excess (0.080 mol) of $NaHCO_3$ and the buffered solution was stirred for 15 min. Analysis of an aliquot showed 3.0 equiv of acid per mole of carbyl sulfate. (This was confirmed with poor precision by a bisulfite additon assay.) The neutralized solution was dried at 50° and reduced pressure and the resulting salt mixture was subjected to a 12-hr Soxhlet extraction with methanol. The extract, containing the organic salt, was divided into aliquots. One portion, treated with *S*-benzylthiuronium chloride, formed the corresponding vinylsulfonate salt, mp 145–146° from ethanol, in good agreement with the reported value.[11] Another portion was dried; the white salt yielded (KBr pellet) major infrared maxima at 1190, 1045, 1620, and 755 cm^{-1}, in the expected regions for $-SO_2-$ asymmetric and symmetric stretch, vinyl, and S–O stretch, respectively. The remaining portion was examined in aqueous solution by nmr, yielding a seven-peak spectrum characteristic of vinyl splitting with $J_{gem} \cong 0$.[12] The three vinylic protons appeared at δ 6.00, 6.04, and 6.86 ppm, similar to those found for methyl vinyl sulfone (5.95, 6.13, and 6.70 ppm)[13] and reasonably close to the values predicted by the Pascual equation[14] for $CH_2{=}CH{-}SO_2-$ (6.23, 6.43, and 6.86 ppm).

Acid–base titrations were carried out using standard 0.10 *N* Na_2CO_3 or NaOH. Since ethionic acid undergoes an acid-generating elimination in near-neutral solutions, it was found useful to make one or two preliminary range-finding titrations, prior to carrying out rapid analytical titrations to first end points.

Reactions in dilute aqueous base were examined by addition of 2–3 mmol of pure carbyl sulfate to 100-ml portions of 0.10 *N* KOH, followed by titration with standard acid. At 25, 50, and 90° the average values of the ratio (equivalents of acid formed):(moles of carbyl sulfate reacted) were found to be 2.7, 2.6, and 2.7. (When carbyl sulfate is predissolved in 10 ml of dry dioxane and this solution is added to the aqueous base, this observed ratio falls to 2.0.) Identification of vinylsulfonate in the product mixture was made by infrared examination and by reaction with measured amounts of bisulfite ion to form potassium ethanedisulfonate.[15]

Quantitative information on the elimination of sulfate by ethionate in near-neutral solutions was sought by combining solutions of ethionic acid and phosphate buffers, then assaying these for vinylsulfonate by the semiquantitative bisulfite method.[15] Vinylsulfonate yields of 80–90% were obtained at pH 7.70, 70–78% at pH 7.01 and 8.90, 45–55% at pH 5.5 and 10.2, and 80–95% with authentic sodium vinylsulfonate. While these data suggest a maximum elimination in nearly neutral solutions, we were unable to obtain acceptably reproducible assays by this procedure.

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Registry No.—Carbyl sulfate, 503-41-3.

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Ester Enolates. A New Preparation of Malonates, Phosphonoacetates, and α-Selenyl and Sulfinyl Esters

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The formation of α carbanions of carboxylic acids and esters by means of nonnucleophilic bases such as disubstituted lithium amides has recently been widely investigated owing to their great synthetic utility.

At the present time, the reactions of these anions with electrophilic substrates are restricted to alkyl halides,[1-6] halogens,[7] epoxides,[1] alkyl nitrates,[8] substituted ammonias,[9] alkyl silyl chlorides,[10] and carbonyl compounds such as CO_2,[11] esters,[8,12] acyl chlorides,[13] aldehydes,[14,15] and ketones.[15]

In this paper we wish to report the extension of this range of substrates to ethyl chloroformate, chlorophosphates, diphenyl disulfide, and benzeneselenenyl bromide. Also included are certain substrates that did not react satisfactorily. Esters of α-branched and straight-chain acids (isobutyric, hexanoic, and acetic acid) were employed to test the general applicability of the investigated reactions in relation with self-condensation reactions. The α anions were prepared with the readily available base lithium diisopropylamide (LDA) using published procedures.[5,6]

The reaction of ethyl chloroformate with these α anions was explored, leading to the expected substituted malonates in yields as high as 70% at −15° and 90% at −78°.

$$R_2CHCO_2R' \xrightarrow[2.\ ClCO_2Et]{1.\ LDA} R_2C(CO_2Et)CO_2R'$$

Of special interest is the facile preparation of ethyl *tert*-butyl malonate,[16] useful in β-keto ester synthesis.[17] This reagent can be obtained in a yield of 70–75%, whereas the normal three-step procedure[16] has an overall yield of 40–45%. This reaction can presumably be extended to the synthesis of other useful mixed malonates.

The synthetic utility of β-carboalkoxy phosphates (phosphonoacetates) and phosphinoxides as starting materials for olefination reactions suggested their preparation by treating the α anions with chlorophosphates and chlorophosphinoxides. Isobutyrates, on reaction with chlorophosphates, gave high yields of the expected products.

$$(CH_3)_2CHCO_2R \xrightarrow[2.\ (R'O)_2POCl]{1.\ LDA} (CH_3)_2C(CO_2R)P(O)(OR')_2$$

a, R = Et; R′ = Et, CH_3
b, R = CH_3; R′ = CH_3

The same reaction attempted with methyl hexanoate and ethyl acetate failed to give the expected products, thus detracting from synthetic use in olefination reactions. As self-condensation products were indicated by nmr spectra, we looked at the analogous *tert*-butyl esters, whose anions are known to be more stable.[5,6,18] The anion of *tert*-butyl acetate gave 65% of the desired reaction with $(EtO)_2P(O)Cl$, indicating the advantages of using hindered esters.

It was observed that $Ph_2P(O)Cl$ was unreactive with isobutyrate and acetate α anions, probably owing to steric crowding, $Ph_2P(O)OH$ being recovered after quenching of the reaction mixture with water. However, the obvious possibility of reaction on oxygen[19] by both sets of phosphorus chloride reagents must be considered, the intermediate phosphates being hydrolized during work-up. The relative success of esters sterically hindered on the α car-

Table I

Ester	Electrophilic reagent	Product	(No.)	Yield, %
$(CH_3)_2CHCO_2Et$	$ClCO_2Et$	$(CH_3)_2C(CO_2Et)_2$	(**1**)	90
CH_3CO_2Et	$ClCO_2Et$	$CH_2(CO_2Et)_2$	(**2**)	88
CH_3CO_2Bu-*t*	$ClCO_2Et$	$CH_2(CO_2Et)CO_2Bu$-*t*	(**3**)	70–75
$(CH_3)_2CHCO_2Et$	$ClP(O)(OEt)_2$	$(CH_3)_2C(CO_2Et)P(O)(OEt)_2$	(**4**)	80
$(CH_3)_2CHCO_2Et$	$ClP(O)(OCH_3)_2$	$(CH_3)_2C(CO_2Et)P(O)(OCH_3)_2$	(**5**)	64
$(CH_3)_2CHCO_2CH_3$	$ClP(O)(OCH_3)_2$	$(CH_3)_2C(CO_2CH_3)P(O)(OCH_3)_2$	(**6**)	62
CH_3CO_2Bu-*t*	$ClP(O)(OEt)_2$	$CH_2(CO_2Bu$-*t*$)P(O)(OEt)_2$	(**7**)	65
$(CH_3)_2CHCO_2Et$	PhSeBr	$(CH_3)_2C(CO_2Et)SePh$	(**8**)	85
n-$C_5H_{11}CO_2CH_3$	PhSeBr	n-$C_4H_9CH(CO_2CH_3)SePh$	(**9**)	60
CH_3CO_2Et	PhSeBr	$CH_2(CO_2Et)SePh$	(**10**)	80
$(CH_3)_2CHCO_2Et$	PhSSPh	$(CH_3)_2C(CO_2Et)SPh$	(**11**)	80
CH_3CO_2Et	PhSSPh	$CH_2(CO_2Et)SPh$	(**12**)	70

bon (isobutyrates) or on alkyl oxygen (*tert*-butyl acetate) indicates steric impedance to Claisen condensation and/or oxygen alkylation as two important side-reactions.[5,6,10,18]

Our interest in organoselenium chemistry and the general synthetic utility of α-thio and α-seleno esters led us to investigate the reaction of ester enolates with diphenyl disulfide and phenyl selenenyl bromide. Recent publications[20-22] concerning similar reactions and the utility of the products in formation of α,β-unsaturated ketones and esters prompt us to include our complementary results.

$$R_2CHCO_2Et \xrightarrow[2.\ PhSSPh]{1.\ LDA} R_2C(CO_2Et)SPh + PhS^- \xrightarrow{H_2O} PhSH$$

$R = CH_3$, H

$$RR'CHCO_2R'' \xrightarrow[2.\ PhSeBr]{1.\ LDA} RR'C(CO_2R'')SePh$$

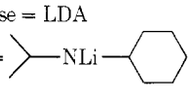
a, $R = R' = CH_3$; $R'' = Et$
b, $R = R' = H$; $R'' = Et$
c, $R = C_4H_9$; $R' = H$; $R'' = CH_3$

The two reactions gave the expected products in high yields. In the first case only half of the disulfide is converted, but the corresponding arylsulfenyl halides are more difficult to prepare.

Two attempted reactions to introduce a β-carbonyl and a γ-formyl functionality failed, giving only unidentified products.

$$R_2CHCO_2Et \xrightarrow[2.\ R'CN\ \ 3.\ H_3O/H^+]{1.\ base} R_2C(COR')CO_2Et$$

a, $R = CH_3$; $R' = CH_3$; base = LDA

b, R = H; R′ = Ph; base = 

$$R_2CHCO_2Et \xrightarrow[2.\ XCH_2CH(OEt)_2\ \ 3.\ H_3O/H^+]{1.\ LDA} R_2C(CO_2Et)CH_2CHO$$

$R = CH_3$; X = Cl, Br

These results are in accord with the known lesser reactivities of nitriles and α-haloacetals toward nucleophiles.

Experimental Section

Infrared spectra were determined using a Perkin-Elmer Infracord or Perkin-Elmer Model 457-A spectrophotometer. Nmr spectra were obtained with a Varian T-60 or HA-100 spectrometer. Chemical shifts (δ) are reported in parts per million downfield from tetramethylsilane (TMS) as internal standard, using conventional notation. Mass spectra were obtained on a Finnigan Model 1015 under the supervision of Dr. Herndon Williams, Universidade de Campinas, Campinas, Brasil. Microanalyses were performed in our department under the supervision of Dr. Riva Moscovici. Boiling points are quoted for the temperature of the oven during evaporative bulb-to-bulb (Kugelröhr) short-path distillation. The esters were prepared in the usual way, distilled, and stored over molecular sieves 4A. Dimethyl and diethyl chlorophosphate were prepared[23] from phosphorus oxychloride and methanol or ethanol, respectively, the products being stored over molecular sieves 4A. Benzeneselenenyl bromide was prepared[21] from diphenyl diselenide and bromine. Diphenyl disulfide was prepared from thiophenol and bromine ($CHCl_3$, 0°, 1 hr) in 75% yield, mp 58–59° (lit.[24] mp 60–61°).

The following general experimental procedure was employed for all the described reactions (see Table I).

To a 50-ml round-bottom flask equipped with septum inlet, magnetic stirring, dropping funnel, and N_2 inlet was added diisopropylamine (0.01 mol) in 10 ml of anhydrous THF and the solution was treated with the equivalent amount of *n*-butyllithium in hexane (0°, 15 min). The colorless solution was cooled with a Dry Ice–acetone bath and treated with the ester (0.01 mol) in 2 ml of THF and after 10 min with the electrophilic reagent (0.01 mol) in 2–5 ml of THF.

After 10–30 min of stirring at −78° the reaction solution was quenched with saturated NH_4Cl solution, extracted with ether, dried with $MgSO_4$, filtered, and evaporated to give the crude product. Depending on purity, distillation or preparative thick plate chromatography and distillation were used to isolate the product in the specified yields.

Owing to water solubility problems the four carboalkoxy dialkylphosphonates were isolated with the minimum amount of water necessary to quench the reaction mixtures. Thiphenol, produced as a by-product in the formation of α-thiophenyl esters, was extracted from the reaction mixture by washing with 10% Na_2CO_3.

Diethyl dimethylmalonate (**1**) from ethyl isobutyrate and ethyl chloroformate (90%): bp 90° (25 mm) [lit.[24] bp 97–98° (22 mm)]; nmr (CCl_4) δ 4.12 (q, 4, J = 7 Hz), 1.35 (s, 6), 1.23 (t, 6, J = 7 Hz).

Diethyl malonate (**2**) from ethyl acetate and ethyl chloroformate (88%): bp 80° (25 mm) (lit.[24] bp 199°); nmr identical with that of authentic sample.

Ethyl *tert*-butylmalonate (**3**) from *tert*-butyl acetate and ethyl chloroformate (70–75%): bp 105° (22 mm) [lit.[16] bp 98–100° (22 mm)]; nmr (CCl_4) δ 4.15 (q, 2, J = 7 Hz), 3.13 (s, 2), 1.45 (s, 9), 1.28 (t, 3, J = 7 Hz).

1-Carbethoxy-1-methylethyl diethyl phosphonate (**4**) from ethyl isobutyrate and diethyl chlorophosphate (80%): bp 55–57° (0.005 mm); nmr ($CDCl_3$) δ 4.22 (q, 2, J = 7 Hz), 4.15 (q, 2, J = 7 Hz), 3.92 (q, 2, J = 7 Hz), 1.65 (s, 3), 1.62 (s, 3), 1.35 (t, 3, J = 7 Hz), 1.33 (t, 3, J = 7 Hz), 1.25 (t, 3, J = 7 Hz); mass spectrum (20 eV) m/e 252 (P).

Anal. Calcd for $C_{10}H_{21}O_5P$: C, 47.61; H, 8.41. Found: C, 46.23; H, 8.31. This compound, although chromatographically pure and spectroscopically consistent, gave inaccurate analyses.

1-Carbethoxy-1-methylethyl dimethyl phosphonate (**5**) from ethyl isobutyrate and dimethyl chlorophosphate (64%): bp 40–42° (0.005 mm); nmr (CCl_4) δ 3.90 (q, 2, J = 7 Hz), 3.87 (s, 3), 3.70 (s, 3), 1.63 (s, 3), 1.58 (s, 3), 1.26 (q, 3, J = 7 Hz); mass spectrum (20 eV) m/e 224 (P).

Anal. Calcd for $C_8H_{17}O_5P$: C, 42.85; H, 7.60. Found: C, 42.73; H, 7.60.

1-Carbomethoxy-1-methylethyl dimethyl phosphonate (**6**) from methyl isobutyrate and dimethyl chlorophosphate (62%): bp 35–37° (0.005 mm); nmr (CCl_4) δ 3.86 (s, 3), 3.67 (s, 3), 3.60 (s, 3), 1.63 (s, 3), 1.58 (s, 3); mass spectrum (20 eV) m/e 210 (P).

Anal. Calcd for $C_7H_{15}O_5P$: C, 40.00; H, 7.21. Found: C, 39.93; H, 7.25.

1-Carbo-*tert*-butoxymethyl diethyl phosphonate (**7**) from *tert*-butyl acetate and diethyl chlorophosphate (65%): bp 50–55° (0.05 mm) [lit.[25] bp 82–82.5° (0.05 mm)]; nmr (CCl_4) δ 4.20 (q, 2, J = 7 Hz), 4.05 (q, 2, J = 7 Hz), 2.73 (d, 2, J = 22 Hz), 1.45 (s, 9), 1.34 (t, 3, J = 7 Hz).

Ethyl α-selenophenylisobutyrate (8) from ethyl isobutyrate and benzeneselenenyl bromide (85%): bp 80–85° (0.025 mm); nmr (CCl_4) δ 7.1–7.6 (m, 5), 4.01 (q, 2, J = 7 Hz), 1.52 (s, 6), 1.17 (t, 3, J = 7 Hz).

Anal. Calcd for $C_{12}H_{16}O_2Se$: C, 53.13; H, 5.90. Found: C, 53.10; H, 5.99.

Methyl α-selenophenylhexanoate (9) from methyl hexanoate and benzeneselenenyl bromide (60%): bp 60–65° (0.05 mm); nmr (CCl_4) δ 7.1–7.7 (m, 5), 3.57 (s, 3), 1.0–2.0 (m, 7), 0.87 (t, 3, J = 6 Hz).

Anal. Calcd for $C_{13}H_{18}O_2Se$: C, 54.74; H, 6.36. Found: C, 55.10; H, 6.41.

Ethyl α-selenophenylacetate (10) from ethyl acetate and benzeneselenenyl bromide (80%): bp 77–80° (0.025 mm); nmr (CCl_4) δ 7.3 (m, 5), 4.10 (q, 2, J = 7 Hz), 3.50 (s, 2), 1.21 (t, 3, J = 7 Hz).

Anal. Calcd for $C_{10}H_{12}O_2Se$: C, 49.43; H, 4.97. Found: C, 49.73; H, 5.05.

Ethyl α-thiophenylisobutyrate (11) from ethyl isobutyrate and diphenyl disulfide (80%): bp 80° (0.025 mm); nmr (CCl_4) δ 7.3 (m, 5), 4.06 (q, 2, J = 7 Hz), 1.42 (s, 6), 1.20 (t, 3, J = 7 Hz).

Anal. Calcd for $C_{12}H_{16}O_2S$: C, 64.28; H, 7.14. Found: C, 64.40; H, 7.21.

Ethyl α-thiophenylacetate (12) from ethyl acetate and diphenyl disulfide (70%): bp 80° (0.05 mm) [lit.[26] bp 118° (2.7 mm)]; nmr (CCl_4) δ 7.1–7.6 (m, 5), 4.07 (q, 2, J = 7 Hz), 3.40 (s, 2), 1.18 (t, 3, J = 7 Hz).

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Reaction of 1,3-Dimethyl-2-pyridone with *N*-Bromosuccinimide. A Reexamination

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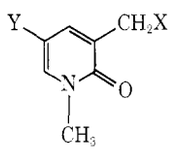
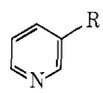
During our recent work on the total synthesis of camptothecin,[1] we had the opportunity to examine the reaction of 3-methyl-2-pyridone systems with *N*-bromosuccinimide (NBS). In a reported application of such a reaction,[2] 1,3-dimethyl-2-pyridone (1) was stated to react with NBS in the presence of dibenzoyl peroxide to yield 3-bromomethyl-1-methyl-2-pyridone (2). Since 1 had been chosen as a model compound, we sought to duplicate this experiment. On each of three attempts, following as closely as we could the experimental procedure described, the only product recovered was 5-bromo-1,3-dimethyl-2-pyridone (3). Comparison of this product with that previously reported proved difficult, since the characterization given[2] included only a melting point (98–99°) and an elemental analysis.





1, X = H; Y = H
2, X = Br; Y = H
3, X = H; Y = Br
4, X = OAc; Y = H
5, X = Cl; Y = H
6, X = OH; Y = H
7, X = OCH=CH_2; Y = H
10, X = $Ph_3P^+Br^-$; Y = H
11, X = OTs; Y = H
12, X = Py^+Br^-; Y = H
13, X = OMs; Y = H

8, R = CHO
9, R = CH_2OH

In characterizing the 5-bromo-1,3-dimethyl-2-pyridone (3) prepared in our study, the major additional datum was its nmr spectrum, which displayed singlets of three-proton intensity at δ 2.17 and 3.54 ppm. These correspond very closely with the methyl singlets at δ 2.14 and 3.52 in 1. The position of the bromine atom in 3 is established by disappearance of a one-proton triplet at δ 6.06 when the spectrum is compared with that of 1. The crude triplet at δ 7.2 corresponding to the remaining protons on the pyridone ring of 1 collapsed to a finely split doublet in the spectrum of 3. To verify that our interpretation of the nmr spectrum of 3 was correct, a series of compounds was prepared, substituted on the 3-methyl group but not at the 5 position of the ring. These included 3-acetoxymethyl-, 3-chloromethyl-, 3-hydroxymethyl-, and 3-vinyloxymethyl-1-methyl-2-pyridone (4, 5, 6, and 7, respectively). In each case, the corresponding nmr spectrum displayed a one-proton triplet near δ 6.0 for the proton on carbon 5 of the ring and a two-proton singlet in the δ 4.5–5.0 range for the methylene group bonded at carbon 3.

Finally, it was reported[2] that compound 2 gave a positive test with alcoholic silver nitrate. It is significant that our product also showed reactivity with alcoholic silver nitrate even after two recrystallizations from petroleum ether, the solvent reported as used for purifying 2. However, an analytically pure sample of 3 prepared by recrystallization and sublimation followed by preparative gc failed to react with silver nitrate and had mp 106–107°