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MANNICH REACTIONS OF ARYLTRIALKYLSTANNANES IN APROTIC SOLVENTS

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Abstract:- Aryltributyl- and aryltrimethyl-stannanes react with a range of N,N-dialkylmethyleneimonium salts to afford N,N-dialkylaminomethyl derivatives in good yields. The method can be used to obtain regioisomers that are not available using classical procedures. "In situ" reactions can also be carried out using alkoxydialkylaminomethanes (aminol ethers) and bis(dialkylamino)methanes (aminals) together with chlorotrimethyl- and trichloromethyl-silanes as the source of the electrophile. However, the "in situ" reactions do not afford good yields in the majority of cases, as a result of the inhibition of imonium salt formation by trialkylchlorostannane.

A wide range of aryltrialkyl-silanes and -stannanes with a pre-determined regiochemistry is available from aryl halides by way of the reactions of Grignard or organolithium reagents. The conversion of these reagents into a number of other derivatives by means of ipso electrophilic addition-with-elimination reactions has been reported.[1] The reactions that have been studied previously have led to the introduction of functionalities such as $-SO_3H$,[2] $-SO_2R$,[3] -NO,[4] $-NO_2$,[5] -CN,[6] -COR,[7] -I,[8] and ^2H.[9] The increased polarity of the carbon-tin bonds as compared to similar carbon-silicon bonds allows reactions of the tin compounds to be carried out under milder conditions or using weak electrophiles that do not react with the corresponding silanes.[10] Hitherto, the weakest electrophile that has been successfully used in reactions with aryltrialkylstannanes is the nitrosonium ion (or its equivalent). The use of aryltrialkyl- silanes[11] constitutes the normal methodology with strong electrophiles, for example as in Friedel-Crafts acylation reactions.

The classical Mannich reaction,[12] in which a labile proton is replaced by an α-aminoalkyl residue, is limited in its aromatic variation to nucleophilic systems. Thus heterocyclic compounds such as indoles[13] and pyrroles[14] have been widely studied as also have carbocyclic amines[15] and phenols.[16] Benzenoid compounds less reactive towards electrophiles than m-dimethoxybenzene[17] have not been reported to undergo Mannich reactions.

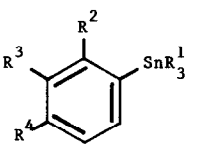
The use of pre-formed methyleneimonium salts in aprotic solvents has been reported to result in useful improvements to both the range of substrates and yields obtained in Mannich reactions.[18] "In situ" reactions may be carried out efficiently with a range of π-excessive aromatic compounds by activating aminals and aminol ethers with either sulphur dioxide[19] or chlorosilanes.[20]

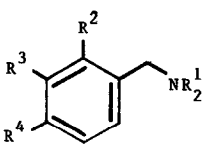
The well-established increase in reactivity towards ipso electrophilic addition-with -elimination reactions of certain aryl-alkylmetallic compounds prompted our study. We now report the results of our investigations of the reactions of a range of aryltrialkylstannanes with pre-formed methyleneimonium salts. Some of these results have been reported in a preliminary communication.[21] We also report the results of our attempted extension of the study to include "in-situ" reactions in which the reactive electrophile was generated by the interaction of an aminal or an aminol ether with either chlorotrimethylsilane or trichloromethylsilane.

A wide range of methyleneimonium chlorides may be made from aminals by reaction with acetyl chloride in ether,[22] or by the reaction of trichloromethylsilane with aminol ethers.[23] These salts can be stored at room temperature, in the absence of moisture, over long periods. We did not detect a reaction when 4-methoxyphenyltrimethylsilane in dichloromethane was stirred with an excess of N,N-dimethylmethyleneimonium chloride over a prolonged period of time. The predictable increase in reactivity using 2-methoxyphenyltrimethylsilane only resulted in the formation of 2-methoxy-N,N-dimethylbenzylamine (**16**) in <5% yield after 24h. It was particularly interesting to study the reaction of 2,4-dimethoxyphenyltrimethylsilane with N-morpholinylmethyleneimonium chloride as this reaction gave a direct comparison with the reaction of the same imonium salt with 1,3-dimethoxybenzene. The yields of (**31**) obtained in the two reactions were comparable, but it is evident that the trimethylsilyl residue does direct the electrophile to ipso substitution since no evidence was obtained for the presence of attack at a non-ipso position.

The increased reactivity towards electrophiles of aryltrialkylstannanes suggested that reactions with those organometallic reagents would be more successful than with the silanes. When a solution of 4-methoxyphenyltributylstannane (**9**) in dichloromethane was stirred with N,N-dimethylmethyleneimonium chloride at room temperature the salt slowly dissolved and after about 30h we isolated 4-methoxy-N,N-dimethylbenzylamine (**17**) in 70% yield.

The generality of the above reaction and its use in carrying out Mannich reactions in the absence of electron-releasing substituents is indicated by **TABLE 1**, and exemplified in structures (**12**)-(**19**). **TABLE 1** also includes examples using a wide range of imonium salts. Reactions of the corresponding iodides, prepared from the aminals by interaction with iodotrimethylsilane[24], gave, in our hands, lower yields than those reported in **TABLE 1**.



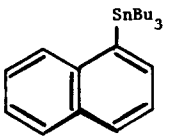


(1; R^1=Bu, R^2=R^3=R^4=H)
(2; R^1=Me, R^2=R^3=R^4=H)
(3; R^1=Bu, R^2=Me, R^3=R^4=H)
(4; R^1=Bu, R^2=R^4=H, R^3=Me)
(5; R^1=Me, R^2=R^4=H, R^3=Me)
(6; R^1=Bu, R^2=R^3=H, R^4=Me)
(7; R^1=Bu, R^2=OMe, R^3=R^4=H)
(8; R^1=Bu, R^2=R^4=H, R^3=OMe)
(9; R^1=Bu, R^2=R^3=H, R^4=OMe)
(10; R^1=Me, R^2=R^3=H, R^4=OMe)
(11; R^1=Bu, R^2=R^4=OMe, R^3=H)

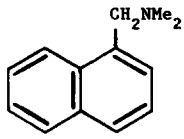
(12; R^1=Me, R^2=R^3=R^4=H)
(13; R^1=Me, R^2=Me, R^3=R^4=H)
(14; R^1=Me, R^2=R^4=H, R^3=Me)
(15; R^1=Me, R^2=R^3=H, R^4=Me)
(16; R^1=Me, R^2=OMe, R^3=R^4=H)
(17; R^1=Me, R^2=R^3=H, R^4=OMe)
(18; R^1=Et, R^2=R^3=H, R^4=OMe)
(19; R^1=Me, R^2=R^4=OMe, R^3=H)

Although the yields reported in **TABLE 1** are similar for the butyl- and methyl-stannanes we originally thought that the reactions of the aryltrimethylstannanes would proceed at faster rates than those of the aryltributylstannanes. This prejudice undoubtedly arises from the more frequent use of aryltrimethylstannanes in electrophilic addition-with-elimination reactions, notwithstanding the greater cost of chlorotrimethylstannane as compared with tributylchloro- stannane. We have carried out a series of competition reactions in order to obtain more information on this point.

A reaction in which N,N-dimethylmethyleneimonium chloride in dichloromethane was allowed to compete for a large excess of equimolar amounts of phenyltrimethylstannane (**2**) and m-tolyltributyl-

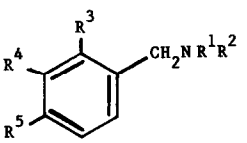


(20)



(21)

butylstannane (**4**) resulted in the formation of N,N-dimethylbenzylamine (**12**) and N,N,3-trimethylbenzylamine (**14**) in the ratio 2 : 8. In a similar reaction using phenyltributylstannane (**1**) and m-tolyltrimethylstannane (**5**) the expected products were obtained in the ratio 2 : 5. It is clear from these results that there is no great advantage in using the aryltrimethylstannane; indeed the results might suggest that the transition state leading to the Wheland intermediate occurs at a later stage than in some other electrophilic destannylation reactions, and that a greater relief of steric strain results using the aryltributylstannanes. However, too much must not be read into these results, since the poor yields obtained with imonium salts other than N,N-dimethylmethyleneimonium chloride show that the reactions are subject to complex steric features. It is noteworthy, in this connection, that an attempted reaction between 4-methoxyphenyltrimethylstannane (**10**) and N,N-di-iso-propylmethyleneimonium chloride (prepared from ethoxy-N,N-di-iso-propylaminomethane) did not afford a Mannich base. Similarly, we did not isolate a Mannich base in an attempted reaction between 1-naphthyltributylstannane (**20**) and N-morpholinylmethyleneimonium chloride in acetontrile under reflux in an atmosphere of dry nitrogen. In this latter case we were able to detect the presence of naphthalene and tributylchlorostannane in the recovered neutral material. The source of the proton in the proto-destannylation reaction is obscure.



(**22**; R^1-R^2= $-(CH_2)_4-$, R^3=R^4=R^5=H)
(**23**; R^1-R^2= $-(CH_2)_2O(CH_2)_2-$, R^3=R^4=R^5=H)
(**24**; R^1-R^2= $-(CH_2)_4-$, R^3=Me, R^4=R^5=H)
(**25**; R^1-R^2= $-(CH_2)_2O(CH_2)_2-$, R^3=Me, R^4=R^5=H)
(**26**; R^1-R^2= $-(CH_2)_5-$, R^3=OMe, R^4=R^5=H)
(**27**; R^1-R^2= $-(CH_2)_4-$, R^3=R^5=H, R^4=OMe)
(**28**; R^1-R^2= $-(CH_2)_2O(CH_2)_2-$, R^3=R^5=H, R^4=OMe)
(**29**; R^1-R^2= $-(CH_2)_4-$, R^3=R^4=H, R^5=OMe)
(**30**; R^1-R^2= $-(CH_2)_2O(CH_2)_2-$, R^3=R^4=H, R^5=OMe)
(**31**; R^1-R^2= $-(CH_2)_2O(CH_2)_2-$, R^3=R^5=OMe, R^4=H)

We also investigated the possible acceleration caused by an ortho- substituent by carrying out a reaction using o-tolyl- and p-tolyl-tributylstannane as the competing pair. Remarkably, the presence of the ortho-methyl group does not cause an increase in the relative rate: the o-methyl : p-methyl isomer ratio was 1.5 : 8.5. A significant effect due to the presence of an ortho- oxygen function was indicated by the use of o-methoxyphenyl- and p-methoxyphenyl- tributyl- stannane in a competition reaction which gave an o- : p- ratio of 6 : 4. We suggest that the electrophile may co-ordinate with the methoxy- group prior to attack at the nucleophilic centre, and hence reaction is more favourable in the case of the o-methoxyphenyl- tributylstannane. It is likely that the results of these competition experiments are subject to problems associated with inefficient mixing and therefore only if kinetic measurements are made will it be possible to evaluate relative reactivities accurately.

TABLE 1

Reactions of Arylstannanes with Eschenmoser Salts ($[R_2N{=}CH_2]^+ \ Cl^-$)[@]

$$Ar\text{-}SnR_3 + [R_2N{=}CH_2]^+ \ Cl^- \longrightarrow Ar\text{-}CH_2NR_2 + R_3SnCl$$

iminium salt R_2 =	aromatic residue	alkyltin residue	solvent	conditions	(structure)	yield[†] %
Me_2	phenyl-	$-SnMe_3$	CH_2Cl_2	24h reflux	(12)	65
$(CH_2)_4$	phenyl-	$-SnBu_3$	CH_3CN	20h reflux	(22)	11
$O(CH_2CH_2)_2$	phenyl-	$-SnBu_3$	CH_3CN	20h reflux	(23)	15
Me_2	o-tolyl-	$-SnBu_3$	CH_2Cl_2	48h reflux	(13)	51
$(CH_2)_4$	o-tolyl-	$-SnBu_3$	CH_3CN	20h reflux	(24)	13
$O(CH_2CH_2)_2$	o-tolyl-	$-SnBu_3$	CH_3CN	20h reflux	(25)	12
Me_2	m-tolyl-	$-SnBu_3$	CH_2Cl_2	48h reflux	(14)	60
Me_2	m-tolyl-	$-SnBu_3$	CH_3CN	4h reflux	(14)	39
Me_2	p-tolyl-	$-SnBu_3$	CH_2Cl_2	24h reflux	(15)	67
Me_2	o-anisyl-	$-SnBu_3$	CH_2Cl_2	15h reflux	(16)	70
$(CH_2)_5$	o-anisyl-	$-SnBu_3$	CH_2Cl_2	24h reflux	(26)	57
$(CH_2)_4$	m-anisyl-	$-SnBu_3$	CH_3CN	19h reflux	(27)	13
$O(CH_2CH_2)_2$	m-anisyl-	$-SnBu_3$	CH_3CN	19h reflux	(28)	17
Me_2	p-anisyl-	$-SnBu_3$	CH_2Cl_2	72h RT	(17)	75
Me_2	p-anisyl-	$-SnBu_3$	CH_2Cl_2	15h reflux	(17)	70
Me_2	p-anisyl-	$-SnMe_3$	CH_2Cl_2	21h RT *	(17)	71
Et_2	p-anisyl-	$-SnBu_3$	CH_3CN	28h reflux	(18)	26
Et_2	p-anisyl-	$-SnMe_3$	CH_3CN	20h reflux	(18)	23
$(CH_2)_4$	p-anisyl-	$-SnBu_3$	CH_3CN	68h reflux	(29)	23
$(CH_2)_4$	p-anisyl-	$-SnMe_3$	CH_3CN	20h reflux	(29)	32
$O(CH_2CH_2)_2$	p-anisyl-	$-SnBu_3$	CH_3CN	42h reflux	(30)	53
$O(CH_2CH_2)_2$	p-anisyl-	$-SnMe_3$	CH_3CN	20h reflux	(30)	59
$O(CH_2CH_2)_2$	2,4-di-$MeOC_6H_3$-	$-SnBu_3$	CH_3CN	23h reflux	(31)	45
Me_2	1-naphthyl-	$-SnBu_3$	CH_2Cl_2	24h reflux	(21)	66
Me_2	1,4-C_6H_4-bis	$-SnBu_3$	CH_3CN	48h reflux	(34)	58$
Me_2	4-thp-oxy-phenyl-	$-SnMe_3$	CH_2Cl_2	15h reflux	(40)	50
Me_2	3-thienyl-	$-SnMe_3$	CH_2Cl_2	60h RT	(36)	66
$(CH_2)_4$	3-thienyl-	$-SnMe_3$	CH_3CN	90h RT	(37)	30
$O(CH_2CH_2)_2$	3-thienyl-	$-SnMe_3$	CH_3CN	94h RT	(38)	59

[@] Reactions carried out using $R_2N\text{-}CH_2\text{-}NR_2$: $ArSnR_3$ = 3 : 2.

[†] Yields not optimised.

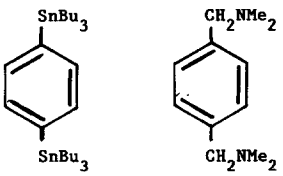
* Reaction preceeded by 3h at -20 C.

$ ratio of $(Me_2N)_2CH_2$: p-$C_6H_4(SnBu_3)_2$ = 6:1;
product p-$C_6H_4(CH_2NMe_2)_2$.

The possibility of carrying out a bis-(dialkylamino)methylation reaction was investigated using 1,4-bis-(tributylstannyl)benzene (**33**) in a reaction with an excess of N,N-dimethylmethylene-imonium chloride. 1,4-Bis-(N,N-dimethylaminomethyl)benzene (**34**) was obtained in 58% yield.

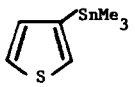
That aminoalkyl-destannylation reactions can also be used to achieve unusual regiospecificity was established by carrying reactions of 3-thienyltrimethylstannane (**35**), which was prepared in 87% yield from 3-thienyllithium and chlorotrimethylstannane. A reaction with N,N-dimethyl- methylene-imonium chloride was carried out room temperature for 60h. 3-(N,N-Dimethylaminomethyl)thiophene

(**36**) was isolated in 66% yield. In other reactions using N-pyrrolidinyl- and N-morpholinyl-methyleneimonium chlorides, reactions were carried out in acetonitrile and gave the expected products (**37**) and (**38**) in 30% and 59% yields repectively. In none of these reactions were we able to detect the presence of the regio-isomers by nmr spectroscopy. 3-Substituted thiophenes are most conveniently distinguished from their regio-isomers by ^{13}C nmr spectroscopy.[25] Thus 2-(N,N-dimethylaminomethyl)thiophene showed the following resonances at δ_c= 45.0(q), 58.3(t), 125.0(d), 125.9(d), 126.4(d), and 142.4(s)ppm, while 3-(N,N-dimethylaminomethyl)thiophene (**36**) showed resonances at δ_c= 45.2(q), 58.8(t), 122.7(d), 125.4(d), 128.4(d), and 139.7(s)ppm. These results are particularly interesting since with very strong electrophiles mixtures of products might have been anticipated. For example, 2-thienyltrimethylsilane is reported to undergo substitution at position-5 in a Friedel-Crafts acylation reaction.[26]

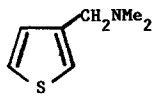


(**33**)

(**34**)

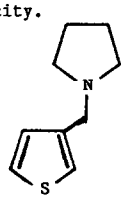


(**35**)

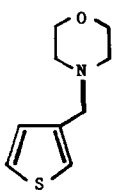


(**36**)

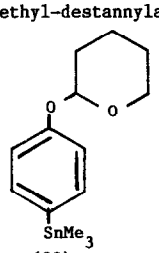
The Mannich reactions of phenols normally proceed regioselectively to afford the ortho-isomer. In order to demonstrate the utility of the present method we carried out a reaction of N,N-dimethylmethyleneimonium chloride with 4-tetrahydropyranyloxyphenyltrimethylstannane (**39**) which gave, after the normal work-up, 4-(N,N-dimethylaminomethyl)phenol (**40**) in 50% yield. The reactions reported show that electrophilic aminomethyl-destannylation reactions proceed with useful regiospecificity.



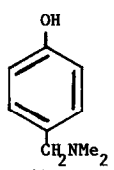
(**37**)



(**38**)



(**39**)



(**40**)

We also attempted to simplify the experimental method by investigating "in situ" reactions of aryltrialkylstannanes by activating aminals and aminol ethers in acetonitrile using chlorosilanes. Our results (**TABLE 2**) show that while satisfactory yields can be obtained with aryltrialkylstannanes which have electron-releasing substituents, other systems give poor yields. An explanation of such results using, for example, phenyltributylstannane (**1**), may relate to the inhibition of the formation of imonium salts by chlorotrialkylstannanes. In separate experiments we found no evidence for the formation of an imonium salt when chorotributylstannane was added to ethoxy-N,N-diethylaminomethane in ether, and when we attempted to carry out a reaction of 2-methylfuran with ethoxy-N,N-diethylaminomethane using chlorotributylstannane as a potential activating agent. Evidently the tin-oxygen bond strength is not great enough to allow the formation of an imonium salt from an aminol ether. We would normally expect to obtain comparable yields from reactions carried out either by using a pre-formed imonium salt or from an "in situ" reaction. For example, N-morpholinylmethylene- imonium chloride gave a 63% yield of the expected product (**31**) with 1,3-dimethoxybenzene, and an "in situ" reaction in which trichloromethylsilane was added to a solution of 1,3-dimethoxy- benzene and ethoxy-N-morpholinylmethane gave the Mannich base (**31**) in 65% yield. In many of the examples quoted in **TABLE 2** the yields reported are significantly lower than those reported in **TABLE 1** for analogous reactions. We presume that an interaction between the aminal or aminol ether and some of the aryltrialkylstannanes can inhibit

the formation of the electrophile that would be involved in the reaction. Only in the reactions of the 4-methoxy- and 2,4-dimethoxy-phenyltrialkylstannanes is there a reasonable correspondence between the two sets of results.

TABLE 2

"In Situ" Reactions of Arylstannanes

aromatic residue	alkyltin residue	reagent	silane	time	(structure)	% yield
phenyl-	$-SnBu_3$	$EtOCH_2N(CH_2CH_2)O$	$MeSiCl_3$	24h	(23)	29
o-tolyl-	$-SnBu_3$	$i\text{-}PrOCH_2NMe_2$	Me_3SiCl	25h	(13)	19
o-tolyl-	$-SnBu_3$	$[O(CH_2CH_2)N]_2CH_2$	$MeSiCl_3$	25h	(25)	18
m-anisyl-	$-SnBu_3$	$EtOCH_2N(CH_2CH_2)O$	$MeSiCl_3$	23h	(28)	28
p-anisyl-	$-SnBu_3$	$(Me_2N)CH_2$	Me_3SiCl	42h	(17)	22
p-anisyl-	$-SnBu_3$	$(Me_2N)CH_2$	$MeSiCl_3$	68h	(17)	65
p-anisyl-	$-SnBu_3$	$i\text{-}PrOCH_2NMe_2$	Me_3SiCl	44h	(17)	48
p-anisyl-	$-SnMe_3$	$i\text{-}PrOCH_2NMe_2$	Me_3SiCl	24h	(17)	62
p-anisyl-	$-SnBu_3$	$i\text{-}PrOCH_2NMe_2$	$MeSiCl_3$	18h	(17)	41
p-anisyl-	$-SnBu_3$	$EtOCH_2NEt_2$	$MeSiCl_3$	42h	(18)	20
p-anisyl-	$-SnBu_3$	$[(CH_2)_4N]_2$	$MeSiCl_3$	42h	(29)	38
p-anisyl-	$-SnBu_3$	$EtOCH_2N(CH_2)_4$	$MeSiCl_3$	68h	(29)	29
p-anisyl-	$-SnMe_3$	$EtOCH_2N(CH_2)_4$	$MeSiCl_3$	22h	(29)	26
p-anisyl-	$-SnBu_3$	$[O(CH_2CH_2)_2N]_2CH_2$	$MeSiCl_3$	28h	(30)	53
p-anisyl-	$-SnBu_3$	$EtOCH_2N(CH_2CH_2)_2O$	$MeSiCl_3$	44h	(30)	63
p-anisyl-	$-SnMe_3$	$EtOCH_2N(CH_2CH_2)_2O$	$MeSiCl_3$	22h	(30)	32
p-anisyl-	$-SnMe_3$	$EtOCH_2N(CH_2CH_2)_2O$	Me_3SiCl	24h	(30)	38
2,4-di-$MeO(C_6H_3)$-	$-SnBu_3$	$i\text{-}PrOCH_2NMe_2$	$MeSiCl_3$	21h	(19)	56
2,4-di-$MeO(C_6H_3)$-	$-SnBu_3$	$EtOCH_2N(CH_2CH_2)_2O$	$MeSiCl_3$	21h	(31)	60
3-thienyl-	$-SnMe_3$	$i\text{-}PrOCH_2NMe_2$	$MeSiCl_3$	23h	(36)	25
3-thienyl-	$-SnMe_3$	$EtOCH_2N(CH_2)_4$	$MeSiCl_3$	90h†	(37)	38
3-thienyl-	$-SnMe_3$	$EtOCH_2N(CH_2CH_2)O$	$MeSiCl_3$	94h†	(38)	51

† Reactions carried out at room temperature.

Finally, we have also looked briefly at reactions of benzyltributylstannane (**41**). The well known importance of β-phenylethylamines suggested that a new alternative route to this class of compounds could be valuable. We found that when benzyltributylstannane and N,N-dimethyl- methyleneimonium chloride were heated under reflux in dichloromethane for 48h we were able to isolate N,N-dimethyl-β-phenylethylamine (**42**) in 46% yield. A reaction of N-morpholinyl- methyleneimonium chloride in acetonitrile gave a 28% yield of the expected product (**43**) and an "in situ" reaction using ethoxy-N-morpholinylmethane and trichloromethylsilane gave the same product in 31% yield.

$PhCH_2SnBu_3$ (**41**)

$PhCH_2CH_2NR^1R^2$

(**42**, $R^1=R^2=Me$)

(**43**, $R^1\text{-}R^2=-(CH_2)_2O(CH_2)_2-$)

The mechanism involved in the reactions of benzyltributylstannane is not obvious. While the electrophilic cleavage of benzyl-tin bonds is not unprecedented those reactions normally occur much less readily than reactions involving the electrophilic cleavage of aryl-tin bonds. Very reactive species such as acids[27] and mercury(II) salts[28] effect electrophilic cleavage, and sulphur dioxide, which is only moderately electrophilic, also reacts with benzylstannanes to

yield the insertion products.[29] Our reactions with benzyltributylstannane did require heating under reflux, whereas in many of our experiments using arylstannanes, satisfactory results could be obtained at room temperature. The addition of fluoride ion did not have a catalytic effect and we therefore exclude the involvement of an intermediate with anionic character. Similarly, we were unable to find evidence for the involvement of the benzyl radical. Allyl- and benzyl- silanes are known[30] to react with pyrrolinium salts by a photochemical process that is thought to involve electron transfer from the silane to the imonium salt. We observed no improvement in the yield on ultraviolet irradiation of a reaction involving N,N-dimethylmethyleneimonium chloride, and reactions of N-morpholinylmethyleneimonium chloride were unaffected when they were conducted in the presence of AIBN, carefully degassed solvent, or when carried out in a solution through which was passed a stream of oxygen.

EXPERIMENTAL SECTION

2-(4-trimethylstannylphenoxy)tetrahydropyran (39). n-Butyllithium (15% in hexane, 0.019 mol) was added to 2-(4-bromophenoxy)tetrahydropyran[31] (4.9g, 0.019 mol) in dry ether at -78 C under a static atmosphere of dry nitrogen. The mixture was stirred at -78 C for 2h and at 0 C for 1h before chlorotrimethylstannane (3.8g, 0.019 mol) was added dropwise. After 6h at room temperature the mixture was heated under reflux for a further 16h. The cooled solution was washed with water, dried (magnesium sulphate), evaporated, and the residue was distilled and gave 3.6g of (**39**), 56% yield, b.p. 170-176/1 mmHg, ^{1}H NMR ($CDCl_3$) δ = 0.30 (s, 9H), 1.40-2.20 (m, 6H), 3.40-4.00 (m, 2H), 5.25 (t, 1H, J=), and 6.75-7.30 (m, 4H, AA'BB', J_{AB}=8Hz)ppm, M^+ found: 342.0618, 340.0613, and 338.0617, $C_{14}H_{22}O_2Sn$ requires 342.0642, 340.0642, and 338.0642.

3-Methoxyphenyltributylstannane (8). Prepared from 3-methoxyphenylmagnesium bromide and tributylchlorostannane in 75% yield, b.p. 125/0.15 mmHg, ^{1}H NMR δ = 0.63-1.83 (m, 27H), 3.74 (s, 3H), and 6.61-7.46 (m, 4H)ppm.

2,4-Dimethoxyphenyltributylstannane (11). Prepared from 2,4-dimethoxyphenylmagnesium bromide and tributylchlorostannane in 61% yield, b.p. 138-142/0.1 mmHg, ^{1}H NMR δ = 0.66-1.82 (m, 27H), 3.75 (s, 3H), 3.80 (s, 3H), 6.35-6.63 (m, 2H), and 7.25 (d, 1H, J_{AB}=7.5Hz), M^+ found: 428.1780, $C_{20}H_{36}O_2Sn$ requires 428.1737.

2,4-Dimethoxyphenyltrimethylsilane. Prepared from 2,4-dimethoxyphenylmagnesium bromide and chlorotrimethylsilane in 69% yield, b.p. 92-93/2.5 mmHg, ^{1}H NMR δ = 0.21 (s, 9H), 3.78 (s, 6H), 6.34-6.60 (m, 2H), and 7.22 (d, 1H, J_{AB}=8 Hz)ppm, M^+ found: 210.1067, $C_{11}H_{18}O_2Si$ requires 210.1076.

General methods for reactions using pre-formed imonium salts

(A) Acetyl chloride (1.18g, 0.015mol) in dry diethyl ether (5ml) was added dropwise to a stirred solution of the aminal[32] (0.015mol) in ether (10ml) at 0 C. After 20min the solvent was removed by means of a filter stick and the salt was washed with several portions of dry ether. Dry dichloromethane (20ml) was then added to the imonium salt and the aryltrialkylstannane (0.01mol) in dichloromethane (10ml) was added dropwise. The mixture was stirred at the specified temperature for the given time and the reaction was terminated by the addition of aqueous sodium hydroxide solution (20ml, 4molar). The two phases were separated, and the aqueous phase was extracted with dichloromethane. The organic phase was extracted with aqueous hydrochloric acid (2molar) and the acidic extracts were washed with dichloromethane. The acidic aqueous phase was then basified with aqueous sodium hydroxide (4molar) and the milky precipitate was extracted into dichloromethane, which was washed with aqueous sodium hydroxide, dried (magnesium sulphate), and evaporated to afford the crude Mannich base, which was purified by distillation (Kugelrohr).

(B) Pre-formed imonium salt (0.005mol) and the aryltrialkylstannane (0.005mol) were heated under reflux for the given time in dry acetonitrile (50ml) in an atmosphere of dry nitrogen. The solvent was evaporated from the cooled reaction mixture after the addition of water, and the aqueous acidic residue (aqueous hydrochloric acid was added if necessary) was extracted with dichloromethane (3 x 30ml). The aqueous layer was basified with aqueous sodium hydroxide (4molar), extracted with dichloromethane (3 x 30ml), dried (magnesium sulphate), evaporated, and distilled (Kugelrohr).

General method for "in situ" reactions

(C) The aryltrialkylstannane (0.005mol) and the aminal or aminol ether (0.005mol) were stirred together under nitrogen in dry acetonitrile (25ml) at 0 C. The silane (0.005mol) in acetonitrile (25ml) was added dropwise and the mixture was heated under reflux for the indicated time. In some reactions a precipitate of an imonium salt was noted before the heating commenced. The reaction mixtures were worked up as in (B) above.

N,N-Dimethylbenzylamine (12). Method (A) using bis(dimethylamino)methane and phenyltrimethylstannane (**2**)[33] gave (**12**), 65% yield, b.p. 82-84/20 mmHg, (lit.[34] b.p. 178-180/760 mmHg), ^{1}H NMR ($CDCl_3$) δ = 2.23 (s, 6H), 3.38 (s, 2H), and 7.30 (s, 5H)ppm.

N-Benzylpyrrolidine (22). Method (B) using N-pyrrolidinylmethyleneimonium chloride and phenyltributylstannane (**1**)[35] gave (**22**), 11% yield, b.p. 55/1.5 mmHg, (lit.[36] b.p. 116-122/22 mmHg), ^{1}H NMR δ = 1.67-1.97 (m, 4H), 2.38-2.77 (m, 4H), 3.64 (s, 2H), and 7.30 (br.s, 5H)ppm.

N-Benzylmorpholine (23). Method (B) using N-morpholinylmethyleneimonium chloride and phenyltributylstannane (**1**) gave (**23**), 15% yield, b.p. 63/1.5 mmHg, (lit.[37] b.p. 128-129/13 mmHg), ^{1}H NMR δ = 2.27-2.58 (m, 4H), 3.47 (s, 2H), 3.55-3.84 (m, 4H), and 7.28 (br.s, 5H)ppm.

N,N,2-Trimethylbenzylamine (13). Method (A) using bis(dimethylamino)methane and o-tolyltributylstannane(**3**) [38] gave (**13**), 51% yield, b.p. 76-78/10 mmHg, (lit.[39] b.p. 73-75/10 mmHg), ^{1}H NMR δ = 2.15 (s, 6H), 2.30 (s, 3H), 3.22 (s, 2H), and 6.92 (m, 4H)ppm.

N-(2-Methylbenzyl)pyrrolidine (24). Method (B) using N-pyrrolidinylmethyleneimonium chloride and o-tolyltributylstannane (**3**) gave (**24**), 13% yield, b.p. 90/0.7 mmHg, (lit.[40] b.p. 113-115/12 mmHg), ^{1}H NMR δ = 1.60-1.92 (m, 4H), 2.35 (s, 3H), 2.34-2.70 (m, 4H), 3.59 (s, 2H), and 7.20 (br.s, 4H)ppm.

N-(2-Methylbenzyl)morpholine (25). Method (B) using N-morpholinylmethyleneimonium chloride and o-tolyltributylstannane (**3**) gave (**25**), 12% yield, b.p. 106/0.9 mmHg, (lit.[41] b.p. 149-151/10 mmHg), ^{1}H NMR δ = 2.35 (s, 3H), 2.30-2.57 (m, 4H), 3.45 (s, 2H), 3.57-3.83 (m, 4H), and 7.17 (br.s, 4H)ppm.

N,N,3-Trimethylbenzylamine (14). Method (A) using bis(dimethylamino)methane and m-tolyltributylstannane (**4**)[38] gave (**14**), 60% yield, b.p. 102-104/28 mmHg, (lit.[42] b.p. 70-72/ 15mmHg), ^{1}H NMR δ = 2.22 (s, 6H), 2.32 (s, 3H), 3.35 (s, 2H), and 6.90-7.25 (m, 4H)ppm. Using method (B) gave (**14**) in 39% yield.

N,N,4-Trimethylbenzylamine (15). Method (A) using bis(dimethylamino)methane and p-tolyltributylstannane (**6**)[43] gave (**15**), 67% yield, b.p. 102/35 mmHg, (lit.[34] b.p. 196-198/760 mmHg), ^{1}H NMR δ = 2.22 (s, 6H), 2.33 (s, 3H), 3.36 (s, 2H), and 7.10 (s, 4H)ppm.

2-Methoxy-N,N-dimethylbenzylamine (16). Method (A) using bis(dimethylamino)methane and 2-methoxyphenyltributylstannane (**7**)[44] gave (**16**), 70% yield, b.p. 102-104/12 mmHg, (lit.[45] b.p. 113/20 mmHg), ^{1}H NMR δ = 2.25 (s, 6H), 3.43 (s, 2H), 3.78 (s, 3H), and 6.70-7.30 (m, 4H)ppm.

N-(2-Methoxybenzyl)piperidine (26). Method (A) using dipiperidylmethane and 2-methoxyphenyltributylstannane (7) gave (26), 58% yield, b.p. 120-124/0.8 mmHg, (lit.[46] b.p. 91/0.3 mmHg), ^{1}H NMR δ = 1.35-1.70 (m, 6H), 2.25-2.55 (m, 4H), 3.45 (s, 2H), 3.68 (s, 3H), and 6.60-7.35 (m, 4H)ppm.

N-(3-Methoxybenzyl)pyrrolidine (27). Method (B) using N-pyrrolidinylmethyleneimonium chloride and 3-methoxyphenyltributylstannane (8) gave (27), 13% yield, b.p.110/0.2 mmHg, ^{1}H NMR δ = 1.57-1.97 (m, 4H), 2.37-2.77 (m, 4H), 3.61 (s, 2H), 3.79 (s, 3H), and 6.58-7.36 (m, 4H)ppm, M^+ found: 191.1301, $C_{12}H_{17}NO$ requires 191.1310.

N-(3-Methoxybenzyl)morpholine (28). Method (B) using N-morpholinylmethyleneimonium chloride and 3-methoxyphenyltributylstannane (8) gave (28), 17% yield, b.p. 120/0.2 mmHg, ^{1}H NMR δ = 2.30-2.60 (m, 4H), 3.46 (s, 2H), 3.53-3.82 (m, 4H), 3.77 (s, 3H), and 6.60-7.34 (m, 4H)ppm, M^+ found: 207.1256, $C_{12}H_{17}NO_2$ requires 207.1259.

4-Methoxy-N,N-dimethylbenzylamine (17). Method (A) using bis(dimethylamino)methane and 4-methoxyphenyltributylstannane(9)[43] gave (17), 70% yield, b.p. 122-124/18 mmHg, (lit.[47] b.p. 104-106/12 mmHg), ^{1}H NMR δ = 2.20 (s, 6H), 3.35 (s, 2H), 3.80 (s, 3H), and 6.75- 7.25 (AA'BB', 4H, J_{AB}= 9Hz), ^{13}C NMR δ = 45.2(q), 55.0(q), 63.8(t), 113.7(d), 130.2(d), 131.1(s), and 158.9(s)ppm. Using 4-methoxyphenyltrimethylstannane(10)[33] gave (17) in 71% yield.

4-Methoxy-N,N-diethylbenzylamine (18). Method (B) using N,N-diethylmethyleneimonium chloride and 4-methoxyphenyltributylstannane (9) gave (18), 26% yield, b.p. 99/1.0 mmHg, (lit.[48] b.p. 126/15 mmHg), ^{1}H NMR δ = 1.03 (t, 6H, J=7.0Hz), 2.48 (q, 4H, J=7.0Hz), 3.46 (s, 2H), 3.68 (s, 3H), and 6.64-7.31 (AA'BB', 4H, J_{AB}=8.5 Hz)ppm. Using 4-methoxyphenyltrimethylstannane (10) gave (18) in 23% yield.

N-(4-Methoxybenzyl)pyrrolidine (29). Method (B) using N-pyrrolidinylmethyleneimonium chloride and 4-methoxyphenyltributylstannane (9) gave (29), 23% yield, b.p. 120/3 mmHg, ^{1}H NMR δ= 1.62-1.96 (m, 4H), 2.29-2.70 (m, 4H), 3.53 (s, 2H), 3.76 (s, 3H), 6.63 -7.47 (AA'BB', 4H, J_{AB}=8 Hz), ^{13}C NMR δ = 23.5(t), 54.1(t), 55.2(q), 60.1(t), 113.7(d), 130.1(d), 131.7(s), 158.8(s)ppm, M^+ found: 191.1310, $C_{12}H_{17}NO$ requires 191.1310. Using 4-methoxyphenyltrimethylstannane (10) gave (29) in 32% yield.

N-(4-Methoxybenzyl)morpholine (30). Method (B) using N-morpholinylmethyleneimonium chloride and 4-methoxyphenyltributylstannane (9) gave (30), 53% yield, b.p. 122/0.8 mmHg, (lit.[49] b.p. 136-139/1 mmHg), ^{1}H NMR δ = 2.23-2.60 (m, 4H), 3.40 (s, 2H), 3.53-3.90 (m, 4H), 3.77 (s, 3H), 6.70-7.40 (AA'BB', 4H, J_{AB}=10Hz), ^{13}C NMR δ = 53.6(t), 55.0(q), 62.8(t), 66.9(t), 113.7(d), 129.9(s), 130.3(d), and 158.9(s)ppm. Using 4-methoxyphenyltrimethylstannane (10) gave (30) in 59% yield.

N-(2,4-Dimethoxybenzyl)morpholine (31). Method (B) using N-morpholinylmethyleneimonium chloride and 2,4-dimethoxyphenyltributylstannane (11) gave (31), 45% yield, b.p. 120/0.07 mmHg, ^{1}H NMR δ = 2.30-2.63 (m, 4H), 3.47 (s, 2H), 3.49-3.81 (m, 4H), 3.77 (s, 6H), 6.33-6.63 (m, 2H), and 7.20 (d, 1H, J_{AB}=8.5 Hz)ppm, M^+ found: 237.1359, $C_{13}H_{19}NO_3$ requires 237.1365.

1-N,N-Dimethylaminomethylnaphthalene (21). Method (A) using bis(dimethylamino)methane and 1-naphthyltributylstannane (20)[50] gave (21), 66% yield, b.p. 135/1.5 mmHg, (lit.[51] b.p. 132-134/2 mmHg), ^{1}H NMR δ= 2.26 (s, 6H), 3.75 (s, 2H), 7.25-7.80 (m, 6H), and 8.05-8.25 (m, 1H)ppm.

1,4-Bis-(N,N-dimethylaminomethyl)benzene (34). Method (A) using bis(dimethylamino)methane and 1,4-bis-(tributylstannyl)benzene (33)[52] (6 mol equivalents) gave (34), 58% yield, b.p. 138-142/8 mmHg, (lit.[53] b.p. 125-127/5 mmHg), ^{1}H NMR δ= 2.22 (s, 12H), 3.35 (s, 4H), and 7.20 (s, 4H)ppm.

4-(N,N-Dimethylaminomethyl)phenol (40). Method (A) using bis(dimethylamino)methane and 2-(4-trimethylstannylphenoxy)tetrahydropyran (**39**) under reflux for 15h gave (**40**), 50% yield, b.p. 138-140/0.8 mmHg, m.p. 102 (lit.[44] m.p. 106), ^{1}H NMR δ = 2.30 (s, 6H), 3.55 (s, 2H), 6.60-7.20 (AA'BB', 4H, J_{AB}= 9Hz), and 10.00 (s, 1H, D_2O ex.)ppm.

3-(N,N-Dimethylaminomethyl)thiophene (36). Method (A) using bis(dimethylamino)methane and 3-thienyltrimethylstannane (**35**)[54] gave (**36**), 66% yield, b.p. 85/12 mmHg, (lit.[55] b.p. 28-32/0.12 mmHg), ^{1}H NMR δ = 2.21 (s, 6H), 3.42 (s, 2H), and 6.90-7.25 (m, 3H)ppm.

3-(N-Pyrrolidylmethyl)thiophene (37). Method (B) using N-pyrrolidinylmethyleneimonium chloride and 3-thienyltrimethylstannane (**35**) gave (**37**), 30% yield,[56] b.p. 90/1 mmHg, ^{1}H NMR δ = 1.62-1.97 (m, 4H), 2.30-2.67 (m,4H), 3.63 (s, 2H), and 6.96-7.35 (m, 3H), ^{13}C NMR δ = 23.4(t), 54.1(t), 55.1(t), 122.3(d), 125.2(d), 128.4(d), and 140.3(s)ppm.

3-(N-Morpholinylmethyl)thiophene (38). Method (B) using N-morpholinylmethyleneimonium chloride and 3-thienyltrimethylstannane (**35**) gave (**38**), 59% yield, b.p. 100/1 mmHg, ^{1}H NMR δ = 2.26-2.54 (m, 4H), 3.53 (s, 2H), 3.55-3.83 (m, 4H), and 6.98-7.37 (m, 3H), ^{13}C NMR δ = 53.3(t), 57.7(t), 66.7(t), 122.7(d), 125.3(d), 128.2(d), and 138.2(s)ppm, M^+ found: 183.0713, $C_9H_{13}NOS$ requires 183.0718.

N-Benzylmorpholine (23). Method (C) using ethoxy-N-morpholinylmethane, phenyltributylstannane (1), and trichloromethylsilane gave (**23**), 29% yield.

N-(2-methylbenzyl)morpholine (25). Method (C) using dimorpholinylmethane, o-tolyltributylstannane (**3**), and trichloromethylsilane gave (**25**), 18% yield.

N,N,2-Trimethylbenzylamine (13). Method (C) using N,N-dimethylamino-iso-propyloxymethane, o-tolyltributylstannane (**3**), and chlorotrimethylsilane gave (**13**), 19% yield.

3-Methoxybenzylmorpholine (28). Method (C) using ethoxy-N-morpholinylmethane, 3-methoxyphenyltributylstannane (**8**), and trichloromethylsilane gave (**28**), 28% yield.

4-Methoxy-N,N-dimethylbenzylamine (17). Method (C) using bis(dimethylamino)methane, 4-methoxyphenyltributylstannane (**9**), and chlorotrimethylsilane gave (**17**) 22% yield. Using trichloromethylsilane gave (**17**) in 65% yield. Using N,N-dimethylamino-iso-propyloxymethane, 4-methoxyphenyltributylstannane (**9**), and chlorotrimethylsilane gave (**17**), 48% yield. Using trichloromethylsilane gave (**17**) in 41% yield. Using N,N-dimethylamino-iso-propyloxymethane, 4-methoxyphenyltrimethylstannane (**10**), and chlorotrimethylsilane gave (**17**), 62% yield.

4-Methoxy-N,N-diethylbenzylamine (18). Method (C) using ethoxy-N,N-diethylaminomethane, 4-methoxyphenyltributylstannane (**9**), and trichloromethylsilane gave (**18**), 20% yield.

N-(4-Methoxybenzyl)pyrrolidine (29). Method (C) using dipyrrolidinylmethane, 4-methoxyphenyltributylstannane (**9**), and trichloromethylsilane gave (**29**), 38% yield. Using ethoxy-N-pyrrolidinylmethane, 4-methoxyphenyltributylstannane (**9**), and trichloromethylsilane gave (**29**) , 29% yield. Using ethoxypyrrolidinylmethane, 4-methoxyphenyltrimethylstannane (**10**), and trichloromethylsilane gave (**29**), 26% yield.

N-(4-Methoxybenzyl)morpholine (30). Method (C) using dimorpholinylmethane, 4-methoxyphenyltributylstannane (**9**), and trichloromethylsilane gave (**30**), 53% yield. Using ethoxy-N-morpholinylmethane, 4-methoxyphenyltributylstannane (**9**), and trichloromethylsilane gave (**30**), 63% yield. Using ethoxy-N-morpholinylmethane, 4-methoxyphenyltrimethylstannane (**10**), and trichloromethylsilane gave (**30**), 32% yield. Using ethoxy-N-morpholinylmethane, 4-methoxyphenyl- trimethylstannane (**10**), and chlorotrimethylsilane gave (**30**), 38% yield.

2,4-Dimethoxy-N,N-dimethylbenzylamine (19). Method (C) using N,N-dimethylamino-iso-propyloxymethane, 2,4-dimethoxyphenyltributylstannane (**11**), and trichloromethylsilane gave (**19**)[57], 56% yield, b.p. 90/0.07 mmHg ^{1}H NMR δ = 2.23 (s, 6H), 3.38 (s, 2H), 3.80 (s, 6H), 6.30-6.70 (m, 2H), and 7.12 (d, 1H, J_{AB}=9Hz)ppm.

N-(2,4-Dimethoxybenzyl)morpholine (31). Method (C) using ethoxy-N-morpholinylmethane, 2,4-dimethoxyphenyltributylstannane (**11**), and trichloromethylsilane gave (**31**), 60% yield.

3-(N,N-Dimethylaminomethyl)thiophene (36). Method (C) using N,N-dimethylamino-iso-propyloxymethane, 3-thienyltrimethylstannane (**35**), and trichloromethylsilane gave (**36**), 25% yield.

3-(N-Pyrrolidinylmethyl)thiophene (37). Method (C), at room temperature, using ethoxy-N-pyrrolidinylmethane, 3-thienyltrimethylstannane (**35**), and trichloromethylsilane gave (**37**), 38% yield.

3-(N-Morpholinylmethyl)thiophene (38). Method (C), at room temperature, using ethoxy-N-morpholinylmethane, 3-thienyltrimethylstannane (**35**), and trichloromethylsilane gave (**38**), 59% yield.

Reactions of benzyltributylstannane (41)

N,N-Dimethyl-β-phenylethylamine (42). Method (A) using bis(dimethylamino)methane and benzyltributylstannane (**41**)[58] gave (**42**), 46% yield, b.p. 76-78/12 mmHg, (lit.[59] b.p. 66-68/6 mmHg), ^{1}H NMRδ = 2.30 (s, 6H), 2.40-3.00 (m, 4H), and 7.18 (s, 5H)ppm.

N-β-Phenylethylmorpholine (43). Method (B) using N-morpholinylmethyleneimonium chloride and benzyltributylstannane (**41**) gave (**43**), 28% yield, b.p. 90/0.07 mmHg, (lit.[60] b.p. 76-78/0.05 mmHg), ^{1}H NMR δ = 2.41-3.12 (m, 8H), 3.67-3.97 (m, 4H), and 7.24 (s, 5H)ppm. Method (C) using ethoxy-N-morpholinylmethane, benzyltributylstannane (**41**), and trichloromethylsilane gave (**43**), 31% yield.

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