. This striking result raises questions about the mode of trifluoroacetyl group participation in π electron delocalization.

Previous papers[1] in this series have reported a systematic investigation of persistent nitrogen-centered radicals designed to give well-resolved ESR spectra. Our research on these captodative nitrogen free radicals leads to the following conclusions. (I) Presence of both an acceptor (Acc) and a donor (Don) group at the radical center, together with steric shielding of the aminyl nitrogen, is responsible for the persistence of these radicals (Don–N–Acc).[2,3] (II) Molecular design of hydrazyl[4-6] and aminyl[7] radicals with the bis(3,5-di-*tert*-butylphenyl)amino group (Ar_2N) as a donor group eliminates hyperfine coupling with the meta protons. The corresponding hydrazyls and aminyls with donor diarylamino groups not substituted in the meta positions give incompletely resolved ESR spectra from which unambiguous hyperfine coupling constants (hfc's) cannot be extracted. In contrast, the ESR spectra of radicals with no meta protons easily give hfc's for all of the nitrogen and hydrogen atoms present. (III) Most of these newly synthesized hydrazyl radicals Ar_2N–N–Acc have two magnetically nonequivalent aromatic nuclei in the donor group at room temperature. Satisfactory simulated ESR spectra are obtained by assuming two sets of three equivalent aromatic hydrogen atoms; this requires that for each aromatic nucleus the two ortho and the one para proton have approximately equal hfc's. (IV) The carbonyl and the sulfonyl groups in 1-benzoyl-[6] and 1-(phenylsulfonyl)-2,2-diarylhydrazyl[4] radicals, respectively, can be said to "insulate" the phenyl rings from the π system over which the electron spin is delocalized. Operationally, this means only that the proton hyperfine coupling constants of the benzene ring protons in these acceptor groups must be less than the ESR line half-width and do not give rise to detectable hyperfine splittings. (V) Analysis of the temperature-dependent ESR spectra in toluene and *n*-pentane shows that the 1-benzoyl-2,2-diarylhydrazyl radical undergoes restricted rotation about the hydrazyl N–N bond. The activation energy calculated from the onset of rotation over the range −25 to +25° is about 32 kJ/mol.[6]

The present paper describes the synthesis and the ESR spectra and their analysis for two new captodative hydrazyl radicals **1a** and **1b**. In both radicals, the donor group is



1a *1b*

again the bis(3,5-di-*tert*-butylphenyl)amino group (Ar_2N), while the acceptor is the trifluoroacetyl group. The two radicals differ in the nitrogen isotope present at position N-1.

Experimental Section

IR spectra were recorded with a Zeiss-Jena UR-10 instrument, and ^1H NMR spectra with a Varian A-60A spectrometer. The ESR spectra were recorded with a JEOL ME-3X instrument at various temperatures over the range −60 to +80 °C, in toluene or pentane solution. Well-resolved spectra are obtained from +13 to +80 °C; below +13 °C the lines are broadened, presumably due to restricted rotation at the N–N bond. Above 80 °C, the spectra are less intense (but otherwise unchanged), due to decomposition to diamagnetic species. The experimental ESR spectra were simulated on a Hewlett-Packard 9830A computer with a program based on the modified Bloch equations.

Preparation of 1,1-Bis(3,5-di-*tert*-butylphenyl)hydrazine (2). This unsymmetrical hydrazine was prepared from toluene by a procedure based upon known steps; our current yields are

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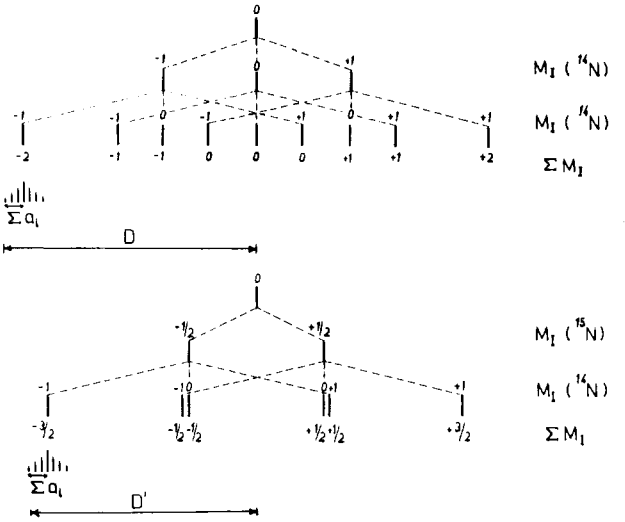

Figure 1. Hyperfine splitting diagrams for unlabeled (upper) and ^{15}N-labeled (lower) 2,2-diarylhydrazyls. In each diagram, the splitting by N-1 is given by the upper half of the pattern and that by N-2 by the lower half.

given in the statements which follow. Toluene was subjected to Friedel–Crafts alkylation with *tert*-butyl chloride in the presence of $AlCl_3$ at room temperature[8] to give the thermodynamically more stable 3,5-di-*tert*-butyltoluene, mp 31–32 °C (50% yield). Oxidation with $KMnO_4$ in pyridine[9] gave 3,5-di-*tert*-butylbenzoic acid, mp 173 °C (60% yield). Schmidt degradation of the azide[10] gave 3,5-di-*tert*-butylaniline, mp 53 °C (80% yield). The secondary amine was obtained (58% yield) by heating equimolar quantities of primary amine and its hydrochloride at 260 °C;[4] mp 117 °C. Nitrosation with $Na^{14}NO_2$ or with $Na^{15}NO_2$ gave the nitrosoamines, mp 108 °C (yields 98%). Reduction with Zn/HOAc at room temperature gave the hydrazines **2a** and **2b**, yields 85–90%. In all cases, the letter **a** designates the compound prepared with ^{14}N, while the letter **b** designates the same compound prepared with ^{15}N-1.

Trifluoracetylation of 2. The unsymmetrical diarylhydrazine **2** (410 mg, 1 mmol) was refluxed in benzene with 105 mg (0.5 mmol) of freshly distilled $(CF_3CO)_2O$. (Trifluoroacetyl)hydrazine (**3**) precipitated on standing overnight. Recrystallization from ethanol gave white crystals, mp 196 °C (yield 60%): ^{1}H NMR δ 1.29 (s, 36 H, *t*-Bu), 7.15 (d, 4 H, 2,6-H), 7.35 (t, 2 H, 4-H); IR (KBr) ν_{max} 3240 vs, 3060 m, 1720 vs, 1600 m, 1500 m, 1200 vs, 920 m, 760 m, 740 w, 710 m, 680 cm^{-1} m.

Anal. Calcd for $C_{24}H_{37}F_3N_2O$: C, 67.60; H, 8.69; N, 6.57. Found: C, 67.59; H, 8.70; N, 6.54.

Oxidation to Free Radicals 1a or 1b. Degassed toluene or pentane solutions of the (trifluoroacetyl)hydrazines were oxidized in a side chamber on the ESR tube with lead dioxide or with lead tetraacetate. The violet radical solutions were decanted from the inorganic salts into the ESR tube for study; these solutions are stable for at least 24 h at room temperature.

Results

The outside halves of the wing multiplets of the ESR spectra are identical for both the labeled and unlabeled radicals because the small hyperfine coupling constants due to the fluorine and hydrogen atoms do not change with the N-1 isotope. Differences appear in the spectra starting from the thirteenth line when counting lines inwards from either margin. These differences arise from the difference in nitrogen hyperfine interactions: two ^{14}N (M_I = 1) nuclei in radical **1a**, while **1b** has one ^{14}N and one ^{15}N (M_I = $^1/_2$) nucleus, with the latter known by the synthesis to be on nitrogen N-1. In the coupling diagrams of Figure 1, D is the distance from the center of the spectrum to a selected line in the outermost multiplet for radical **1a**, while D' is the distance from the center to the corresponding line for radical **1b**. Equations 1 and 2 give expressions for D and D'. Both include the term $\sum_i a_i$, which describes the fluorine and proton couplings that produce corresponding lines in the lateral multiplets. The terms in eq 1 are obvious from inspection of the upper diagram in Figure 1. Use of the multiplicities of lines produced by the nuclear spins M_I and the ratio 1.403 between gyromagnetic ratios of the ^{15}N and ^{14}N nuclei gives eq 2. One of the two

$$D = a(^{14}\text{N-1}) + a(^{14}\text{N-2}) + \sum_i a_i \quad (1)$$

$$D' = \tfrac{1}{2}a(^{15}\text{N-1}) + a(^{14}\text{N-2}) + \sum_i a_i = \tfrac{1}{2}(1.403a(^{14}\text{N-1})) + a(^{14}\text{N-2}) + \sum_i a_i \quad (2)$$

$$a(^{14}\text{N-1}) = (D - D')/0.299 \quad (3)$$

nitrogen hfc's (for **1a**) can be calculated by eq 3 from the values of D and D' measured directly on the experimental spectra and that for **1b** from the ratio 1.403. This gives the values $a(^{14}$N-1) = 0.670 mT and $a(^{15}$N-1) = 0.939 mT.

If the middle peaks of the outer multiplets can be identified in the experimental spectra, it is possible to determine D and D' without the last terms in eq 1 and 2 by measurement from these peaks to the centers of the spectra. This gives $a(^{14}$N-2) = 1.040 mT for both radicals. With these values and trial values for a(F) and a(H), the fit to the experimental spectra can be optimized by adjustment of these smaller hfc's in successive simulations. Results are shown in Figures 2 and 3; it can be seen that the agreement of simulated with experimental spectra is good. The small hyperfine constants are the same for both radicals: three equal values of 0.250 mT and six equal hyperfine constants of 0.195 mT for magnetically equivalent nuclei with M_I = $^1/_2$. We assign the smaller hfc's (a(H) = 0.195 mT) to the six aromatic protons and the larger (a(F) = 0.250 mT) to the three equivalent fluorine atoms. Thus in this case the carbonyl group does not "insulate" the trifluoroacetyl group from the N–N π system, as it appears to do in 1-benzoyl-2,2-diarylhydrazyl.[6] The a(H) value agrees fairly well with values found for the related radicals 1-(phenylsulfonyl)-2,2-diarylhydrazyl (a(H) = 0.181 mT)[4] and 1-benzoyl-2,2-diarylhydrazyl (a(H) = 0.162 mT).[6] The hfc's of the *tert*-butyl protons on the donor groups are smaller than the line half-width and thus unresolved, as has been found for other hydrazyl radicals which contain these groups.

Discussion

In all 1,2,2-triarylhydrazyl radicals with electron-acceptor groups bonded to the aromatic ring on N-1 thus far investigated, including 1-picryl-2,2-diphenylhydrazyl (DPPH),[11,12] the a(N-1) value is larger than a(N-2). The crystallographic bond angles in DPPH show that both N-1 and N-2 are close to planar and sp^2 hybridized.[13] We

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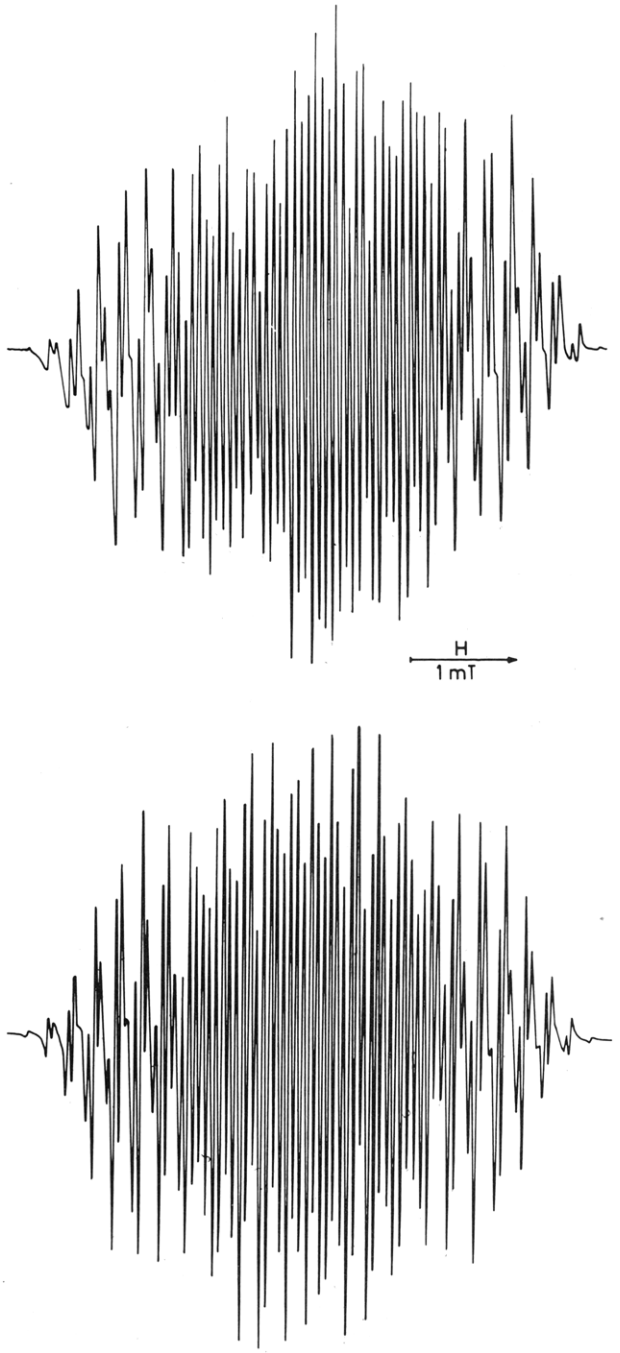

Figure 2. Upper plot: experimental first-derivative ESR spectrum of 1-(trifluoroacetyl)-2,2-diarylhydrazyl in toluene at 50 °C. Lower plot: simulated ESR spectrum.

assume for purposes of this discussion that spin density on N-2 is stabilized by delocalization of an unshared electron pair on N-1 to the acceptor groups on the aromatic ring bonded to that atom.

An acyl group on N-1 appears to be more effective in stabilizing structures with the unpaired electron on N-2 than is any acceptor-substituted aromatic ring. Thus, the ratio a(N-1)/a(N-2) is close to unity for the 1-benzoyl-2,2-diarylhydrazyl radical.[6] (However, this radical is much less persistent than DPPH.) In part, the effectiveness of acyl groups must be due to their smaller steric requirements compared to those of acceptor-substituted aromtic rings such as picryl. In DPPH, the space requirements of the picryl ring make it impossible for that ring to rotate

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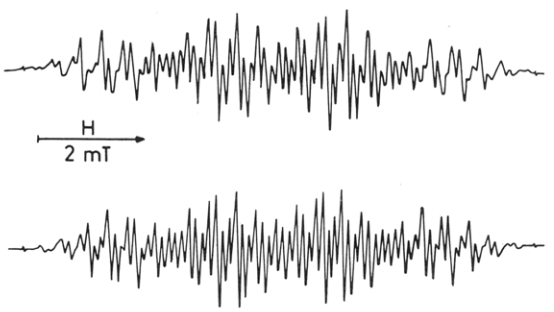
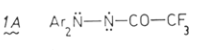
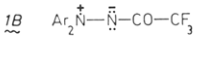
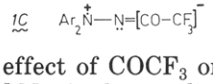


Figure 3. Upper trace: experimental first-derivative ESR spectrum of [1-^{15}N]-1-(trifluoroacetyl)-2,2-diarylhydrazyl in toluene at 60 °C. Lower trace: simulated ESR spectrum. This spectrum is much less intense than that in Figure 1, due to differences in concentration and instrument settings.

into the plane of the central N–N system with its directly bonded carbon atoms,[13] for optimum overlap of the two π systems. The trifluoroacetyl group on N-1 decreases the coupling constant ratio still further to 0.64 and thus is even more effective than benzoyl in stabilizing structures with the spin on N-2. In this case limiting structure **1A** contributes less than **1B** together with **1C** to the ground state of the π system. **1C** is intended to represent all structures in which an unshared electron pair and negative charge is delocalized from nitrogen N-1 to the carbonyl oxygen (or possibly fluorine).







This very large effect of $COCF_3$ on the relative spin densities at N-1 and N-2 in these radicals requires that an efficient electron pair delocalization mechanism be available to the $COCF_3$ group, so it can stabilize **1C** effectively. Trifluoroacetyl is recognized to be a strong inductive electron-withdrawing group, presumably through the σ-bond network. This is the accepted explanation for the ratio (factor of 10^4) of ionization constants for trifluoroacetic and acetic acids. These groups also differ drastically in their ability to stabilize hydrazyl radicals. Thus, the acetyl group fails to give a stable radical when 1-acetyl-2,2-diphenylhydrazine is shaken with PbO_2;[14] the dimeric tetrazane is formed instead. A few reactions have been shown to undergo rate enhancements by a factor of about 10^5 upon substitution with the $COCF_3$ group.[15] The Hammett σ parameter for m-$COCF_3$ has been estimated to be 0.65;[16] no experimental values are available. In any case, parameters evaluated for substituents on aliphatic systems would be more directly applicable here. Holtz has reviewed the evidence on fluorine hyperconjugation in the CF_3 group and concluded that this does not contribute significantly to substituent effects.[17] His conclusion is confirmed by more recent surveys of the problem.[18] A number of authors have invoked a "π inductive effect" to account for stabilization of structures like **1C**, but a recent

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review on the question concludes that this effect is small, if it operates at all.[19] Our intuition in this case calls for interpretation of the effects of the trifluoroacetyl group on spin distribution in terms of electron pair delocalization through the π system, but the reviews cited above appear to leave us with little basis for proposing this. We prefer to postpone further discussion of the problem until the results of our further studies and calculations on these systems become available.

Acknowledgment. We are indebted to Dr. H. Caldararu for recording reference ESR spectra of Fremy salt in water.

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Ethylene Biosynthesis. 8. Structural and Theoretical Studies

Michael C. Pirrung

Department of Chemistry, Stanford University, Stanford, California 94305

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The use of semiempirical molecular orbital methods for study of enzymatic reaction mechanisms has been further demonstrated by an investigation of ethylene biosynthesis. Calculations on the neutral forms of amino acids give excellent agreement to experiment. Large variances are found in the energies, however. An X-ray crystal structure of 1-aminocyclopropanecarboxylic acid was carried out to provide a comparison to the calculation. The structural data agree closely with what has previously been found for related molecules. The qualitative findings of the reaction pathway investigation include the following: that the radical SOMO's are carbon-centered; that ring-opening is irreversible; and that the second single-electron oxidation occurs to generate a zwitterion that fragments to ethylene and cyanoformic acid. This hitherto unknown species is calculated to be several kilocalories less stable than its constituents, CO_2 and HCN.

Because of ethylene's importance as a plant ripening hormone, study of its biosynthesis was rejuvenated by the 1979 demonstration that 1-aminocyclopropanecarboxylic acid (ACC, **1**) is its immediate biosynthetic precursor.[1] Research in this area has taken several forms. The feeding of isotopically labeled substrates,[2] the development of chemical models for ethylene production,[3] the evaluation of cell-free systems for ethylene biosynthesis,[4] and the study of substrate analogues have all been used.[5] Currently, the most defensible view of the mechanism of ethylene biosynthesis is that proposed in 1983: namely, the sequential single-electron-transfer mechanism[2a] pictured in Chart I. Some modifications have been made to this scheme to encompass specific oxidants such as are found in the chemical models,[4] and recently a partial kinetic mechanism has been proposed.[2g] While in vivo studies with (sometimes) labeled substrate analogues have given considerable information about the internal workings of the mechanism,[5ac] it seemed necessary to seriously examine the structures and reactivity of some of the intermediates that have previously been postulated. While the enzyme involved in ethylene biosynthesis will clearly have

Table I. Crystal and Data Parameters of 1

A. Crystal Parameters at $T = 25^{a,b}$

empirical formula $C_4H_7NO_2 \cdot {}^1/_2H_2O$

a = 6.2687 (4) Å	space Group $P1$
b = 8.5514 (11) Å	formula weight = 110.2 amu
c = 10.1467 (11) Å	Z = 4
α = 101.763 (10)°	d(calc) = 1.39 g cm^{-3}
β = 96.709 (8)°	μ(calc) = 1.08 cm^{-1}
γ = 94.057 (9)°	
V = 526.3 (2) Å^3	

size: 0.17 × 0.23 × 0.28 mm

B. Data Measurement Parameters[10]

radiation: Mo Kα (λ = 0.71073 Å)
monochromator highly oriented graphite (2θ = 12.2)
detector: crystal scintillation counter, with PHA
reflections measured: $+h, +/-k, +/-l$
2θ range: 3° → 55° scan type: θ–2θ
scan width: $\Delta\theta = 0.65 + 0.35 \tan\theta$
scan speed: 0.78 → 6.7 (θ, deg/min)
background: measured over 0.25(scan width) added to each end of the scan
vert. aperture = 3.0 mm horiz. aperture = 2.3 + 1.0 tan θ mm
no. of unique reflctns collected: 2407
intensity standards (412), (1, −4, −4), (1, −6, 5); measured every hour of X-ray exposure time. Over the data collection period no decrease in intensity was observed.
orientation: Three reflections were checked after every 200 measurements. Crystal orientation was redetermined if any of the reflections were offset by more than 0.1° from their predicted positions. Reorientation was not needed during data collection.

[a] Unit cell parameters and their esd's were derived by at least-squares fit to the setting angles of the unresolved Mo Kα components of 24 reflections with 2θ between 27° and 31°. [b] In this and all subsequent tables the esd's of all parameters are given in parentheses, after the least significant digit(s) of the reported value.

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