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Mechanisms of Elimination Reactions. 37. Secondary β-Tritium Isotope Effects in Eliminations from 2-Arylethyl Derivatives[1,2]

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Abstract: In E2 reactions of $PhCH_2CH_2X$ containing tracer amounts of $PhCHTCH_2X$, secondary β-tritium isotope effects can be determined from the activity of reactant (R_o) and of the styrene product (isolated as the dibromide) at low extents of reaction ($R_s{}^0$): $(k_H/k_T)_{sec} = {}^1/_2 R_o/R_s{}^0$. Isotope effects determined in this manner at 50 °C (leaving group, base/solvent, $(k_H/k_T)_{sec}$): NMe_3, EtO^-/EtOH, 1.26 (40 °C); NMe_3, OH^-/30% Me_2SO, 1.24; NMe_3, OH^-40% Me_2SO, 1.25; NMe_3, OH^-/50% Me_2SO, 1.24; NMe_3 (p-ClC_6H_4 on β-carbon), EtO^-/EtOH, 1.28; SMe_2, EtO^-/EtOH, 1.16; SMe_2, OH^-/30% Me_2SO, 1.12; SMe_2, OH^-/40% Me_2SO, 1.14; SMe_2, OH^-/50% Me_2SO, 1.13; OTs, t-BuO^-/t-BuOH, 1.24; Br, EtO^-/EtOH, 1.11; Br, t-BuO^-/t-BuOH, 1.07. Errors ran 0.01–0.03. The larger of these values substantially exceed the equilibrium isotope effect (k_H/k_T = 1.17) calculated from the fractionation factors of Hartshorn and Shiner. Calculations showing that tunneling could be the cause of this discrepancy are quoted. The contribution of the secondary isotope effect to the measured k_H/k_D for substrates such as $ArCH_2CH_2X$ vs. $ArCD_2CH_2X$ is discussed.

The literature on primary hydrogen isotope effects in proton abstraction from carbon is extensive, but the secondary isotope effects incurred when a proton is removed from a carbon atom bearing one or two deuterons have been all but completely ignored. For example, we and others have determined isotope effects in E2 reactions by measuring the rates of elimination from $ArCH_2CH_2X$ and $ArCD_2CH_2X$ derivatives.[3] In these cases the observed k_H/k_D is actually the product of $(k_H/k_D)_{prim}$ and $(k_H/k_D)_{sec}$. Since conclusions are based mainly on *relative* k_H/k_D values, this practice would make no difference if $(k_H/k_D)_{sec}$ were small and approximately constant. The evidence we present below shows, however, that the secondary isotope effect is not usually small and is by no means constant with changing substrate and reaction conditions.

Another motive for studying the secondary isotope effect is the evidence it can give about bonding changes at the β-carbon atom between the reactant and the transition state. More specifically, the secondary isotope effect might be expected to depend upon the extent of rehybridization from sp^3 toward sp^2 in the transition state.[4,5] Such information is obviously of importance in the development of a comprehensive theory of transition-state structure in E2 and other proton-transfer reactions.

The earliest workers to measure β-secondary isotope effects in elimination reactions used tritiated substrates and essentially the same procedures as the present work. They studied base- and solvent-promoted decompositions of quaternary ammonium salts and found $(k_H/k_T)_{sec}$ values from 0.97 to 1.33.[6-9] These correspond to $(k_H/k_D)_{sec}$ values of 0.98–1.22.[10] The reactions were run under a variety of conditions and at a variety of temperatures, however, which makes it difficult to perceive any trends or draw any conclusions.

Another approach to β-secondary isotope effects in eliminations involves the use of a cyclic reactant stereospecifically labeled with deuterium in the β-position such that protium is lost in the elimination reaction. This has been done with reactions of *cis*-cyclohexyl-*2-d* tosylate **1**. Finley and Saunders[11] reported k_H/k_D values of 1.36 (ethoxide in ethanol) and 1.51 (*tert*-butoxide in *tert*-butyl alcohol) for base-promoted eliminations of **1**. They assumed a negligible isotope effect on elimination into the undeuterated branch of **1**, an assumption later shown to be incorrect.[12] Revised values that take this factor into account are 1.15 and 1.25, respectively.[12]

For our present work we chose the 2-arylethyl system because of the large amount of data already available on primary hydrogen and other isotope effects. A 2-arylethyl derivative tracer-labeled with tritium in the 2-position can undergo the following E2 reactions:

$$ArCH_2CH_2X + OR^- \xrightarrow{2k_1} ArCH{=}CH_2 + ROH + X^- \quad (1)$$

$$ArCHTCH_2X + OR^- \xrightarrow{k_2} ArCH{=}CH_2 + ROT + X^- \quad (2)$$

$$ArCHTCH_2X + OR^- \xrightarrow{k_3} ArCT{=}CH_2 + ROH + X^- \quad (3)$$

$(k_H/k_T)_{prim}$ is k_1/k_2, and $(k_H/k_T)_{sec}$ is k_1/k_3. To evaluate both of these ratios, two different experiments are needed.

In our previous work,[13] we determined the activity of original reactant (R_o) and of recovered reactant (R) after fraction of reaction F_H. Then[14]

$$\frac{2k_1}{k_2 + k_3} = \frac{\log (1 - F_H)}{\log [(1 - F_H)R/R_o]} \quad (4)$$

Usually k_1, $k_3 > k_2$, and the ratio in eq 4 is much more sensitive to k_1/k_3 than to k_1/k_2. Thus if k_1/k_2 can be determined separately, it can be combined with the ratio in eq 4 to give k_1/k_3 with good precision. If the activity of ROH (ROT) is determined at low (<5%) extents of reaction ($R^0{}_{ROH}$), then[14]

$$k_1/k_2 = \tfrac{1}{2}R_o/R^0{}_{ROH} \quad (5)$$

The qualitative basis of eq 5 can easily be understood as follows. While ROH is produced in both reactions 1 and 3, the relative amount produced in reaction 3 is negligible because $ArCHTCH_2X$

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Table I. Secondary Isotope Effects in E2 Reactions of $PhCHTCH_2X$ at 50 °C

leaving group, X	base/solvent	data pts., range[a]	k_1/k_3[b]	k_H/k_D[c]
NMe_3	$EtO^-/EtOH$	9, 14–35	1.259 ± 0.010[d]	1.17
NMe_3	$EtO^-/EtOH$		1.311 ± 0.014[d e]	1.21
NMe_3	OH^-/30% Me_2SO	9, 17–38	1.235 ± 0.016	1.16
NMe_3	OH^-/40% Me_2SO	5, 13–44	1.250 ± 0.023	1.17
NMe_3	OH^-/50% Me_2SO	7, 14–51	1.243 ± 0.031	1.16
NMe_3[f]	$EtO^-/EtOH$	9, 32–69	1.284 ± 0.030	1.19
SMe_2	$EtO^-/EtOH$	5, 20–73	1.157 ± 0.022	1.11
SMe	OH^-/30% Me_2SO	6, 16–46	1.119 ± 0.023	1.08
SMe_2	OH^-/40% Me_2SO	6, 30–64	1.144 ± 0.026	1.10
SMe_2	OH^-/50% Me_2SO	6, 20–50	1.134 ± 0.026	1.09
OTs	t-BuO^-/t-BuOH	6, 43–75	1.239 ± 0.023	1.16
Br	$EtO^-/EtOH$	6, 23–69	1.110 ± 0.024	1.08
Br	t-BuO^-/t-BuOH	5, 33–61	1.071 ± 0.026	1.05

[a] Number of separate experiments and the range of percent completion of reaction they cover, respectively. [b] Rate of proton removal from unlabeled substrate divided by rate of proton removal from labeled substrate. Error limits reflect combined standard deviations of R_o and R_p^0. [c] Calculated from $k_H/k_D = (k_1/k_3)^{1/1.44}$ (ref 10). [d] At 40 °C. [e] Data from ref 13. Obtained by combining $2k_1/(k_2 + k_3)$ and k_1/k_2. [f] For p-$ClC_6H_4CHTCH_2NMe_3^+$.

is present only in tracer amounts. Thus the activity of ROH is a measure of the relative amounts of ROH and ROT produced in reactions 1 and 2, and R_{ROH} is inversely related to k_1/k_2 (eq 5) under conditions where insufficient starting material has been consumed to change its isotopic composition appreciably.

We followed this procedure for the reaction of 2-phenylethyltrimethylammonium ion with ethoxide ion in ethanol at 40 °C and obtained $k_1/k_3 = 1.311 \pm 0.014$.[13] While the precision of this result is quite acceptable, we encountered difficulty in obtaining comparably precise results in other solvent-base systems. The probable cause of this difficulty is revealed by error analysis.[15] The ratio $2k_1/(k_2 + k_3)$ of eq 4 is quite sensitive to error in the fraction of reaction, F_H. An error of 1% in F_H becomes an error of 3–4% in the ratio at $F_H = 0.3 - 0.8$.

Fortunately, an alternate method of determining k_1/k_3 is available. If the activity of styrene isolated at low extents of reaction (R_s^0) is available, then[14]

$$k_1/k_3 = \tfrac{1}{2}R_o/R_s^0 \tag{6}$$

The qualitative basis of eq 6 can be understood in a way analogous to that for eq 5. Unlabeled styrene from reaction 2 can be neglected, so that the activity of the styrene reflects the relative amounts produced by reactions 1 and 3. In practice the styrene was isolated as the dibromide, which is more stable and easier to purify. Because small amounts were difficult to isolate, we isolated styrene dibromide at various values of F_H in separate experiments, and plotted R_s vs. F_H. Then R_s^0 is obtained by extrapolation to $F_H = 0$. In theory this extrapolation is not quite linear, especially when F_H values above 0.6–0.7 are included. In practice a linear least-squares fit was found to be more reliable than a quadratic least-squares fit, because the quadratic fit was too sensitive to random error in the data, sometimes showing curvature opposite that predicted by the full equation.[14]

The secondary tritium isotope effects determined in this way are shown in Table I. Entries 1 and 2 are for the same reaction; the first entry by the present method, and the second by our previous method of combining $2k_1/(k_2 + k_3)$ and k_1/k_2.[13] These two values differ from each other by somewhat more than the combined experimental errors. The first is probably more reliable, given the sensitivity of the second to errors in the fraction of reaction (see above).

We will first discuss the overall features of the results and their probable meaning in mechanistic terms. As noted above, a reasonable a priori hypothesis would be that k_1/k_3 reflects the extent to which the β-C–H (or C–D) bond has changed in the transition state from the sp^3 hybridization of the reactant toward the sp^2 hybridization of the product. By this line of reasoning, the maximum kinetic secondary isotope effect should closely approximate the equilibrium secondary isotope effect. Unfortunately the position of equilibrium for E2 reactions lies so far on the side of products that it is impossible to measure equilibrium constants. The equilibrium isotope effect can, however, be reliably estimated.

Hartshorn and Shiner[16,17] have calculated fractionation factors for isotopic exchange between small molecules for which force fields consistent with spectroscopic data could be obtained. The fractionation factors are tabulated with reference to a common reactant, acetylene, which permits the generation of a wide variety of other factors from the tabulated ones. In the present case, those for reactions 7 and 8 give the desired value for reaction 9. Thus

$$HC{\equiv}CD + CH_3CH_2CH_3 \rightleftharpoons HC{\equiv}CH + CH_3CHDCH_3 \tag{7}$$

$$HC{\equiv}CD + CH_2{=}CHCH_3 \rightleftharpoons HC{\equiv}CH + CH_2{=}CDCH_3 \tag{8}$$

$$CH_3CH_2CH_3 + CH_2{=}CDCH_3 \rightleftharpoons CH_3CHDCH_3 + CH_2{=}CHCH_3 \tag{9}$$

$K_9 = K_7/K_8 = 1.501/1.336 = 1.1235$ at 25 °C. Assuming exponential temperature dependence, K_9 becomes 1.117 at 40 °C and 1.113 at 50 °C, our two experimental temperatures. For tritium, the corresponding values[10] are 1.173 and 1.167, respectively.

Although the substrates of eq 9 are not identical with those of eq 1 and 3, it is hard to imagine that the isotope effects could be significantly different. The effect of solvent, of the temperature extrapolation, and of the conversion from deuterium to tritium isotope effects should not introduce more than a few percent error. It is thus apparent that at least six of the reactions in the table have secondary kinetic isotope effects larger than the corresponding equilibrium isotope effect. One would not expect them to be even as large if the kinetic isotope effect reflected only the extent of rehybridization at the β-carbon from sp^3 to sp^2 in the transition state. Primary deuterium kinetic isotope effects are known for most of these reactions,[18-20] and they all are large enough to suggest that the transition states are not extremely productlike. Complete rehybridization at the β-carbon in the transition state is therefore improbable.

The conclusion is inescapable that our secondary isotope effects cannot result solely from the effect of rehybridization on the forces restraining the motions of the nontransferred β-hydrogen. Secondary deuterium isotope effects larger than the equilibrium effects have also been observed in hydride-transfer reactions of $NAD^+/NADH$ systems, both enzymic[21,22] and nonenzymic.[23] These observations were tentatively explained as arising from a contribution of the nontransferred hydrogen to the motion along the reaction coordinate.[21,23] This suggestion was carried further by Huskey and Schowen,[24] who performed model calculations showing that such motion could lead to a substantial tunnel correction to the secondary isotope effect.

In work more closely related to the present results, Saunders[25] reported calculations of isotope effects in E2 reactions where the

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bending modes of the nontransferred β-hydrogen were coupled by means of off-diagonal **F** matrix elements to the C–H stretch of the transferred β-hydrogen. The maximum $(k_H/k_D)_{sec}$ values at 45 °C of his model 4 (1.18–1.20) correspond to $(k_H/k_T)_{sec}$ values of 1.27–1.30, comparable to the larger values found in the present work. Furthermore, the tunnel correction represents the major part of the effect; $(Q_{tH}/Q_{tD})_{sec}$ is 1.15 and 1.13, respectively, for $(k_H/k_D)_{sec}$ of 1.18 and 1.20. There is a nontunneling contribution of the motion along the reaction coordinate, because $\nu^{\ddagger}_{LH}/\nu^{\ddagger}_{LD} = 1.037$ and 1.039, respectively, but it is clearly insufficient to account for the magnitudes of the observed isotope effects. Saunders' calculations also make the interesting prediction that tunneling will noticeably steepen the temperature dependence of $(k_H/k_D)_{sec}$. We are attempting to test this prediction.

In summary, the calculations strongly suggest that tunneling is responsible when the kinetic secondary isotope effect exceeds the equilibrium secondary isotope effect. Furthermore, when tunneling is significant the kinetic secondary isotope effect does not reflect in any simple way the extent of rehybridization at the β-carbon in the transition state. Instead, it is largest when the hydrogen is 30–50% transferred to base in the transition state, because this is the region in which tunneling is most prominent.[25] The most important single contribution to the magnitude of the kinetic secondary isotope effect thus appears to be the extent to which motion of the nontransferred hydrogen contributes to the motion along the reaction coordinate, for it is this contribution which leads to the tunnel correction. In its absence, the tunnel correction is negligible.[25]

Returning to the data in the table, the major factor leading to differences in the secondary kinetic isotope effects is the nature of the leaving group, which runs $NMe_3 > OTs > SMe_2 > Br$. This is essentially the order of decreasing carbanion character in the transition state, although the relative order of OTs and SMe_2 is not unambiguously fixed by the Hammett ρ values and the primary deuterium isotope effects.[26]

In contrast to the leaving-group effect, the influence of solvent on the secondary isotope effects seems small or negligible. There are no trends clearly outside experimental error as the solvent/base system is changed for NMe_3, SMe_2, or Br. Likewise, substituting *p*-chlorophenyl for phenyl in the quaternary ammonium salt (entry 6 vs. entry 1) does not significantly increase the isotope effect. Evidently these changes do not have very much effect on the carbanion character of the transition state. Indeed, the extent to which transition-state structure changes as the composition of mixtures of water and dimethyl sulfoxide varies is not at all clear, for primary deuterium isotope effects suggest more marked changes than do Hammett ρ values or nitrogen isotope effects.[18] Whatever the change, it is insufficient to influence the secondary isotope effect. For the present, then, the secondary isotope effect appears to be a useful measure of carbanion or E1cB-like character in an E2 transition state, but it is not capable of making fine distinctions.

The final point that needs to be addressed is the meaning of these results for interpretation of isotope effects measured by determining the rates of elimination of $ArCH_2CH_2X$ and $ArCD_2CH_2X$. The last column of the table seems to suggest that these contain a variable contribution from a secondary isotopic effect of up to 1.19 at 45 °C. If this were so, then only substantial changes in the observed k_H/k_D could be safely ascribed to the primary isotope effect. Fortunately, the problem is of somewhat smaller magnitude than would seem the case from this simple analysis.

The isotope effects in the last line of the table are $k_H{}^H/k_H{}^D$, where the subscript represents the atom transferred, and the superscript the atom left behind. The secondary isotope effect that contributes to the overall $k_H{}^H/k_D{}^D$ effect is, however, $k_D{}^H/k_D{}^D$, as can be seen from $k_H{}^H/k_D{}^D = (k_H{}^H/k_D{}^H) \times (k_D{}^H/k_D{}^D)$. Because deuterium is being transferred instead of protium, the tunnel correction to the secondary isotope is expected to be less, making $k_D{}^H/k_D{}^D < k_H{}^H/k_H{}^D$.

How much less can be estimated from calculations like those reported earlier. Model 4 of ref 25 gives $k_H{}^H/k_H{}^D$ of 1.184 and 1.197, respectively, for n_{OH} values (extent of hydrogen transfer in the transition state) of 0.3 and 0.5 at 45 °C. The corresponding values of $k_D{}^H/k_D{}^D$ for the same model are 1.104 and 1.134. Thus the spread in $k_D{}^H/k_D{}^D$ should be correspondingly less than the spread in $k_H{}^H/k_H{}^D$, for it is the larger secondary effects (with more tunneling) that will be more attenuated when deuterium rather than protium is the atom transferred. The present results thus do not seem to demand major changes in past qualitative interpretations of $k_H{}^H/k_D{}^D$ values. In fact, correction of the observed isotope effects for $PhCD_2CH_2X$, where X = NMe_3, SMe_2, OTs, and Br, would have the effect of increasing the spread in $k_H{}^H/k_D{}^H$ compared to that in $k_H{}^H/k_D{}^D$, for the larger experimental values of the latter[26] tend to be associated with the smaller values of the secondary isotope effects in the table and vice-versa.

Experimental Section

Solvents. Distilled water was redistilled over potassium permanganate. Dimethyl sulfoxide was refluxed over calcium hybride under reduced pressure for 16 h and distilled. *tert*-Butyl alcohol was refluxed over potassium *tert*-butoxide for 12 h and distilled. Ethanol was refluxed over magnesium and a catalytic amount of iodine for 12 h and distilled. The alkoxide bases were prepared by dissolving the metal in the appropriate alcohol under nitrogen.

Phenylacetic-α-*t* Acid. Phenylacetic acid (0.184 mol) was refluxed with 40 mL of tritiated water (1 mCi/mL) and sodium hydroxide (0.25 mol) for 60 h. The mixture was cooled and enough 10% sulfuric acid added to make it just acidic. The mixture was filtered and the precipitate washed with water and dried to give an essentially quantitative yield of phenylacetic-α-*t* acid, 8.51 mCi/mol. Recrystallization from water gave material of mp 77 °C (lit.[27] mp 77 °C).

2-Phenylethanol-*2-t* was obtained by the reduction of 0.18 mol of phenylacetic-α-*t* acid with 0.24 mol of lithium aluminum hydride in ether, followed by the work-up procedure of Amundsen and Nelson.[28] Distillation gave 72% of 2-phenylethanol-*2-t*, bp 96–97 °C (10 mm) (lit.[29] bp 102–103 °C (15 mm)).

2-Phenylethyl-*2-t* Tosylate. Treatment of 2-phenylethanol-*2-t* with tosyl chloride in pyridine according to Tipson's procedure[30] gave 89% of 2-phenylethyl-*2-t* tosylate. Recrystallization from a mixture of ether and petroleum ether resulted in material of mp 35 °C (lit.[31] mp 35.5–36.6 °C).

(2-Phenylethyl-*2-t*)dimethylamine was prepared in 61% yield from dimethylamine and 2-phenylethyl-*2-t* tosylate by the procedure of Saunders and Edison,[19] bp 95 °C (10 mm) [lit.[19] bp 111 °C (20 mm)].

(2-Phenylethyl-*2-t*)trimethylammonium bromide was obtained by the reaction of 2-phenylethyl-*2-t*-dimethylamine (0.07 mol) with methyl bromide (0.14 mol) in nitromethane (100 mL) for 1 day at room temperature.[19,32] Removal of solvent under reduced pressure and recrystallization from ethanol–ether gave 85% of product, mp 239 °C (lit.[19] 238–239 °C).

[2-(*p*-Chlorophenyl)ethyl-*2-t*]trimethylammonium bromide was prepared from (*p*-chlorophenyl)acetic acid by utilizing the sequence of reactions described above for the unsubstituted compound. The product had mp 242–243 °C (lit.[33] mp 242.3–242.6 °C).

2-Phenylethyl-*2-t* Bromide. A solution of 0.07 mol of 2-phenylethyl-*2-t* tosylate and 0.14 mol of lithium bromide in 100 mL of dry acetone was allowed to stand at room temperature for 2 days. It was concentrated to 25 mL, 75 mL of water added, and the mixture extracted three times with ether. The combined extracts were dried over sodium sulfate, the ether was removed, and the residue was distilled to give 68% of 2-phenylethyl-*2-t* bromide, bp 95 °C (15 mm) (lit.[19] bp 94 °C (15 mm)).

Methyl 2-Phenylethyl-*2-t* sulfide was prepared in 70% yield from sodium methyl mercaptide and 2-phenylethyl-*2-t* tosylate by the proce-

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dure of Saunders and Edison,[19] bp 120 °C (75 mm) (lit.[19] 121 °C (75 mm)).

(2-Phenylethyl-*2-t*)dimethylsulfonium bromide was obtained in 75% yield by the reaction of 0.07 mol methyl 2-phenylethyl-*2-t* sulfide with 0.14 mol of methyl bromide in 100 mL of nitromethane for 12 h. The product was precipitated by the addition of ether and recrystallized from ethanol-ether, mp 136-137 °C (lit.[19] 136.5-137 °C).

Determination of Isotope Effects. Separate solutions of the substrate and the freshly prepared base were equilibrated for 1 h in a bath maintained within ±0.05 °C of the stated temperature. Sufficient base solution was added to the substrate solution to give final concentrations of 0.1-0.3 M and a reaction half life of 1-10 h. Aliquots of the reaction mixture were withdrawn periodically and diluted with ethanol for measuring the styrene absorbance. The molar absorbances of Saunders and Williams[34] were used in calculating the fraction of reaction. At the desired extent of reaction the reaction mixture was quenched by acidification with hydrochloric acid. The quenched reaction mixture was added to 25 mL of pentane, 100 mL of water was added, and the pentane layer separated. The aqueous layer was extracted five times with 10-mL portions of pentane, and the combined extracts washed with water and dried over anhydrous potassium carbonate. The pentane solution was treated with bromine until the color persisted, the pentane removed, water added to the residue, and the precipitated styrene dibromide recrystallized from methanol-water, mp 74 °C (lit.[35] 73 °C).

Counting of substrate and styrene dibromide was done on 10-50 mg samples in 15 mL of scintillation cocktail to ±0.2% precision using a Beckman LS-100C liquid scintillation counter. The cocktail consisted of 26.6 g of BuPBD and 0.4 g of Me_2POPOP in 4 L of toluene. For the sulfonium and ammonium salts, 20 mg of the salt sample was dissolved in 1 mL of distilled water and 15 mL of Beckman Ready-Solv HP added to give a clear solution. Quench corrections were determined by the external standard channels ratio method. Counting efficiencies were in the 35-45% range. Each vial was counted twice, and the activities used in calculating the isotope effects were based on 2-4 separate weighings of each sample.

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Reaction of α-(Phenylsulfinyl)acetonitrile with Aldehydes and Ketones to γ-Hydroxyalkenenitriles and Syntheses of Terpenoids

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Abstract: Reaction of α-(phenylsulfinyl)acetonitrile (**1**) with aldehydes or ketones in the presence of base directly affords γ-hydroxyalkenenitriles. Some terpenoids, such as dendrolasin (**9**), sirenin (**17**), and conjugated trienoic acid (3,7,11,15-tetramethylhexadeca-2,4,6,10,14-pentenoic acid (**24**)), were synthesized by employing the new C^2 unit homologation method.

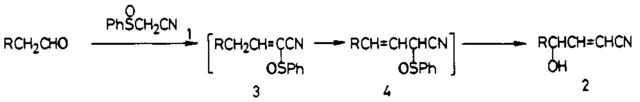
As part of our continuing interest in the reaction of organosulfur compounds, the reaction of the carbanion, derived from a sulfinyl-activated methylene compound, with electrophile became a matter of prime interest because of the versatility in functionalization of the products by the sulfinyl group.[1] Here, we describe one of our current developments on organosulfur-mediated synthetic method; the reaction of α-(phenylsulfinyl)acetonitrile (**1**) with aldehydes or ketones in the presence of base to give γ-hydroxyalkenenitriles.[2] We also report the syntheses of several terpenoids by use of the methodology.

Results and Discussion

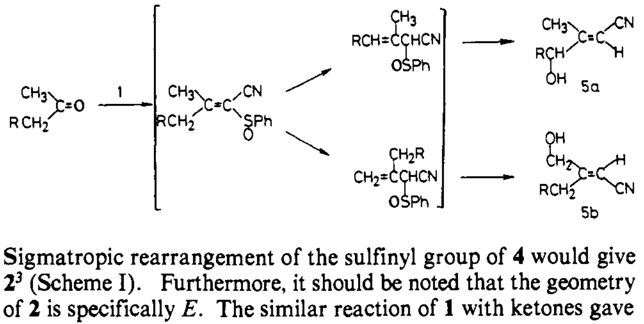
Reaction of α-(Phenylsulfinyl)acetonitrile (1) with Aldehydes or Ketones. α-(Phenylsulfinyl)acetonitrile (**1**) was readily obtained by treatment of α-chloroacetonitrile with thiophenol and sodium carbonate, followed by oxidation of the resulting α-(phenylthio)acetonitrile with sodium periodate or hydrogen peroxide.

As an interesting fact, we have found out that the room-temperature reaction of **1** with aldehydes and piperidine in methanol directly affords γ-hydroxyalkenenitriles **2** in quantitative yield without contamination of α-(phenylsulfinyl)alkenenitriles **3** or **4**. As a working hypothesis, it was assumed that **2** should be derived from **3**, which in turn is converted to **4** by double bond migration. Sigmatropic rearrangement of the sulfinyl group of **4** would give **2**[3] (Scheme I). Furthermore, it should be noted that the geometry of **2** is specifically *E*. The similar reaction of **1** with ketones gave the corresponding γ-hydroxyalkenenitrile. In particular, room-temperature treatment of **1** with methyl ketone such as octan-2-one and piperidine in methanol selectively gave 3-methyl-4-hydroxynon-2-enenitrile (**5a**) in 84% yield. In contrast, the re-

Scheme I



Scheme II



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