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Aqueous Organotin Chemistry: Tin Hydride Mediated Dehalogenation of Organohalides and A Novel Organotin Mediated Nucleophilic Substitution on 2-Iodobenzoates *in Water*

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Abstract: This paper describes the dehalogenation of water soluble and water insoluble organohalides in water by tri-*n*-butyltin hydride (TBTH), preformed TBTH and triphenyltin hydride (TPTH) *in water*. TBTH in the presence of a radical trap, and Ph_4Sn were also found to effect nucleophilic substitution of 2-iodobenzoates in the presence of various nucleophiles.

INTRODUCTION

Tri-*n*-butyltin hydride (TBTH) and triphenyltin hydride (TPTH) are two of the most used organotin reagents in organic synthesis. They have found many applications in the generation of carbon radicals by atom abstraction (halides, selenides, sulfides), or by the addition to a multiple bond (alkene, alkyne and carbonyl compounds).[1] They are also used as a hydrogen donor for radicals,[1(d), (e)] for hydrostannylation of alkenes, alkynes[2] and carbonyl compounds,[3] in radical ring expansions,[4] radical oxygenations,[5] deoxygenations,[6] carbonylations[7] and reduction of carbonyl compounds.[8] The use of TBTH as a source of Bu_3Sn^- and TPTH for hole-transfer-promoted hydrogenation are also known.[9,10] TBTH has been shown to act as a source of Nucleophilic hydride.[11] Polymer supported tin hydrides[12] and internally coordinated tin reagents have also been described in the literature.[13] Though the applications of organotin reagents in organic synthesis are well explored, their solubility has limited them to organic solvents only.

In recent years, the use of water as a solvent for organic synthesis has increased considerably.[14] However, because of the chemical incompatibility of many reducing agents with water, it is rarely used as a solvent in reductions.[15] We recently communicated a simple methodology to effect dehalogenation with TBTH in aqueous

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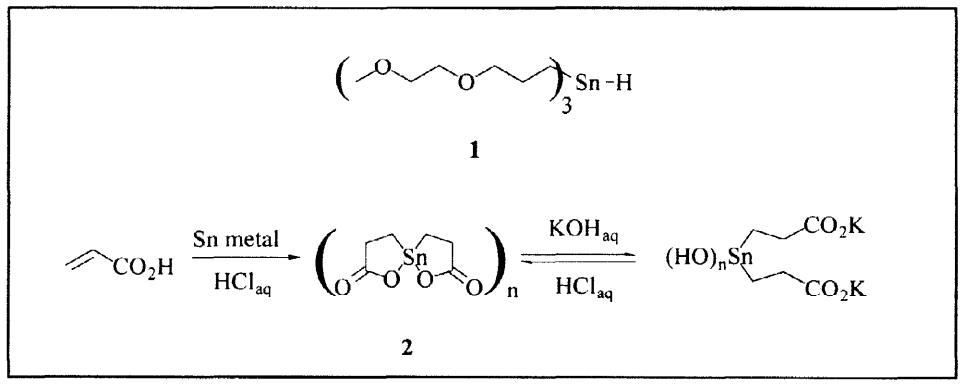
suspensions.[16] In this paper we report in detail the use of organotin reagents in the dehalogenation of organohalides and report a new Nucleophilic substitution on 2-iodobenzoates *in water*.

DEHALOGENATION OF ORGANOHALIDES

a) Tri-n-butyltin hydride (TBTH) mediated dehalogenation

For the dehalogenation of water soluble substrates a water soluble tin hydride (**1**) was reported by Breslow.[17] Although this reagent gave good yields in the dehalogenation of a number of water soluble substrates, the synthesis of **1** takes several steps. There was another report on the reduction and free radical cyclizations of alkyl and aryl bromides carried out in aqueous base by $NaBH_4$ in the presence of a base-soluble dialkyltin(IV) reagent (**2**) and 4,4'-azobis(4-cyanovaleric acid).[18]



We felt that TBTH chemistry could be carried out in water if it could be solubilized by a suitable detergent. In the presence of aqueous CTAB/CTAC, SDS[19] or Triton-X-100, TBTH was found to reduce 3-bromobenzoate efficiently. However, a control reaction (no detergent) showed that the detergent was not necessary! A few other substrates were examined under thermal as well as photochemical conditions and the results are summarized in Table 1. Even water insoluble substrates could be reduced in high yields. It is interesting to note that for 9-bromoanthracene the presence of a detergent was necessary, since the reaction carried out without a detergent for 48 h was not complete. However, cholesterol dibromide underwent smooth reduction to cholesterol (84%) in the absence of any detergent with 2 equiv of TBTH.

b) Dehalogenation mediated by preformed tin hydride

Several attempts were subsequently made to effect the dehalogenation of these substrates in water using a catalytic amount of TBTH in the presence of an excess of $NaBH_4$ for regenerating the tin hydride.[20] However, 4-iodobenzoic acid yielded approximately the same quantity of benzoic acid with 1 equiv of TBTH in the presence or absence of *ca.* 3 equiv of $NaBH_4$. No benzoic acid was obtained from tri-*n*-butyltin chloride (TBTC)

mediated reactions of 3-bromo- and 4-iodobenzoic acids in the presence of a large excess of $NaBH_4$. It seemed that the trialkyltin halide generated/added in the reaction medium was hydrolyzing very rapidly, and that the regeneration of the hydride from the halide by $NaBH_4$ was slow under the reaction conditions.[21] This suggested that dehalogenation in aqueous media could still be carried out by adding preformed tin hydride generated (from an organotin chloride and $NaBH_4$) *in a solvent less reactive towards the tin chloride than water, and carrying out this transformation at a lower temperature.* Ethanol was chosen as the solvent for preforming TBTH and it was done simply by stirring TBTC/$NaBH_4$ in EtOH for *ca.* 10 min at *ca.* 10°C. The results summarized in Table 1 (last column) show that under this set of conditions it is indeed possible to effect the dehalogenation of organohalides in water using an inexpensive primary reducing agent.

Table 1: Reduction of organohalides with TBTH/ preformed TBTH in water[a]

Entry	Substrate	%Yield (TBTH)	%Yield ($TBTH_{preformed}$)
1	3-$BrC_6H_4CO_2H$	95	84
2	2-$BrC_6H_4CO_2H$	–	84
3	4-$BrC_6H_4CO_2H$	89	98
4	2-$IC_6H_4CO_2H$	95	–
5	4-$IC_6H_4CO_2H$	–	90
6	3-$BrC_6H_4CO_2H$[b]	93	–
7	5-Br uracil[c]	>95[d]	82[d]
8	9-Br anthracene[e]	85	80
9	Cholesterol dibromide[f]	84	92

[a] Unless otherwise mentioned the temperature and reaction times were 90°C and 24 h, respectively with 3 equiv. of TBTH or preformed TBTH in presence of $NaHCO_3$ as the additive. [b] Photolysis (300 nm) at room temperature. [c] No additive was used. [d] The yield was measured by ^1H NMR using an internal standard. [d] CTAB was also added. [f] 2 equiv. of TBTH or preformed TBTH was used.

c) Triphenyltin hydride (TPTH) mediated dehalogenation

Triphenyltin hydride was also found to effect the dehalogenation with high yields in aqueous suspensions. These results are summarized in Table 2. Dehalogenations mediated by TPTH were found to be complete in 6 h compared to 24 h with TBTH.

Table 2: Reduction of organohalides with 3 equiv of TPTH in water[a]

Entry	Substrate	%Yield
1	4-$IC_6H_4CO_2H$	92
2	2-$IC_6H_4CH_2CO_2H$	87
3	3-$BrC_6H_4CO_2H$	82
4	4-$BrC_6H_4CO_2H$	94

[a] Unless otherwise mentioned the temperature and reaction times were 90°C and 6 h, respectively, $NaHCO_3$ was used as additive.

TIN MEDIATED NUCLEOPHILIC SUBSTITUTION ON *2*-IODOBENZOATES

a) Nucleophilic Substitution by TBTH

i) Introduction and results. In connection with the studies on dehalogenation reactions mediated by aqueous TBTH suspensions, it was found that a reaction of 2-iodobenzoic acid with TBTH in the *absence of a* radical initiator (AIBN) yielded benzoic acid with a small amount of salicylic acid. Interestingly, in the *presence* of 3,5-dinitrobenzoic acid a complete conversion (^{1}H NMR) to salicylic acid was observed. A control reaction carried out in the absence of both TBTH and 3,5-dinitrobenzoic acid yielded only 20% of salicylic acid.[22] Complete conversion to salicylic acid was also observed[23] using anthraquinone-2-carboxylate (partially water soluble) and 1,4-(or 1,3)dinitrobenzene (water insoluble). 2,5-Diiodobenzoic acid yielded 70% of 5-iodosalicylic acid under identical conditions. However, 2-bromo-(or 2-chloro)benzoic acid gave only a trace amount of salicylic acid, whereas with 2-fluorobenzoic acid, 3-bromobenzoic acid and 4-iodobenzoic acid no hydroxybenzoic acid was detected.

Nucleophilic substitution reactions were subsequently attempted with carbon nucleophiles. Good yields were achieved with 2-iodobenzoic acid and 2,5-diiodobenzoic acid using acetylacetone and ethyl acetoacetate as the carbon nucleophile source (Table 3). Interestingly, 2,5-diiodobenzoic acid yielded only a trace amount of the product with acetylacetone for reasons not clear to us. It is also interesting to note that in all the cases, possibly because of the anchimeric assistance of the *ortho*-carboxylate group, the products are derived by the *retro*-Claisen reaction of the initially formed arylated β-dicarbonyl compounds.

ii) Discussion. The salient features of these observations can be summarized as follows:

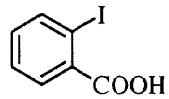
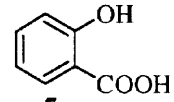
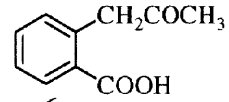
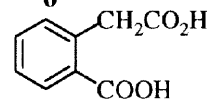
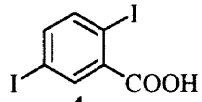
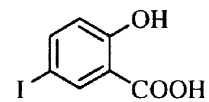
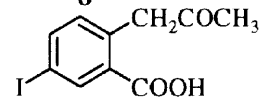
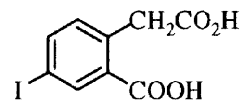
1. The use of a radical quencher is necessary. The reaction done with 2-iodobenzoic acid without a radical quencher yielded the normal reduction product with only a trace amount of salicylic acid. This clearly indicates that the reactions do not take place *via* a radical pathway.

2. A reaction performed with 2-iodobenzoic acid in a mixture of equimolar amounts of methanol and water resulted in approximately equal amounts of 2-methoxybenzoic acid and salicylic acid, along with some unreacted starting material. This result provides evidence that a common intermediate is involved.

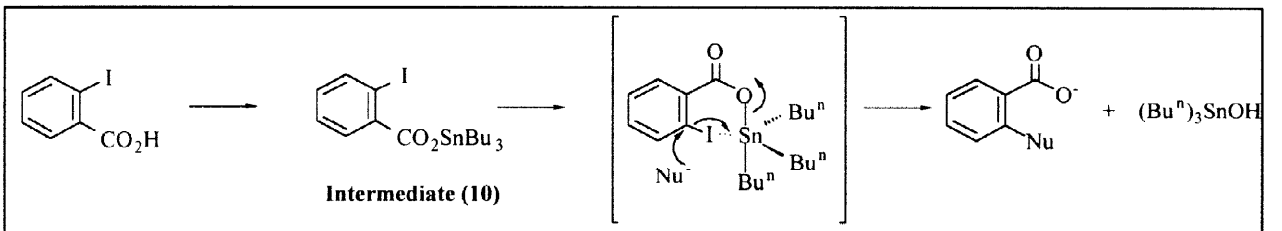
3. The reaction did not occur with ^{n}Bu$_3$SnCl in place of TBTH. Trimethyltin halides (Cl, Br or I) are known[24] to dissolve in water to form a diaquo cation $[Me_3Sn(H_2O)_2]^+$.[25] R_3SnX reacts with aqueous alkali to form R_3SnOH or $(R_3Sn)_2O$ depending on the nature of R. Organotin hydrides have been reported to react with carboxylic acids to form esters with the evolution of hydrogen.[26] Though these reactions have not been investigated in aqueous media a reasonable mechanistic interpretation to our observations would be to postulate the formation of tri-*n*-butyltin carboxylates (e.g., **10**) under the reaction conditions.[27]

4. Though the associative nature of organotin carboxylates in aqueous medium is unknown it is expected that in dilute aqueous solutions, as is known for organic solvents, they will be monomeric in nature.[28] It has also been reported that the presence of electron-withdrawing organic groups attached to the tin and/or the carboxylate moiety favor complex formation, *e.g.*, $Me_3SnOCOC_5H_4N$-2.H_2O.[29] Consequently, considering the fact that the reactions proceeded with 2-iodocarboxylates and not with 4-iodobenzoic acid, it may be inferred that in course of the reaction the iodine atom at C-2 coordinates with the tin center to generate a trigonal bipyramidal complex (**I**). Then the course of the reaction can be explained by the abstraction of the iodine by the tin center and the subsequent attack by the nucleophile (Scheme 1.). The low reactivity of 2-bromobenzoic acid can be explained by the smaller atomic radius of the Br atom which makes it unsuitable for internal coordination and/or because

Table 3: TBTH and TPT Mediated Nucleophilic Substitution on 2-iodobenzoates

Substrate	Nucleophile	Additive	Product	% Yield (TBTH)	% Yield (Ph_4Sn)
 **3**	OH^-	$NaHCO_3$	 **5**	86[a]	78[a,c]
	$(CH_3CO)_2CH^-$	$NaHCO_3$	 **6**	83[b]	84[b]
	$(CH_3COCHCO_2Et)^-$	Na_2CO_3	 **7**	76[b]	75[b]
 **4**	OH^-	$NaHCO_3$	 **8**	70[a]	73[a,c]
	$(CH_3CO)_2CH^-$	$NaHCO_3$	 **9**	—	81[b]
	$(CH_3COCHCO_2Et)^-$	Na_2CO_3	 **11**	79[b]	80[b]

[a] Isolated yield. [b] Yields as measured after esterification of the products with CH_2N_2. [c] Toluene was used as an additive.



Scheme 1

of higher C-Br bond strength.

iii) Studies with the tin ester. In order to provide evidence for the intermediacy of the proposed tin ester, tri-*n*-butyltin-2-iodobenzoate (**10**) was prepared by reacting TBTC with a suspension of sodium 2-iodobenzoate in benzene. When subjected to the reaction conditions with different nucleophiles the tin ester yielded salicylic acid, 2-acetonylbenzoic acid and homophthalic acid in high yields (Table 4). These observations support the predictions made about the mechanism of the reactions in Scheme 1. ^{119}Sn NMR shows a modest downfield shift of 13.46 ppm for the Sn peak as compared to that for tri-*n*-butyltin benzoate. This probably implies Sn-I coordination becoming more important in the transition state. The same type of transition state effect was also observed by Vedejs *et al.* for their internally activated tin hydride with enhanced reducing ability.[13]

Table 4: Nucleophilic Substitutions with 10 in water[a]

Entry	Nucleophile	Product	%Yield
1	OH^-	$2\text{-}OHC_6H_4CO_2H$	80
2	Ac_2CH^-	$2\text{-}(CH_2Ac)C_6H_4CO_2H$	75
3	$(AcCHCO_2H)^-$	$2\text{-}(CH_2CO_2H)C_6H_4CO_2H$	73

[a] Yields as measured after esterification of the products with CH_2N_2, $NaHCO_3$ was used as additive.

b) Tetraphenyltin Mediated Nucleophilic Substitutions

Organotin esters can be prepared by the cleavage of one or more organic groups from tetraorganotin compounds by carboxylic acids, and tetraphenyltin (Ph_4Sn) has been demonstrated to react faster than any other tetraorganotin compound.[30] As the Nucleophilic substitutions are preceded by the formation of the tin ester we felt that it should be possible to achieve the same transformation using tetraphenyltin instead of TBTH. Indeed, the reactions performed with Ph_4Sn gave the expected products in high yields (Table 3). Interestingly, the reaction between 2,5-diiodobenzoic acid and acetylacetone took place with a high yield, which could not be achieved with TBTH.

CONCLUSIONS

The chemistry of TBTH, TPTH and Ph_4Sn have been explored for the first time in water. We believe that our dehalogenation methodology in aqueous medium with TBTH, preformed TBTH and TPTH should be of general interest in organic synthesis. To the best of our knowledge this work represents the first report of organotin mediated Nucleophilic substitution. Though Hurtley reactions, *i.e.*, copper-catalyzed direct arylation of β-dicarbonyl compounds with 2-bromobenzoic acids are known, none of these reactions was reported to have been done in *aqueous* medium.[31] An interesting feature of our observations is the formation of *retro*-Claisen

reaction products from β-dicarbonyl compounds, which was also observed in Hurtley reactions. At present we are exploring other organotin mediated transformations in water and the results will be reported in due course of time.

EXPERIMENTAL

All reactions were done under argon atmosphere in deoxygenated water.

TBTH mediated dehalogenation: (a) Water soluble substrates:

Representative example for the reduction of halo-benzoic acids; reduction of 3-bromobenzoic acid: A mixture of 3-bromobenzoic acid (0.203g, 1.01 mmol), $NaHCO_3$ (0.129 g, 1.53 mmol) and AIBN (0.04 g, 0.27 mmol) in water (40 mL) was stirred for 15 min. TBTH (0.84 mL, 3.12 mmol) was added and the mixture was stirred at *ca.* 90°C for 24 h. The reaction mixture was cooled, made alkaline with 1 M NaOH and washed with $CHCl_3$. The aqueous phase was acidified with conc. HCl and the product was extracted with $CHCl_3$. The $CHCl_3$ extract was dried to yield benzoic acid (95%). The same procedure was followed for other halo-benzoic acids (entries 2 and 3, Table 1).

Reduction of 5-bromouracil: A suspension of 5-bromouracil (0.028 g, 0.15 mmol) and AIBN (0.006 g, 0.04 mmol) in 5 mL water was stirred at *ca.* 90°C for 15 min. TBTH (0.124 mL, 0.46 mmol) was added dropwise to it and the mixture was stirred at *ca.* 90°C for 24 h. The reaction mixture was cooled and washed with $CHCl_3$. Then the aq. solution was dried under high vacuum and the product composition was determined by ^1H NMR using methyl 4-nitrobenzoate as the internal standard.

Reduction of 3-bromobenzoic acid under photochemical condition: A mixture of 3-bromobenzoic acid (0.026 g, 0.13 mmol) and $NaHCO_3$ (0.017 g, 0.198 mmol) in water (5 mL) was stirred for 15 min. TBTH (0.106 mL, 0.39 mmol) was added and the mixture was photolyzed (300 nm) with stirring at room teperature for 24 h. Work up as mentioned above yielded 0.015 g of benzoic acid (93%).

(b) Water insoluble substrates:

Reduction of 9-bromoanthracene: $NaHCO_3$ (0.006 g, 0.08 mmol), 9-bromoanthracene (0.032 g, 0.13mmol), CTAB (0.021 g, 0.06 mmol) and AIBN (0.006 g, 0.04 mmol) were taken in water (5 mL) in an argon atmosphere and stirred for 1 h. TBTH (104 μL) was added and the reaction mixture was stirred at *ca.* 90°C for 24 h. The reaction mixture was cooled, diluted to 60 mL, $Al_2(SO_4)_3$ (2 g) was added and extracted with $CHCl_3$. The organic extract was washed with 5% aq. NH_3 and the crude product was purified by column chromatography on silica gel using hexane to afford 19 mg of anthracene (85%).

Reduction of cholesterol dibromide: TBTH (0.046 mL, 0.17 mmol) was added to a suspension of cholesterol dibromide (0.042 g, 0.08 mmol), $NaHCO_3$ (0.007 g, 0.08 mmol) and AIBN (0.006 g, 0.04 mmol) and stirred at *ca.* 90°C for 24 h. The reaction mixture was cooled and extracted with $CHCl_3$. The organic extract was washed with 5% aq. NH_3 and the crude product was purified by column chromatography on silica gel using hexane/ethylacetate to afford 0.025g of cholesterol (84%).

Dehalogenation by TPTH:

Representative example: A mixture of 4-bromobenzoic acid (0.102 g, 0.51 mmol), $NaHCO_3$ (0.062 g, 0.74 mmol) and AIBN (0.031 g, 0.24 mmol) in water was stirred for 30 min. at *ca.* 90°C. TPTH (0.39 mL, 1.53 mmol) was added and the mixture was stirred at *ca.* 90°C for 6 h. The reaction mixture was cooled, made alkaline with 1 M NaOH and washed with $CHCl_3$. The aqueous phase was acidified with conc. HCl and the

product was extracted with $CHCl_3$. The $CHCl_3$ extract was dried to yield 0.058 g benzoic acid (94%). Same procedure was followed for other halo-benzoic acids (entries 1-3, Table 2).

Dehalogenation by *preformed* TBTH: (a) Water soluble substrates:

Representative examples for the reduction of halo-benzoic acids

Method A; Reduction of 4-iodobenzoic acid: A mixture of 4-iodobenzoic acid (0.11 g, 0.45 mmol), $NaHCO_3$ (0.114 g, 1.35 mmol) and AIBN (0.021 g, 0.13 mmol) in water (16 mL) was warmed to *ca.* 90°C with stirring for 30 min. TBTC (0.37 mL, 1.36 mmol) was added to a cooled (*ca.* 10°C) suspension of $NaBH_4$ (0.083 g, 2.18 mmol) in EtOH (2 mL) with constant stirring. Stirring was continued for 10 min, and then this solution was added dropwise to the reaction mixture (2 min.). EtOH (2 x 1 mL) used for washing was also added to the reaction mixture which was stirred at *ca.* 90°C for 24 h. It was then cooled, made alkaline with 1 M NaOH and washed with $CHCl_3$ (6 x 10 mL). The aqueous phase was acidified with conc. HCl and the product was extracted with $CHCl_3$ (5 x 10 mL). The $CHCl_3$ extract was dried over anhyd. Na_2SO_4 and solvent was removed to yield 0.049 g of benzoic acid (90%).

Method B; Reduction of 4-bromobenzoic acid: TBTC (0.43 mL, 1.57 mmol) was added to a cooled (*ca.* 10°C) suspension of $NaBH_4$ (0.112 g, 2.96 mmol) in EtOH (4 mL) with constant stirring. Stirring was continued for 10 min. To it was added a solution of 4-bromobenzoic acid (0.104 g, 0.52 mmol) and $NaHCO_3$ (0.152 g, 1.81 mmol) in water (16 mL) followed by AIBN (0.023 g, 0.14 mmol). The mixture was stirred at *ca.* 90°C for 24 h. Work up as described above yielded 0.062 g of benzoic acid (98%).

Method B was followed for the substrates in entries 1 and 2, Table 1.

Reduction of 5-bromouracil: A suspension of 5-bromouracil (0.030 g, 0.16 mmol) and AIBN (0.007 g, 0.05 mmol) in 5 mL water was stirred at *ca.* 90°C for 15 min. TBTH (from 0.129 mL of TBTC, **Method A**) was added dropwise to it and the mixture was stirred at *ca.* 90°C for 24 h. The reaction mixture was cooled and washed with $CHCl_3$. Then the aqueous soln. was dried under high vacuum and the product composition was found out by ^1H NMR using methyl 4-nitrobenzoate as the internal standard.

(b) Water insoluble substrates:

Reduction of 9-bromoanthracene: $NaHCO_3$ (0.083 g, 0.99 mmol), 9-bromoanthracene (0.112 g, 0.44 mmol), CTAB (0.084 g, 0.23 mmol) and AIBN (0.022 g, 0.13 mmol) were taken in water (16 mL) in an argon atmosphere and stirred for 2.5 h. TBTH (from 0.36 mL of TBTC, **Method A**) was added and the reaction mixture was stirred at 90°C for 24 h. The reaction was worked up as described before to yield 0.062 g of anthracene (80%).

Reduction of cholesteroldibromide: TBTH (from 0.043 mL of TBTC, **Method A**) was added to a suspension of cholesterol dibromide (0.043 g, 0.08 mmol), $NaHCO_3$ (0.008 g, 0.09 mmol) and AIBN (0.009 g, 0.06 mmol) and stirred at *ca.* 90°C for 24 h. Work up as described before yielded 0.028 g of cholesterol (92%).

TBTH mediated Nucleophilic substitutions: All the reactions were done at *ca.* 95°C in the presence of 3.0 equiv. each of TBTH and 1,3-dinitrobenzene (DNB). Reactions were performed with 0.51 mmol and 0.34 mmol of 2-iodobenzoic (**3**) acid and 2,5-diiodobenzoic acid (**4**) respectively.

Salicylic acid (5): A mixture of **3**, DNB and $NaHCO_3$ (2.7 equiv.) were stirred with water (17 mL) for 10 min. TBTH was added dropwise to the reaction mixture and the mixture was heated with stirring for 24 h. The reaction mixture was cooled, made alkaline (pH ≈ 10) with 1 M NaOH and washed with $CHCl_3$. The aqueous phase was acidified (pH ≈ 2) with conc. HCl and the product was extracted with $CHCl_3$. The $CHCl_3$ extract was dried to yield 86% of salicylic acid.

Methyl 2-acetonylbenzoate (6):[32] A mixture of **3**, DNB, $NaHCO_3$ (4.4 equiv.) and acetylacetone (5.3 equiv.) were heated with stirring with water (18 mL) for *ca.* 30 min. TBTH was added dropwise and heating was continued for 24 h with continuous stirring. The reaction mixture was cooled, made alkaline (pH ≈ 10) with 1 M NaOH and washed with $CHCl_3$. The aqueous phase was acidified (pH ≈ 2) with conc. HCl and the product was extracted with $CHCl_3$. The $CHCl_3$ extract was dried and the crude product was reacted with an excess of CH_2N_2 in ether. The esterified product was purified by column chromatography on silica gel using 6% ethyl acetate in hexane to afford 0.082 g (83%) of the title compound. **^{1}H NMR**[32] ($CDCl_3$, 270 MHZ), δ: 2.27 (s, 3 H), 3.85 (s, 3 H), 4.09 (s, 2 H), 7.18 (d, J = 8.1 Hz, 1 H), 7.35 (t, J = 8.1 Hz, 1 H), 7.48 (t, J = 8.4 Hz, 1 H), 8.02 (d, J = 9.2, 1 H).

Methyl 2-(methoxycarbonylmethyl)benzoate (7):[33] TBTH was added dropwise to a soln of **3**, DNB, Na_2CO_3 (15.9 equiv.) and ethyl acetoacetate (*ca.* 43 equiv.) in water (16 mL). Work up was as described for **6** except diethyl ether (10 x 10 mL) was used for the extraction after acidification, yield 76%. **^{1}H NMR** ($CDCl_3$, 270 MHZ), δ: 3.69 (s, 3 H), 3.86 (s, 3 H), 4.01 (s, 2 H), 7.25 (d, J = 8.6 Hz, 1 H), 7.35 (t, J = 4.0 Hz, 1 H), 7.48 (t, J = 5.3 Hz, 1 H), 7.98 (d, J = 9.3 Hz, 1 H). **LRMS**: m/z (rel intensity) 208 (M^+, 5), 176 (100), 148 (85), 91 (50). On hydrolysis the product melted at 170-2 °C (*lit.*[34] mp: 172-4 °C)

5-Iodosalicylic acid (8):[35] A mixture of **4**, DNB and $NaHCO_3$ (3.9 equiv.) was stirred with water (17 mL) for 30 min. TBTH was added dropwise to the reaction mixture and heated with stirring for 24 h. The reaction mixture was cooled, made alkaline (pH ≈ 10) with 1 M NaOH and washed with $CHCl_3$. The aqueous phase was acidified (pH ≈ 2) with conc. HCl and the product was extracted with ether. The ether extract was dried over anhyd. Na_2SO_4 and solvent was removed. The crude product was purified by crystallization from boiling water to yield 0.063 g (70%) of the acid (mp: 195-7 °C, *lit.*[8] mp: 198 °C).

Methyl 2-(methoxycarbonylmethyl)-5-iodobenzoate (9): TBTH was added dropwise to a soln of **4**, DNB, Na_2CO_3 (17.2 equiv.) and ethyl acetoacetate (42.0 equiv.) in water (12 mL). Work up was as described for **7**. Yield 79%. **^{1}H NMR** ($CDCl_3$, 270 MHZ), δ: 3.70 (s, 3 H), 3.88 (s, 3 H), 3.96 (s, 2 H), 7.00 (d, J = 8.02 Hz, 1 H), 7.80 (dd, J = 8.1, 1.9 Hz, 1 H), 8.34 (d, J = 1.8 Hz, 1 H). **^{13}C NMR** ($CDCl_3$, 22.5 MHZ), δ: 39.37, 51.58, 52.00, 92.13, 131.16, 133.70, 135.36, 139.34, 140.89, 165.65, 170.96. **LRMS**: m/z (rel intensity) 334 (M^+, 15), 302 (100), 274 (50). **HRMS**: calcd. for $C_{11}H_{11}IO_4$, 333.9702, found 333.9719.

Tri-n-butylstannyl 2-iodobenzoate (10): TBTC (1.11 mL, 4.09 mmol) was added to a suspension of sodium 2-iodobenzoate (from 1.02 g, 4.09 mmol of 2-iodobenzoic acid) in benzene (10 mL). The mixture was stirred at room temperature for 24 h. The solution was filtered through a fritted glass funnel, washed with $CHCl_3$ (3x5 mL) and the combined organic layer was dried under high vacuum to yield 2.17 g of a light brown solid (yield 99%). A part of the product was further purified by dissolving it in hexanes followed by precipitating it out by cooling to *ca.* 0°C as a white mass, mp: 42-3 °C. **IR** (neat): 1630, 1580, 1460 cm^{-1}. **^{1}H NMR** ($CDCl_3$, 270 MHZ), δ: 0.94 (t, J = 7.1 Hz, 9 H), 1.39 (t, J = 8.2 Hz, 6 H), 1.71 (m, 12 H), 7.07 (t, J = 7.5 Hz, 1 H), 7.36 (t, J = 7.4 Hz, 1 H), 7.78 (d, J = 7.7 Hz, 1 H), 7.94 (d, J = 7.9 Hz, 1 H). **^{13}C NMR** ($CDCl_3$, 22.5 MHZ), δ: 13.64, 16.84, 27.01, 27.90, 94.01, 127.62, 130.72, 131.49, 138.46, 140.67, 171.84. **^{119}Sn NMR** ($CHCl_3$, D_2O Lock, 149 MHZ), δ: 125.70. **LRMS**: m/z (rel intensity) 537 (M^+, 1), 481 (M - Bu, 100), 269 (95), 248 (65). Anal. Calcd for $C_{19}H_{31}IO_2Sn$: C, 42.49; H, 5.82. Found: C, 42.81; H, 5.86.

Nucleophilic substitutions with the tin ester: All the reactions were done at *ca.* 95 °C with 0.19 mmol of **10**.

Salicylic acid (5): A mixture of **10** and $NaHCO_3$ (3.2 equiv.) were stirred in 6 mL of water for 24 h. Work up as before yielded 80% of **5**.

Methyl 2-acetonylbenzoate (6): A mixture of **10**, $NaHCO_3$ (4.1 equiv.) and acetylacetone (5.9 equiv.) was heated with stirring with 6 mL of water. Work up as before yielded 75% of the compound **6**.

Methyl 2-(methoxycarbonylmethyl)benzoate (7): A mixture of **10**, Na_2CO_3 (16.0 equiv.) and ethyl acetoacetate (40 equiv.) in water (5.5 mL) was used. Work up as described before yielded 73% of **7**.

Ph_4Sn (TPT) mediated Nucleophilic substitutions: All the reactions were done at *ca.* 95 °C with 3.0 equiv. of TPT. Reactions were performed with 0.51 mmol and 0.34 mmol of 2-iodobenzoic (**3**) acid and 2,5-diiodobenzoic acid (**4**) respectively.

Salicylic acid (5): A mixture of compound **3**, $NaHCO_3$ (2.4 equiv.) and TPT was stirred with water (15 mL) and toluene (2 mL) for 10 min, followed by heating with constant stirring. Work up as before yielded 78% of compound **5**.

Methyl 2-acetonylbenzoate (6): A mixture of **3**, TPT, $NaHCO_3$ (3.8 equiv.) and acetylacetone (28 equiv.) was stirred with water (15 mL) for *ca.* 30 min followed by heating with continuous stirring. Work up as before yielded 84%of compound **6**.

Methyl 2-(methoxycarbonylmethyl)benzoate (7): A mixture of **3**, TPT, Na_2CO_3 (13 equiv.) and ethyl acetoacetate (46 equiv.) in water (13 mL) was used. Work up as described before yielded 75% of compound **7**.

5-Iodosalicylic acid (8): A mixture of **4**, TPT and $NaHCO_3$ (3.7 equiv.) in a mixture of 15 mL of water and 2 mL of toluene were used. Work up as before yielded 73% of compound **8**.

Methyl 2-acetonyl-5-iodobenzoate (11): A mixture of compound **4**, $NaHCO_3$ (5.2 equiv.), acetylacetone (41 equiv.) and TPT in 12 mL of water was used. Work up as described for **7** yielded 81% of compound **11**. **^{1}H NMR** ($CDCl_3$, 90 MHZ), δ: 2.26 (s, 3 H), 3.84 (s, 3 H), 4.04 (s, 2 H), 6.91 (d, J = 8.1 Hz, 1 H), 7.78 (dd, J = 8.9, 1.8, 1 H), 8.33 (d, J = 1.8 Hz, 1 H). **^{13}C NMR** ($CDCl_3$, 22.5 MHZ), δ: 29.78, 49.02, 52.11, 90.02, 130.83, 134.03, 136.36, 139.56, 141.11, 165.76, 204.79. **LRMS**: m/z (rel intensity) 318 (M^+, 20), 286 (55), 43 (100). **HRMS**: calcd. for $C_{11}H_{11}IO_3$, 317.9753, found 317.9760.

Methyl 2-(methoxycarbonylmethyl)-5-iodobenzoate (9): A mixture of **4**, TPT, Na_2CO_3 (17equiv.) and ethyl acetoacetate (42 equiv.) in water (12 mL) was used. Work up was as described for before yielded 80% of compound **9**.

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