Phenylthioacetic Acid Dianion: Latent Vinyl, Oxiranyl, and Acyl Carbanion Equivalents

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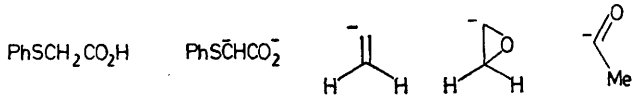
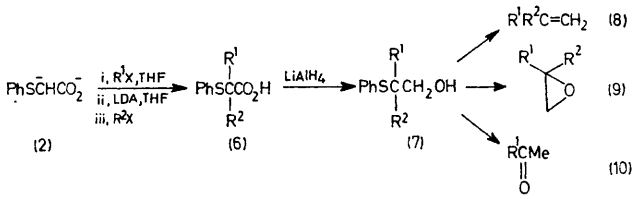
Summary The α-metallated carboxylate salt of phenylthioacetic acid provides access to a wide variety of β-hydroxy sulphides which are key intermediates for the synthesis of olefins, oxirans, and ketones.

DIANIONS derived from carboxylic acids have provided means for derivatizing long-chain fatty acids at the α carbon atom.[1] We report our results with the dianion (**2**) obtained from commercially available phenylthioacetic acid (**1**). The α-metallated dianion (**2**) represents latent vinyl (**3**), oxiranyl (**4**), and acyl (**5**) carbanion equivalents which are of considerable synthetic interest.[2]



(1) (2) (3) (4) (5)

As illustrated in the Scheme, the dianion (**2**) can be cleanly alkylated (see Table) providing the carboxylic acid (**6**) which is smoothly reduced to the β-hydroxy sulphide (**7**). β-Hydroxy sulphides provide routes to (a) olefins, *via* reductive elimination (Li–NH_3) of the corresponding benzoates,[3] (b) oxirans, *via* base treatment of the corresponding sulphonium salt,[4] and (c) ketones, *via* elimination followed by unmasking.[5] Unlike its corresponding methyl ester, the phenylthioacetic acid dianion (**2**) [prepared by treatment of (**1**) with 2·0 equiv. of lithium di-isopropylamide in tetrahydrofuran at 0°] undergoes high-yield alkylation (Table) providing access to a wide variety of fully substituted phenylthio carboxylic acids. The advantages of preparing β-hydroxy sulphides *via* the dianion route over existing methods are (a) ready availability of the starting material, (b) dianion reactions can be conducted at room or reflux temperature, and (c) the present method avoids α-sulphenylation of enolates at low temperature.



SCHEME

The olefination sequence reported herein complements previous approaches involving condensation of ketones and aldehydes with either methylenetriphenylphosphorane or phenylthiomethyl-lithium. The method obviates the necessity of directly employing ketones or aldehydes in which competition may exist between proton transfer and carbonyl addition with the risk of isomerization in the case of the former. In addition, the method circumvents the problem of preparing regiospecifically 1,4-dienes from the not so readily accessible βγ-unsaturated ketones [Table, entry (III)].[6] Likewise, previous oxiran syntheses have involved condensation of nucleophilic alkylidene sulphur reagents or phenylthiomethyl-lithium with either aldehydes or ketones.

It has recently been demonstrated by Trost[5] that β-hydroxy sulphides, prepared by direct α-phenylsulphenylation, at low temperature, of appropriately substituted esters followed by reduction, represent masked ketones.

TABLE. Olefin and oxiran synthesis *via* phenylthioacetic acid dianion

Entry	1st alkylation[a] of (2) yield (%) R^1–X	2nd alkylation[a] of (2) yield (%)[b] R^2–X	Alcohol[c] yield (%)[b]	Benzoate[f] yield (%)[b]	Olefin[g] yield (%)[b]	Oxiran[i] yield (%)[b]
(I)	$Me[CH_2]_{11}I$ (98)	—	88	86	(**11**) 65	66
(II)	,,	Me (98)	85	91	(**12**) 64	66
(III)	$Me[CH_2]_3I$ (96)	$C_{10}H_{17}Br$[j] (90)	89	98	(**13**)[k] 54	–
(IV)	,,	$Me[CH_2]_{11}I$ (97)	87	77	(**14**) 52	70
(V)	$Br[CH_2]_4Br$[e] (75)		50	98	(**15**)[h] 70	–
(VI)	Me_2CHI (99)	$Me[CH_2]_{11}I$ (95)	55	99	(**16**) 67	65

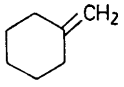
[a] Formation of the dianion was achieved by dilithiation [2·0 equiv. of lithium di-isopropylamide (LDA)–THF–0°–30 min] followed by addition (0°) of R–X and warming to room temperature (3 h). [b] Reported yields are based on isolated analytically pure products unless stated otherwise. [c] A mixture of the dianion (**2**) in THF and 1,4-dibromobutane was heated to reflux and after 15 h, 1·0 equiv. of LDA were added (0°) and refluxing was continued for an additional 3 h. [d] After addition of alkyl halide, the reaction was heated to reflux for 5 h. [e] Conversion into the alcohol was achieved by reduction (LiAlH–THF–reflux–5 h). [f] Formation of benzoate ester was carried out by lithiation (1·0 equiv. of Bu^nLi–THF) followed by addition of benzoyl chloride. [g] Lithium–ammonia reduction. [h] Yield by g.l.c. analysis. [i] β-Hydroxy sulphide was alkylated with trimethyloxonium fluoroborate in CH_2Cl_2 followed by treatment with 0·5 N NaOH. [j] $C_{10}H_{17}Br$ = geranyl bromide. [k] Ref. 6.

$Me[CH_2]_{11}CH{=}CH_2$ (11)

$Me[CH_2]_{11}C(Me){=}CH_2$ (12)

$Me_2C{=}CH[CH_2]_2C(Me){=}CHCH_2C(Bu){=}CH_2$ (13)

$Me[CH_2]_{11}C(Bu^n){=}CH_2$ (14)



(15)

$Me[CH_2]_{11}C(Pr^i){=}CH_2$ (16)

The β-hydroxy sulphide (**7**) (R^1 = dodecyl, R^2 = H) [(Table, entry (I)] prepared from the dianion (**2**) was efficiently converted into methyldodecyl ketone in > 85% overall yield from phenylthioacetic acid.[7]

In summary, the thiophenylthioacetic acid dianion (**2**) furnishes a highly efficient route to β-hydroxy sulphides which can be transformed into a variety of useful functional groups. Furthermore, reduction of the substituted phenylthioacetic acids with $LiAlD_4$ constitutes a highly specific method for the preparation of deuterium labelled terminal olefins and oxirans.

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