use of chiralcel OB.[20] These are the first reported optically active building blocks having fluorine and other labile groups directly attached to the chiral center.

Since the compounds **3–9** still possess a functionality to be used for further elaboration, including C–C bond formation, and are readily prepared from **1**,[22] these sequences have the potential of being versatile starting points for the construction of many monofluorinated compounds. Studies for application of the methodology are in progress.

Supplementary Material Available: Experimental details and spectral data for new compounds (11 pages). Ordering information is given on any current masthead page.

(20) Racemic **2d** was resolved on a Chiralcel OB column[21] by eluting with hexane/*i*-PrOH (9/1) to afford (+)-**2d**, $[\alpha]^{26}_D$ +42.2° (*c* 1.88, $CHCl_3$), and (−)-**2d**, $[\alpha]^{26}_D$ −42.8° (*c* 0.46 in $CHCl_3$), in 75% yields.

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(22) The analytical and spectral data (including ^{19}F NMR) for all new compounds were in accord with the structures proposed.

Yoshio Takeuchi,* Kazuhiro Nagata, Toru Koizumi

Faculty of Pharmaceutical Sciences
Toyama Medical & Pharmaceutical University
Sugitani 2630, Toyama 930-01, Japan

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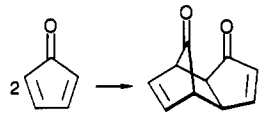
Decreased and Increased Solution Electron Affinities via the Replacement of a Single ^{12}C with ^{13}C

Summary: The reduction of a mixture of fluorenone and fluorenone with carbonyl-^{13}C with a very molar deficient quantity of sodium metal in HMPA leads to the formation of both anion radicals; ESR and ^{13}C NMR data show that the anion radical of the heavy isotopic isomer is present in a higher concentration than that of the light isotopic isomer. Similar experiments with benzophenone yield contrasting results.

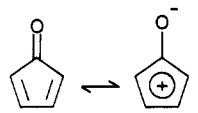
Sir: A ^{12}C–^{13}C isotope effect of unprecedented magnitude has been observed, which should lead to an enrichment procedure that is orders of magnitude more efficient than any used today.[1]

In a manner that is reminiscent of the situation with cyclobutadiene, neutral cyclopentadienone is very unstable toward dimerization[2] (reaction 1). This high reactivity



(1)

of cyclopentadienone may be seen as a reflection of the antiaromaticity contributed by the polarized structure, structure II in reaction 2, involving the cyclopentadienium



(2)

I II

(1) (a) Most of the world's ^{13}C is now produced by the cryogenic distillation of CO. The separation factor at the operating temperature is 1.008.[1b] (b) Lockhart, I. M. In *Isotopes: Essential Chemistry & Applications*; Elvidge, J. A., Jones, J. R., Eds.; The Chemical Society: London, 1979.

(2) Garbisch, E. W.; Sprecher, R. F. *J. Am. Chem. Soc.* **1969**, *91*, 6785.

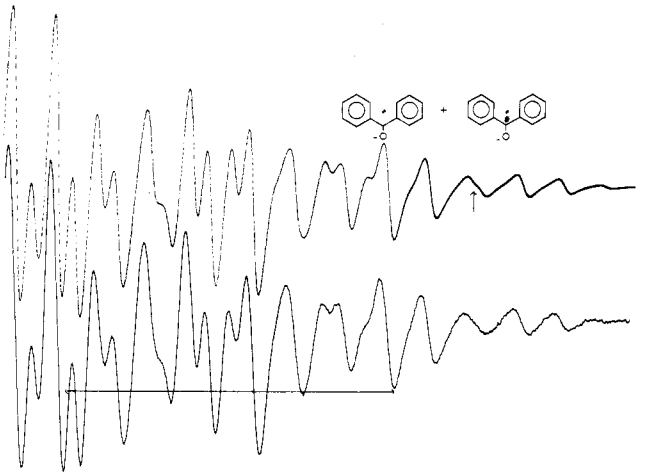


Figure 1. (Bottom) The first 22 lines of the ESR spectrum of a sample containing 0.089 M BZO + 0.10 M BZO-^{13}C reduced with a very small amount of sodium metal in HMPA. (Top) A computer simulation. This best simulation was obtained using a ratio of [BZO-$^{13}C^{\bullet-}$]/[BZO$^{\bullet-}$] = 0.65. The coupling constants used in the simulation are 3.49 (2 H), 2.40 (4 H), and 0.74 G (4 H). A 6.36-G (the arrow is 6.36 G long) splitting for the ^{13}C was added to the simulation of the spectrum for BZO-$^{13}C^{\bullet-}$. These parameters correspond to an equilibrium constant of 0.58. The vertical arrow indicates the first line in the BZO$^{\bullet-}$ spectrum. Continued reduction of this mixture results in dramatic increases in the relative intensity of the ESR signal for BZO-$^{13}C^{\bullet-}$. When the reduction of this same solution was continued until the number of moles of sodium was equal to that of the benzophenones, the best computer simulation was obtained by using a ratio of [BZO-$^{13}C^{\bullet-}$]/[BZO$^{\bullet-}$] = 1.1.

cation.[3] The addition of an extra electron results in some divergence from the 4n π character of the five-member ring system in cyclopentadienone, and the corresponding anion radical endures long enough for ESR observation at room temperature.[4] Very recent theoretical work on benzophenone[5] as well as the Raman and IR studies carried out upon the anion radicals and neutral molecules of tetracyanoethylene[6] and benzene[7] shows that the effect of an added electron is best characterized as resulting in a weakening of multiple bonds and a strengthening of single bonds coupled with a net reduction in bond order. Thus, the addition of an extra electron to a fully conjugated ketone to yield the ketyl should result in a general bond lengthening. From this it is predicted that the zero-point energy (ZPE) effects[8] would result in benzophenone (BZO) having a higher electron affinity than benzophenone substituted at the carbonyl position with a ^{13}C (BZO-^{13}C). On the other hand, a general bond order increase is to be expected when an electron is added to a substituted cyclopentadienone such as fluorenone (FLU = dibenzocyclopentadienone) for the reasons mentioned above.

A simple competition between BZO and BZO-^{13}C for an added electron can be staged by reducing a carefully prepared mixture of BZO and BZO-^{13}C with a very deficient amount of sodium metal. When this reaction is carried out in hexamethylphosphoramide (HMPA) the solvated ketyls are free of ion association,[9] and the equi-

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(7) Moore, J. C.; Thornton, C.; Collier, W. B.; Devlin, J. P. *J. Phys. Chem.* **1981**, *85*, 350.

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librium constant for reaction 3 is found to be well below unity. K_{eq} was determined by monitoring the relative

$$BZO^{\bullet-} + BZO\text{-}^{13}C \rightleftharpoons BZO + BZO\text{-}^{13}C^{\bullet-} \quad (3)$$

$$K_{eq} = 0.58 \pm 0.04 \text{ at } 25\ ^\circ C$$

intensities of the ESR signals for $BZO^{\bullet-}$ and $BZO\text{-}^{13}C^{\bullet-}$ using simulation techniques previously described[8] (the ^{13}C coupling constant for the free solvated ketyl in HMPA is 6.36 G) (Figure 1).

The reduction of FLU in HMPA with sodium metal also results in the formation of the free solvated anion radical ($A_{^{13}C}$ = 3.00 G). However, in strong contrast with the benzophenone system, the partial reduction of a 1:1 mixture of FLU and FLU-^{13}C results in a solution that contains much more of the isotopically heavy anion radical than of the light anion radical. Five separate experiments have shown that the equilibrium constant for the electron transfer from $FLU^{\bullet-}$ to FLU-^{13}C (reaction 4) is about five times greater than that for the transfer from $BZO^{\bullet-}$ to BZO-^{13}C.

$$FLU^{\bullet-} + FLU\text{-}^{13}C \rightleftharpoons FLU + FLU\text{-}^{13}C^{\bullet-} \quad (4)$$

$$K_{eq} = 2.74 \pm 0.34 \text{ at } 25\ ^\circ C$$

The addition of the extra electron to benzophenone results in a general bond loosening. Thus, the sum of all of the frequencies over all of the vibrational degrees of freedom ($3n - 6 = 66$) in benzophenone ($\sum \upsilon_{BZO}$) is larger than this same sum for the benzophenone ketyl ($\sum \upsilon_{BZO^{\bullet-}}$). Since the vibrational frequencies are inversely proportional to the square root of the reduced masses of the atoms involved, the difference in the two sums is greater for the ^{13}C-substituted system than it is for the ^{12}C system (eq 5). This difference is simply the difference in the solution electron affinities of BZO and BZO-^{13}C or the free energy of reaction 3.

$$\tfrac{1}{2}h([\textstyle\sum \upsilon_{BZO\text{-}^{13}C} - \sum \upsilon_{BZO\text{-}^{13}C^{\bullet-}}] - [\sum \upsilon_{BZO} - \sum \upsilon_{BZO^{\bullet-}}]) = \Delta G^\circ(\text{eq } 3) > 0 \quad (5)$$

For the case of FLU the situation is reversed. Since bonds are tightened upon electron addition, they are tightened more for ^{13}C-substituted material than for the FLU itself (eq 6). Unfortunately, present day quantum

$$\tfrac{1}{2}h([\textstyle\sum \upsilon_{FLU\text{-}^{13}C} - \sum \upsilon_{FLU\text{-}^{13}C^{\bullet-}}] - [\sum \upsilon_{FLU} - \sum \upsilon_{FLU^{\bullet-}}]) = \Delta G^\circ(\text{eq } 4) < 0 \quad (6)$$

mechanical calculations are not sufficiently advanced to allow quantitative predictions of the free energies described in eq 5 or 6. This is due, in part, to the fact that the resulting free energies reflect relatively small differences between large numbers.

What is described above is, by far, the largest thermodynamic isotope effect yet observed. Further, since the chemical properties of ketyls and ketones are very different, they can be easily separated allowing enrichment of the ^{13}C materials with an efficiency that is literally orders of magnitude greater than those of enrichment techniques used today. Enrichment of the ^{13}C carbonyl systems can be accomplished by harvesting either the neutral molecule or the anion radical as electrons are easy to put on or take off of these stable systems.[10] Indeed, we have demonstrated that enriched material can be obtained from these anion radical solutions.

The reduction of FLU containing ^{13}C in natural abundance in tetrahydrofuran (THF) with about $^1/_2$ of the stoichiometric amount of sodium metal followed by the removal of the solvent under reduced pressure leaves the solid ketone–ketyl mixture in the reaction apparatus. The ketone was selectively dissolved from the mixture in warm hexane. This recovered ketone was then sublimed, mixed with an equal number of moles of 3-pentanone, dissolved in 10 mL of $CDCl_3$, and submitted to ^{13}C NMR analysis. A control NMR sample was made with the untreated fluorenone. In each of five such experiments, it was clear that the ratio of the intensities of the FLU carbonyl carbon signal to the carbonyl carbon signal for 3-pentanone is less than the equivalent ratio based on the control sample. The two NMR spectra were obtained in exactly the same manner (same pulse delay, pulse width, number of pulses, etc.). When 50% of the FLU is reduced to the ketyl, the recovered ketone has a carbonyl ^{13}C content of 0.98 ± 0.04% as compared to 1.11% in the original ketone. The solid ketyl remaining after the removal of the ketone was then reacted with I_2 to oxidize it back to the ketone. This reconstituted ketone was sublimed and submitted to the same ^{13}C NMR analysis. It proved to be significantly enriched in carbonyl ^{13}C content (1.24 ± 0.05%). We have realized significant carbonyl ^{13}C enrichment from just a single pass of the ketone through the reduction–oxidation cycle.

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Registry No. Benzophenone, 119-61-9; fluorenone, 486-25-9; carbon-13, 14762-74-4.

Gerald R. Stevenson,* Richard C. Reiter
Wai-shun Au-Yeung, John A. Pescatore, Jr.
Randal D. Stevenson
Department of Chemistry
Illinois State University
Normal, Illinois 61761
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Synthetic 1-Methoxybenzo[*d*]naphtho[1,2-*b*]pyran-6-one C-Glycosides

Summary: The first synthetic benzo[*d*]naphtho[1,2-*b*]-pyran-6-one C-glycosides related to the antibiotics ravidomycin, the gilvocarcins (toromycin), and chrysomycin A and B (virenomycin) have been achieved by palladium-mediated coupling of furanoid glycals with 1-methoxy-4-(tri-*n*-butylstannyl)benzo[*d*]naphtho[1,2-*b*]pyran-6-one.

Sir: The procedure for synthesis of C-glycosides (C-nucleosides)[1] by palladium-mediated coupling of glycals with aryl or heterocyclic aglycon derivatives, which was developed in our laboratory,[2] was used to prepare the 1-methoxybenzo[*d*]naphtho[1,2-*b*]pyran-6-one furanosyl

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