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"Metallo-Fries" Rearrangements of 2-lithio-6-nitrophenol derivatives

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Abstract: *2-Bromo-6-nitrophenyl trialkylsilylethers, esters, carbamates and carbonates undergo "metallo-Fries" rearrangements to the C-silyl compounds, ketones, amides and esters respectively.*

"Metallo-Fries" rearrangements have been observed with a number of classes of compounds, notably trialkylsilyl ethers, esters and carbamates providing the C-trialkylsilyl compounds, ketones and amides respectively[1,2,3]. The reactions occur when the electrophilic centre acts as a bridge to transfer the negative charge from the aromatic carbon to the phenolic oxygen. In the case of trialkylsilyl ethers and esters, the reaction has been shown to proceed *via* an intramolecular mechanism[1,2]. We now report the analogous reactions of derivatives of 2-bromo-4-methyl-6-nitrophenol, and the rearrangement of the benzyl carbonate derivative to the corresponding benzyl ester in moderate yield.

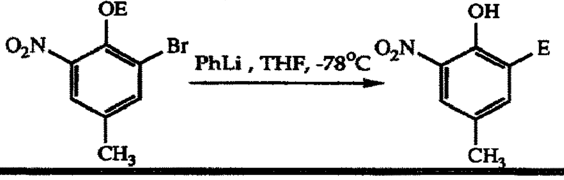
A variety of trialkylsilyl ethers (**Table**, substrates (1)-(4)) were prepared from 2-bromo-4-methyl-6-nitrophenol under standard conditions[4]. Upon halogen-metal exchange (PhLi, THF, -78°C) an instantaneous reaction occurred giving a deep red solution. On work-up the corresponding 2-trialkylsilyl-6-nitrophenols were obtained in moderate to good yields (**Table**, entries 1-4). In contrast, when the supposed dianion formed from 2-bromo-4-methyl-6-nitrophenol (PhLi, 2 eq.; THF; -78°C) was quenched with TMSCl, a complex mixture of products resulted.

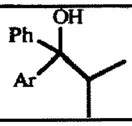
2-Lithioaryl carbamates are stable at -78°C but are observed to rearrange on warming[3]. Upon halogen-metal exchange at -78°C the carbamate[5] (**5**) rapidly rearranged to give the amide (**6**) in 49% yield (**Table**, entry 5). Similarly reaction of the isopropylester (**7**) with phenyllithium (1 eq.; THF; -78°C) resulted in the isolation of an inseparable mixture of the ketone (**8**) and the carbinol (**9**), formed from the addition of phenyllithium to the rearranged ketone (**8**), (**Table**, entry 6). Reduction of the temperature to -100°C had no significant effect on the product distribution. When the reaction was attempted using ^{t}butyllihium (1 eq.; THF; -78°C) the ketone (**8**) was isolated in low yield.

To our knowledge there have been no reports of similar reactions of carbonates, hence the readily available[6] benzylcarbonate (**10**) was subjected to our standard rearrangement conditions (PhLi, 1eq; THF; -78°C), resulting in the isolation of the benzyl ester (**11**) in 54% yield (**Table**, entry 7).

Although detailed kinetic studies have not been undertaken, the o-nitro group has a dramatic effect upon the rate on this rearrangement reaction, presumably by stabilisation of the resulting phenolate anion[7]. This is most

Table: O-C Rearrangements of Substituted o-Nitrophenols



Entry / Substrate	E	Product Yield (%)[a]
1; (**1**)	$-SiMe_3$	72
2; (**2**)	$-Si(CH_3)_2{}^tBu$	53
3; (**3**)	$-Si^iPr_3$	84
4; (**4**)	$-SiPh_2{}^tBu$	59
5; (**5**)	$-CONEt_2$	(**6**); 49
6; (**7**)	$-COCH(CH_3)_2$	(**8**)+(**9**) ((3:2)); 65
7; (**10**)	$-CO_2Bn$	(**11**); 54
a: isolated yields	By-product (**9**) = 	

evident in the case of the 2-lithioarylcarbamate species which is stable at low temperature in the absence of the nitro group.

In conclusion, we have demonstrated that "metallo-Fries" rearrangements of a wide variety of 2-lithio-6-nitrophenol derivatives occur rapidly at low temperature[8,9] affording new synthetic routes to highly functionalised aromatic compounds.

References and Notes

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4. Prepared from 2-bromo-4-methyl-6-nitrophenol: substrate:- (**1**) HMDS, reflux, 2 hours; substrates (**2**) to (**4**):- (i) NaH; THF, (ii) $R'R_2SiCl$.
5. Prepared from 2-bromo-4-methyl-6-nitrophenol: (i) NaH; THF, (ii) Et_2NCOCl, reflux; 22%.
6. Prepared from 2-bromo-4-methyl-6-nitrophenol: (i) NaH; THF, (ii) $PhCH_2COCl$; 90%.
7. pKa values for phenol and 2-nitrophenol are 9.89 and 7.17 respectively.
8. All new compounds have analytical and spectral (^1H nmr, ir, ms) data consistent with the indicated structures.
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