has been an important method for the study of carbonium ion reactions[2] but has been applied less frequently to reactions leading to the formation of free radicals.[3]

The substrates chosen for study were the *tert*-butyl peresters of aliphatic acids completely substituted at the 2 position with alkyl groups that were expected to lead directly to the corresponding tertiary radicals in one-step unimolecular decompositions. Ionizations leading to the corresponding carbonium ions were known to involve sizable rate accelerations attributable to steric effects. The peresters, their rates of decomposition, and the derived activation parameters are reported in Table I.[4] Rates for the corresponding carbonium ion reactions are presented in Table II for comparison, along with data for formation of radicals from azo compounds.[3f]

The rates for the peresters provide compelling confirmation of the mechanism in eq 1 for the reaction of peresters where the group R is a tertiary radical. The rapid rate of *tert*-butyl triisopropylperacetate relative to the less crowded peresters must be largely due to relief of steric strain on fragmentation of the molecule. The inductive effects may make a small contribution to the observed rate increases, but the nonlinear dependence of the rates on the degree of β substitution shows this is a minor factor. Models suggest negligible steric interaction between the developing alkyl radical and the departing *tert*-butoxy group. Therefore the possible sources of the steric acceleration are (a) rehybridization at the quaternary carbon to relieve "B" strain between the isopropyl groups, and (b) relief of "F" strain between the alkyl groups and the carboxy group by stretching the connecting bond. The latter effect is analogous to the steric repulsion of the leaving group which has been proposed to contribute to steric acceleration of carbonium ion formation.[2,5] It is not yet possible to define the specific contribution of these two effects to the observed rate increase, but it is clear the bond between R and the CO_2 group in 1 must be stretched for either effect to operate.

Comparison of the radical and carbonium ion forming reactions (Table II) shows that all are accelerated by bulky groups. The total effects are largest in the azo compounds, but these have two bulky groups present which each contribute to the observed acceleration.

Another conceivable contributing factor to these effects is a polar enhancement of reactivity due to rehybridization.[1d] As we have discussed for carbonium ion formation,[2] bulky groups may increase the p character in the carbon orbital bonded to the leaving group, and this rehybridization may enhance the formation of electron-deficient transition states. Since the generation of carbon free radicals is often assisted by the same electronic factors which favor carbonium ions,[1] strain-induced rehybridization would equally likely be a factor in perester decompositions as in ionization reactions.

Other effects which have been ascribed to steric factors in free radical formation include small increases in the rate of formation of secondary alkyl radicals from peresters[3a] and reactivity increases of 15–30 in hydrogen abstraction reactions where relief of back-strain is possible.[3b] Bulky ortho substituents also increase the rates of decomposition of *tert*-butyl perbenzoates.[3e] It is becoming clear that the atom rehybridizations and bond stretchings which lead to steric acceleration can make substantial net contributions to observed reactivities in formation of both radicals and carbonium ions from various types of precursors.

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(4) The peresters were all oils prepared from the known corresponding acids by conversion to the acid chlorides and reaction with sodium *tert*-butyl hydroperoxide in ether with purification by column chromatography. The new peresters gave the expected spectral parameters [**2:** ir (CCl_4) 1752 cm^{-1}; nmr (CCl_4) δ 1.03 (d, J = 7 Hz, 18, $\mathbf{Me_2}$CH), 1.28 (s, 9, *t*-Bu), 2.40 (heptet, J = 7 Hz, 3, $Me_2\mathbf{CH}$). **3:** ir (CCl_4) 1752 cm^{-1}; nmr (CCl_4) δ 0.95 (s, 9, *t*-$BuCH_2$), 1.23 (6, s, Me_2), 1.28 (s, 9, *t*-BuO), 1.60 (s, 2, CH_2). **4:** ir (CCl_4) 1765 cm^{-1}; nmr (CCl_4) δ 0.97 (s, 9, *t*-BuC), 1.14 (s, 6, Me_2), 1.28 (s, 9, *t*-BuO)]. Acceptable elemental analyses were obtained for **3** and **4,** but that for **2** (*Anal.* Calcd for $C_{15}H_{30}O_3$ (258.39): C, 69.73; H, 11.70. Found: C, 68.03; H, 11.40) deviated, apparently because of the thermal instability of this compound at room temperature. The products from the peresters are under investigation and will be reported as part of a general study of the reactivity of crowded radicals. The triisopropylemethyl radical from the corresponding perester has been observed by esr and is extremely long lived at room temperature: S. Icli, C. Thankachan, and T. T. Tidwell, *J. Chem. Soc., Chem. Commun.*, in press.

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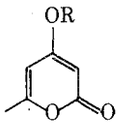
A New Polyketide Synthon

Summary: A phosphonium ylide derived from triacetic acid lactone has been prepared and used in the synthesis of tetraacetic acid lactone and other acetogenins.

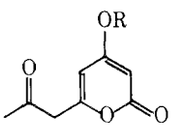
Sir: Although Collie's hypothesis of the "multiple keten group" [1] lay fallow for decades in the literature, its resurrection as Birch's "Acetate hypothesis" [2] has proven of immense significance in fungal metabolism.[3] Of special interest are derivatives of 4-hydroxy-2-pyrone and, in particular, triacetic acid lactone **1**[4,5] and tetraacetic acid lactone **2**,[5] as these compounds represent the closest approximation of true "polyketides." A number of related pyrones have been biomimetically transformed into phenols of naturally occurring types.[6-9]

After repetition of reported syntheses of **2** from **1** *via* **3**,[9] the 6-carboxy derivative of **4** *via* carboxylation of the 6-methyl anion,[8] and **5** from **3** *via* **6**,[10] it became clear to us that none of these were readily adaptable to isotopic labeling studies, in addition to their other drawbacks.

This report deals with the preparation of a reagent which produces polyketide-related materials under relatively mild and selective conditions from carbonyl substrates



1, R = H
4, R = Me



2, R = H
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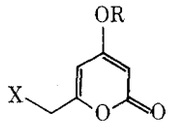
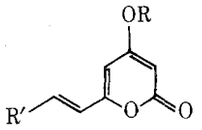
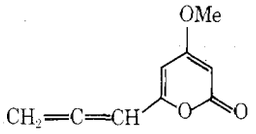


7, R = Me; X = Br
8–13 X = $Ph_3P^+Br^-$
8, R = Me
10, R = Ac
11, R = H
12, R = $COCMe_3$
13, R = $SiMe_3$



5, R = H; R′ = Me
6, R = Me; R′ = Me
16, R = Me; R′ = *n*-Pr



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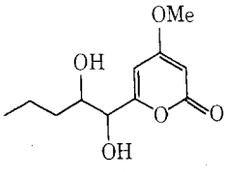

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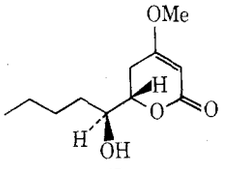

15

(stereochemistry uncertain)

available commercially with a variety of substituents and/or isotopic labels.

Allylic bromination of **4**[11] (NBS, CCl_4, reflux, di-*tert*-butyl peroxide initiator) gave as the major product **7**,[12] mp 93–95° [nmr δ ($CDCl_3$) 3.85 (3 H, s, $-OCH_3$), 4.13 (2 H, s, $BrCH_2-$), 5.51 (1 H, d, J = 1.5 Hz, vinylic), 6.12 (1 H, d, J = 1.5 Hz, vinylic); ir ($CHCl_3$) 1724 (C=O), 1655, 1572 cm^{-1} (C=C)], together with minor products due to ring bromination.

Since the starting material and minor products were all unreactive toward Ph_3P, it was most efficient to treat the bromide mixture directly with Ph_3P (PhH, reflux, under N_2) to give a 70% yield of the phosphonium salt **8**,[13] mp 224–226° dec: nmr δ (F_3CCO_2H) 3.95 (3 H, s, CH_3O-), 4.75 (2 H, d, broadened, J = 14 Hz, $Ph_3P^+-CH_2-$), 6.00 (1 H, d, 1.5 Hz, vinylic), 6.45 (1 H, m, vinylic), 7.65–7.89 (15 H, m, C_6H_5); ir (KBr) 3030, 2816, 2739 (C–H), 1715 (C=O), 1639, 1552 cm^{-1} (C=C). As no special storage precautions are necessary with salt **8**, it represents a convenient source of the ylide, which is readily generated from **8** in THF at ambient temperature (*n*-BuLi, 1 hr).

Although direct acylation of the ylide from **8** was not useful, tetraacetic acid lactone **2** was readily approached *via* treatment of the ylide with an equivalent of ketene[14] and letting the reaction stand 2–3 days to give 68%[15] of the allene **9**, mp 115–116°: nmr δ ($CDCl_3$) 3.86 (3 H, s, $-OCH_3$), 5.33–6.03 (5 H, complex, vinylic and allenic);[16] ir (KBr) 3415 (C–H), 1945 (allene), 1706 (C=O), 1629, 1550 cm^{-1} (C=C); uv λ_{max} 310 nm (ϵ 10,000). Hydration of **9** (80% H_2SO_4, ambient temperature, 20 hr) gave a 90% yield of **3**, identical with material synthesized by the recently reported method of Scott.[9] This material has been demethylated by ourselves and others[9] to tetraacetic acid lactone **2**.

A particularly effective application of our reagent was to the synthesis of **5**, a synthetic[10] and possibly biogenetic[17] precursor of radicinin. The only previous synthetic approach to **5**, which proceeded *via* demethylation[10] of **6**, involved several steps from the difficultly accessible **3**. Using our method, acetaldehyde can be converted into **6** in one step in 80% yield[18] by generation of the ylide from **8** by lithium diisopropylamide at −20–0° over 2 hr, followed by an equivalent of the carbonyl, gradual warming to ambient temperature, and standing 2–3 days. Since acetaldehyde is available with a number of isotopic labels, this process represents a most effective labeling process for **5**.

By similar reactions we have prepared a series of phosphonium salts **10–12**;[19] however, none of these systems has proven useful in direct synthesis of the enolic forms of polyketides. Attempts to produce **13** in pure form have not been successful. We note that the methoxy series of compounds is of interest *per se*, owing to the recent isolation of the *Penicillium* metabolite **14**[20] and the gibberellin synergist pestalotin (**15**).[20,21] Synthetic approaches to **14** *via* **16** are in progress, as well as extensions of our studies to polypyrones, dialdehydes, branched polyketides, and pyridones, whose *N*-ribosyl derivatives are of current interest as cytotoxic uridine analogs.[22] Yields of compounds **6** and **9** were for material chromatographed on silica gel (activity 1, $CHCl_3$ eluent). Satisfactory analytical and/or mass spectral data were obtained for all new compounds reported.

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(15) Prepared as above by the standard *n*-BuLi method. The yield should be significantly improved by the diisopropylamide procedure below.
(16) This appears to contain δ 5.43 (1 H, d, J = 2 Hz, vinylic), 5.90 (1 H, m, vinylic), 5.21 (1 H, s, allenic), 5.45 (1 H, s, allenic), and one other proton. Decoupling experiments failed due to the proximity of coupled protons.
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