gation from the lactyl methyl group of the coenzyme adduct.

Jordan, O'Leary, Deniro, and their co-workers have investigated ^{13}C isotope effects (for the carboxyl group of pyruvate) in pyruvate decarboxylase.[8,9] These groups have concluded that decarboxylation is partially rate determining (for V_{max}) in the enzymic reaction. The intrinsic ^{13}C effect for decarboxylation as measured by Jordan in a model system is roughly a measure of the extent of rehybridization in the transition state along the coordinate corresponding to the breaking of the C1–C2 bond of pyruvate and is not complicated by the rate at which the product is released.[29] The isotope effect increases by about 5% in going from the reaction in water to 30% aqueous ethanol, indicative of a slightly more extensive change of structure in arriving at the transition state in the presence of the cosolvent. Since the reaction is faster in the cosolvent, this result indicates that the transtion state becomes more productlike in the cosolvent. This is a reasonable conclusion since it is assumed that the reaction involves conversion of a polar molecule to a less polar intermediate.[1,28] In our study, the β-deuterium isotope effect provides information which is complementary to that from the ^{13}C isotope effect. Although the decarboxylation is faster and the transition state is more productlike, there is little change in the amount of stabilization provided by the β-substituent. The type of stabilization offered by the β-substituents is localized and does not compete with that offered by the solvent. Thus, the two types of isotope effects are consistent with a transition state which is more advanced in the more reactive system but which has a fixed amount of hyperconjugative interaction.

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Conclusion

It is clear that β-deuterium isotope effects are significant in the decarboxylation and elimination reactions of lactylthiamin and are directly comparable to the values obtained with pyruvate decarboxylase from yeast. The magnitude of the isotope effect is consistent with considerable stabilization by negative hyperconjugation. This stabilization is unaffected by the factors which accelerate the reaction in a nonpolar solvent. Therefore, the value we measure can be used confidently for the intrinsic isotope effect on the decarboxylation step in enzymic reactions. Since lactylthiamin diphosphate is a central intermediate in other enzymes (pyruvate oxidase, pyruvate dehydrogenase, acetolactate synthetase), the effects on V_{max} by pyruvic-d_3 acid will provide information on differences in the electronic demand of the transition states. For example, the coupling of oxidation to decarboxylation should drastically reduce the need for negative hyperconjugation by the adjacent methyl group. Further enzymic and nonenzymic studies will extend the utility of the methodology that our study has established.

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Communications to the Editor

Acetylenic Esters. Preparation and Characterization of Hitherto Unknown Alkynyl Carboxylate, RC≡COCOR′, and Alkynyl Phosphate, RC≡COPO(OR′)$_2$, Esters

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Carboxylate **1** as well as phosphate **2** esters are important chemical[2] and biochemical[3] functionalities. Likewise, acetylenes are well-known and useful molecules.[4] Despite the ubiquitous nature and importance of esters[2] and the diversity of functionalized acetylenes,[4] alkynyl carboxylate **3** and alkynyl phosphate **4** esters are hitherto unknown. Recently we reported[5] the first synthesis of the related alkynyl sulfonate esters **5** and in this paper we wish to disclose our preliminary results for the preparation and characterization of **3** and **4**.

$$\underset{\mathbf{1}}{RC(=O)OR} \qquad \underset{\mathbf{2}}{ROP(=O)(OR')_2} \qquad \underset{\mathbf{3}}{RC{\equiv}COC(=O)R'}$$

$$\underset{\mathbf{4}}{RC{\equiv}COP(=O)(OR')_2} \qquad \underset{\mathbf{5}}{RC{\equiv}COSO_2Ar}$$

The synthesis of representative alkynyl carboxylate and phosphate esters is outlined in Scheme I. Anion exchange, under strictly anhydrous conditions,[6] of known[5,7] alkynylphenyliodonium tosylates **6** with benzoate and diethyl phosphate ions gives the respective, new, iodonium salts **7** and **9**. Because of the considerable nucleophilicity of benzoate anions, the iodonium carboxylate salts **7** could not be isolated, with decomposition to the desired carboxylate esters **8** and iodobenzene being complete during anion exchange. In contrast, the iodonium phosphate salt **9a** could be isolated as a stable, crystalline salt in 80% yield, while **9b** could not be obtained pure. However, in solution, e.g., in CH_2Cl_2 at room temperature, these iodonium phosphate salts, **9**, smoothly and quantitatively convert to the desired phosphate ester **10** and the expected iodobenzene in 12–36 h.

We believe that the conversion of iodonium salts **7** and **9** to their respective esters **8** and **10**, with concomitant loss of C_6H_5I, is a result of a "nucleophilic acetylenic displacement" via an addition–elimination process as shown in Scheme II. Similar processes, namely, nucleophilic vinylic substitutions[8] via addition–elimination pathway, are well-known but are less common in acetylene chemistry.[9] This reaction is clearly dependent upon

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(6) These exchanges were carried out on pretreated, anion-saturated, Amberlyst A-26, dried at 100 °C for 48 h, by passage of the tosylate salts **6** through the appropriate column, analogous to column chromatography using anhydrous CH_2Cl_2 as solvent. Separation of the respective esters from iodobenzene was accomplished by silica gel column chromatography using CH_2Cl_2 (CH_2Cl_2/hexanes) as eluent.
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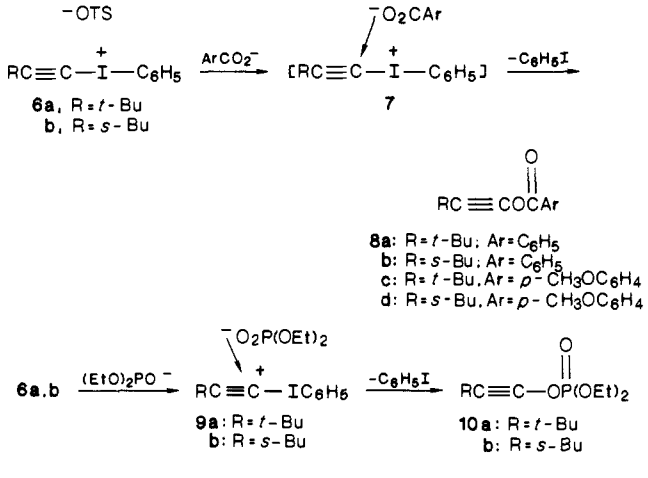
Table I. Spectral Data for Alkynyl Esters **8** and **10** and Iodonium Salt **9a**

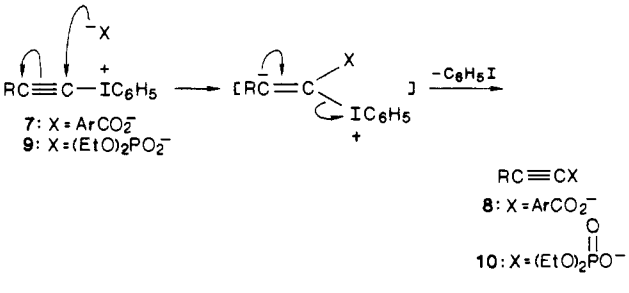
compound	IR (neat), cm^{-1}	^1H NMR ($CDCl_3$, δ)	^{13}C NMR ($CDCl_3$, δ)	EI-mass spectrum, *m/e* [%]
8a	2965–2900 (vs), 2865 (s) CH, 2285 (s), 2255 (sh) C≡C, 1770 (vs) C=O, 1250–1230 (vs), 1125 (vs) C—O	8.15–7.95 (m, 2 H, arene H), 7.75–7.35 (m, 3 H, arene H), 1.32 (s, 9 H, *t*-Bu)[a]	163.20 (CO), 134.81, 130.51, 129.13, 126.93 (arene C), 79.09 (C-1), 59.95 (C-2), 31.55 [(CH_3)$_3$], 27.15 (CMe_3)[a]	202 [3.5] M^+, 201 [9.6] M^+ – H, 146 [3.7] M^+ – =<, 105 [100] PhCO, 77 [3.0] Ph
8b	2965 (vs), 2930 (s), 2875 (s) CH, 2275 (s) C≡C, 1770 (vs) C=O, 1250–1210 (vs), 1000–980 (vs) C=O	8.05–7.85 (m, 2 H, arene H), 7.55–7.20 (m, 3 H, arene H), 2.47 (m, 1 H, H-3), 1.48 (m, 2 H, H-4), 1.19 (d, $^3J_{H,H}$ = 7.0 Hz, 3 H, H-6), 1.02 (t, $^3J_{H,H}$ = 7.0 Hz, 3 H, H-5)	163.05 (CO), 134.38, 130.24, 128.70, 126.57 (arene C), 79.82 (C-1), 55.92 (C-2), 30.21, 26.62, 21.07, 11.82 (C-3 to C-6)	203 [1.3], 202 [0.2] M^+, 201 [0.5] M^+ – H, 105 [100] PhCO, 77 [6.5] Ph
8c	2960–2900 (vs), 2860 (s) CH, 2283 (s), 2250 (sh) C≡C, 1765 (vs) C=O, 1270–1240 (vs), 1128 (vs), 980 (vs) C—O	7.40 (AA′XX′ system, J = 9.5 Hz, δ_A 7.92, δ_x 6.88, each 2 H, arene H), 3.80 (s, 3 H, OMe) 1.26 (s, 9 H, *t*-Bu)	164.41 (MeO*C*), 162.42 (CO), 132.41, 118.61, 114.02 (arene C), 78.80 (C-1), 59.30 (C-2), 55.13 (OCH_3), 31.41 [(CH_3)$_3$], 26.77 (CMe_3)	232 [2.0] M^+, 201 [2.1] M^+ – OMe, 176 [1.7] M^+ – =<, 135 [100] *p*-MeOPhCO, 107 [1.4] *p*-MeOPh
8d	2965 (vs), 2930 nvs), 2875 (s) CH, 2275 (s) C≡C, 1760 (vs) C=O, 1265–1240 (vs), 1215 (s), 1165 (s), 1015 (s) C—O	7.40 (AA′XX′ system, J = 9.5 Hz, δ_A 7.92, δ_x 6.88, each 2 H, arene H), 3.82 (s, 3 H, OMe), 2.48 (m, 1 H, H-3), 1.50 (m, 2 H, H-4), 1.20 (d, $^3J_{H,H}$ = 7.0 Hz, 3 H, H-6), 1.03 (t, $^3J_{H,H}$ = 7.0 Hz, 3 H, H-5)	164.38 (MeO*C*), 162.47 (CO), 132.37, 118.50, 113.96 (arene C), 79.96 (C-1), 55.46 (OCH_3), 55.30 (C-2), 30.17, 26.53, 21.04, 11.76 (C-3 to C-6)	232 [1.1] M^+, 201 [0.2] M^+ – OMe, 135 [100] *p*-MeOPhCO, 107 [0.9] *p*-MeOPh
9a	2970 (s), 2925 (m), 2895 (m) CH, 2165 (m), 2135 (w) C≡C, 1438 (m), 1245–1220 (vs) PO, 1060–1040 (vs) POEt[b]	8.25–8.07 (m, 2 H, arene H), 7.50–7.20 (m, 3 H, arene H), 3.85 (quin, $^3J_{P,H}$ = $^3J_{H,H}$ = 7.5 Hz, 4 H, $POCH_2$), 1.25 (s, 9 H, *t*-Bu), 1.23 (t, $^3J_{H,H}$ = 7.5 Hz, 6 H, $POCCH_3$)	132.65, 130.98, 130.63, 120.41 (arene C), 113.26 (C-2), 61.00 (d, $^2J_{P,C}$ = 5 Hz, $POCH_2$), 35.28 (C-1), 30.11 [(CH_3)$_3$], 29.10 (CMe_3), 16.31 (d, $^3J_{P,C}$ = 9 Hz, $POCCH_3$)	
10a	2965–2910 (vs), 2865 (s) CH, 2290 (sh), 2270 (s) C≡C, 1475 (s), 1305–1280 (vs) PO, 1060–1010 (vs) POEt	4.23 (dq, $^3J_{H,H}$ = 7.5, $^3J_{P,H}$ = 8.5 Hz, 4 H, $POCH_2$), 1.36 (dt, $^3J_{H,H}$ = 7.5, $^4J_{P,H}$ = 1.3 Hz, 6 H, $POCCH_3$), 1.17 (s, 9 H, *t*-Bu)	79.07 (d, $^2J_{P,C}$ = 11.4 Hz, C-1), 65.84 (d, $^2J_{P,C}$ = 6 Hz, $POCH_2$), 47.75 (d, $^3J_{P,C}$ = 6 Hz, C-2), 31.24 [(CH_3)$_3$], 26.18 CMe_3, 15.98 (d, $^3J_{P,C}$ = 6 Hz, $POCCH_3$)	234 [15] M^+, 137 [23.9] $PO(OEt)_2$, 109 [100] OPOH (OEt), 97 [46.7] *t*-BuC≡C—O
10b	2965, 2930 (vs), 2875 (s) CH, 2280 (vs) C≡C, 1455 (s), 1305–1280 (vs) PO, 1230 (vs), 1060–1010 (vs) POEt	4.28 (dq, $^3J_{H,H}$ = 7.5, $^3J_{P,H}$ = 8.5 Hz, 4 H, $POCH_2$), 2.34 (m, 1 H, H-3), 1.40 (m, 2 H, H-4 and dt, $^3J_{H,H}$ = 7.5, $^4J_{P,H}$ = 1.3 Hz, 6 H, $POCCH_3$), 1.13 (d, $^3J_{H,H}$ = 7.0 Hz, 3 H, H-6), 0.97 (t, $^3J_{H,H}$ = 7.5 Hz, 3 H, H-5)	80.16 (d, $^2J_{P,C}$ = 9 Hz, C-1), 65.88 (d, $^2J_{P,C}$ = 6 Hz, $POCH_2$), 43.86 (d, $^3J_{P,C}$ = 6 Hz, C-2), 30.09, 26.01, 20.98, 11.71 (C-3 to C-6), 16.02 (d, $^3J_{P,C}$ = 8 Hz, $POCCH_3$)	234 [4.9] M^+, 177 [25.2] M^+ – *s*-Bu, 137 [20.7] $PO(OEt)_2$, 109 [100] OPOH(OEt), 97 [74.5] *s*-BuC≡CO

[a] In CD_2Cl_2. [b] KBr pellet.

Scheme I



Scheme II



the nucleophilicity of the anion and greatly facilitated by the loss of neutral C_6H_5I from the iodonium salt, analogous to the loss of N_2 from a diazonium ion.

Iodonium salt **9a**, as well as alkynyl benzoates **8** and alkynyl phosphates **10**, was characterized[10] by spectral means as summarized in Table I. Specifically, iodonium phosphates **9** show characteristic IR absorptions at 2135–2165 cm^{-1} and the ^1H and ^{13}C NMR spectrum of **9a** is in accord with its structure. The infrared spectra of benzoates **8** display an intense acetylenic absorption at 2275–2285 cm^{-1} and a very strong carbonyl stretch at 1760–1770 cm^{-1}. Whereas, the phosphate esters **10** show very strong acetylenic absorptions at 2270–2280 cm^{-1} and the characteristic P=O absorption at 1280–1305 cm^{-1}. The ^1H and ^{13}C NMR data are in accord with expectations. In particular, the ^{13}C NMR spectra show the expected, characteristic chemical shifts for the two acetylenic carbons including the familiar 40–60 ppm

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(10) All new compounds reported gave satisfactory elemental (C, H. **9a**: C,H,P,I) analyses.

upfield shift of the β-C's (C-2), unique for all known, related, oxygen-functionalized acetylenes ($C_\beta \equiv C_\alpha OR$: R = SO_2Ar;[5] R = Si≡;[11] R = Alkyl[12]). The mass spectra show appropriate molecular ions and fragmentation patterns. Moreover, phosphate esters **10** were independently prepared by the $(EtO)_2P(O)Cl$ trapping of the recently reported[14] alkynolate ions $(RC\equiv CO)^-Li^+$ and found to be identical in all respects. Hence, there is no doubt about the identity of these novel acetylenic esters.

Alkynyl benzoates **8** are reasonably stable, colorless liquids that decompose upon standing at room temperature over several days. The alkynyl diethyl phosphate esters **10** are also colorless liquids and even more stable than the corresponding benzoates but do undergo slow decomposition (over several weeks) upon standing neat at room temperature.

In summary, we have developed a simple, mild, general means of preparing novel alkynyl carboxylate and phosphate esters from readily available tricoordinate iodonium tosylate precursors. These new acetylenic esters have characteristic spectral properties consistent with their proposed structures and are isolable, reasonably stable, colorless liquids. The full scope of this methodology, along with the chemistry of these new esters, including the potential uses as possible enzyme-activated inhibitors,[14] are under active study and will be the subject of future papers.

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Registry No. 6a, 92473-47-7; **6b**, 92473-43-3; **8a**, 104911-35-5; **8b**, 104911-36-6; **8c**, 104911-37-7; **8d**, 104911-38-8; **9a**, 104911-39-9; **10a**, 104911-40-2; **10b**, 104911-41-3; $C_6H_5CO_2^-$, 766-76-7; p-$CH_3C_6H_4CO_2^-$, 5118-31-0; $(EtO)_2PO_2^-$, 48042-47-3.

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Oxygen Activation by Metalloporphyrins Related to Peroxidase and Cytochrome P-450. Direct Observation of the O–O Bond Cleavage Step

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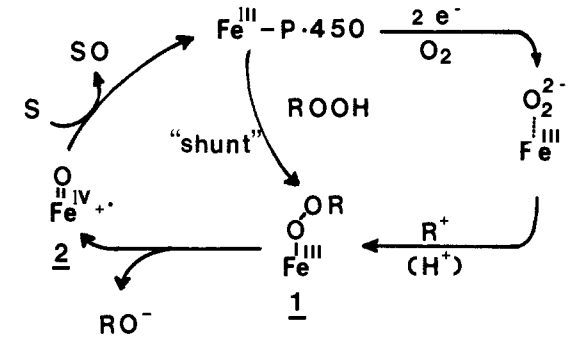
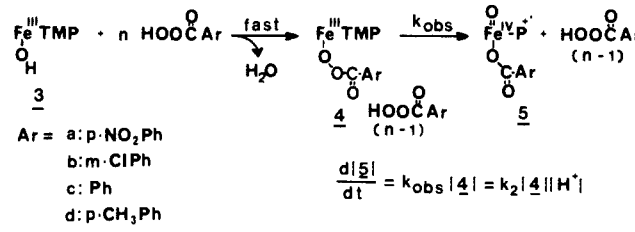
The reductive activation and transfer of dioxygen mediated by cytochrome P-450 is unique among the hemoproteins.[1] That two one-electron reductions are required for each cycle with dioxygen, and the apparent circumvention of this multistep process with exogenous peroxides,[2] has suggested the intermediacy of peroxyiron(III) species such as **1**.[1c,3] Heterolytic cleavage of the O–O bond in such a complex could give rise to an oxoiron(IV) porphyrin cation radical (**2**) (Scheme I). Support for this view derives from the oxidation of synthetic iron(III) porphyrins to

Scheme I



Scheme II



reactive complexes analogous to **2**.[4]

We describe here the formation of an (acylperoxy)iron(III) porphyrin complex analogous to **1** and its reaction to form an oxoiron(IV) porphyrin cation radical (**2**); the first direct observation of an iron-catalyzed O–O bond cleavage.

Attempts to follow the kinetics of the oxidation of chloro(5,10,15,20-tetramesitylporphyrinato)iron(III) [Fe^{III}(TMP)(Cl)] with peroxy acids at low temperature led to complicated sigmoidal rate profiles. By contrast the oxidation of *hydroxo* Fe(III)TMP was well behaved. Thus, Fe^{III}TMP(OH)[5] (**3**) was found to react with *p*-nitroperoxybenzoic acid instantaneously at −46 °C (1.48×10^{-5} M in CH_2Cl_2) to produce an intermediate (**4a**) which exhibited a visible spectrum typical of a five-coordinate, high-spin Fe(III) complex (λ_{max} 419, 508, 666, and 682 nm in CH_2Cl_2).[6] However, **4a** was not stable even under these mild conditions, and it decomposed to a bright green species **5a** (Figure 1). Intermediate **5a** was characterized as an oxoiron(IV) porphyrin cation radical (**2**) by comparison with authentic sample prepared by the reaction of Fe^{III}(TMP)(Cl) with mCPBA in CH_2Cl_2 at −50 °C.[7] Furthermore, **5a** reacted with added cyclooctene whereas $[Fe^{III}(TMP^{\bullet})(ClO_4)]^+$ was stable under these conditions. The similarity of the visible spectrum of **4a** to that of Fe^{III}(TMP)(*p*-nitrobenzoate),[8] its facile conversion at low temperature to **5a**, and the 1.2:1 stoichiometry of its formation from Fe^{III}(TMP)(OH) are consistnet with an Fe^{III}(TMP)(peroxybenzoate) formulation. The corresponding (acylperoxy)*manganese*(III) porphyrin complex has been formed in the same way.[9]

The conversion of **4** to **5** could be monitored conveniently by observing changes in the visible spectrum upon the addition of at least 1.2 equiv of peroxy acid. Lines A and B in Figure 1 represent the time-dependent changes of absorbances at 418 and 363 nm upon the addition of 3 equiv of *p*-nitroperoxybenzoic acid to a CH_2Cl_2 solution of **3** (1.48×10^{-5} M) at −46 °C. Several clear isosbestic points were evident. The formation of **5** was found

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