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SILICON-MEDIATED C-ISOPRENYLATION OF PHENOLS

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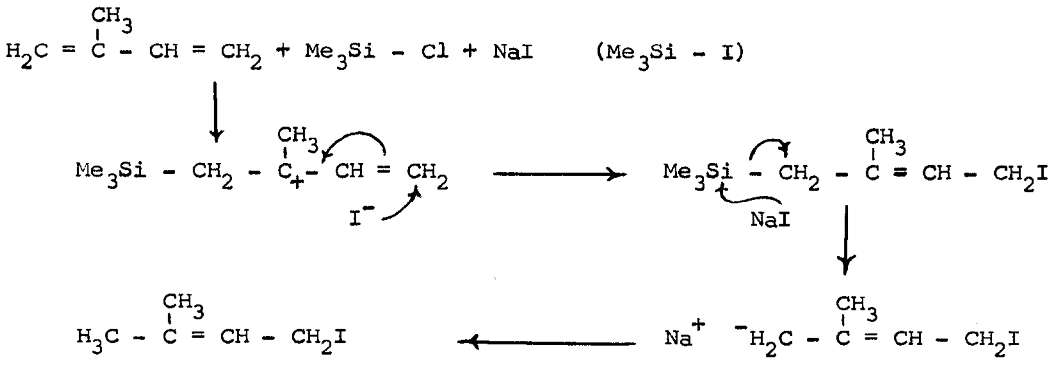
Summary: C-isoprenylation of phenols has been effected using a combination of isoprene and in situ generated iodotrimethylsilane or hydrogen iodide.

Natural products bearing an isoprenyl group as such or in the modified form have been exceedingly coming into light during the past two decades[1,2] and some of them exhibit important biological properties[3-6]. In continuation of our studies on the use of silicon reagents[7], we explored C-isoprenylation of phenols with isoprene and iodotrimethylsilane generated in situ from chlorotrimethylsilane (CTMS) and sodium iodide[8] - a combination which we thought would be a potential source of 3,3-dimethylallyl iodide (Scheme 1).



Scheme 1

We have earlier demonstrated that toluene-p-sulphonic acid and sodium iodide is an excellent reagent combination for in situ generation of hydrogen iodide[9]. Therefore, we argued that this reagent combination on exposure to isoprene would also generate 3,3-dimethylallyl iodide capable of effecting C-isoprenylation[10]. It is evident from the results described in Table 1 that these two methods indeed could be useful alternatives to the earlier methods which employ 2-methyl-but-3-ene-2-ol/BF_3[11] and 3,3-dimethylallyl bromide/sodium methoxide[12] and where moderate yields of C-isoprenylated compounds have been reported. To our knowledge this is the first report of direct C-isoprenylation of phenols with isoprene.

All attempts to obtain **5** or its double bond isomer from **1** using a combination of the epoxide **12** and excess CTMS/NaI (or TsOH/NaI) resulted in the formation of the corresponding isoprenylated compound **2**.[13,14]

Table 1[a]:

Substrate	Procedure used (Method)	Time/hr	Product (% yield)[b]
1	(A)	1.0	**2** (60)
	(B)	3.5	**2** (30
3	(A)	1.5	**4** (50)
	(B)	4.0	**4** (50)
6	(A)	3.0	**7** (40)
	(B)	4.5	**7** (25)
8	(A)	4.0	**9** (50)
	(B)		No reaction
10	(A)	18.0	**11** (60)
	(B)	3.0	**11** (40)

[a] In each case some amount of the cyclised product (i.e. the corresponding chromane compound) was formed.[15]

[b] Yields refer to the isolated products of >90% purity as determined by TLC and NMR.

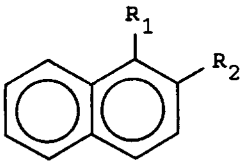
A typical Experimental Procedure

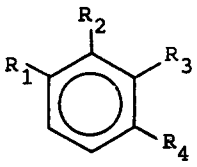
Method (A) :

To a solution of 100 mg of **1** in 4 ml dry acetonitrile was added 400 mg of NaI, and 0.5 ml of isoprene followed by 0.5 ml of chlorotrimethylsilane. The reaction mixture was stirred at r.t. monitoring by TLC. It was quenched with 200 ml water and extracted with chloroform. The washed ($Na_2S_2O_3$ solution and water) and dried extract was evaporated and the residue purified by preparative TLC to furnish 2. Addition of a small amount of imidazole in the reaction mixture to quench hydrogen iodide which may have been formed due to decomposition of iodotrimethylsilane led to identical yield of the product 2.

Method (B) :

A solution of 100 mg of 1 in 4 ml dry acetonitrile was treated with 200 mg of NaI and 200 mg of p-TsOH with stirring at r.t. for 5 mints and then 0.5 ml of isoprene was added to it. The reaction mixture was stirred at r.t. monitoring by TLC and worked up as described in method A. Reaction of 1 with isoprene/HI gave only 10% yield of 2.





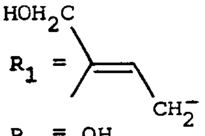
1 $R_1 = H, R_2 = OH$

2 $R_1 = Pr, R_2 = OH$

3 $R_1 = OH, R_2 = H$

4 $R_1 = OH, R_2 = Pr$

5 R_1 =



$R_2 = OH$

6 $R_1 = R_3 = OH, R_2 = R_4 = H$

7 $R_1 = R_3 = OH, R_2 = H, R_4 = Pr$

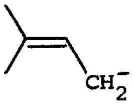
8 $R_1 = R_4 = H, R_2 = R_3 = OH$

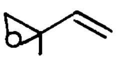
9 $R_1 = R_4 = Pr, R_2 = R_3 = OH$

10 $R_1 = R_3 = OH, R_2 = H, R_4 = COCH_3$

11 $R_1 = R_3 = OH, R_2 = Pr, R_4 = COCH_3$

Pr =





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