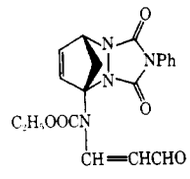
(3) The elemental composition of this substance was established by C. H, and N combustion analysis.
(4) Separation of the mixture into its individual components was accomplished by column chromatography at −15 °C.
(5) This substance was characterized by fully consistent spectroscopic (^{1}H NMR, ^{13}C NMR, IR, UV, mass spectrum) data.
(6) All efforts to purify this substance by column chromatography at −15 °C were frustrated by its tendency to undergo overall dehydration to **6**.
(7) The structure of **5** was further confirmed through low-temperature (−78 °C) cycloadditive coupling with *N*-phenyltriazolinedione to produce a single cycloadduct (mp 70–72 °C dec) whose spectroscopic characteristics (IR, ^{1}H NMR, ^{13}C NMR, mass spectrum) are fully consistent with the structure shown as ii.



ii

(8) For obvious reasons, the primary product generated in the thermolytic ring contraction of **4** must be the symmetrically substituted counterpart of **5** and one which is related to the observed product, **5**, by a simple (1,5) hydrogen shift.
(9) Chemically, the structure of **6** receives unequivocal support from its reductive ($LiAlH_4$) conversion to the previously described [A. G. Anderson, Jr., and H. I. Ammon, *Tetrahedron Lett.*, 2579 (1966)] mixture of 5*H*- and 7*H*-1-pyrindines (^{1}H NMR, UV, IR).
(10) It is significant to note in this connection that compounds **4**, **5**, and A cleanly dehydrate to **6** on passage through alumina at ca. −15 °C.
(11) For pertinent information in this connection see W. Grimme and K. Seel, *Angew. Chem.*, **85**, 514 (1973).
(12) C. Weizmann postdoctoral fellow.

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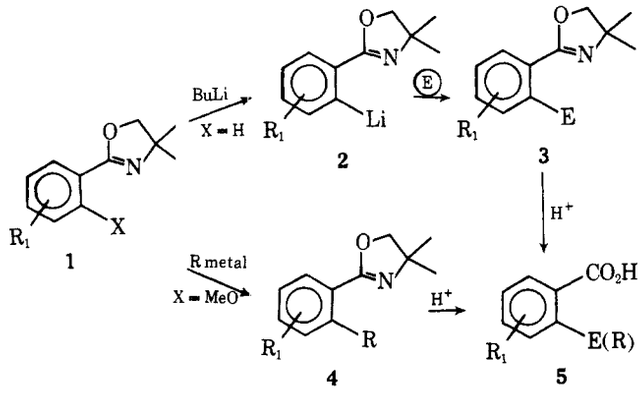
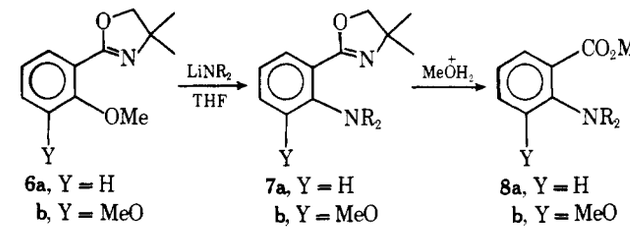
The Displacement of Methoxy by Amino Groups in Aryloxazolines. A Novel Approach to *o*-Amino-, *o*-Alkylamino-, and *o*-Dialkylaminobenzoic Acids

Summary: Treatment of *o*-(methoxyaryl)oxazolines with lithio amides at room temperature results in a facile methoxy displacement furnishing the *o*-(aminoaryl)oxazolines.

Sir: The synthetic utility of aryloxazolines as precursors to various substituted benzoic acids has been demonstrated in this and other laboratories.[1,2] Thus, 2-aryloxazolines **1** (X = H) may be readily metalated using *n*-butyllithium furnishing exclusively the *o*-lithio derivative **2** which, when treated with various electrophiles (E), affords the ortho-substituted aryloxazolines **3**. In contrast to the above, 2-(*o*-methoxyphenyl)oxazolines **1** (X = MeO) were found to react with organometallics (RLi, RMgX) not by metalation, but by direct substitution of the methoxyl group furnishing the *o*-alkyl or *o*-aryl derivative **4**. This latter process occurs under unexpectedly mild conditions (−45–25 °C, THF) in high yields. Both electrophilic (**1** → **3**) and nucleophilic (**1** → **4**) routes lead ultimately to elaborated benzoic acids **5**.



We now wish to describe a significant extension to the methoxy-displacement reaction using various lithio salts of primary and secondary amines as well as lithium amide.[3] When lithio amides are treated with either **6a** or **6b** at room temperature (THF, 1–6 h), the *o*-amino substituent is directly introduced in place of the *o*-methoxyl group in fair-to-excellent yields. The only other major product observed is the starting methoxy derivative which was readily separated and recovered by column or preparative layer chromatography. The aminated oxazolines were transformed into their corresponding methyl benzoates **8** by acidic hydrolysis (3 N HCl, 12–24 h, reflux) followed by esterification using methanolic hydrogen chloride.[4] The versatility of this substitution process can be seen by the examples listed in Table I. Most striking are those examples using so called "nonnucleophilic" bases such as LDA and *tert*-butylamine, indicating that there are virtually no steric effects to inhibit methoxy displacement.[5] In fact, the methoxy group displaced in **6b** is one which is flanked by two ortho substituents and seemingly sterically encumbered. The process may be envisioned as a nucleophilic addition followed by elimination of lithium methoxide en-



6a, Y = H
b, Y = MeO

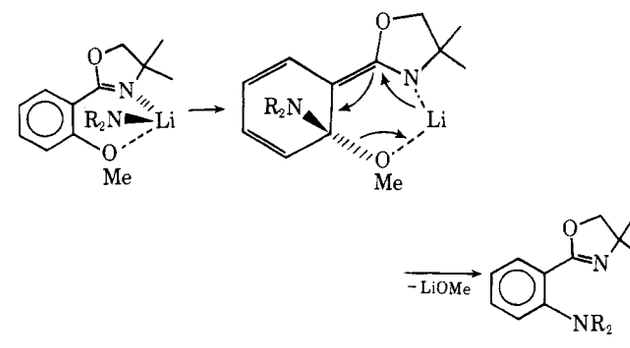
7a, Y = H
b, Y = MeO

8a, Y = H
b, Y = MeO

Table I. Amination of 2-(*o*-Methoxyphenyl)oxazolines 6 Leading to *o*-Aminated Benzoic Esters

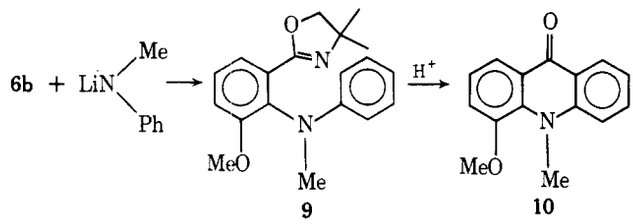
Oxazoline	$LiNR_2$	% 7[a]	% 8[b]
6a	$LiNH_2$	58	45
6a	$LiNEt_2$	98	*c*
6a	$LiN(i\text{-}Pr)_2$	78	*c*
6a	$LiNH(t\text{-}Bu)$	41	*c*
6b	$LiNH_2$	59	72
6b	$LiNEt_2$	93	40
6b	$LiN(i\text{-}Pr)_2$	78	*c*
6b	$LiNH(t\text{-}Bu)$	63	75[d-f]

[a] Yields are those for pure, isolated material. [b] Obtained by heating **7** in 3 N HCl (15–20 h) followed by treatment with methanolic hydrogen chloride. These conditions have not as yet been optimized. [c] Not attempted. [d] Hydrolysis proceeds with dealkylation producing methyl 2-amino-3-methoxy benzoate. [e] All new compounds gave correct analytical data. [f] The alternative basic hydrolysis to remove the oxazoline should allow the *tert*-butyl group to remain intact (see ref 2).



hanced by strong chelation of the lithium cation. This mode of entry would be relatively free of nonbonded interactions thus allowing bulky amino substituents easy access to the sp^2 carbon at the ortho position. There exists the remote possibility that these displacements as well as those previously reported[2] using alkyl metallics are proceeding via an electron-transfer process and this aspect is currently under investigation.

An interesting example which may have considerable potential in heterocyclic syntheses is given by the reaction of **6b** with the lithio salt of *N*-methylaniline. The adduct **9** was



9 10

formed in 50% yield (+50% recovery of **6b**) which gave, after acidic hydrolysis, the acridone **10** (mp 91 °C, 40%)[6] and the expected uncyclized benzoic acid (25%).

These preliminary results indicate that the amination of *o*-(methoxyaryl)oxazolines may provide additional methodology to aromatic substitution and further studies in this respect are in progress.

Acknowledgment. The authors wish to express their gratitude to the Army Research Office (Durham) for financial support of this work.

References and Notes

(1) A. I. Meyers and E. D. Mihelich, *J. Org. Chem.*, **40**, 3158 (1975); H. W. Geschwend and A. Hamdam, *ibid.*, **40**, 2008 (1975).
(2) A. I. Meyers and E. D. Mihelich, *J. Am. Chem. Soc.*, **97**, 7383 (1975).
(3) A number of nucleophilic reagents have been surveyed in addition to alkyl and aryl metallics and the results to date indicate that enamines, thiolates, enolates, and other "soft" anions fail to substitute the methoxyl group. The reactions observed with these nucleophiles are those which cleave the methyl–oxygen bond. Details of these reactions will be reported in the full account of this work.
(4) The oxazolines **6a** and **6b** were prepared from the corresponding *o*-methoxybenzoic acids, thionyl chloride, and 2-amino-2-methylpropanol as described previously [A. I. Meyers et al., *J. Org. Chem.*, **39**, 2787 (1974)].
(5) At this time, the only lithio amine which failed to displace the methoxy group is 2,2,6,6-tetramethylpiperidine.
(6) G. K. Hughes, N. K. Matheson, A. T. Norman, and E. Ritchie [*Aust. J. Sci. Res., Ser. B*, **5**, 206 (1952)] report mp 89–91 °C.

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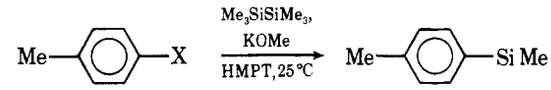
Trimethylsilyl Anions. Direct Synthesis of Trimethylsilylbenzenes

Summary: The reaction of aryl halides with hexamethyldisilane and potassium methoxide (or sodium methoxide or methyllithium) in hexamethylphosphoric triamide (HMPT) affords the corresponding trimethylsilyl-substituted benzene and some reduction product.

Sir: Silyl anions are highly reactive nucleophiles and one-electron-transfer reagents.[1,2] The synthetic utility of trimethylsilylpotassium,[2g,h] -sodium,[2d] and -lithium,[2j] (TMSK, TMSNa, TMSLi, respectively) has increased owing to recently reported convenient methods of in situ generation from the reaction of hexamethyldisilane and potassium methoxide, sodium methoxide, and methyllithium, respectively. The reaction of silyl anions and aromatic halides has been known in the literature for over 20 years but the chemistry reported to date has not been very clean.[2a,d] We report a mild one-step procedure at 25 °C for the conversion of aryl halides to trimethylsilylbenzenes, formally a trimethylsilyldehalogenation on an aromatic compound.[3] Trimethylsilyl-substituted benzenes are very useful intermediates for directing specific mild electrophilic substitution on carbon as shown in the work of Eaborn and coworkers.[4]

Reaction of aryl halides, ArX (X = Cl, Br, I), with hexamethyldisilane and KOMe (or NaOMe or MeLi) in anhydrous

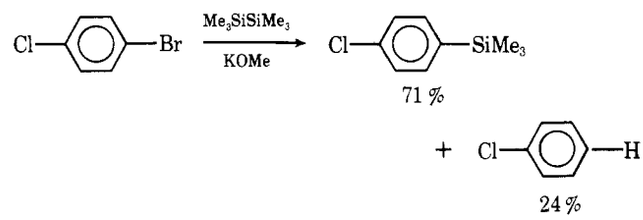


ArX, X = Cl, Br, I ArTMS

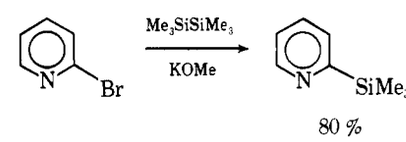
HMPT at 25 °C under argon for 3 h affords the corresponding substitution product $ArSiMe_3$ (92–63%) and some reduction product ArH (4–26%) depending mostly on the choice of aryl halide. Typical yields are shown in Table I.

In general we find that (1) the ratio of substitution/reduction increases in the direction I < Br < Cl; (2) this ratio is relatively insensitive to the choice of metal cation; (3) the rates of reaction appear to decrease in the direction I, Br > Cl; (4) substitution occurs exclusively on the carbon bearing the halogen substituent; (5) the ratio of substitution/reduction increases as substituent position on the aromatic ring changes from ortho > meta > para;[5] (6) yields and substitution/reduction ratios are sensitive to temperature.[6]

Differences in reactivity of the halogen substituent could be distinguished on the same molecule. 1-Bromo-4-chlorobenzene reacts with hexamethyldisilane and KOMe to afford



reaction mostly (>95%) at the carbon bearing bromine.[7] Substitution also occurs in heteroaromatic molecules, for example, 2-bromopyridine. No reduction product was found in this case.



80 %

The mechanisms of these reactions are not yet known. In a formal sense, the silylated product is derived from a nucleophilic aromatic substitution reaction. At least four mechanisms can be considered: (1) the aryne mechanism, (2) direct nucleophilic substitution (S_NAr), (3) halogen–metal interchange to afford an ArM (M = K, Na, Li) intermediate, (4) radical-anion chain reaction ($S_{RN}1$).[8] The aryne pathway can be excluded based on the stereochemical results. Concerted nucleophilic displacement at aromatic carbon is more difficult to eliminate,[8b] especially in view of the strong nucleophilicity of silyl anions. However, this S_NAr mechanism is seldom encountered with unactivated aryl halides and requires a second competing pathway for reduction product. Quenching the reaction mixture of iodobenzene and TMSK with D_2O after 5 min affords reduction product (benzene) with 30% d_1 incorporation.[9] This is permissive evidence that at least