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Combined directed *ortho*-metalation, remote metalation, and Stille cross-coupling strategies. Concise stereoselective synthesis of polysubstituted 9*H*-fluoren-9-ones

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Abstract

The new sequential stereoselective synthesis of diversely substituted 9*H*-fluoren-9-ones by *ortho*-lithiation/Bu_3SnCl quench of unprotected benzoic acids followed by Stille cross-coupling reaction and remote metalation is reported.

Keywords: *ortho* and Remote metalations; Stille reaction; Benzoic acids

1. Introduction

Substituted fluorenones and fluorenes are interesting target molecules in organic synthesis. The 9*H*-fluoren-9-one skeleton occurs inter alia in a wide range of substrates, including marine sediments,[1] kerogen pyrolyzates,[2] weathered surface retorted oil shales, and Wilmington petroleum.[3] 9*H*-Fluoren-9-ones are also known to function as photoinitiators in various photochemical reactions.[4] Both 9*H*-fluoren-9-ones and 2-nitrofluorene behave as acceptors in photoinduced electron transfer.[4a] On the other hand, non-peptidic compounds that contain a biphenylcarboxylic acid group have shown to inhibit HIV-1 protease.[5] Biphenylcarboxylic acids are potential objects of interesting photophysical studies in view of our recent findings[6] on photoinduced electron transfer in carboxylic acids.

We recently reported on a general method for the construction of fluorenones by thematic variation of inter-connecting synthetic methodologies. 2-Biphenylcarboxylic acid (**1**) readily undergoes metalation *ortho* to the carboxylate substituent (C_3)[7] when treated with *s*-butyllithium (*s*-BuLi) in THF at −78 °C (reaction A).[8] Trapping with a variety of electrophiles gives diversely 3-substituted 2-biphenylcarboxylic acids **2** with good yields. Treatment of **2** with the Lochmann–Schlosser superbase (*n*-butyllithium/*t*-BuOK) (LICKOR)[9] affords the fluorenone skeleton **3** arising from the metalation of the remote $C_{2'}$ site (reaction B).[10]

On the other hand, 2-biphenylcarboxylic acid (**1**), when treated successively with (1) LICKOR (3.5 equiv) in THF or benzene at 20–60 °C, (2) *n*-BuLi (2 equiv, rt to 60 °C), and (3) an electrophile (EX), gives the fluorenone skeleton **3** that arises from the metalation of the remote $C_{2'}$ site (reaction C). We have shown[11] that the doubly charged dimetallo dialkoxide group $C(OM)_2$ (M=Li, K) of **4** acts as a new director of *ortho*-metalation and presumably directs a second metalation in the adjacent position (C_1) affording the stable 1-metallo-9*H*-fluoren-9,9-dimetallo dialkoxide **5** that can be trapped by electrophiles.

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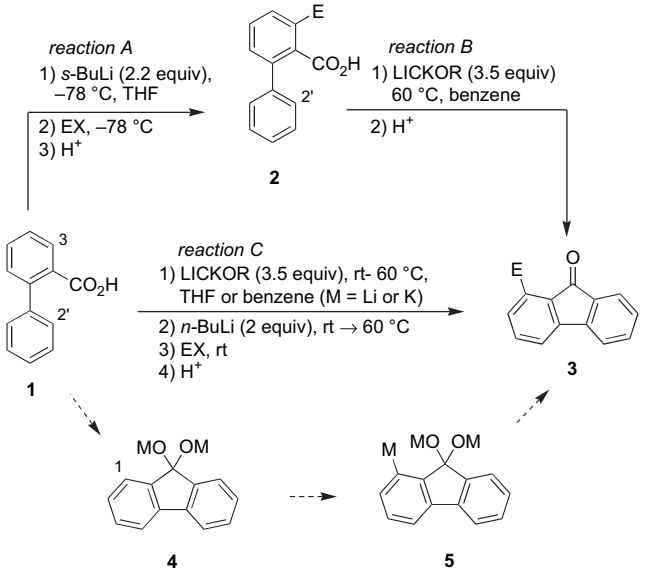


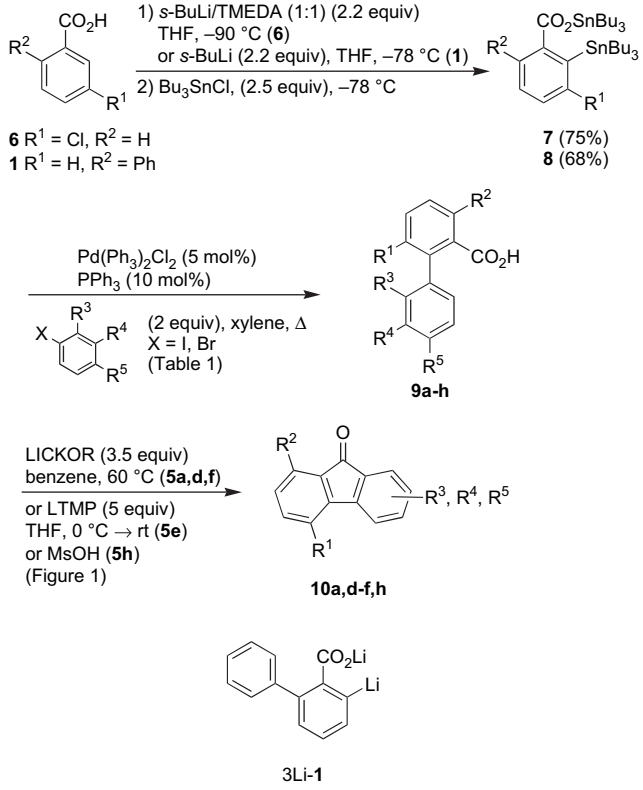
The present manuscript which describes a complementary synthesis of asymmetrically polysubstituted fluorenones seeks to provide additional proof of the synthetic potential of these techniques which thereof could appear to match if not exceed that of tertiary benzamides as metalation directing group. The synthesis involves the sequential *ortho*-lithiation/Bu_3SnCl quench of unprotected benzoic acids followed by Stille cross-coupling and remote metalation procedures.

2. Results and discussion

The carboxylic acid group deserves to occupy a prominent position in the repertoire of directed metalation strategies and its use in conjunction with other directing groups opens new methodological possibilities.[12,13] The presence of the carboxylate functionality makes benzoic acids more reactive and therefore more sensitive than their amide and oxazoline counterparts,[14] thus requiring a gentler approach to lithiation.

Tributylstannyl 3-chloro-2-(tributylstannyl)benzoate (**7**) was prepared by metalation of 3-chlorobenzoic acid (**6**) with *s*-BuLi/TMEDA (1:1 complex, 2.2 equiv) in THF at −90 °C[12] (Scheme 1). The lithiated species was trapped by Bu_3SnCl (2.5 equiv) at −78 °C and the reaction mixture was allowed to warm to rt. The electrophile in excess and the solvents were removed under reduced pressure to give **7** (75%), which was sufficiently pure for the subsequent step and did not require purification.

Smooth deprotonation of 2-biphenylcarboxylic acid (**1**) with *s*-BuLi at −78 °C afforded lithium 3-lithiobiphenyl-2-carboxylate which is remarkably stable over hours in THF at rt and does not give autocondensation products.[15] Quenching with Bu_3SnCl led to tributylstannyl 3-(tributylstannyl)biphenyl-2-carboxylate (**8**) (68%).[8,10] Although TMEDA is known as an accelerator of metalation reactions due to its disaggregation effect on butyllithium oligomers,[16] its use resulted in lower yield.[17,18] When stored under dry nitrogen at rt, **7** and **8** are indefinitely stable.



Scheme 1. Stereoselective synthesis of polysubstituted 9*H*-fluoren-9-ones.

Organostannanes **7** and **8** were submitted to the Stille conditions [$Pd(PPh_3)_2Cl_2$, 5 mol %; PPh_3, 10 mol %; substituted halobenzene, 2 equiv; refluxing xylene, 24 h] (Table 1).[19,20] Iodobenzene, *meta*- and *para*-substituted bromobenzenes led to the expected coupling products **9a**,**d**–**h** in moderate purified yields whereas the reaction of *ortho*-substituted bromobenzenes (1-bromo-2-methylbenzene and 1-bromo-2-methoxybenzene) leading to **9b** and **9c** was sluggish. *meta*-Terphenyl-2-carboxylic acid (**9h**) was prepared by treatment of **8** with iodobenzene (59%).[8,21,22]

In the literature, the most useful syntheses of 9*H*-fluoren-9-ones include Friedel–Crafts closures of biarylcarboxylic acids and derivatives,[23] intramolecular [4+2] cycloaddition reactions of conjugated enynes,[24] and oxidation of fluorenes.[25] Fluorenones have been synthesized by palladium-catalyzed

Table 1
Stille cross-coupling reactions of tributylstannyl 3-chloro-2-(tributylstannyl)-benzoate (**7**) and tributylstannyl 3-(tributylstannyl)biphenyl-2-carboxylate (**8**) with halobenzenes

7 or **8**	R^1	R^2	R^3	R^4	R^5	X	**9a**–**h**[a] (%)
7	Cl	H	H	H	H	I	**9a** (59)
7	Cl	H	Me	H	H	Br	**9b** (11)
7	Cl	H	OMe	H	H	Br	**9c** (11)
7	Cl	H	H	H	Me	Br	**9d** (53)
7	Cl	H	H	OMe	H	Br	**9e** (75)
7	Cl	H	H	H	OMe	Br	**9f** (44)
7	Cl	H	H	OMe	OMe	Br	**9g** (44)
8	H	Ph	H	H	H	I	**9h** (59)

[a] Purified yields (chromatography). Product characterization was completed by ^1H NMR, ^{13}C NMR, and FTIR.

cyclization of 2-iodobenzophenones[26] and by palladium-catalyzed cyclocarbonylation of 2-halobiaryls.[27] Fluorenones containing an aryl substituent in the position C_1 can be prepared either by radical procedures[28] or via fluorenones-1-boronic acid coupling with the corresponding aryl halides.[29] The direct *ortho*-lithiation of the aminoalkoxide derived from parent 9*H*-fluoren-9-one and lithium 4-methylpiperazin-1-ide has also been reported.[29b] Attention paid to asymmetrically polysubstituted fluorenones has been sparse, presumably due to difficulty of access.

Reaction of 2-biphenylcarboxylic acids **9a**,**d**,**f** with LICKOR[9,13c,h] (3.5 equiv) in benzene at 60 °C led to the fluorenones **10a**,**d**,**f** after hydrolysis of the stable dialkoxides **11a**,**d**,**f** which arise from the metalation of **9a**,**d**,**f** at the remote $C_{2'}$ site (Fig. 1). It is presumed that the moderate yields obtained for this cyclization are due to competing reduction of the C–Cl bond, and (in the case of **10d**) to side-reactions that arise from the lateral deprotonation of the methyl group by the superbase.[13c] Recently, the use of aryl chlorides in Suzuki–Miyaura and Sonogashira coupling reactions has been reported.[21c,30] Therefore 4-chloro-9*H*-fluoren-9-ones **10a–f** are potential precursors for the synthesis of polyfunctionally substituted 4-aryl- and 4-alkynyl-9*H*-fluoren-9-ones, which are not easy to prepare.[1–6] Intramolecular Friedel–Crafts acylation carried out by treatment of the teraryl carboxylic acid **9h** with methanesulfonic acid at 50–60 °C[31] led to 1-phenyl-9*H*-fluoren-9-one (**10h**, 41%).[8]

The reaction of **9e** with LTMP (5 equiv) in THF at −20 °C gave 1-methoxy-5-chlorofluoren-9-one (**10e**) as the *sole* product (60%), without any traces of the regioisomer **10e′**. LTMP presumably approaches **9e** in the initial step by a strong coordination of the lithium with *both* the highly electron-rich π-system of the carboxylate and the methoxy group, leading to a pre-lithiation complex **12** (Complex Induced Proximity Effect (CIPE) Process) (Fig. 2).[32] Complexation between the organolithium base and the directing group is a fast, reversible process, which is followed by a much slower deprotonation step.[13g,33]

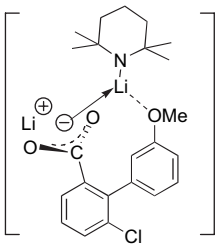


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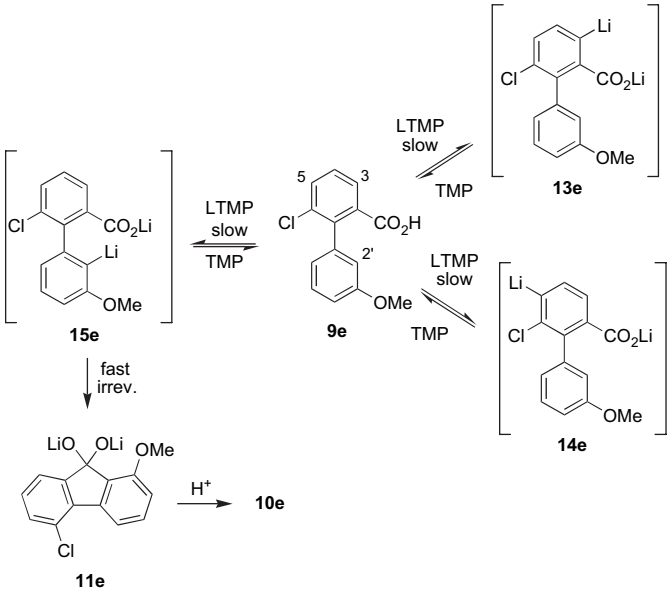
Figure 2. Pre-lithiation complex **12**.

The results obtained with LTMP attest to the thermodynamic control of the regiochemistry of the lithiation of **9e**. Since deuterolysis experiments have shown that both *ortho* (C_3) and remote ($C_{2'}$) positions of the parent 2-biphenylcarboxylic acid (**1**) are metalated under these conditions,[13c] LTMP more probably metalates randomly the C_3 and $C_{2'}$ sites, as well as the C_5 site of **9e** (Scheme 2). Due to the presence of the residual, potentially coordinated 2,2,6,6-tetramethylpiperidine (TMP), there is possible interconversion of the resulting organometallic species **13e**, **14e**, and **15e**. While the formation of **13e** and **14e** are non-issues, the carboxylate group of the $C_{2'}$-metalated species **15e** acts as an in situ trap. Cyclization of **15e** is fast and irreversible and the equilibria **13e**⇋**15e** and **14e**⇋**15e** are shifted toward the formation of **15e** by Le Châtelier's principle.



Scheme 2. Mechanism of formation of **10e**.

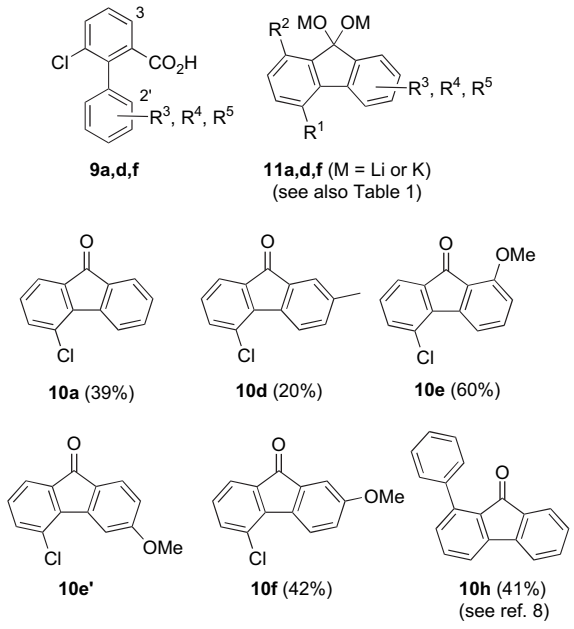


Figure 1.

Prior to hydrolysis, the stable species present in the reaction mixture is the cyclic tetrahedral dilithio dialkoxide **11e** which, only upon hydrolysis, leads to fluorenone **10e**. Obviously

directed remote metalations outperform poorly regioselective Friedel–Crafts substitutions.[34]

3. Conclusion

The results reported in this article corroborate the recently developed concept of the means of achieving chemo or regiocontrol in hydrogen/metal exchange processes through mechanism-based matching of substituents and reagents.[13,14b] Although yields in this preliminary study are only fair, the fact that no protection and deprotection steps of the reactive carboxylic acid group are needed makes this methodology a methodology of choice. We are continuing a full generalization of the reactions described here, as well as an investigation of the ability of the CO_2H group to effect *ortho* and remote lithiations in larger fused aromatic ring systems.

4. Experimental section

4.1. General

For standard working practice, see Ref. 16a. Reactions were carried out under argon in heat gun-dried glassware. Tetrahydrofuran was dried from sodium benzophenone ketyl. NMR spectra were recorded on a 200- or 400-MHz spectrometer. ^{13}C NMR spectra were obtained with broadband proton decoupling. For spectra recorded in $CDCl_3$, chemical shifts were recorded relative to the internal TMS (tetramethylsilane) reference signal. For DMSO-d_6, chemical shifts are given relative to the solvent signal. IR spectra were recorded on a FT-IR spectrophotometer. All melting points are uncorrected. Commercial reagents were used without further purification. Chromatography was performed with silica gel (40–60 μm). Procedures for the preparation and characterization of tributylstannyl 3-(tributylstannyl)biphenyl-2-carboxylate (**8**), *meta*-terphenyl-2′-carboxylic acid (**9h**), and 1-phenyl-9*H*-fluoren-9-one (**10h**) are given in Ref. 10.

4.2. Tributylstannyl 3-chloro-2-(tributylstannyl)benzoate (*7*)

At −90 °C, 3-chlorobenzoic acid (**6**) (1.1 g, 7 mmol) in THF (8 mL) was added dropwise—over a period of 30 min—to a vigorously stirred solution of the complex *s*-BuLi (1.3 M in cyclohexane–hexane, 13.3 mL, 17.3 mmol)/TMEDA (2.7 mL, 17.3 mmol) in THF (20 mL) under argon atmosphere. After 1 h at −90 °C, the mixture was warmed at −78 °C and treated with tributyltin chloride (5.35 mL, 17.3 mmol) in THF (10 mL). The resulting solution was allowed to warm up to ambient temperature, and concentrated in vacuo. Dry heptane (15 mL) was added and the solution was left to stand overnight at ≈5 °C. After filtration of the insoluble, the organic layer was concentrated, and the excess of Bu_3SnCl was eliminated at 100 °C/4 mbar to give **7** which was sufficiently pure for the subsequent step and did not require purification (3.87 g, 75%). ^1H NMR (DMSO-d_6, 400 MHz) δ: 7.94 (d, 1H, J=6.4 Hz), 7.34 (d, 1H, J=7.1 Hz), 7.25–7.31 (m, 1H), 1.38–1.70 (m, 12H), 1.20–1.34 (m, 12H), 0.93–1.17 (m, 12H), 0.75–0.85 (m, 18H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 172.1, 147.3, 143.7, 140.2, 132.0, 128.8, 128.6, 29.3 (d, J=19 Hz), 27.9 (d, J=20 Hz), 27.5 (2d, J=64, 67 Hz), 27.1 (d, J=64 Hz), 16.6 (d, J=354 Hz), 15.3 (2d, J=357, 373 Hz), 13.7, 13.6.

4.3. Stille cross-coupling reactions of tributylstannyl 3-chloro-2-(tributylstannyl)benzoate (*7*) with halobenzenes. General procedure for the preparation of *9a*,*c*–*g* (Table 1)

Under an argon atmosphere, triphenylphosphine (95 mg, 0.36 mmol), bistriphenylphosphine dichloropalladium (134 mg, 0.18 mmol), and the halobenzene (7.2 mmol) were successively added to a solution of **7** (2.65 g, 3.6 mmol) in *p*-xylene (10 mL). After being refluxed for 24 h, the mixture was cooled to rt, filtered, and extracted with aq 2 M NaOH. The aqueous layer was washed twice with diethyl ether (40 mL), acidified with aq 4 M HCl (4 mL), and extracted with diethyl ether (2×60 mL). The combined ether layers were combined and dried over $MgSO_4$, filtered, and concentrated in vacuo to give a residue which was purified by recrystallization or chromatography.

4.3.1. 6-Chlorobiphenyl-2-carboxylic acid (*9a*)

According to the general procedure, recrystallization (heptane) afforded **9a** (496 mg, 59%) as a white solid (mp 157–160 °C). ^1H NMR ($CDCl_3$, 400 MHz) δ: 7.82 (t, 1H, J=8.9 Hz), 7.64 (dd, 1H, J=7.9, 1.2 Hz), 7.38 (m, 4H), 7.21 (m, 2H). ^{13}C NMR ($CDCl_3$, 50 MHz) δ: 172.6, 141.2, 137.6, 135.0, 133.4, 131.9, 128.8, 128.7, 128.3, 127.8, 127.7. Anal. Calcd for $C_{13}H_9ClO_2$: C, 67.11; H, 3.90. Found: C, 66.91; H, 3.92.

4.3.2. 6-Chloro-6′-methoxybiphenyl-2-carboxylic acid (*9c*)

According to the general procedure, recrystallization (heptane) afforded **9c** (104 mg, 11%) as a white solid (mp 142–144 °C). ^1H NMR ($CDCl_3$, 400 MHz) δ: 7.87 (dd, 1H, J=7.9, 1.5 Hz), 7.65 (dd, 1H, J=7.9, 1.5 Hz), 7.09 (dd, 1H, J=7.4, 2 Hz), 7.36 (m, 2H), 7.01 (t, 1H, J=7.4 Hz), 6.94 (d, 1H, J=8.4 Hz), 3.71 (s, 3H). ^{13}C NMR ($CDCl_3$, 50 MHz) δ: 172.1, 156.4, 138.5, 135.5, 133.5, 132.2, 130.1, 129.4, 128.7, 128.2, 126.7, 120.3, 110.8, 55.5.

4.3.3. 6-Chloro-4′-methylbiphenyl-2-carboxylic acid (*9d*)

According to the general procedure, recrystallization (heptane) afforded **9d** (477 mg, 53%) as a white solid (mp 146–149 °C). ^1H NMR ($CDCl_3$, 400 MHz) δ: 7.82 (dd, 1H, J=7.9, 1.0 Hz), 7.63 (dd, 1H, J=8.1, 1.2 Hz), 7.35 (t, 1H, J=7.9 Hz), 7.16 (t, 1H, J=8.1 Hz), 2.41 (s, 3H). ^{13}C NMR ($CDCl_3$, 50 MHz) δ: 172.6, 141.1, 137.4, 135.1, 134.5, 133.3, 132.2, 128.7, 128.7, 128.6, 128.1, 21.3. Anal. Calcd for $C_{14}H_{11}ClO_2$: C, 68.16; H, 4.49. Found: C, 68.01; H, 4.46.

4.3.4. 6-Chloro-5′-methoxybiphenyl-2-carboxylic acid (*9e*)

According to the general procedure, chromatography (cyclohexane/ethyl acetate 9:1) afforded **9e** (0.71 g, 75%) as a yellow oil. ^1H NMR ($CDCl_3$, 400 MHz) δ: 7.82 (dd, 1H,

J=7.9, 1.5 Hz), 7.63 (dd, 1H, J=8.3, 1.2 Hz), 7.37 (t, 1H, J=7.9 Hz), 7.31 (t, 1H, J=7.7 Hz), 6.92 (dd, 1H, J=8.4, 1.7 Hz), 6.80 (m, 2H), 3.81 (s, 3H). ^{13}C NMR ($CDCl_3$, 50 MHz) δ: 172.5, 159.0, 140.8, 138.9, 134.8, 133.1, 132.3, 128.9, 128.5, 128.3, 121.44, 114.7, 113.3.

4.3.5. 6-Chloro-4′-methoxybiphenyl-2-carboxylic acid (**9f**)

According to the general procedure, recrystallization (heptane) afforded **9f** (427 mg, 44%) as a white solid (mp 137–139 °C). ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.81 (dd, 1H, J=7.6, 1.2 Hz), 7.63 (dd, 1H, J=8.1 Hz), 7.34 (t, 1H, J=7.8 Hz), 7.04 (m, 4H), 3.85 (s, 3H). ^{13}C NMR ($CDCl_3$, 50 MHz) δ: 172.5, 159.1, 140.8, 135.3, 133.3, 132.4, 130.2, 129.8, 128.7, 128.1, 113.4. Anal. Calcd for $C_{14}H_{11}ClO_3$: C, 64.01; H, 4.22. Found: C, 63.66; H, 4.28.

4.3.6. 6-Chloro-4′,5′-dimethoxybiphenyl-2-carboxylic acid (**9g**)

According to the general procedure, recrystallization (heptane) afforded **9g** (467 mg, 44%) as a white solid (mp 153–155 °C). ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.80 (dd, 1H, J=8.1, 1.2 Hz), 7.64 (dd, 1H, J=7.6, 1.2 Hz), 7.36 (t, 1H, J=7.9 Hz), 3.92 (s, 3H), 3.86 (s, 3H). ^{13}C NMR ($CDCl_3$, 50 MHz) δ: 172.4, 148.5, 148.2, 140.5, 135.1, 133.1, 132.6, 130.0, 128.1, 128.4, 121.4, 112.5, 110.5, 55.8, 55.6.

4.4. Remote metalation reactions of 2-biphenylcarboxylic acids **9a**,**d**,**f** with LICKOR. General procedure for the preparation of 9H-fluoren-9-ones **10a**,**d**,**f**

n-Butyllithium (1.85 mL, 3 mmol of a solution 1.6 M in hexanes) was added to a suspension of potassium *tert*-butoxide (339 mg, 3 mmol) in benzene (15 mL) at ambient temperature. After 5 min stirring, the LICKOR base was transferred into a round flask containing 2-biphenylcarboxylic acid **9a**,**d**,**f** (0.85 mmol) in benzene (10 mL). Stirring was maintained for 3 h at 60 °C. After being cooled gradually to rt, the solution was quenched with water (15 mL). The aqueous layer was extracted with ethyl acetate (3×30 mL), acidified with aq HCl (2 M), extracted with diethyl ether (3×30 mL), and dried ($MgSO_4$). After concentration in vacuo, the crude 9*H*-fluoren-9-ones **10a**,**d**,**f** were purified by chromatography on silica gel.

4.4.1. 4-Chloro-9H-fluoren-9-one (**10a**)

According to the general procedure, chromatography (cyclohexane/ethyl acetate 9:1) afforded **10a** (71 mg, 39%) as a yellow solid (mp 136 °C). ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.17 (dd, 1H, J=6.9, 1.0 Hz), 7.71 (d, 1H, J=7.9 Hz), 7.59 (dd, 1H, J=7.4, 1.0 Hz), 7.54–7.56 (m, 1H), 7.44 (dd, 1H, J=7.9, 1.0 Hz), 7.35–7.36 (m, 1H), 7.23–7.24 (m, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 192.4, 143.2, 140.7, 136.4, 136.2, 135.0, 134.0, 124.9, 129.6, 129.4, 124.4, 124.1, 122.5. IR (neat): 1709, 1599, 1447, 1298, 1192, 1153, 917, 734, 698 cm^{-1}. HRMS (EI) m/z calcd for $C_{13}H_7^{35}ClO_3$ ($M^{+\bullet}$): 214.0185. Found: 214.0183.

4.4.2. 5-Chloro-2-methyl-9H-fluoren-9-one (**10d**)

According to the general procedure, chromatography (cyclohexane/ethyl acetate 9:1) afforded **10d** (39 mg, 20%) as a yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.59–7.61 (m, 2H), 7.43–7.44 (m, 2H), 7.34–7.36 (m, 1H), 7.29 (d, 1H), 2.39 (s, 3H, Me). IR (neat): 1712, 1657, 1610, 1447, 1299, 1276, 1151, 917, 733, 699 cm^{-1}. HRMS (EI) m/z calcd for $C_{14}H_9^{35}ClO$ ($M^{+\bullet}$): 228.0342. Found: 228.0326.

4.4.3. 5-Chloro-2-methoxy-9H-fluoren-9-one (**10f**)

According to the general procedure, chromatography (cyclohexane/ethyl acetate 9:1) afforded **10f** (88 mg, 42%) as a yellow solid (mp 113 °C). ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.04 (d, 1H, J=8.4 Hz), 7.53 (dd, 1H, J=6.7, 1.0 Hz), 7.38 (dd, 1H, J=7.9, 1.0 Hz), 7.24 (d, 1H, H_1, J=2.5 Hz), 7.14 (dd, 1H, J=7.9, 1 Hz), 7.02 (dd, 1H, H_3, J=8.4, 2.5 Hz), 3.87 (s, 3H, OMe). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 192.3, 160.8, 141.1, 136.4, 136.1, 135.9, 135.6, 128.9, 128.54, 125.1, 122.5, 120.1, 109.6, 55.7. HRMS (EI) m/z calcd for $C_{14}H_9^{35}ClO_2$ ($M^{+\bullet}$): 244.0291. Found: 244.0294.

4.4.4. 5-Chloro-1-methoxy-9H-fluoren-9-one (**10e**)

To a stirred solution of LTMP (4.75 mmol) in THF (5 mL) at −20 °C was added dropwise 6-chloro-5′-methoxy-2-biphenylcarboxylic acid (**9e**, 250 mg, 0.95 mmol) in THF (10 mL). The solution was then allowed to warm to rt and stirring was maintained for 12 h. After hydrolysis with water (15 mL), pH of the solution was adjusted to 12. The aqueous layer was washed with ethyl acetate (3×30 mL) and the aqueous phase was acidified with aq (2 M) HCl to pH 1. The aqueous layer was then extracted with ether (3×30 mL), the organic layer was dried ($MgSO_4$), and concentrated in vacuo to give a residue which was chromatographed on silica gel (cyclohexane/ethyl acetate 9:1) to give 5-chloro-1-methoxy-9*H*-fluoren-9-one (**10e**) as a single product (yellow oil, 139 mg, 0.57 mmol, 60%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.85 (d, 1H, J=8.4 Hz), 6.86–6.88 (m, 3H), 6.61 (dd, 1H, J=2.5, 8.9 Hz), 6.48 (d, 1H, J=2.5 Hz), 3.82 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 187.0, 159.0, 150.2, 145.9, 133.5, 128.6, 124.0, 121.1, 116.8, 114.1, 112.7, 112.2, 110.2, 55.3. IR (neat): 1715, 1597, 1461, 1295, 1163, 1127, 1038, 967, 745 cm^{-1}. HRMS (EI) m/z calcd for $C_{14}H_9^{35}ClO_2$ ($M^{+\bullet}$): 244.0291. Found: 244.0287.

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