

Directed Metalation of Diaryl Sulfone 2-Amides and 2-*O*-Carbamates. Regiospecific General Route to Thioxanthen-9-one 10,10-Dioxides via Anionic Friedel–Crafts and Remote Fries Rearrangement Equivalents

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Summary: 2-Carboxamido- and 2-*O*-carbamoyldiaryl sulfones **5**, DMG = CONEt₂ and DMG = OCONEt₂, undergo LDA-mediated amide alternate ring migration and cyclization to thioxanthen-9-one 10,10-dioxides **6** and **8**, respectively, in a general, synthetically useful reaction.

The recent demonstration¹ that diarylamides and *O*-carbamates are converted into fluorenones and 2-carboxamido-2'-hydroxybiaryls, **1** → **2** and **1** → **3**, respectively (Scheme 1), provides a conceptual platform, based qualitatively on the complex induced proximity effect,² for new synthetic aromatic chemistry. As a rational extension of this work into other useful synthetic arenas, we have initiated the study of heteroatom-bridged biaryl metalation, and we report preliminary observations on LDA-mediated reactions of 2-carboxamido- and 2-*O*-carbamoyl diaryl sulfones³ leading to thioxanthen-9-one 10,10-dioxides, **5** → **6** and **5** → **8**, respectively (Scheme 2). These new processes, formally anionic equivalents of the Friedel–Crafts and sequential remote Fries rearrangement (via **7**) and Friedel–Crafts reactions, constitute prototypes of regiospecific, mild, and potentially general approaches for the construction of condensed heterocycles from heteroatom-bridged biaryl systems⁴ which supersede or effectively compete with classical routes.⁵

When *N,N*-diethyl-2-carboxamidodiphenyl sulfone, prepared by metalation–phenyl sulfonylation of the corresponding benzamide, **4** → **5**, DMG = CONEt₂, PG = H,⁶ was subjected to reaction with LDA (2 equiv/THF/0 °C → rt/0.5 h), a smooth conversion to thioxanthen-9-one 10,10-dioxide was observed (entry 1, Table 1). Similarly, methoxy-substituted amido diaryl sulfones provided corresponding thioxanthenones (entries 2 and 3) which are tedious to obtain by conventional routes.⁵ The synthesis

Table 1. Synthesis of Thioxanthen-9-one 10,10-Dioxides

Entry	Diarylsulfone	Cond ^a	Product	Yield, % ^b
1		A		73
2		A		81
3		A		86
4		A		57
5		A		62
6		B		62 ^c
7		B		96
8		C		71

^aA: 2.0 equiv of LDA/THF/0 °C; B: 3.0 equiv of LDA/THF/0 °C; C: 3.0 equiv of LDA/THF/-78 °C → 0 °C. ^bYields of chromatographed and recrystallized material. ^c Thioxanthen-9-ol 10,10-dioxide, undoubtedly resulting from LDA reduction, was also obtained (22%).

of silylated (entry 4) and condensed (entry 5) thioxanthenones illustrates further scope of this reaction.

As expected from analogous diaryl *O*-carbamate metalation results,^{1b} the unprotected 2-*O*-carbamate diaryl sulfone **9^b** (Scheme 3) underwent rapid anionic *ortho*-Fries rearrangement to give **10** in modest yield. However, with *ortho*-TMS protection,^{1b} a sequence of ring-to-ring amide migration followed by anionic cyclization was observed to afford a hydroxy thioxanthenone (entry 6) as the major product. Under similar conditions, a more highly substituted thioxanthenone (entry 7) and an aza-thioxanthenone (entry 8), representing a new heterocyclic system, were obtained.

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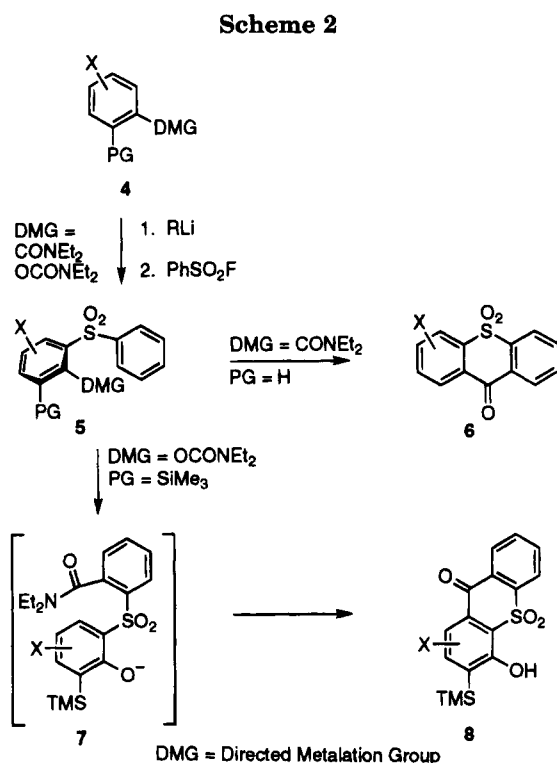
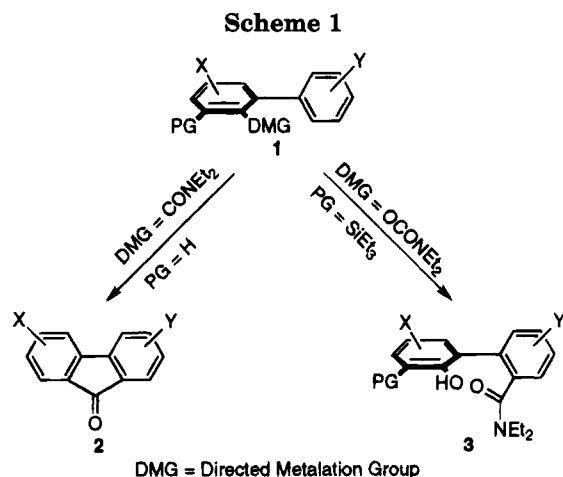
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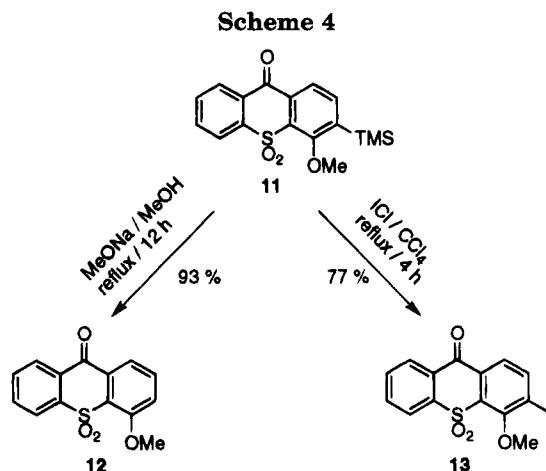
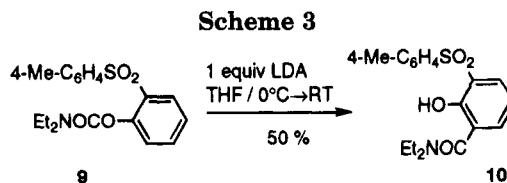
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In attempts to probe the operation of the CIPE in these reactions, the 2-carboxamido diphenylsulfone (entry 1) was subjected to kinetic deprotonation (1.1 equiv of *s*-BuLi/TMEDA/ $-78\text{ }^{\circ}\text{C}$ or $-100\text{ }^{\circ}\text{C}$). Quenching after 5 min and 1 h resulted in recovery of starting material or intractable mixtures, respectively. Treatment with LDA and TMSCl in sequence (THF/ $-78\text{ }^{\circ}\text{C}$ /1 h) led to the formation of thioxanthene-9-one 10,10-dioxide as the sole isolable product (45%) while using the *in situ* LDA/TMSCl (THF/ $-78\text{ }^{\circ}\text{C}$ /1 h) conditions⁷ afforded starting



material (47%), 4-(trimethylsilyl)thioxanthene-9-one 10,10-dioxide [(8%, different from the 1-silyl derivative (entry 4) by direct comparison)]. Control experiments demonstrated that the latter is not formed from thioxanthene-9-one 10,10-dioxide and that diphenyl sulfone is metalated-silylated under the sequential LDA/TMSCl/THF/ $0\text{ }^{\circ}\text{C}$ conditions to yield 26% of 2-trimethylsilyldiphenyl sulfone⁸ in addition to 59% of recovered starting material. These results allow tentative conclusions that (a) cyclization is fast with respect to trapping by external TMSCl electrophile and (b) low-temperature metalation occurs at the 6- or the 2'-position of the starting material to a minor degree. Since, under the reaction conditions, diphenyl sulfone is metalated to a minor degree compared to the 2-carboxamidodiphenyl sulfone, we tentatively conclude that the amide and *O*-carbamate functionalities play a role, perhaps by a CIPE, in the overall anionic transformations (Scheme 2).

The conversions of the derived thioxanthenes, illustrated by desilylation, 11 \rightarrow 12, and iodination, 11 \rightarrow 13, are indicative of potentially useful chemistry for further functionalization. These transformations, together with the rich chemistry of thioxanthenes,⁹ provide reinforcement of the new anionic methodology. Furthermore, its extension to other heteroatom-inserted biaryl derivatives may be anticipated.^{10,11}

Supplementary Material Available: General experimental and characterization data (18 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.

(6) These compounds were first obtained as products of reactions of the corresponding *ortho*-lithiated benzamide and phenyl *O*-carbamate with $(\text{PhSO}_2)_2\text{NF}$ in attempts to *ortho* fluorinate; see: Snieckus, V.; Beaulieu, F.; Mohri, K.; Han, W.; Murphy, C. K.; Davis, F. A. *Tetrahedron Lett.* **1994**, 35, 3465. In general, they were prepared by the method of Truce; see: Truce, W. E.; Ray, W. J., Jr. *J. Am. Chem. Soc.* **1959**, 81, 481. See also: Köbrich, G., *Chem. Ber.* **1959**, 92, 2981. See also: Frye, L. L.; Sullivan, E. L.; Cusack, K. P.; Funaro, J. M. *J. Org. Chem.* **1992**, 57, 697 and references cited therein. For classical routes to diaryl sulfones, see ref 3b. For recent work, via Friedel-Crafts reaction, see: Tanaka, M.; Souma, Y. *J. Org. Chem.* **1992**, 57, 1338. Via reaction of sulfonates with chloronitrobenzenes by nucleophilic aromatic substitution, see: Srinivasan, K. V.; Kumar, S. M.; Ayyangar, N. R. *Synthesis* **1992**, 825. Via phenoxide displacement with ArLi on arylsulfonate esters, see: Baarschers, W. H. *Can. J. Chem.* **1976**, 54, 3056.

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(10) All new compounds show analytical and spectral (^1H , ^{13}C NMR, MS, IR) data consistent with the depicted structures.

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