Reaction of Aryl Triflates with Heteroaryllithiums via Aryne Intermediates

Kelly Hardee Reuter[1a] and William J. Scott[*,1b]

Department of Chemistry, The University of Iowa, Iowa City, Iowa 52242

Received February 13, 1992 (Revised Manuscript Received May 25, 1993)

Unhindered aryl triflates react with a mixture of 1.5 equiv of LDA and 8–10 equiv of 2-lithiofuran at −78 °C to form 2-arylfurans in 50–60% yield via the corresponding arynes. Regioisomeric ratios of products are similar to those observed for reactions of arynes with well-precedented nucleophiles, such as metal amides. Steric hindrance ortho to the triflate increases the *cine* to *ipso* ratio, but lowers overall yields due to enhanced nucleophilic attack at sulfur leading to formation of the corresponding phenol. Use of 2-lithiothiophene affords the analogous arylthiophene.

Substituted furans have become increasingly important synthetic intermediates both as masked 1,4-dicarbonyls and as Diels–Alder dienes.[2] The furan moiety also comprises an integral part of a multitude of natural products.[3] These attributes have stimulated interest into new methods for the construction of functionalized furans. Synthesis of substituted furans may involve *de novo* construction of the furan ring. For example, Mukaiyama demonstrated that furanoids could be synthesized from the $TiCl_4$-promoted reaction of α-bromo acetals with silyl enol ethers.[4] Similarly, palladium salts have been used to catalyze cyclization of acetylenic diols into furans.[5]

Another general approach to the synthesis of aryl furans involves the coupling of an electrophile with a preexisting furan ring. Johnson found that furan will react with aryl diazonium chlorides to yield 2-arylfurans.[6] More recently, Group 10 metal catalysts have been shown to mediate the cross-coupling of aryl electrophiles with furan directly,[7] or with a wide variety of furyl nucleophiles, including 2-lithiofuran,[8] (2-furyl)magnesium halide,[9] (2-furyl)zinc halide,[8b,10] and (2-furyl)trimethylstannane.[11] When substituted aryls are used, cross-coupling reactions result in the *ipso*-furyl product.

We have recently shown that treatment of aryl triflates with LDA in either ethereal solvents or in *N,N*-diisopropylamine at −78 °C rapidly forms the corresponding aryne, which is then trapped with *N,N*-diisopropylamine to afford the corresponding *N,N*-diisopropylaniline.[12] Substituted phenyl triflates gave regioisomeric mixtures of substituted *N,N*-diisopropylanilines in ratios similar to those observed for aniline formation using the analogous aryl halides.[12] Typically, use of *ortho*-substituted aryl triflates affords largely *cine* (meta) rather than *ipso* (ortho) products, while *para*-substituted aryl triflates gave more nearly 1:1 mixtures of *cine* (meta) and *ipso* (para) products.[12]

As part of our continuing interest in the aryne-mediated reactions of aryl triflates,[12] we chose to study reactions which might demonstrate the advantages of the generation of arynes under such gentle conditions (−78 °C). We were accordingly attracted to the possibility of synthesizing arylfurans by attack of a furyl nucleophile on an aryne intermediate. This approach to the synthesis of arylfurans would complement the use of palladium-mediated cross-coupling reactions, which can only afford the *ipso* product, in that the *cine* product would be available from the reaction mixture. Though the reaction of carbanions with arynes is well known, the use of heteroaryl nucleophiles appears to be unprecedented.[13–17] We have found 2-lithio-

---

[1] (a) Department of Exploratory Research; Land O'Lakes, Inc.; P.O. Box 116; Minneapolis MN 55440-0116. (b) Institute for Chemistry; Pharmaceutical Division; Miles, Inc.; 400 Morgan Lane; West Haven, CT 06516-4175.

[2] (a) Lipshutz, B. H. *Chem. Rev.* **1986,** *86,* 795-819. (b) Meyers, A. I. *Heterocycles in Organic Synthesis*; John Wiley: New York, 1974.

[3] (a) Dean, F. M. *Adv. Heterocycl. Chem.* **1982,** *30,* 168–238. (b) Padwa, A.; Murphree, S. S. *Org. Prep. Proc. Ed. Int.* **1991,** *23,* 547-568.

[4] Mukaiyama, T.; Ishihara, H.; Inomata, K. *Chem. Lett.* **1975,** 527-530.

[5] Camus, F.; Hasiak, B.; Martin, M.; Couturier, D. *Synth. Commun.* **1982,** *12,* 647–650.

[6] Johnson, A. W. *J. Chem. Soc.* **1946,** 895–899.

[7] Ohta, A.; Akita, Y.; Ohkuwa, T.; Chiba, M.; Fukunaga, R.; Miyafuji, A.; Nakata, T.; Tani, N.; Aoyagi, Y. *Heterocycles* **1990,** *31,* 1951–1958.

[8] (a) Murahashi, S.; Yamamura, M.; Yanagisawa, K.; Mita, N.; Kondo, K. *J. Org. Chem.* **1979,** *44,* 2408–2417. (b) Pelter, A.; Rowlands, M.; Clements, G. *Synthesis* **1987,** 51–53.

[9] Pridgen, L. N.; Jones, S. S. *J. Org. Chem.* **1982,** *47,* 1590–1592.

[10] (a) Negishi, E.; Luo, F.; Frisbee, R.; Matsushita, H. *Heterocycles* **1982,** *18,* 117–122. (b) Pelter, A.; Rowlands, M.; Jenkins, I. H. *Tetrahedron Lett.* **1987,** *28,* 5213–5216. (c) Negishi, E.; Takahashi, T.; King, A. O. *Org. Synth.* **1988,** *66,* 67–74. (d) Arcadi, A.; Burini, A.; Cacchi, S.; Delmastro, M.; Pietroni, B. *Synlett* **1990,** 47–48. (e) Roth, G. P.; Fuller, C. E. *J. Org. Chem.* **1991,** *56,* 3493–3496.

[11] (a) Bailey, T. R. *Tetrahedron Lett.* **1986,** *27,* 4407–4410. (b) Katsumura, S.; Fujiwara, S.; Isoe, S. *Tetrahedron Lett.* **1987,** *28,* 1191–1194.

[12] Wickham, P. P.; Hazen, K. H.; Guo, H.; Jones, G.; Reuter, K. H.; Scott, W. J. *J. Org. Chem.* **1991,** *56,* 2045–2050.

[13] For some reviews on the reaction of carbon nucleophiles with aryne intermediates, see: (a) Hoffman, R. W. *Dehydrobenzene and Cycloalkynes*; Academic Press: New York, 1967. (b) Caubere, P. *Acc. Chem. Res.* **1974,** *7,* 301–308. (c) Biehl, E. R.; Khanapure, S. P. *Acc. Chem. Res.* **1989,** *22,* 275–281.

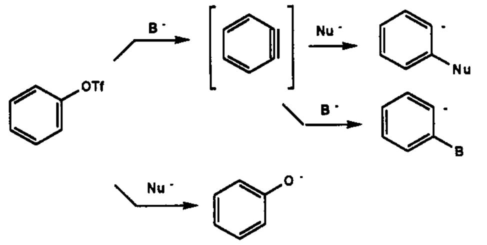
[14] For examples of the reaction of aryl and vinyl nucleophiles with aryne intermediates, see: (a) Wittig, G.; Fuhrmann, G. *Chem. Ber.* **1940,** *73,* 1197–1218. (b) Huisgen, R.; Zirngibl, L. *Chem. Ber.* **1958,** *91,* 1438–1452. (c) Gilman, H.; Gorsich, R. D. *J. Am. Chem. Soc.* **1956,** *78,* 2217–2222. (d) Furukawa, N.; Shibutani, T.; Fujihara, H. *Tetrahedron Lett.* **1987,** *28,* 2727–2730. (e) Vinod, T. K.; Hart, H. *J. Org. Chem.* **1990,** *55,* 5461–5466.

[15] For selected examples of the reaction of stabilized and unstabilized alkyl nucleophiles with aryne intermediates, see: (a) Wright, R. E.; Bergstrom, F. W. *J. Org. Chem.* **1936,** *1,* 179–188. (b) Dirstine, P. H.; Bergstrom, F. W. *J. Org. Chem.* **1946,** *11,* 55–59. (c) Pansegrau, P. D.; Rieker, W. F.; Meyers, A. I. *J. Am. Chem. Soc.* **1988,** *110,* 7178–7184.

[16] For examples of the reaction of enolates and analogous nucleophiles with aryne intermediates, see: (a) Bergstrom, F. W.; Agostinho, R. *J. Am. Chem. Soc.* **1945,** *67,* 2152–2154. (b) Hauser, C. R.; Harris, T. M. *J. Am. Chem. Soc.* **1958,** *80,* 6360–6363. (c) Bunnett, J. F.; Brotherton, T. K. *J. Org. Chem.* **1958,** *23,* 904–906. (d) Leake, W. W.; Levine, R. *J. Am. Chem. Soc.* **1959,** *81,* 1627–1630. (e) Meyers, A. I.; Pansegrau, P. D. *Tetrahedron Lett.* **1984,** *25,* 2941–2944. (f) Gregoire, B.; Carre, M.-C.; Caubere, P. *J. Org. Chem.* **1986,** *51,* 1419–1427. (g) Carre, M. C.; Aatif, A. A.; Geoffroy, P.; Caubere, P. *Synth. Commun.* **1990,** *19,* 2523–2550. (h) Bhawal, B. M.; Khanapure, S. P.; Zhang, H.; Biehl, E. R. *J. Org. Chem.* **1991,** *56,* 2846–2849. (i) Desmukh, A. R.; Zhong, H.; Tran, L.; Biehl, E. *J. Org. Chem.* **1992,** *57,* 2485–2486. (j) Desmukh, A. R.; Biehl, E. R. *Heterocycles* **1992,** *34,* 99–102.

0022-3263/93/1958-4722$04.00/0

Scheme I. Strategy for the Nucleophilic Substitution of Aryl Triflates via Aryne Intermediates



furan,[18] generated between -80 and -20 °C, not to be stable at or above room temperature, conditions commonly used for generation of benzyne from phenyl halides. Herein, the first synthesis of arylfurans via aryne intermediates is described.

Results and Discussion

Our initial approach to the synthesis of aryl furans involved the use of 2-lithiofuran[18] (**2**) as both base and nucleophile. However, treatment of phenyl triflate (**1**) with excess 2-lithiofuran in ethereal solvents at -78 °C afforded only small amounts of 2-phenylfuran (10–15%). The remainder of the arene was returned as phenol. Nucleophiles such as NaOH,[19] *n*-butyllithium,[20,21] NaH,[21] and $LiAlH_4$[20] have been reported to attack vinyl and aryl triflates at sulfur generating the corresponding enolates and phenoxide ions. We have since found that *tert*-butyllithium, $NaNH_2$, and 2-lithiofuran react with phenyl triflate in a similar manner. Conversely, use of the highly hindered amide base, LiTMP, returned the phenyl triflate unchanged. LDA therefore remains the base of choice for aryne generation from aryl triflates.

Given the need for a hindered amide base, nucleophilic substitution of the aryne intermediate would appear to require a very narrow window of reactivity (Scheme I). The reaction must include both a base (B^-, the amide) and a nucleophile (Nu^-, the metallofuran). The base must be reactive enough to deprotonate the aryl triflate more rapidly than the nucleophile can react at sulfur. However, after deprotonation and elimination, the aryne intermediate must react preferentially with the nucleophile in the presence of any remaining base.

Addition of a -78 °C solution of phenyl triflate (**1**) in THF to a -78 °C solution of 1.5 equiv of LDA and 9.5 equiv of 2-lithiofuran (**2**) in THF afforded the desired arylfuran **3** in 52% yield (Table I). Under these conditions, only trace amounts of phenol and *N,N*-diisopropylaniline[12] were observed. Increased levels of LDA or decreased levels of 2-lithiofuran led to the formation of significant amounts of *N,N*-diisopropylaniline due to competitive attack of *N,N*-diisopropylamine with benzyne. Similarly, increased levels of 2-lithiofuran, or warming of either solution prior to mixing gave phenol as the major product due to the apparently facile attack of the nucleophile at sulfur.

As shown in entry 4, reaction of 2-methoxyphenyl triflate (**8**) under the above conditions gave only the *meta*-product **9**. The regiochemistry of the product was assigned from the ^1H NMR chemical shifts. In addition to furanoid absorptions at 6.47, 6.64, and 7.46 ppm, a ddd at 6.82 ppm (J = 7.1, 2.4, 2.4 Hz) was consistent with the calculated value for a proton at C-4 (6.8 ppm), and the three remaining phenyl protons were observed between 7.2 and 7.3 ppm as expected.[21] The regiochemistry and selectivity of this reaction are analogous to those observed in previous reactions involving 3-methoxybenzyne.[12,24]

Treatment of 2-methylphenyl triflate (**6**) with LDA in the presence of excess 2-lithiofuran gave a 2:1 mixture of 2-arylfurans accompanied by a small amount (<5% by GC analysis) of a third adduct, which could not be separated from the product mixture (entry 3).[24] ^1H NMR analysis of the reaction mixture showed signals for the major isomer at δ 2.37 (s), 6.44 (dd, J = 3.4, 1.8 Hz) and 6.62 (dd, J = 3.4, 0.7 Hz), which agreed well with the partial spectrum reported for furan ***m*-7** (δ 2.30, 6.35, 6.55),[8b] and were readily distinguished from the minor isomer ***o*-7**, which displayed signals at δ 2.48 (s), 6.48 (dd, J = 3.4, 1.8 Hz) and 6.52 (dd, J = 3.4, 0.7 Hz). Assignment of the major and minor isomers as 2-(3-methylphenyl)furan (***m*-7**) and the ortho isomer ***o*-7**, respectively, is consistent with the generalizations that electron-withdrawing groups deshield an *o*-methyl group 0.10–0.25 ppm relative to the analogous *m*-methyl group, and is also consistent with product ratios reported from reactions of nucleophiles with 3-methylbenzyne.[12,27c] Further confirmation of the assignments of ***o*-7** and ***m*-7** was obtained by independently synthesizing the ortho isomer via $dppfPdCl_2$-mediated cross-coupling of triflate **6** with (2-furyl)tributylstannane in the presence of excess LiCl (unoptimized procedure in supplementary material). The 2-(2-methylphenyl)furan (***o*-7**) thus obtained displayed identical properties (NMR, GC, MS, and IR) with the minor component of the isomer mixture resulting from the aryne reaction.

Treatment of 4-phenylphenyl triflate (**4**) under the standard reaction conditions gave two isomeric bipheny-

---

(17) For selected examples of ring formation via reaction of carbon nucleophiles with aryne intermediates, see: (a) Hrutfiord, B. F.; Bunnett, J. F. *J. Am. Chem. Soc.* **1958**, *80*, 2021–2022. (b) Bunnett, J. F.; Kato, T.; Flynn, R. R.; Skorcz, J. A. *J. Org. Chem.* **1963**, *28*, 1–6. (c) Beam, C. F.; Bissell, R. L.; Hauser, C. R. *J. Org. Chem.* **1970**, *35*, 2083–2085. (d) Sammes, P. G.; Wallace, T. W. *J. Chem. Soc., Chem. Commun.* **1973**, 524. (e) Loubinoux, B.; Caubere, P. *Synthesis* **1974**, 201–203. (f) Jung, M. E. Lowen, G. T. *Tetrahedron Lett.* **1986**, *27*, 5319–5322.

(18) Ramanathan, V.; Levine, R. *J. Org. Chem.* **1962**, *27*, 1216–1219.

(19) Summerville, R. H.; Senkler, C. A.; Schleyer, P. v. R.; Dueber, T. E.; Stang, P. J. *J. Am. Chem. Soc.* **1974**, *96*, 1100–1110.

(20) Garcia Martinez, A.; Espada Rios, I.; Martinez Alvarez, R.; Gomez Anton, M. R.; Teso Vilar, E. *An. Quim., Ser. C* **1981**, *77*, 150–152.

(21) Stang, P. J.; Mangum, M. G.; Fox, D. P.; Haak, P. *J. Am. Chem. Soc.* **1974**, *96*, 4562–4569.

(22) Predicted chemical shifts of the phenyl ring protons were calculated using the literature method and literature substituent values.[23] 2-Furyl substituent effects of Z_2 = 0.42, Z_3 = 0.12, Z_4 = -0.01 were based on the ^1H NMR of 2-phenylfuran.

(23) Pretsch, E.; Seibl, J.; Simon, W.; Clerc, T. *Tables of Spectral Data for Structure Determination of Organic Compounds*; Springer-Verlag: New York, 1983; pp H255–H260.

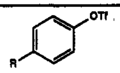
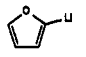
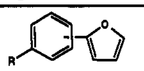
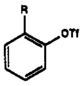
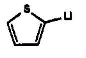
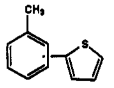
(24) (a) Benkeser, R. A.; DeBoer, C. E. *J. Org. Chem.* **1956**, *21*, 281–284. (b) Huisgen, R.; Rist, H. *Justus Liebigs Ann. Chem.* **1955**, *594*, 137–158. (c) Gilman, H.; Kyle, R. H. *J. Am. Chem. Soc.* **1952**, *74*, 3027–3029. (d) Zbiral, E. *Tetrahedron Lett.* **1964**, *5*, 1649–1652.

(25) To date the side product of the aryne reaction using triflate **6** has eluded identification. The impurity shows identical TLC and similar GC characteristics to those of furans *m*-7 and *o*-7. The mass spectrum of the adduct was indistinguishable from that of an authentic sample of 1-methylnaphthalene (*m/z* 142, 139, 115), a substance which is readily differentiated from arylfurans *m*-7 and *o*-7 by both TLC and GC. No NMR evidence for the presence of the 1-methylnaphthalene, 1,4-epoxy-1,4-dihydro-8-methylnaphthalene (the product of a Diels–Alder reaction between3-methylbenzyneandfuran),[26a] 1-hydroxy-5-methylnaphthalene,[26b] or 1-hydroxy-8-methylnaphthalene[26b] could be obtained from the reaction mixture.

(26) (a) Harrison, R.; Heaney, H.; Lees, P. *Tetrahedron* **1968**, *24*, 4589–4594. (b) Batt, D. G.; Jones, D. G.; La Greca, S. *J. Org. Chem.* **1991**, *56*, 6704–6708.

(27) (a) Tanaka, Y.; Tsujimoto, K.; Ohashi, M. *Bull. Chem. Soc. Jpn.* **1987**, *60*, 788–790. (b) Huisgen, R.; Sauer, J.; Hauser, A. *Chem. Ber.* **1958**, *91*, 2366–2374. (c) Huisgen, R.; Sauer, J. *Angew. Chem.* **1960**, *72*, 91–108.

Table I. Reaction of Aryl Triflates with LDA in the Presence of Lithiated Heteroaryl Nucleophiles

entry	aryl triflate	R	no.	nucleophile	no.	product(s)	no.	isomer ratio	isolated yield (%)
1		H	1		2		3		52
2		Ph	4		2		m-5/p-5	58:42	52[a]
3		Me	6		2		o-7/m-7	32:68	54[b]
4		MeO	8		2		o-9/m-9	0:100	58
5		H	1		10		11		49
6		Me	6		10		o-12/m-12	43:57	54[c]
7		MeO	8		10		o-13/m-13	0:100	35

[a] Product ratio determined by GC. [b] Arylfurans *o*-7 and *m*-7 were isolated along with an impurity (>5%). [c] Regiochemistry of isomers was tentatively assigned by analogy to the corresponding aryne reaction with 2-lithiofuran.

lylfurans in a 3:2 GC ratio (entry 2). Because spectral analysis of the product mixture would not permit unambiguous determination of the relative regiochemistry of the two products, the para isomer ***p*-5** was synthesized independently via the palladium-mediated cross-coupling reaction (unoptimized procedure in supplementary material). The product thus obtained displayed identical properties (NMR, GC, and IR) with the minor component of the isomeric biphenylyl mixture, allowing assignment of the major component of the mixture as the meta isomer. The ratio of *m*- (***m*-5**) to *p*-biphenylylfuran (***p*-5**) was similar to that previously obtained for aryne-mediated reactions of triflate **4** with diisopropylamine as the nucleophile.[12]

Reaction of 2-*tert*-butylphenyl triflate (**14**) with LDA in the presence of excess 2-lithiofuran gave a mixture of 2-*tert*-butylphenol and 2-(3-*tert*-butylphenyl)furan in a 3:1 ratio, from which the furan could be isolated in 20% yield. Interestingly, only the *meta*-substituted furan was produced from the hindered triflate, while 2-methylphenyl triflate had given a 1:2 mixture of *ortho*- and *meta*-substituted products. Similarly, treatment of 2-phenylphenyl triflate (**15**) under the reaction conditions gave only trace amounts of the desired furan product with the major product being 2-phenylphenol. These results may be contrasted with the successful reactions of 4-phenylphenyl triflate and 2-methylphenyl triflate (entries 2 and 3). The poor reactivity of triflates **14** and **15** may be rationalized as being due to a steric-related change in conformation of the sulfonate ester causing increased susceptibility to nucleophilic attack at sulfur and/or decreased ability for the ester to assist in deprotonation.

Thiophenes are synthetically useful heterocycles, with applications in medicinal chemistry and agrochemical research.[28] Substituted thiophenes have found use as high intensity sweeteners[29] and flavoring agents.[30] 2-Arylthiophenes have also been used in the synthesis of conducting polymers.[31] As with the synthesis of furanoids, a variety of methods have been developed for the synthesis of substituted thiophenes.[28] Recently, Group 10 metal-mediated cross-coupling reactions have emerged as the methods of choice for these transformations. Palladium or nickel catalysts have been used to couple electrophiles with thiophene directly,[7] or with metallothiophenes including magnesium,[31b,32] zinc,[10a–c,31a] and tin nucleophiles.[11a,33]

In a brief extension of the aryne–lithiofuran chemistry to the synthesis of aryl thiophenes, aryl triflates were found to react with 2-lithiothiophene in the presence of LDA in a manner analogous to that described for 2-lithiofuran (entries 5–7). Treatment of phenyl triflate (**1**) with LDA in the presence of 10 equiv of 2-lithiothiophene afforded 2-phenylthiophene (**11**) in 49% yield. *o*-Tolyl triflate (**6**) reacted similarly to give the corresponding *ortho*- and *meta*-substituted products (**12**) in good yield. Reaction of 2-methoxyphenyl triflate (**8**) with LDA and 2-lithiothiophene gave the 3-methoxyphenyl product **13** as the only product observed.

Conclusions

Aryl triflates react with a mixture of LDA and a 10-fold excess of either 2-lithiofuran or 2-lithiothiophene to give arylfurans or arylthiophenes via the aryne. Where relevant, mixtures of the *cine* and *ipso* products are formed in ratios similar to those commonly observed for nucleophilic attack on substituted arynes. To our knowledge, this is the first report of the use of 2-lithiofuran as a nucleophile in aryne-mediated reactions. This methodology demonstrates that aryl triflates can be used to generate arynes at low temperatures, and that these arynes can then be trapped with lithiated carbon nucleophiles which might not normally be stable under normal aryne-generating reaction conditions.

Aryne generation appears to be sensitive to the presence of bulky substituents ortho to the triflate. The reaction of aryne intermediates generated from aryl triflates with other carbon and heteronucleophiles is currently under investigation and will be reported in due course.

Experimental Section

^{1}H and ^{13}C NMR spectra were obtained in CDCl$_3$. Low resolution GC-mass spectra (GC-LRMS) were obtained at an ionization potential of 70 eV. Capillary GC analyses were run

---

(28) Hartough, H. D., Ed. *Chemistry of Heterocyclic Compounds - Thiophene and Derivatives*; Wiley Interscience: New York, 1952.

(29) Janusz, J. M.; Young, P. A.; Blum, R. B.; Riley, C. M. *J. Med. Chem.* **1990**, *33*, 1676–1682.

(30) (a) Min, D. B. S; Ina, K.; Peterson, R. J.; Chang, S. S. *J. Food Sci.* **1979**, *44*, 639–642. (b) Vernin, G.; Vernin, G. In *Heterocyclic Flavouring and Aroma Compounds*; Vernin, G., Ed.; Ellis Horwood: Chichester, 1982; Chapter II.

(31) (a) Pelter, A.; Maud, J. A.; Jenkins, I.; Sadeka, C.; Coles, G. *Tetrahedron Lett.* **1989**, *30*, 3461–3464. (b) Reynolds, J. R.; Ruiz, J. P.; Child, A. D.; Nayak, K.; Marynick, D. M. *Macromolecules* **1991**, *24*, 678–687.

(32) (a) Tamao, K.; Kodama, S.; Nakajima, I.; Kumada, M.; Minato, A.; Suzuki, K. *Tetrahedron* **1982**, *38*, 3347–3354. (b) Rossi, R.; Carpita, A.; Lezzi, A. *Tetrahedron* **1984**, *40*, 2773–2779.

(33) Crisp, G. T. *Synth. Commun.* **1989**, *19*, 307–316.

on a chromatograph equipped with a 0.53 mm × 5 m methyl silicone column and a flame ionization detector. TLC was conducted on EM silica gel 60F-254 plates. No attempt was made to separate isomeric arenes. All mixtures of furanoids were >95% pure as determined by GC, TLC, ^{1}H NMR, and ^{13}C NMR analyses except where noted. All spectral information reported is for the mixture of isomers described in Table I.

Phenyl triflate,[34] 2-methoxyphenyl triflate,[35] 2-methylphenyl triflate,[34] 4-phenylphenyl triflate,[36] and 2-phenylphenyl triflate[32] were prepared according to literature methods.[37] (2-Furyl)-tributylstannane was synthesized according to the literature method.[38] THF was double distilled from potassium. *N,N*-Diisopropylamine was freshly distilled from CaH_2. Furan and thiophene were freshly distilled from KOH immediately before use. All reactions were performed under positive argon pressure.

General Procedure. Aryne Reaction with Heteroaryl Lithiums. 2-(3-Methoxyphenyl)furan (9, entry 4): To a solution of furan (0.73 mL, 10 mmol, 9.43 equiv) in THF (10 mL) at −78 °C was added *n*-BuLi (4.42 mL, 2.26 M in hexanes, 10.0 mmol, 9.43 equiv). The mixture was allowed to warm to rt for 2 h and recooled to −78 °C. To the furyllithium solution was added a solution of LDA (diisopropylamine [0.21 mL, 1.5 mmol, 1.41 equiv]; *n*-BuLi [0.66 mL, 2.26 *M* in hexanes, 1.41 equiv]) in THF (10 mL) at −78 °C via cannula, followed by a solution of 2-methoxyphenyl triflate (0.27 g, 1.06 mmol) in THF (5 mL). This mixture was maintained at −78 °C for 2 h, warmed to rt, and stirred for 10 h. The resulting slurry was separated between water (50 mL) and CH_2Cl_2 (50 mL) and the aqueous layer was back-extracted with CH_2Cl_2 (3 × 25 mL). The combined organic layers were washed with a 10% HCl solution (50 mL), a 10% NaOH solution (50 mL), water (50 mL), and a saturated NaCl solution (50 mL), dried ($MgSO_4$), and concentrated under reduced pressure to afford a dark brown viscous oil, which was adhered onto silica gel (0.5–1.0 g) and was purified by column chromatography (SiO_2, hexane) to give **9** (0.11 g, 58%) as a colorless oil: IR (CH_2Cl_2) 1580, 1470, 1270, 1210, 1030, 780, 685 cm^{-1}; ^{1}H NMR (300 MHz) δ 3.85 (s, 3H), 6.47 (dd, J = 3.4, 1.7 Hz, 1H), 6.64 (d, J = 3.4 Hz, 1H), 6.82 (ddd, J = 7.1, 2.4, 2.4 Hz, 1H), 7.22–732 (m, 3H), 7.46 (d, J = 3.4 Hz, 1H); ^{13}C NMR (75 MHz) δ 55.3, 105.3, 109.1, 111.6, 113.2, 116.4, 129.7, 132.2, 142.0, 153.8, 159.9; GC-LRMS m/z (rel abundance) 174 (100%, M^+).

2-Phenylfuran (3; entry 1): yield, 0.082 g (52%); TLC (hexane) R_f 0.40; ^{1}H and ^{13}C NMR spectra for **3** were in agreement with those previously reported.[8b,10a,39]

2-(3-Phenylphenyl)furan and 2-(4-Phenylphenyl)furan (*m*-5, *p*-5; entry 2): yield, 0.12 g, (54%); TLC (hexane) R_f 0.45; IR ($CDCl_3$) 1610, 1500, 1480, 1230, 1120, 1030 cm^{-1}; ^{1}H NMR (300 MHz) δ 6.48 (dd, J = 3.3, 1.8 Hz, 1H), 6.69 (dd, J = 3.3, 0.6 Hz, 1H), 7.33–7.75 (m, 9H), 7.89–7.91 (m, 1H). Anal. Calcd for $C_{16}H_{12}O$: C, 87.24; H, 5.49. Found: C, 86.92; H, 5.28.

Meta isomer (*m*-5): ^{13}C NMR (75 MHz) δ 105.2, 111.7, 122.6, 122.7, 126.2, 127.2 (2C), 127.5, 128.8 (2C), 129.1, 131.4, 141.0, 141.7, 142.2, 153.9; GC rel retention (ratio) 1.05 (0.58); GC-LRMS m/z (rel abundance) 220 (100%, M^+); HRMS for $C_{16}H_{12}O$, calcd 220.0888, found 220.0884.

Para isomer (*p*-5): ^{13}C NMR (75 MHz) δ 105.1, 111.7, 124.2 (2C) 126.9 (2C), 127.4 (3C), 128.8 (2C), 129.9, 140.0, 140.6, 142.2, 153.8; GC rel retention (ratio) 1.00 (0.42); GC-LRMS m/z (rel abundance) 220 (100%, M^+); HRMS for $C_{16}H_{12}O$, calcd 220.0888, found 220.0864. No attempt was made to separate the isomeric aryl furans. The ratio of products was determined by GC analysis assuming equal FID response factors for ***m*-5** and ***p*-5**. ***p*-5** showed identical properties (^{1}H NMR, ^{13}C NMR, MS, GC, IR) with an independently synthesized sample. It was not possible to assign absorbances in the aromatic region of the ^{1}H NMR spectrum of the product mixture to specific isomers.

2-(2-Methylphenyl)furan and 2-(3-methylphenyl)furan (*o*-7, *m*-7; entry 3): yield, 0.085 g (54%); IR (CH_2Cl_2) 1620, 1490, 1230, 1070, 1030 cm^{-1}.

***ortho*-Isomer** (*o*-7): TLC (hexane) R_f 0.20; ^{1}H NMR (300 MHz) δ 2.48 (s, 3 H), 6.48 (dd, J = 3.4, 1.8 Hz, 1H), 6.52 (dd, J = 3.3, 0.6 Hz, 1H), 7.05–7.70 (m, 4H), 7.49 (dm, J = 1.6 Hz, 1H); ^{13}C NMR (75 MHz) δ 21.8, 108.5, 111.3, 126.0, 127.1, 127.4, 130.8, 131.1, 134.6, 141.6, 153.6; GC rel retention (ratio) 1.00 (0.32); GC-LRMS m/z (rel abundance) 158 (100%, M^+).

***meta*-Isomer (*m*-7)**: TLC (hexane) R_f 0.11; ^{1}H NMR (300 MHz) δ 2.37 (s, 3 H), 6.44 (dd, J = 3.4, 1.8 Hz, 1H), 6.62 (dd, J = 3.3, 0.6 Hz, 1H), 7.05–7.70 (m, 4H), 7.49 (dm, J = 1.6 Hz, 1H); ^{13}C NMR (75 MHz) δ 21.5, 104.8, 111.6, 121.0, 124.1, 124.4, 128.1, 128.6, 138.2, 141.9, 154.1; GC rel retention (ratio) 1.06 (0.68); GC-LRMS m/z (rel abundance) 158 (100%, M^+). No attempt was made to separate the isomeric arylfurans. The ratio of products, determined by GC analysis assuming equal FID response factors for ***o*-7** and ***m*-7**, was in agreement with the ratio of methyl singlets for ***o*-7** (δ 2.48) and ***m*-7** (δ 2.37) in the ^{1}H NMR. The ^{1}H and ^{13}C NMR of ***m*-7** were similar to those reported.[8b] ***o*-7** displayed identical properties (^{1}H NMR, ^{13}C NMR, MS, GC, IR) with an authentic sample.

The mixture of ***o*-7** and ***m*-7** was accompanied by ~5% of an impurity. Partial characterization included the following: ^{1}H NMR (300 MHz) δ 2.68 (s), 7.83 (dm, J = 7.4 Hz), 7.99 (dm, J = 8.0 Hz); ^{13}C NMR (75 MHz) δ 19.4, 125.5, 125.7, 126.3, 126.5, 130.2; GC rel retention 1.04; GC-LRMS m/z (rel abundance) 142 (97%), 141 (100%), 139 (12%), 115 (34%).

2-Phenylthiophene (11; entry 5): yield, 0.099 g (49%); TLC (hexane) R_f 0.43; ^{1}H and ^{13}C NMR spectra and LRMS were similar to those previously reported for 11.[40]

2-(2-Methylphenyl)thiophene and 2-(3-methylphenyl)-thiophene (*o*-12, *m*-12; entry 6): yield, 0.10 g (54%); TLC (hexane) R_f 0.40; IR (CH_2Cl_2) 1580, 1470 cm^{-1}; ^{1}H NMR (300 MHz) δ 2.36 (s, 1.6H), 2.41 (s, 1.4H) 7.03–7.08 (m, 2H), 7.17–7.42 (m, 5H); ^{13}C NMR (75 MHz) δ 21.1, 21.4, 122.9, 123.1, 124.6-128.7 (10C), 130.4, 130.7, 134.1, 134.3, 136.0, 138.5, 143.1, 144.5. Anal. Calcd for $C_{11}H_{10}S$: C, 75.82; H, 5.78. Found: C, 75.90; H, 5.75.

***ortho*-Isomer (*o*-12)**: GC rel retention (ratio) 1.00 (43%); GC-LRMS m/z (rel abundance) 174 (100%, M^+).

***meta*-Isomer (*m*-12)**: GC rel retention (ratio) 1.13 (57%); GC-LRMS m/z (rel abundance) 174 (100%, M^+).

The product mixture displayed only one spot in the TLC. No attempt was made to separate the isomeric arylthiophenes. The ratio of products, determined by GC analysis assuming equal FID response factors for ***m*-11** and ***o*-11**, was consistent with the ratio of methyl singlets in the ^{1}H NMR. It was not possible to assign peaks in the aromatic region of the ^{1}H NMR spectrum of the mixture to specific isomers. The regiochemistry of the major and minor isomers was assigned by analogy to reaction of 3-methylbenzyne with 2-lithiofuran and is consistent with the ratio of isomers found for reaction of 1-methyl-2,3-benzyne with nucleophiles.[12,27]

2-(3-Methoxyphenyl)thiophene (13; entry 7): yield, 0.072 g (34%); TLC (hexane) R_f 0.40; IR (neat) 1610, 1580, 1490, 800, 730 cm^{-1}; ^{1}H NMR (300 MHz) δ 3.81 (s, 3H), 6.83 (ddm, J = 8.0, 2.6 Hz, 1H), 7.04 (dd, J = 5.1, 3.7 1H), 7.14–7.29 (m, 5H); ^{13}C NMR (75 MHz) δ 55.2, 111.6, 112.9, 118.5, 123.2, 124.8, 127.9, 129.8, 135.7, 144.2, 159.9; GC-LRMS m/z (rel abundance) 190 (100%, M^+). Anal. Calcd for $C_{11}H_{10}OS$: C, 69.42; H, 5.30. Found: C, 69.34; H, 5.35.

Acknowledgment. The authors gratefully acknowledge support for this research by the Office of the Vice President for Research at The University of Iowa. NMR spectra were obtained at the University of Iowa High Field NMR Facility and mass spectra at the University of Iowa High Resolution Mass Spectrometry Facility. HRMS were

---

[34] Subramanian, L. R.; Hanack, M.; Chang, L. W. K.; Imhoff, M. A.; Schleyer, P.v.R.; Effenberger, F.; Kurtz, W.; Stang, P. J.; Dueber, T. E. *J. Org. Chem.* **1976**, *41*, 4099–4103.

[35] Yamashita, J.; Inoue, Y.; Kondo, T.; Hashimoto, H. *Chem. Lett.* **1986**, 407–408.

[36] Hansen, R. L. U.S. Patent 3,346,612 (10 Oct 1967); *Chem. Abstr.* **1968**, *68*, 21698c.

[37] (a) Stang, P. J.; Hanack, M. C.; Subramanian, L. R. *Synthesis* **1982**, 85–126 and references therein. (b) Echavarren, A. M.; Stille, J. K. *J. Am. Chem. Soc.* **1988**, *110*, 1557–1565 and references therein.

[38] Pinhey, J. T.; Roche, E. G. *J. Chem. Soc., Perkins Trans. 1*, **1988**, 2415–2421.

[39] Dana, G.; Convert, O.; Girault, J.-P.; Mulliez, E. *Can. J. Chem.* **1976**, *54*, 1827–1836.

[40] (a) Del Mazza, D.; Reinecke, M. G.; Smith, W. B. *Magn. Reson. Chem.* **1989**, *27*, 187–190. (b) Segard, C.; Roques, B.-P.; Pommier, C.; Guiochon, G. *J. Organomet. Chem.* **1974**, *77*, 59–68. (c) Janssen, M. J.; de Jong, F. Z. *Chem.* **1970**, *10*, 216–219.

taken by Dr. Larry M. Mallis. Preliminary experiments were conducted by Professor Peter P. Wickham (Coe College) and Garth S. Jones (University of Iowa) for which the authors are grateful.

Supplementary Material Available: General, unoptimized procedure for the dppfPdCl$_2$-catalyzed cross-coupling of aryl triflates with 2-tributylstannylfuran, as well as ^{1}H and ^{13}C NMR spectra of the arylfuran mixtures reported in entries 2, 3, and 4, of the arylthiophene mixture reported in entry 6 of Table I, and of ***o*-7**, and ***p*-5** (14 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.