Unprecedented Iridium Catalysed Group Transfer Reactions of 1,3-Thiazanes

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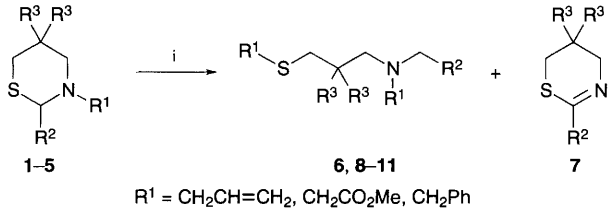
Intramolecular allyl, benzyl or methylene ester transfer is observed upon treatment of suitably functionalized 1,3-thiazanes with catalytic amounts of either anhydrous iridium trichloride or chlorotricarbonyliridium in benzene under a carbon monoxide atmosphere (*e.g. N*-allyl-2-phenyl-1,3-thiazane is converted to *N,S*-diallyl-*N*-benzyl-1,3-aminothiol; the allyl unit is provided by a second molecule of the thiazane, which is in turn converted into the corresponding thiazine by formal loss of propene).

In continuation of the pursuit of our research into the carbonylation of carbon–heteroatom bonds in both cyclic and acyclic compounds,[1–6] we investigated the carbonylation of the thiazane substrates **1–5** (Scheme 1). Surprisingly, these compounds did not undergo carbonylation as previously observed,[1–6] but instead participated in an unprecedented allyl transfer/disproportionation reaction to form **6** and **8–11**. We now report the fascinating results of this investigation.

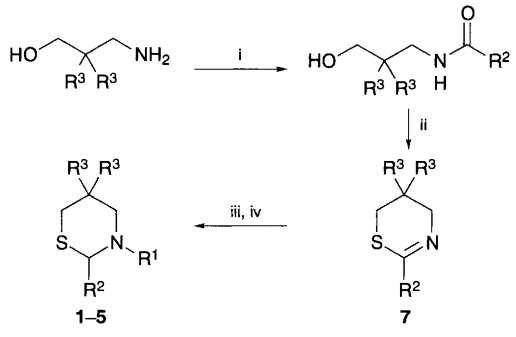
The required thiazanes **1–5** were prepared *via* the thiazine **7**, which was readily synthesized following literature procedures (Scheme 2).[7] Reductive alkylation of **7** was then effected by stirring the thiazine in a neat or concentrated solution of the required allyl or benzyl halide followed by reduction with $NaBH_4$.[8]

The carbonylation of **1** (Table 1) was first attempted under the conditions previously shown to be effective in the thiazolidine series, namely $[Rh(cod)Cl]_2/KI$.[4a] There was no reaction using this catalyst system [under 68 atm (1 atm ≃ 101.325 kPa) of CO at 180 °C]. However, catalytic amounts of $[Ir(CO)_3Cl]$ or anhydrous $IrCl_3$ [which forms $Ir(CO)_3Cl$ on exposure to CO at 150 °C or higher[9]] did catalyse the reaction, the product did not contain carbon monoxide, and spectral analysis indicated that an allyl transposition had taken place (Scheme 1). It is obvious from the nature of the product that two molecules of starting material were consumed during the production of **6** from **1**. The yield of the diallylated material **6** (86%) was excellent, with the thiazine **7** (R^1 = H,R^2 = Ph) formed as the accompanying product.

This novel reaction was applied to several other thiazines, and the results are presented in Table 1. The methylene ester **2** was exposed to the iridium catalyst under the reaction conditions described, affording the amino thioether diester **8** in good yield (64%) and thus there is transfer of the methylene ester unit. The *N*-benzyl analogue **3** was also transferred in good yield affording **9** in 66% yield. 5,5-Dimethyl-2-phenylthiazane **4** also underwent the allyl transposition reaction, but the yield of **10** was lower than that of **6**. Finally, 2-benzylthiazane **5** was converted into product **13** in 56% yield. *N*-Methyl- and *N*-ethyl-2-phenylthiazanes and *N*-allyl-2-methylthiazane were recovered unchanged upon attempting the transposition reaction.



Scheme 1 *Reagents and conditions*: i, $Ir(CO)_3Cl$, CO, heat

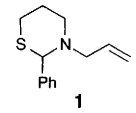
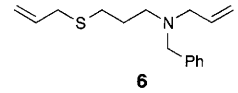
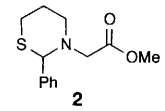
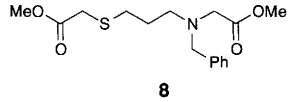
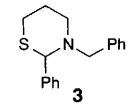
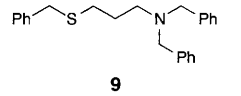
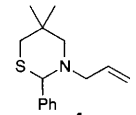
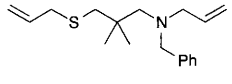
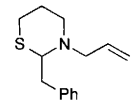
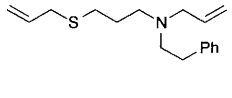


Scheme 2 *Reagents and conditions*: i, R^2COCl, NEt_3, CH_2Cl_2; ii, P_2S_5, heat; iii, R^1Br, neat; iv, $NaBH_4$, MeOH

Having determined which substrates were susceptible to the transposition process, we performed several reactions to gain some insight into the reaction mechanism. The reaction is indeed metal catalysed, since substrate **1** was recovered unchanged after heating to 170 °C in benzene in the absence of iridium. Also, since carbon monoxide was not incorporated into the product, we attempted the reaction under nitrogen by heating compound **1** to 170 °C under 20 atm of nitrogen in the presence of 1% $Ir(CO)_3Cl$. Again there was no reaction, indicating that carbon monoxide binding to iridium is required to stabilize one or more of the reaction intermediates.

Palladium catalysed disproportionation reactions have been reported for amine systems, and in these cases the mechanism of the reaction involves the generation of iminium salts by C–H activation.[10] If a similar mechanism was operative in the present

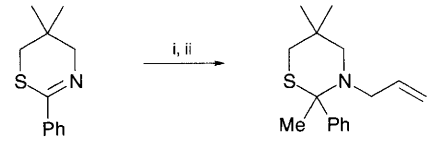
Table 1 Reaction of *N*-alkyl thiazanes with $Ir(CO)_3Cl$ or anh. $IrCl_3$ under CO[a]

Entry	Substrate	Product	Yield (%)[b]
1	 **1**	 **6**	86
2	 **2**	 **8**	64
3	 **3**	 **9**	66
4	 **4**	 **10**	52
5	 **5**	 **11**	56

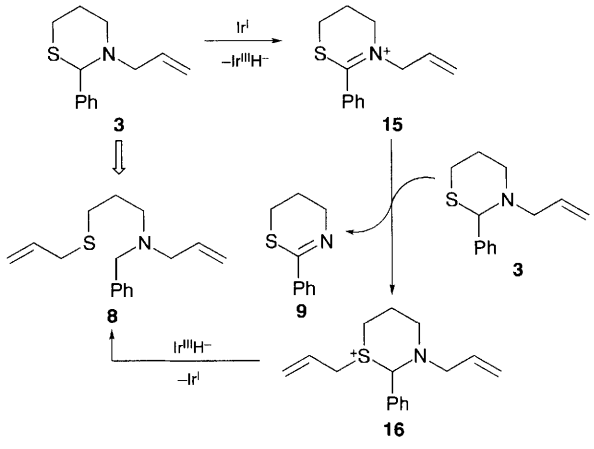
[a] *Reaction conditions*: 5 mmol substrate, 1% (0.05 mmol) Ir catalyst, 10 ml benzene, 68 atm CO, 170 °C, 24—36 h. [b] Isolated yield (following purification by preparative TLC using 30% ethyl acetate in hexanes as the developer). The products were identified on the basis of analytical and spectral (IR, NMR, HMQC, COSY, MS) data.

system, then replacement of hydrogen at C-2 by a methyl group should inhibit reaction. Thus compound **12** was prepared by a route similar to that described in Scheme 1, but using methylmagnesium bromide instead of sodium borohydride (Scheme 3). When **12** was subjected to the usual reaction conditions [1% $Ir(CO)_3Cl$, 68 atm CO, 170 °C, 36 h] only decomposition products could be isolated, with none of the allyl transposition product observed in the reaction mixture.

Given these results, and the fact that the thiazine **7** was formed along with the diallylated product **6** from **1**, one can propose the mechanism outlined in Scheme 4 for the transposition reaction. The initial step may involve the generation of an iminium ion **13** by oxidative addition of iridium into the C–H bond at C-2 followed by loss of an anionic iridium hydride. Deallylation by a second molecule of starting material generates thiazine **7** and bisallylated **14**. Finally, the catalytic cycle is completed by reduction of compound **14** using the iridium hydride previously eliminated. This sequence would yield the observed products of the reaction and regenerate the iridium catalyst.



Scheme 3 *Reagents and conditions*: i, Allyl bromide, neat; ii, MeMgBr, THF



Scheme 4

In conclusion, we have established that a variety of substituted thiazanes are able to undergo a unique iridium catalysed disproportionation reaction in moderate to good yields. Although the reaction is limited to 2-phenyl- or 2-benzyl-thiazanes, a variety of groups can be transferred including allyl, benzyl and methylene ester. The substrates are readily prepared in 3 steps from the corresponding amino alcohols, and the sequence described constitutes a convenient method for the preparation of allyl or benzylated amino thioethers.

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