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METALLATION OF BENZYL SELENIDES AND OF α-ARYL SELENOACETALS. SCOPE AND LIMITATIONS.

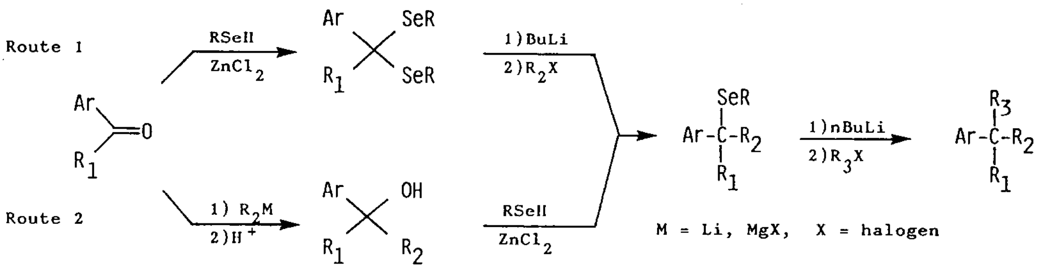
M. Clarembeau and A. Krief

Facultés Universitaires Notre-Dame de la Paix
Laboratoire de Chimie Organique
61, rue de Bruxelles
B-5000 NAMUR (Belgium)

α-Metallo benzylselenides and α-metallo selenoacetals derived from aromatic aldehydes have been conveniently prepared by metallation of the corresponding carbon acids. KDA in THF proved among the various basic systems tested, the most efficient.

α-Arylselenoacetals and benzylselenides are valuable starting materials for the synthesis of α-selenobenzyllithiums [1,2] and benzyllithiums [2,3] respectively and have been used as intermediates for the geminal dialkylation [1] of the carbonyl group of aromatic aldehydes and ketones (Scheme 1).

Scheme 1



Selenoacetals have been usually prepared [4] from the corresponding carbonyl compounds and selenols. Benzylselenides have, for their part, been generated from the corresponding alcohols [5] or halides [6-9] and selenols or selenolates, or by a stepwise reduction-alkylation sequence from selenoacetals [1]. There remain however cases in both series for which the transformations are difficult or even impossible.

This is particularly the case - i - for selenoacetals derived from aromatic ketones [1,4,10]. The selenoacetalisation of these ketones, with the exception of the first member of the series (i.e. methyl and ethyl aryl ketones) is quite slow, and large amounts of benzylselenides are formed [4,10] as side products - ii - for benzylselenides, which are rather difficult to prepare from selenolates or selenols and benzylhalides bearing a quarternary benzylic center and from benzyl alcohols bearing bulky alkyl groups on the benzylic carbon [2].

We therefore thought that the tandem metallation-alkylation reaction applied to readily available selenoacetals derived from aromatic aldehydes [4] or to unsubstituted or monosubstituted benzylselenides [5-9] should provide a very good entry to higher homologues, especially the hindered ones. To our knowledge [11] metallation of selenoacetals derived from aromatic aldehydes has not been reported and although benzylphenylselenide has been metallated [8,9] with lithium diisopropylamine (LDA) in THF-hexane, it has been described [9] that the reaction does not apply to higher homologues.

We now report on the aptitude of strong non nucleophilic bases such as LDA, lithium tetramethyl piperidide (LTMP) [12,13] and lithium diisopropylamine/potassium t-butoxide (KDA) [11b,14] in THF or in THF-HMPA to metallate a series of phenylseleno and methylseleno acetals derived from aromatic aldehydes as well as phenyl and methyl benzyl selenides.

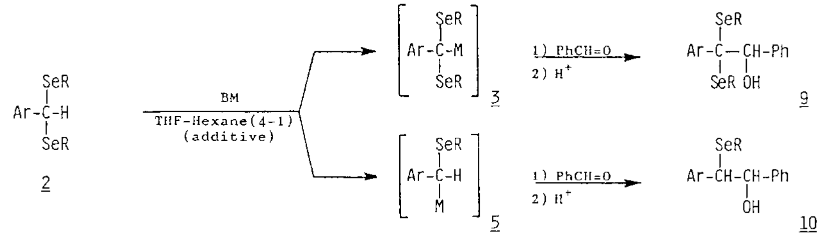
Typically the metallation reactions have been carried out in THF-hexane, with or without HMPA as additive and performed between -78° and 0° according to the cases. The reaction medium is then cooled down to -78° if necessary and benzaldehyde is added at this temperature.

Among the different systems we tested, we found that KDA in THF is the most efficient one. At temperatures around -78° to -50°, it allows the efficient metallation of a series of phenylselenoacetals and their methylseleno analogues as well as of benzylphenylselenides bearing hydrogens or one alkyl substituent on the benzylic carbon. The resulting organometallics have been trapped with benzaldehyde at -78°, and lead to good yields of β-hydroxyselenoacetals 9 in the first cases (Scheme 2) and of β-hydroxyselenides 10 in the second (Scheme 3). Benzylmethylselenides bearing two hydrogens on the benzylic carbon behave similarly (Scheme 3, entries g-k). Higher homologues (6 $R = R_1 = Me$, Ar = Ph, 2-MeO-Ph, 4-CN-Ph) however, do not produce the expected alcohols 10. Styrenes have in some cases been observed (Scheme 3, entries l,m) and may arise 1 from the selenides 6 by a β-elimination reaction [15] or from the organometallics 5 via a sequence involving carbene formation and its rearrangement [16].

Other basic systems tried, such as LDA (Scheme 2 , entries b,c,i, Scheme 3, entries a,c,h) or LTMP (Scheme , entries d,e,j, Scheme , entries d,i) proved less successful with α-phenylselenoacetals and benzylselenides. Substantial amounts of the starting material are isolated on reaction of both series of compounds with these bases and subsequent addition of benzaldehyde to the reaction medium. Surprisingly in the case of selenoacetals, appreciable quantities of β-hydroxyselenides (10, Scheme 2) are also isolated besides the expected β-hydroxyselenoacetals (9, Scheme 2). These could result from a selenium-metal exchange rather than a hydrogen-metal exchange, occurring on reaction of these selenoacetals with LDA or LTMP acting as nucleophiles.

Finally, the α-potassio selenoacetals have been successfully alkylated (Scheme 4) and have permitted the synthesis of the selenoacetals which are difficult or even impossible to

Scheme 2

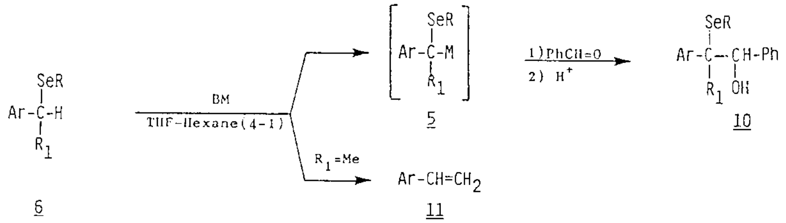


	Ar	R	Condition used	Yield* in 9(%)	recovered* 2(%)	Yield* in 10(%)
a	Ph	Me	KDA, -78°, 0.3h	79	00	--
b			LDA, -78°, 0.3h	50+	50+	--
c			LDA, -50°, 0.3h	68	19	--
d			LTMP, -78°, 0.3h	16	54	31
e			LTMP, (1.1HMPA) -78°, 0.3h	52	13	17
f	4-MeOPh	Me	KDA, -78°, 0.3h	79	--	--
g	3,5-MeOPh	Me	KDA, -78°, 0.3h	82	--	--
h	Ph	Ph	KDA, -78°, 0.3h	79	--	--
i			LDA, -78°, 0.3h	26	50	11
j			LTMP, -78°, 0.3h	63	16	--
k	4-MeOPh		KDA, -78°, 0.3h	81	--	--

* Except otherwise stated (+) the yield refers to pure product with analytical data confirming the proposed structure.

\+ Estimated by NMR.

Scheme 3



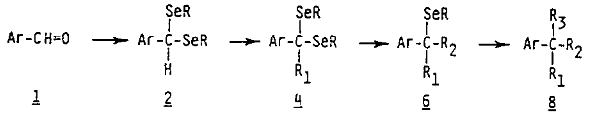
	Ar	R	R_1	Conditions	yield* in 10(%)	recovered* 6(%)	yield* in 11(%)
a	Ph	Ph	H	LDA, -78°, 0.5h	65	16	
b			Me	KDA, -50°, 0.3h	87	00	
c				LDA, 0°, 0.5h	15	85	
d				LTMP, 20°, 0.5h	62	--	
e	Ph	Ph	nBu	KDA, -50°, 0.3h	70	17	
f	4-MeOPh	Ph	nBu	KDA, -50°, 0.3h	64	22	
g	Ph	Me	H	KDA, -78°, 0.3h	79	--	
h				LDA, -50°, 0.3h	61	16	
i				LTMP, -78°, 0.3h	67	17	
j	2-MeOPh	Me	H	KDA, -78°, 0.3h	68	--	
k	4-CNPh	Me	H	KDA, -78°, 0.3h	82	--	
l	Ph	Me	Me	KDA, -78°, 0.3h	00	49	**
m	2-MeOPh	Me	Me	KDA, -78°, 0.3h	00	27	19

* The yield refers to pure product with analytical data confirming the proposed structure.

** Present in ~20% yield in the crude reaction mixture.

prepare from aryl ketones and selenols [1,4]. Therefore this reaction, coupled with those reported in the accompanying paper, allow the efficient synthesis of arylalkanes, including those bearing a fully alkylated benzylic carbon, from aromatic aldehydes, by three stepwise alkylation reactions (Scheme 4).

Scheme 4



Ar	R	method⁺ used	yield in 2* (%)	R_1X	yield in 4* (recovered 2%)	R_2X	yield in 6* (%)	R_3X	yield in 8* (%)
Ph	Me	A	92	MeI	70 (15)	MeI	79	MeI	72
						nPrBr	88	sBuBr	93 §
						iPrI	86	iPrI	87
4-MeOPh	Me	A	78	nBuI	81 (--)	MeI	84	sBuI	78
3,5-MeOPh	Me	A	85	nBuI	51 (--)	nBuI	82	nBuI	81
Ph	Ph	B	64	MeI	72 (00)				
				iPrI	27** (00)				
				tBuI	00 (81)				
4-MeOPh	Ph	B	52	nBuI	52 (00)				

+ Method A : $2MeSeH/0.5ZnCl_2$, CCl_4, 20°, 2 h
Method B : $2PhSeH/0.3TiCl_4$, CH_2Cl_2, -50°, 72 h

* The yield refers to pure product with analytical data confirming the proposed structure.

**This product rapidly decomposes on standing or during the purification by chromatography on SiO_2 or Al_2O_3. The yield in crude alkylated product can be estimated to be more than 70%.

§ This reaction has been performed by Ph. Barbeaux in our laboratory.

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