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AN UMPOLUNG OF ARYL AND VINYL HALIDES USING TRIS-(TRIMETHYLSILYL)ALUMINUM AN APPROACH TO META- AND PARA-BRIDGED AROMATICS

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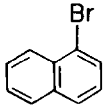
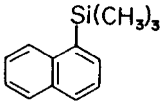
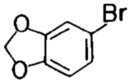
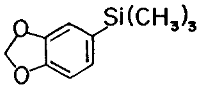
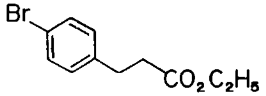
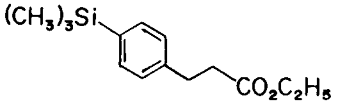
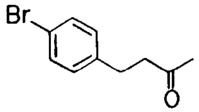
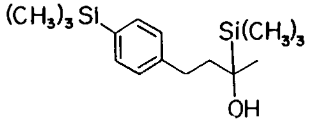
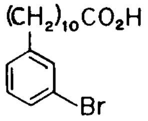
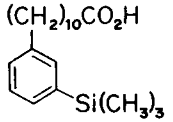
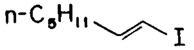
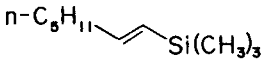
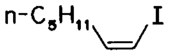
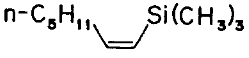
SUMMARY: Nickel and palladium catalysts effect the chemoselective and stereocontrolled umpolung of aryl and vinyl halides to trimethylsilyl derivatives; this reaction permits a regioselective approach to cyclophanes.

A major application of aryl and vinyl halides in organic chemistry is their metal-halogen exchange to form magnesium and lithium derivatives in order to facilitate formation of new C-C bonds. Such a transformation converts an electrophilic center into a nucleophilic one but will be restricted due to the compatibility of functionality with such a transformation. The usefulness of aryl and vinyl silanes in reactions with electrophiles[1] has suggested the need for a chemoselective conversion of an aryl or vinyl halide to their corresponding silane. In this paper, we wish to report the use of tris(trimethylsilyl)aluminum etherate (1)[2,3,4] and transition metal catalysts to effect such a reaction and the utility of such an approach to make aromatic compounds bridged on non-adjacent carbons.

Bromobenzene was chosen as a simple model to explore reaction conditions. A 1.5:1 mol ratio of 1 and bromobenzene was allowed to reflux in dioxane in the presence of bis(triphenylphosphine)nickel dichloride or dibromide and analyzed by VPC.[5,6a] Trimethylsilylbenzene formed in 81-2% yield after 1 h reaction time. The importance of the phosphine ligands was demonstrated by use of nickel bromide alone (28% yield) and various other phosphines such as dppp[6b] (34% yield) or dppe[6b] (37% yield). The requirement for a nickel catalyst was demonstrated by the absence of any product by simply allowing 1 and bromobenzene to reflux. Solvent proved to be very important. Hydrocarbon solvents like pentane (18% yield) and benzene (19% yield) were inferior to ethereal solvents like diethyl ether (27% yield), THF (61% yield), and dioxane (82% yield). The higher yields in dioxane are attributed to both its Lewis basicity which, by coordinating to the aluminum, facilitates transfer of the trimethylsilyl group, and its higher reflux temperature. In a standard synthetic procedure, an aliquot of a standardized pentane solution of 1 (3.6 mmol) was evaporated to dryness (a white solid results) and taken up in dioxane. The resultant solution was added to a mixture of the aryl bromide (3.0 mmol) and $(Ph_3P)_2NiCl_2$ (0.15 mmol) in dioxane and then allowed to reflux 1 h. After cooling and partitioning between ether and water, the ether layers were dried. After removal of the ether by distillation, the residue was distilled to give the silylated product. The Table summarizes the results.

TABLE. Silylation of Aryl and Vinyl Halides

Entry	Halide	Time	Product[a]	Isolated Yield[b]
1^c	PhBr	1	$PhSi(CH_3)_3$	65 (82)
2^c	$4\text{-}CH_3OC_6H_4Br$	1	$4\text{-}CH_3OC_6H_4Si(CH_3)_3$	79 (92)
3^c		1		56
4^c		1		71
5^c		1		64
6^c		1		68
7^c		15 min		51^e
$8^{d,i}$	 f	4		83^f
$9^{d,j}$	 g	4		71^h

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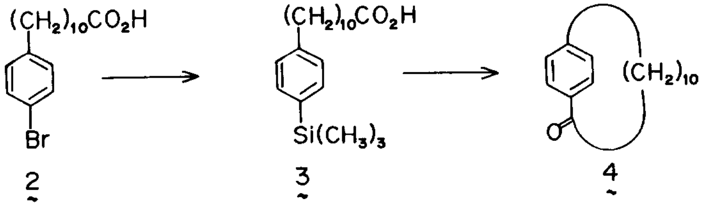
(a) All new products have been fully characterized. (b) Yields given are for isolated pure material. Yields in parenthesis are vpc determined. Isolation is by distillation except where otherwise noted. (c) This reaction utilized 5 mol% of $(Ph_3P)_2NiCl_2$ in refluxing dioxane. (d) This reaction utilized $(Ph_3P)_4Pd$ in ether-pentane at room temperature. (e) Isolated by plc using hexane-ethyl acetate. (f) This compound was ≥ 95% E as determined by nmr analysis. (g) The compound was 92/8 Z/E as determined by nmr analysis. (h) The compound was 89/11 Z/E as determined by nmr analysis. (i) 5 mol% of catalyst employed. (j) 11 mol% of catalyst employed.

The positional identity of the bromide is fully retained in the product. Most significantly, both an ester and carboxylic acid (entries 5 and 7) are compatible. The reaction of a ketone (entry 6) is most interesting. The silyl group added to the carbonyl group as well as effect the replacement of the bromide.[7] Such an adduct allows easy regeneration of the ketone by oxidation or cleavage to the simple alcohol by treatment with KH[8] - two facts that offer flexibility to this method of replacement of bromide by silicon. Thus, unprotected ketones can also be present and their ultimate fate determined by a simple further reaction.

In extending the reaction to vinyl derivatives, we found that vinyl bromides reacted under the above conditions with loss of stereochemistry. Switching to a palladium catalyst led to a very slow reaction. On the other hand, vinyl iodides react at room temperature with 1 in an ether-pentane mixture in the presence of tetrakis(triphenylphosphine)palladium[9] as catalyst (entries 8 and 9). Within experimental error, olefin geometry is maintained.

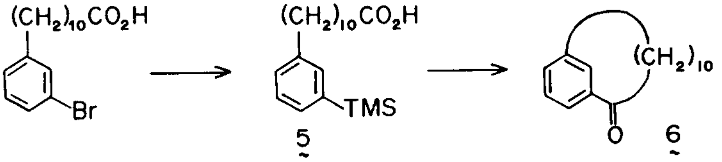
The usefulness of this approach in synthesis can be illustrated by a synthesis of meta and para bridged aromatic derivatives. 11-(4'-Bromophenyl)undecanoic acid (2) was silylated under the standard conditions to give 3[10] in 51% yield but using a mole ratio of 1 to bromoacid of 1.5 (see eq 1).



(1)

Conversion of 3 to its acid chloride [(COCl)$_2$, PhH] in benzene, evaporation *in vacuo*, and then adding a methylene chloride solution of the resultant acid chloride to a stirred suspension of aluminum chloride over 30 min at -28° followed by continued stirring for 19 h gave a 58% yield of 4 , mp 41-42.5° (unrecrystallized) (lit.[11] mp 44.5-45°).[10,11]

In similar fashion, the meta derivative 5 was prepared in 51% yield (see eq 2). Slow addition of the acid chloride derived from 5 to a methylene chloride suspension of aluminum chloride at -28° produced an isomer of 4 in 45% unoptimized yield, whose NMR spectrum clearly showed it was the meta bridged analog 6.[10] Thus, tris(trimethylsilyl)aluminum combined with transition metal catalysts permits facile exchange of halide for the trimethylsilyl group.[12] The utility and spectroscopic advantages of the trimethylsilyl group as well as the high chemoselectivity of this approach makes it a highly promising method for the umpolung of halides. In addition to the utility in synthesis, the ability of tris(trimethylsilyl)aluminum to participate in such a cross coupling is mechanistically interesting since the presence of β-H in the group being transferred normally leads the reaction in a different direction and the effect of ligands is the opposite to that normally seen where bidentate ligands are preferred to monodentate ligands. The dependence on the nature of the catalyst is also noteworthy. However, such mechanistic questions remain the province of future investigations.



(2)

Acknowledgment. We wish to thank the National Science Foundation for their generous support of our programs. We thank Johnson Matthey and Englehard

Industries for their generous supplies of palladium salts.

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3. Prepared as a standardized solution in pentane[4]. Its NMR spectra show absorptions for ^{29}Si at -19.73 and for ^{1}H at 0.17 in pentane-C_6D_6 both relative to TMS.

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6. a) Analyzed on a 5% SE-30 column at 50°. b) Abbreviations: dppp=1,3-bis(diphenylphosphino)propane; dppe= 1,2-bis(diphenylphosphino)ethane.

7. Cf ref 2.

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10. **3** ^{1}H NMR ($CDCl_3$, 200 MHz) 0.24 (s, 9H), 1.29 (m, 12H), 1.60 (m, 4H), 2.33 (t, J=7.4 Hz, 2H), 2.58 (t, J=7.6 Hz, 2H), 7.16 (d, J=7.8 Hz, 2H), 7.42 (d, J=7.8 Hz, 2H). ^{13}C NMR -0.85, 24.88, 29.33, 29.34, 29.56, 31.38, 34.14, 36.12, 127.80, 133.20, 137.00, 143.40, 179.04. IR ($CDCl_3$): 1708, 1600 cm^{-1}. Calc'd for $C_{20}H_{34}O_2Si$: 334.2328. Found: 334.2328.

4 ^{1}H NMR ($CDCl_3$, 200 MHz): 0.45-1.4 (m, 12H), 1.68 (m, 4H), 2.70 (m, 2H), 2.86 (m, 2H), 7.29 (d, J=8.3 Hz, 2H), 7.70 (d, J=8.3 Hz, 2H). ^{13}C NMR ($CDCl_3$): 25.53, 26.94, 27.32, 28.03, 29.06, 29.33, 36.21, 38.75, 128.19, 129.55, 137.78, 147.43, 205.56. IR ($CDCl_3$): 1677, 1607 cm^{-1}. Calc'd for $C_{17}H_{24}O$: 244.1828. Found: 244.1828.

5 ^{1}H NMR ($CDCl_3$, 200 MHz) 0.30 (s, 9H), 1.2-1.5 (m, 12H), 1.5-1.75 (m, 4H), 2.38 (t, J=7.4 Hz, 2H), 2.64 (t, J=7.7 Hz, 2H), 7.15-7.4 (m, 4H). IR ($CDCl_3$) 3510, 3400-2400 (br), 1700 $cm.^{-1}$ Calc'd for $C_{20}H_{34}O_2Si$: 334.2328. Found: 334.2328.

6 ^{1}H NMR ($CDCl_3$, 200 MHz) 1.0-1.45 (m, 12H), 1.5-1.8 (m, 4H), 2.7-2.8 (m, 2H), 2.8-2.95 (m, 2H), 7.3-7.45 (m, 2H), 7.70 (bs, 1H), 7.75-7.85 (m, 1H). 13^{C} NMR ($CDCl_3$): 24.18, 25.13, 25.45, 26.71, 27.22, 28.23, 30.62, 33.29, 37.34, 125.52, 129.52, 129.0, 133.62, 136.78, 141.90, 203.01. IR ($CDCl_3$): 1678, 1610, 1587 cm^{-1}. Calc'd for $C_{17}H_{24}O$: 244.1827. Found: 244.1828.

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12. For related work with phosphates and diethyl(phenyldimethylsilyl)aluminum which appeared after completion of our work see: Okuda, Y.; Sato, M.; Oshima, K.; Nozaki, H. Tetrahedron Lett. 1983, 24, 2015. It is stated that nickel catalysts are ineffective in this reaction.

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