JOC The Journal of Organic Chemistry

Note

pubs.acs.org/joc

Chemoselective Deprotonative Lithiation of Azobenzenes: Reactions and Mechanisms

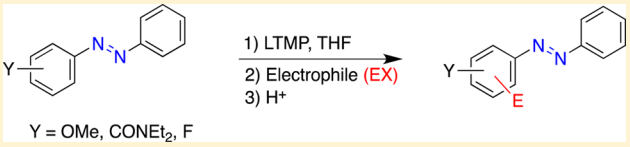
Thi Thanh Thuy Nguyen,[†] Anne Boussonnière,[†] Estelle Banaszak,[†] Anne-Sophie Castanet,[†] Kim Phi Phung Nguyen,[‡] and Jacques Mortier*[,†]

[†]Institut des Molécules et Matériaux du Mans, Faculté des Sciences et Techniques, Université du Maine and CNRS UMR 6283, Avenue Olivier Messiaen, 72085 Le Mans Cedex 9, France

[‡]École des Sciences Naturelles, Laboratoire de Chimie Organique, Université Nationale de Ho-Chi-Minh-Ville, 283/2 Nguyen Van Cu. Arrondissement 5, Ho Chi Minh Ville, Vietnam

Supporting Information

ABSTRACT: Whereas standard strong bases (*n*-BuLi, *s*-BuLi/TMEDA, *n*-BuLi/*t*-BuOK, TMPMgCl·LiCl, and LDA) reduce the N=N bond of the parent azobenzene (Y = H), aromatic H→Li permutation occurs with LTMP when a suitable director of lithiation (Y = OMe, $CONEt_2$, F) is present in the benzene residue of the azo compound. The method allows direct access to new substituted azobenzenes.



Chemistry of aromatic azobenzenes is well studied because of the ease of the N=N bond *E*/*Z* photoisomerization.[1,2] Azobenzene exists mainly as the *E* isomer but upon photoexcitation converts to the *Z* isomer. Azobenzenes are widely and commercially used as dyes and, more recently, have been applied to photoresponsive molecular switches and materials by taking advantage of this photoisomerization.[3]

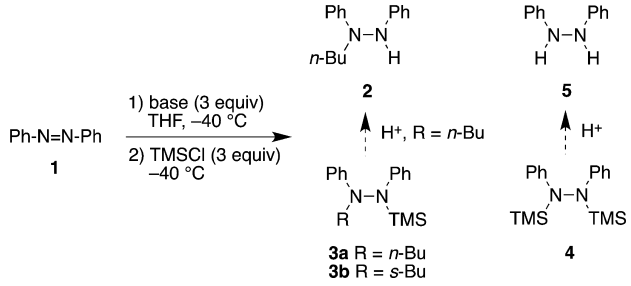
The synthesis of lithiated azobenzene derivatives represents a difficult challenge resulting from the high electrophilicity of the azo functionality.[1] The only approach to these carbanions is the halogen−lithium exchange at very low temperature.[4] In this note, we wish to report conditions for chemoselective deprotonative lithiation of substituted azobenzenes.

Efforts were initially directed toward interacting alkyllithium and sterically hindered lithium amide bases with the parent azobenzene **1** under the conditions depicted in Table 1. In agreement with the previous work of Katritzky[5] among others,[6] *n*-BuLi does not work as a base and only has the strength to react with the N=N bond of **1** to afford a mixture of tri and tetrasubstituted hydrazines **2** and **3a** after the addition of TMSCl (entry 1).

It is well-known that the use of *s*-BuLi/TMEDA (1:1 complex) provides optimal and highly reliable conditions for ortholithiation of many aromatic compounds.[7] Treatment of **1** with 3 equiv of *s*-BuLi/TMEDA followed by quench with TMSCl afforded hydrazine **3b** in high yield (entry 2). Both the ^1H and ^{13}C NMR spectra showed two sets of signals indicating the existence of two stable conformers resulting from the slow flipping of the N-atom to which the chiral C-atom of the *s*-butyl group is attached (See Supporting Information).

Lithium diisopropyl amide (LDA) equally acts as a reductor (entry 3);[8] however, the reaction proceeds only sluggishly as evidenced by a meager 32% yield of **4**. The probable mechanism is given in Scheme 1. In the initial (reversible) step, azobenzene (**1**) interacts with LDA and forms a complex **A***.[8] Transfer of a hydride ion within the complex results in the reduction of the N=N bond leading to lithium 1,2-diphenylhydrazin-1-ide (**6**) and oxidation of the amide to the corresponding imine. Compound **6** can react further with the excess of base to give **4** via the dilithio compound **7** (path a).[9]

Table 1. Reactions of Azobenzene (1) with Strong Bases



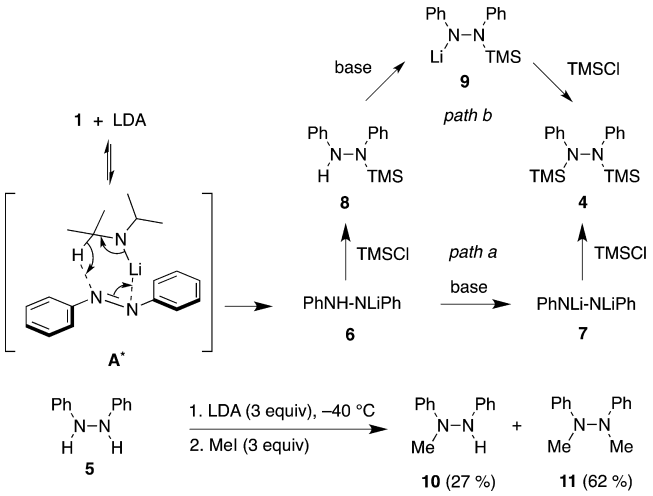
entry[a]	base[b]	2−5 (%)[c]
1	*n*-BuLi	**2** (40) + **3a** (46)
2	*s*-BuLi/TMEDA	**3b** (89)[d]
3	LDA	**4** (32)
4	LTMP	*e*
5	LICKOR	**4** (14) + **5** (36)
6	TMPMgCl·LiCl	**4** (22) + **5** (50)

[a]Lithiation attempts at −78 °C failed. [b]Azobenzene (**1**) in THF was allowed to react with the base at −40 °C, and the electrophile was added (external quench conditions). [c]Purified yields. [d]Two stable conformers (1:1 ratio) in $CDCl_3$ or DMSO-d_6 at rt. [e]Complex mixture of products.

Received: January 29, 2014
Published: February 26, 2014

   dx.doi.org/10.1021/jo500230q | J. Org. Chem. 2014, 79, 2775−2780

Scheme 1. Mechanism of Reduction of Azobenzene by LDA



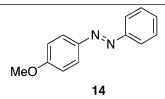
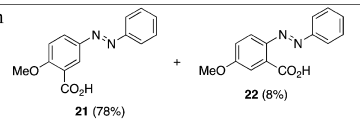
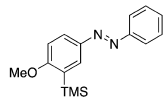
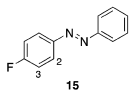
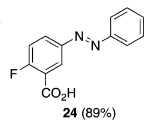
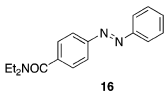
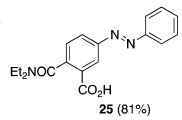
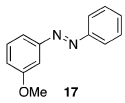
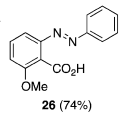
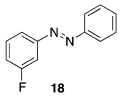
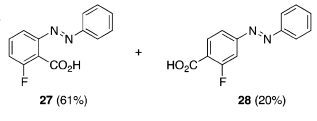
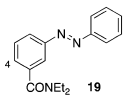
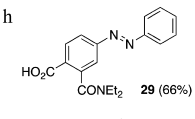
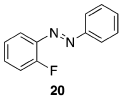
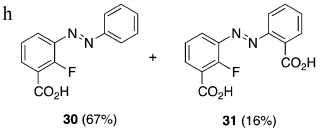
TMSCl is a treacherous electrophile since it reacts slowly with bulky bases such as LDA and LTMP, coexisting with them at low temperatures over hours.[10,11] A silylation step could then be interposed between the first and the second H→Li permutation (path b). As a result, lithio compound **6** could be the stable species prior to the addition of TMSCl. The reaction of **8** with LDA giving monolithio compound **9** could be faster than the expected rapid degradation of LDA by TMSCl. Since the reaction of hydrazobenzene (**5**) with LDA (3 equiv) at −40 °C followed by quench with MeI provided a mixture of **10** (27%) and **11** (62%), it is likely that the reaction proceeds via **7**.

Treatment of **1** with lithium 2,2,6,6-tetramethylpiperidide (LTMP) followed by quench with TMSCl led to a complex mixture of products (Table 1, entry 4). In these reactions, hydrazines **2** and **5** could result, at least partially, from the protodesilylation of **3** and **4** during aqueous workup.

The Lochmann-Schlosser superbase *n*-BuLi/*t*-BuOK (LICKOR)[12] and the Hauser base TMPMgCl·LiCl[13] are strong metalating agents of poor nucleophilicity[13,14] which nevertheless also reduced the N═N bond of **1** to give mixtures of 1,2-diphenyl-1,2-bis(trimethylsilyl)hydrazine (**4**) and 1,2-diphenylhydrazine (**5**) (entries 5 and 6).

It was found that introduction of a director of lithiation (OMe, F, and $CONEt_2$)[7,15] in the phenyl group of the azo compound changed radically the pattern of the reaction (Table

Table 2. Lithiation of Substituted Azobenzenes 14−20 with LTMP

entry	AzB (**14-20**)	conditions	**21-31**
1	 **14**	1) LTMP (5 equiv), –78 °C, 2 h 2) CO_2	 **21** (78%) + **22** (8%)
2	**14**	1:1 LTMP/TMSCl (5 equiv), –45 °C, 2 h, ISQ See ref[10]	 **23** (52%)
3	 **15**	1) LTMP (3 equiv), –78 °C, 2 h 2) CO_2	 **24** (89%)
4	 **16**	1) LTMP (5 equiv), –78 °C, 2 h 2) CO_2	 **25** (81%)
5	 **17**	1) LTMP (5 equiv), –78 °C, 2 h 2) CO_2	 **26** (74%)
6	 **18**	1) LTMP (3 equiv), –78 °C, 2 h 2) CO_2	 **27** (61%) + **28** (20%)
7	 **19**	1) LTMP (5 equiv), –78 °C, 2 h 2) CO_2	 **29** (66%)
8	 **20**	1) LTMP (3 equiv), –78 °C, 2 h 2) CO_2	 **30** (67%) + **31** (16%)

dx.doi.org/10.1021/jo500230q | J. Org. Chem. 2014, 79, 2775−2780

2). In the literature, Kauffmann showed that methyllithium reacts with electron-rich azobenzene derivatives (4-NMe_2, 4-NH_2, and 4-OMe) by nucleophilic addition to the electron-rich phenyl group, while Me_3FeLi ortho-methylates the less electron-rich phenyl group.[16] Less reactive organometallic compounds (M = Zn and Mn) give reduction products when applied at higher temperatures.[17]

Metalation conditions were initially explored with a methoxy group in para position. This directing metalation group (DMG) is moderately powerful with regard to directing ability but of high synthetic value.[7] To our delight, treatment of (*E*)-1-(4-methoxyphenyl)-2-phenyldiazene (**14**) with LTMP (5 equiv) at −78 °C followed by trapping with dry ice and aqueous quenching provided the acids **21** and **22** in good yields (entry 1).[18] The azo bond was not affected, and lithiation occurred preferentially ortho to the methoxy.[19]

Aside from some polysilylated products (<10%), the reaction of **14** with a 1:1 mixture of LTMP/TMSCl (5 equiv) at −45 °C under *in situ* quench (ISQ) conditions[10] followed by warming to rt gave the substituted azobenzene **23** arising from silylation in the position adjacent to the methoxy. This experiment strongly suggests that **23**-formation is a kinetically controlled process (CIPE effect).[20] The diethyl carboxamide is a strong DMG which has the requirements for good coordination to the lithium reagent and the electron-withdrawing properties to cause the ortho-protons to become acidic enough for efficient and rapid deprotonation.[7,15] Halogens direct by an inductive, acidifying effect alone. Deprotonation of 1-(4-fluorophenyl)-2-phenyldiazene (**15**) and *N*,*N*-diethyl-4-(phenyldiazenyl)-benzamide (**16**) occurred exclusively in C3 providing carboxylic acid derivatives **24** (89%) and **25** (81%) after quenching with CO_2.

In principle, 1,3-interrelated DMGs promote metalation at the common ortho site. This was indeed the case with a methoxy located meta with respect to the azo group (entry 5) but not with a diethylamido group where lithiation occurred exclusively in position C4 (entry 7). With a fluorine atom occupying a meta position to the azo group, a 3:1 mixture of 2- and 4-substituted azobenzenes **27** and **28** was obtained.

It was also desirable to ascertain whether the reaction of 1-(2-fluorophenyl)-2-phenyldiazene (**20**) with LTMP would proceed with lithiation ortho to the azo group or the fluorine atom. Exposing **20** to LTMP followed by quench with dry ice led to carboxylation exclusively ortho to the fluorine functionality. The dicarboxylated azobenzene **31** was isolated in a yield of 70% when 5 equiv of LTMP was used.

Suitable conditions have indeed been found under which substituted azobenzenes can undergo effective and regioselective lithiation, as evidenced by several trapping experiments. Despite the modest strength of N=N-Ph group as an ortho-lithiation director, the synthetic potential of this new reaction which allows a late-stage functionnalization of the azobenzene scaffold is clearly enormous. Conceptually, this methodology complements palladium-catalyzed regioselective functionalization reactions of aromatic azo compounds which only lead to ortho-substituted azobenzenes.[21] This reaction could play a crucial role particularly in tuning the functional features of azobenzene-containing monolayers with photoswitchable wettability.[3,22]

EXPERIMENTAL SECTION

General Experimental Methods. ^1H and ^{13}C NMR spectra were obtained on a 200 MHz or a 400 MHz spectrometer in $CDCl_3$ unless otherwise indicated. Chemical shifts are reported in δ (ppm downfield from tetramethylsilane) and are referenced to the residual solvent peak of $CDCl_3$ at δ 7.26 and δ 77.00 in ^1H and ^{13}C NMR, respectively. Coupling constants are reported in Hz with multiplicities denoted as s (singlet), d (doublet), t (triplet), q (quartet), p (pentet), m (multiplet), and br (broad). IR spectra were acquired by an FT-IR spectrometer and are reported in wave numbers (cm^{-1}).

All experiments were carried out under argon with anhydrous solvents in dried glassware, using syringe−septum cap techniques. For standard working practice, see ref 23. THF was dried using the drying station. *n*-BuLi (1.6 M in hexanes) and *s*-BuLi (1.3 M in a mixture of cyclohexane and hexanes) were titrated periodically against *N*-benzylbenzamide.[24] 2,2,6,6-Tetramethylpiperidine (TMP) was prepared from 2,2,6,6-tetramethyl-4-piperidinone by Wolff−Kishner−Huang reduction.[25] The Hauser base TMPMgCl·LiCl was prepared according to a literature procedure.[13] *N*,*N*,*N*′,*N*′-Tetramethyl-1,2-ethylenediamine (TMEDA), TMP, and chlorotrimethylsilane (TMSCl) were distilled from CaH_2 and stored under argon. Potassium *tert*-butoxide (*t*-BuOK) was sublimated prior to use.

Reactions of Parent Azobenzene (1) and Hydrazobenzene (5) with Strong Bases (Table 1 and Scheme 1). *1-n-Butyl-1,2-diphenylhydrazine (**2**) and 1-n-Butyl-1,2-diphenyl-2-(trimethylsilyl)-hydrazine (**3a**) (Entry 1).* To a stirred solution of azobenzene (**1**) (364 mg, 2 mmol) in THF (20 mL) at −40 °C was added dropwise *n*-butyllithium (3.8 mL, 1.6 M in hexanes, 6 mmol). The reaction mixture was stirred for 2 h, after which TMSCl (0.8 mL, 6 mmol) was added. Stirring was maintained for 2 additional hours. The reaction mixture was then allowed to warm to room temperature and hydrolyzed with water (20 mL). The aqueous layer was extracted with ethylacetate (3 × 10 mL), the combined organic layers were dried ($MgSO_4$), and concentrated in vaccuo. Purification by chromatography (cyclohexane/ethylacetate 10:0 → 8:2) afforded a mixture of **2** (190 mg, 40%, yellow oil) and **3a** (286 mg, 46%, orange oil).

*1-n-Butyl-1,2-diphenylhydrazine (**2**).* ^1H NMR (400 MHz, $CDCl_3$, Litt.[5]) δ: 7.26−7.20 (m, 4H), 6.93−6.90 (m, 2H), 6.85−6.77 (m, 4H), 5.60 (br s, 1H), 3.51 (t, *J* = 7.5 Hz, 2H), 1.67 (p, *J* = 7.5 Hz, 2H), 1.67 (sext, *J* = 7.5 Hz, 2H), 0.96 (t, *J* = 7.5 Hz, 3H).

*1-n-Butyl-1,2-diphenyl-2-(trimethylsilyl)hydrazine (**3a**).* ^1H NMR (400 MHz, $CDCl_3$) δ: 7.21−7.15 (m, 4H), 6.84−6.77 (m, 3H), 6.72−6.64 (m, 3H), 3.51−3.43 (m, 2H), 1.76−1.65 (m, 2H), 1.40−1.30 (m, 2H), 0.94 (t, *J* = 7.2 Hz, 3H), 0.34 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 150.0 (C), 148.0 (C), 129.4 (2CH), 129.0 (2CH), 118.9 (CH), 116.9 (CH), 115.1 (2CH), 111.0 (2CH), 53.4 (CH_2), 30.6 (CH_2), 20.6 (CH_2), 14.1 (CH_3), 1.0 ($3CH_3$). IR (neat): 2959, 2855, 1594, 1497, 1255, 838, 693 cm^{-1}. HRMS (TOF MS FI) calcd for $C_{19}H_{28}N_2Si$, $[M]^+$ 312.2022; found, 312.2029.

*1-(sec-Butyl)-1,2-diphenyl-2-(trimethylsilyl)hydrazine (**3b**) (entry 2).* Following the procedure described above for entry 1, azobenzene (**1**) (182 mg, 1 mmol) was allowed to react with *s*-BuLi/TMEDA (1:1 complex). Standard workup followed by chromatography (cyclohexane/ethylacetate 10:0 → 8:2) afforded 1-(*sec*-butyl)-1,2-diphenyl-2-(trimethylsilyl)hydrazine (**3b**) (277 mg, 89%, yellow oil). The ^1H and ^{13}C NMR spectra of **3b** in $CDCl_3$ at room temperature consist in two sets of signals, indicating an equilibrium of two invertomers (isomers stemming from slow nitrogen inversion) in a 1:1 ratio. ^1H NMR (400 MHz, $CDCl_3$) δ: 7.22−7.13 (m, 8H), 6.90 (d, *J* = 8.1 Hz, 2H), 6.85−6.77 (m, 4H), 6.70 (t, *J* = 7.2 Hz, 2H), 6.64 (d, *J* = 7.9 Hz, 4H), 3.84−3.72 (m, 2H), 2.01−1.91 (m, 2H), 1.49−1.33 (m, 2H), 1.29 (d, *J* = 6.6 Hz, 3H), 1.17 (d, *J* = 6.5 Hz, 3H), 1.00 (t, *J* = 7.5 Hz, 3H), 0.92 (t, *J* = 7.5 Hz, 3H), 0.35 (s, 9H), 0.35 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 150.5 (C), 150.3 (C), 149.1 (C), 149.1 (C), 129.4 (2CH), 129.3 (2CH), 129.0 (2CH), 128.8 (2CH), 128.7 (2CH), 119.1 (CH), 119.0 (CH), 118.4 (CH), 116.6 (CH), 116.5 (CH), 115.7 (CH), 115.4 (CH), 114.4 (CH), 112.1 (CH), 111.7 (CH), 58.3 (CH), 58.2 (CH), 28.2 (CH_2), 28.1 (CH_2), 17.3 (CH_3), 16.9 (CH_3), 11.9 (CH_3), 11.4 (CH_3), 1.2 (3 CH_3), 1.1 (3 CH_3). IR (neat): 2959, 2900, 1592, 1497, 1488, 1255, 924, 838, 694 cm^{-1}. HRMS (TOF MS ESI) calcd for $C_{19}H_{28}N_2NaSi$, $[M+Na^+]^+$ 335.1914; found, 335.1919.

The presence of invertomers was confirmed by variable-temperature ^1H NMR spectra in DMSO-d_6. The CH_3c and CH_3d signals at ambient temperature appear, respectively, as two doublets (δ_H = 1.29

dx.doi.org/10.1021/jo500230q | J. Org. Chem. 2014, 79, 2775−2780

and 1.17) and two triplets (δ_H = 1.00 and 0.92) that coalesce on warning the sample to 90 °C. Degradation products were observed above 60 °C. See Supporting Information.

*1,2-Diphenyl-1,2-bis(trimethylsilyl)hydrazine (**4**) and 1,2-Diphenylhydrazine (**5**) (Entries 3, 5, and 6).* Following the procedure described above for entry 1, azobenzene (**1**) (182 mg, 1 mmol) was allowed to react with LDA (entry 3), LICKOR (entry 5),[26] or TMPMgCl·LiCl (entry 6). With LDA, 1,2-diphenyl-1,2-bis-(trimethylsilyl)hydrazine (**4**) (103 mg, 32%, white solid) was the only product isolated. With the Schlosser-Lochmann superbase (LICKOR), standard workup followed by chromatography (cyclohexane/ethylacetate 10:0 → 8:2) gave a mixture of **4** (45 mg, 14%) and **5** (66 mg, 36%, yellow solid). With TMPMgCl·LiCl, a literature procedure[13] led to compounds **4** (22%) and **5** (50%), which were separated and purified by column chromatography.

*1,2-Diphenyl-1,2-bis(trimethylsilyl)hydrazine (**4**).* ^{1}H NMR (400 MHz, $CDCl_3$, Litt.[27]) δ: 7.19−7.14 (m, 4H), 6.84−6.74 (m, 6H), 0.32 (s, 18H).

*1,2-Diphenylhydrazine (**5**).* ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.25−7.20 (m, 4H), 6.87−6.83 (m, 6H), 5.63 (s, 2H).

*1-Methyl-1,2-diphenylhydrazine (**10**) and 1,2-dimethyl-1,2-diphenylhydrazine (**11**).* 1,2-Diphenylhydrazine (**5**) (182 mg, 1 mmol) in THF (10 mL) was slowly added to a solution of LDA (3 mmol) in THF (10 mL) at −40 °C. The resulting mixture was stirred for 2 h at this temperature, and iodomethane (0.18 mL, 3 mmol) in THF (3 mL) was added. The mixture was allowed to warm to room temperature and hydrolyzed with water (20 mL). The aqueous layer was extracted with ethylacetate (3 × 10 mL), and the combined organic layers were dried ($MgSO_4$) and concentrated in vaccuo. Purification by chromatography (cyclohexane/ethylacetate/Et_3N 10:0:0 → 9:0.5:0.5) afforded **10** (53 mg, 27%) and **11** (131 mg, 62%) as yellow oils.

*1-Methyl-1,2-diphenylhydrazine (**10**).* ^{1}H NMR (400 MHz, $CDCl_3$, Litt.[28]) δ: 7.28−7.22 (m, 4H), 6.98−6.95 (m, 2H), 6.87−6.81 (m, 4H), 5.47 (s, 1H), 3.17 (s, 3H).

*1,2-Dimethyl-1,2-diphenylhydrazine (**11**).* ^{1}H NMR (400 MHz, $CDCl_3$, Litt.[28]) δ: 7.28−7.23 (m, 4H), 6.86−6.80 (m, 6H), 3.00 (s, 6H).

-Deprotonative Lithiation of Azobenzenes 14−20 with LTMP: Reactions and Structural Elucidation (Table 2). 1-(4-Methoxyphenyl)-2-phenyldiazene (**14**) is commercially available from a chemical supplier. 1-(4-Fluorophenyl)-2-phenyldiazene (**15**),[29] 1-(3-fluorophenyl)-2-phenyldiazene (**18**),[30] 1-(2-fluorophenyl)-2-phenyldiazene (**20**),[31] and 1-(3-methoxyphenyl)-2-phenyldiazene (**17**)[32] were synthesized by condensation of nitrosobenzene with, respectively, 4-fluoroaniline, 3-fluoroaniline, 2-fluoroaniline, and 3-methoxyaniline. *N*,*N*-Diethyl-4-(phenyldiazenyl)benzamide (**16**) and the meta isomer **19** were synthesized from the corresponding phenyldiazenylbenzoyl chlorides and diethylamine in dry dichloromethane under nitrogen.[33] Phenyldiazenylbenzoyl chlorides were themselves prepared by reaction of the corresponding phenyldiazenylbenzoic acids with thionyl chloride in the presence of anhydrous sodium carbonate.[34] (*E*)-4-(Phenyldiazenyl)benzoic acid and the corresponding meta isomer were prepared by the reaction of 4-aminobenzoic acid and 3-aminobenzoic acid with nitrosobenzene in glacial acetic acid.[35]

General Procedure. To a solution of TMP (3−5 mmol) in THF (10 mL) at −20 °C under argon was added dropwise *n*-butyllithium in hexanes (3−5 mmol). The resulting LTMP solution was stirred at 0 °C for 30 min and cooled to −78 °C, and a solution of the azo compound (1 mmol) in THF (10 mL) was slowly added. Stirring was maintained for 2 h at −78 °C, after which the mixture was poured into an excess of freshly crushed carbon dioxide. The solution was then allowed to warm up to 20 °C. Water (10 mL) was added, and the resulting mixture was basified to pH 13 with a 1 M NaOH aq. solution. The aqueous layer was separated, washed with diethyl ether (3 × 10 mL), acidified to pH 1 with 2 M HCl, and extracted with ethylacetate (3 × 10 mL). The combined organic layers were dried ($MgSO_4$) and concentrated in vaccuo. The residue was purified by chromatography or recrystallization.

*2-Methoxy-5-(phenyldiazenyl)benzoic Acid (**21**) and 5-methoxy-2-(phenyldiazenyl)benzoic Acid (**22**) (Entry 1).* According to the general procedure, a solution of 1-(4-methoxyphenyl)-2-phenyldiazene (**14**) (212 mg, 1 mmol) in THF (10 mL) was added to a THF solution of LTMP (5 mmol) at −78 °C. The resulting mixture was stirred at this temperature for 2 h and poured onto dry ice. Standard workup followed by chromatography (cyclohexane/ethylacetate 9:1 → 0:10) afforded **21** (200 mg, 78%) and **22** (20 mg, 8%) as yellow solids.

*2-Methoxy-5-(phenyldiazenyl)benzoic acid (**21**).* Mp 168−169 °C. ^{1}H NMR (400 MHz) δ: 8.76 (d, J = 2.6 Hz, 1H), 8.15 (dd, J = 8.9 Hz, J = 2.6 Hz, 1H), 7.92−7.89 (m, 2H), 7.54−7.46 (m, 3H), 7.19 (d, J = 8.9 Hz, 1H), 4.15 (s, 3H). ^{13}C NMR (100 MHz) δ: 165.3 (C), 159.8 (C), 152.5 (C), 147.3 (C), 131.4 (CH), 129.3 (2CH), 129.0 (CH), 128.9 (CH), 123.0 (2CH), 118.5 (C), 112.3 (CH), 57.3 (CH_3). IR (neat): 3000−2400 (br), 2920, 1688, 1663, 1608, 1571, 1496, 1418, 1254, 768, 689 cm^{-1}. HRMS (TOF MS CI) calcd for $C_{14}H_{13}N_2O_3$, $[M+H]^+$ 257.0926; found, 257.0927.

*5-Methoxy-2-(phenyldiazenyl)benzoic Acid (**22**).* Mp 141−142 °C. ^{1}H NMR (400 MHz) δ: 8.06 (d, J = 9.0 Hz, 1H), 7.90 (d, J = 2.9 Hz, 1H), 7.83−7.80 (m, 2H), 7.59−7.55 (m, 3H), 7.20 (dd, J = 9.0 Hz, J = 2.9 Hz, 1H), 3.97 (s, 3H). ^{13}C NMR (100 MHz) δ: 166.2 (C), 163.4 (C), 151.7 (C), 144.1 (C), 132.8 (CH), 129.9 (2CH), 129.2 (C), 123.4 (2CH), 121.5 (CH), 118.1 (CH), 115.4 (CH), 56.2 (CH_3). IR (neat): 3000−2500 (br), 2970, 1738, 1593, 1490, 1438, 1337, 1232, 1068, 1019, 779, 679 cm^{-1}. HRMS (TOF MS CI) calcd for $C_{14}H_{13}N_2O_3$, $[M+H]^+$ 257.0926; found, 257.0918.

*1-(4-Methoxy-3-(trimethylsilyl)phenyl)-2-phenyldiazene (**23**) (Entry 2).* According to the general procedure, a stirred solution of LTMP (5 mmol) in THF (10 mL) was added dropwise to a solution of 1-(4-methoxyphenyl)-2-phenyldiazene (**14**) (212 mg, 1 mmol) and TMSCl (0.63 mL, 5 mmol) in THF (10 mL) at −45 °C. The resulting mixture was stirred for 2 h at this temperature and then hydrolyzed with water (10 mL). The aqueous phase was extracted with diethyl ether (3 × 10 mL), and the combined organic layers were dried ($MgSO_4$) and concentrated in vaccuo. Purification by chromatography (cyclohexane/ethylacetate 10:0 → 8:2) afforded **23** (148 mg, 52%) as a red solid. Mp 61−65 °C. ^{1}H NMR (400 MHz) δ: 8.05 (d, J = 2.4 Hz, 1H), 7.98 (dd, J = 8.8 Hz, J = 2.4 Hz, 1H), 7.93−7.90 (m, 2H), 7.54−7.50 (m, 2H), 7.45 (m, 1H), 6.96 (d, J = 8.8 Hz, 1H), 3.90 (s, 3H), 0.37 (s, 9H). ^{13}C NMR (100 MHz) δ: 166.9 (C), 153.1 (C), 146.8 (C), 130.6 (CH), 130.3 (CH), 129.1 (2CH), 129.0 (C), 125.7 (CH), 122.6 (2CH), 109.8 (CH), 55.6 (CH_3), −0.9 ($3CH_3$). IR (neat): 2953, 2898, 1578, 1462, 1386, 1238, 1067, 833, 762, 687 cm^{-1}. HRMS (TOF MS CI) calcd for $C_{16}H_{21}N_2OSi$, $[M+H]^+$ 285.1422; found, 285.1423.

*2-Fluoro-5-(phenyldiazenyl)benzoic Acid (**24**) (Entry 3).* According to the general procedure, 4-fluoroazobenzene (**15**) (200 mg, 1 mmol) in THF (10 mL) was added dropwise to LTMP (3 mmol) at −78 °C. The resulting mixture was stirred for 2 h and poured onto dry ice. Standard workup followed by chromatography (cyclohexane/ethylacetate 8:2 → 0:10) gave **24** (217 mg, 89%) as an orange solid. Mp 172−175 °C. ^{1}H NMR (400 MHz) δ: 8.64 (dd, J_{H-F} = 6.8 Hz, J = 2.6 Hz, 1H), 8.16 (ddd, J = 8.8 Hz, J_{H-F}= 4.4 Hz, J = 2.6 Hz, 1H), 7.96−7.92 (m, 2H), 7.56−7.48 (m, 3H), 7.33 (dd, J_{H-F} = 10.0 Hz, J = 8.8 Hz, 1H). ^{13}C NMR (100 MHz) δ: 168.5 (d, J_{C-F} = 3.3 Hz, C), 163.9 (d, J_{C-F} = 265.7 Hz, C), 152.6 (C), 148.9 (d, J_{C-F} = 3.4 Hz, C), 131.7 (CH), 129.3 (2CH), 129.1 (d, J_{C-F} = 9.7 Hz, CH), 128.2 (CH), 123.2 (2CH), 118.5 (d, J_{C-F} = 10.5 Hz, C), 118.2 (d, J_{C-F} = 23.8 Hz, CH). ^{19}F (376 MHz) δ: −105.7 (ddd, J_{H-F} = 10.0 Hz, J_{H-F} = 6.8 Hz, J_{H-F} = 4.4 Hz). IR (neat) 2800−2600 (br), 1687, 1618, 1444, 1283, 1237, 924, 843, 766, 679 cm^{-1}. HRMS (TOF MS FI) $C_{13}H_9FN_2O_2$, $[M]^+$ calcd 244.0648; found, 244.0653.

*2-(Diethylcarbamoyl)-5-(phenyldiazenyl)benzoic Acid (**25**) (Entry 4).* According to the general procedure, *N*,*N*-diethyl-4-(phenyldiazenyl)benzamide (**16**) (282 mg, 1 mmol) in THF (10 mL) was added dropwise to a THF solution of LTMP (5 mmol) at −78 °C. The mixture was stirred at this temperature for 2 h and then poured onto dry ice. Standard workup followed by recrystallization (ethylacetate) afforded **25** as an orange solid (263 mg, 81%). Mp 159−161 °C. ^{1}H NMR (400 MHz) δ: 8.62 (d, J = 2.0 Hz, 1H), 8.11

dx.doi.org/10.1021/jo500230q | J. Org. Chem. 2014, 79, 2775−2780

(dd, J = 8.0, J = 2.0 Hz, 1H), 7.96−7.93 (m, 2H), 7.56−7.49 (m, 3H), 7.45 (d, J = 8.0 Hz, 1H), 3.61 (br s, 2H), 3.16 (q, J = 7.4 Hz, 2H), 1.30 (t, J = 7.2 Hz, 3H), 1.07 (t, J = 7.4 Hz, 3H). ^{13}C NMR (100 MHz) δ: 170.4 (C), 168.8 (C), 152.5 (C), 152.4 (C), 141.0 (C), 131.8 (CH), 129.3 (2CH), 128.9 (C, observed in HMBC spectrum, see below), 127.9 (CH), 126.5 (CH), 126.4 (CH), 123.3 (2CH), 43.1 (CH_2), 39.2 (CH_2), 13.7 (CH_3), 12.2 (CH_3). IR (neat): 3000−2600 (br), 2978, 2877, 1710 (2), 1588, 1443, 1240, 767, 689 cm^{-1}. HRMS (TOF MS FD) $C_{18}H_{19}N_3O_3$, $[M]^+$calcd 325.1426; found, 325.1423.

*2-Methoxy-6-(phenyldiazenyl)benzoic Acid (**26**) (Entry 5).* According to the general procedure, 1-(3-methoxyphenyl)-2-phenyldiazene (**17**) (212 mg, 1 mmol) in THF (10 mL) was added to a THF solution of lithium LTMP (5 mmol) at −78 °C. Standard workup and purification by chromatography (cyclohexane/ethylacetate 9:1 → 0:10) gave **26** as an orange solid (189 mg, 74%). Mp 171−173 °C. ^{1}H NMR (400 MHz, acetone-d_6) δ: 7.90−7.87 (m, 2H), 7.61−7.55 (m, 3H), 7.54 (dd, J = 8.1 Hz, J = 8.2 Hz, 1H), 7.42 (br d, J = 8.1 Hz, 1H), 7.27 (br d, J = 8.2 Hz, 1H), 3.94 (s, 3H). ^{13}C NMR (100 MHz, acetone-d_6) δ: 167.3 (C), 157.7 (C), 153.4 (C), 150.3 (C), 132.6 (CH), 131.2 (CH), 130.2 (2CH), 125.9 (C), 123.8 (2CH), 114.7 (CH), 109.8 (CH), 56.7 (CH_3). IR (neat): 2800−2550 (br), 1687, 1469, 1270, 1093, 747, 687 cm^{-1}. HRMS (TOF MS FD) calcd for $C_{14}H_{12}N_2O_3$, $[M]^+$ 256.0848; found, 256.0851.

*2-Fluoro-6-(phenyldiazenyl)benzoic Acid (**27**) and 2-Fluoro-4-(phenyldiazenyl)benzoic Acid (**28**) (Entry 6).* According to the general procedure, 1-(3-fluorophenyl)-2-phenyldiazene (**18**) (200 mg, 1 mmol) in THF (10 mL) was added dropwise to a THF solution of LTMP (3 mmol) at −78 °C. The mixture was stirred at this temperature for 2 h and poured onto dry ice. Standard workup followed by chromatography (cyclohexane/ethylacetate 9:1 → 0:10) gave **27** (149 mg, 61%) and **28** (49 mg, 20%) as orange-yellow solids.

*2-Fluoro-6-(phenyldiazenyl)benzoic acid (**27**).* Mp 116−118 °C. ^{1}H NMR (400 MHz) δ: 7.91−7.89 (m, 2H), 7.72 (d, J = 8.1 Hz, 1H), 7.59 (td, J = 8.1 Hz, J_{H-F} = 5.6 Hz, 1H), 7.52−7.48 (m, 3H), 7.31 (ddd, J_{H-F} = 9.2 Hz, J = 8.1 Hz, J = 0.8 Hz, 1H). ^{13}C NMR (100 MHz) δ: 168.1 (C), 160.8 (d, J_{C-F} = 253.8 Hz, C), 152.0 (C), 150.8 (d, J_{C-F} = 2.1 Hz, C), 132.6 (CH), 132.4 (d, J_{C-F} = 9.2 Hz, CH), 129.5 (2CH), 123.6 (2CH), 118.7 (d, J_{C-F} = 22.0 Hz, CH), 117.8 (d, J_{C-F} = 15.4 Hz, C), 115.6 (d, J_{C-F} = 3.3 Hz, CH). ^{19}F (376 MHz) δ: −123.57 (bs). IR (neat): 3000−2500 (br), 2802, 1687, 1615, 1575, 1460, 1294, 1244, 797, 683 cm^{-1}. HRMS (TOF MS CI) calcd for $C_{13}H_{10}FN_2O_2$, $[M+H]^+$ 245.0726; found, 245.0718.

*2-Fluoro-4-(phenyldiazenyl)benzoic acid (**28**).* Mp 216−218 °C. ^{1}H NMR (400 MHz, acetone-d_6) δ: 8.19 (dd, J = 8.1 Hz, J_{H-F} = 8.0 Hz, 1H), 8.02−7.94 (m, 2H) 7.87 (ddd, J = 8.1 Hz, J = 1.7 Hz, J_{H-F} = 0.4 Hz, 1H), 7.72 (dd, J_{H-F} = 11.6 Hz, J = 1.7 Hz, 1H), 7.65−7.62 (m, 3H). ^{13}C NMR (100 MHz, acetone-d_6) δ: 164.7 (d, J_{C-F} = 3.5 Hz, C), 163.3 (d, J_{C-F} = 258.4 Hz, C), 157.2 (d, J_{C-F} = 7.6 Hz, C), 153.2 (C), 134.2 (d, J_{C-F} = 1.6 Hz, CH), 133.3 (CH), 130.4 (2CH), 124.1 (2CH), 121.6 (d, J_{C-F} = 11.3 Hz, C), 120.2 (d, J_{C-F} = 3.6 Hz, CH), 110.4 (d, J_{C-F} = 24.3 Hz, CH). ^{19}F (376 MHz, acetone-d_6) δ: −109.78 (dd, J_{F-H} = 11.6 Hz, J_{F-H} = 8.0 Hz). IR (neat): 3000−2500 (br), 2817, 1682, 1613, 1575, 1447, 1295, 1280, 778, 688 cm^{-1}. HRMS (TOF MS CI) calcd for $C_{13}H_{10}FN_2O_2$, $[M+H]^+$ 245.0726; found, 245.0729.

*2-(Diethylcarbamoyl)-4-(phenyldiazenyl)benzoic Acid (**29**) (Entry 7).* According to the general procedure, *N*,*N*-diethyl-3-(phenyldiazenyl)benzamide (**19**) (282 mg, 1 mmol) in THF (10 mL) was added dropwise to a THF solution of LTMP (5 mmol) at −78 °C. The resulting mixture was stirred at this temperature for 2 h and poured onto dry ice. Standard workup and purification by recrystallization (ethylacetate) gave **29** as a red solid (214 mg, 66%). Mp 138−140 °C. ^{1}H NMR (400 MHz) δ: 8.24 (d, J = 8.0 Hz, 1H), 7.98−7.94 (m, 3H), 7.83 (d, J = 1.6 Hz, 1H), 7.56−7.52 (m, 3H), 3.63 (br s, 2H), 3.20 (q, J = 6.8 Hz, 2H), 1.31 (t, J = 6.8 Hz, 3H), 1.09 (t, J = 7.4 Hz, 3H). ^{13}C NMR (100 MHz) δ: 170.4 (C), 168.9 (C), 154.8 (C), 152.6 (C), 140.3 (C), 132.6 (CH), 132.1 (CH), 129.5 (C), 129.3 (2CH), 123.4 (2CH), 122.9 (CH), 121.1 (CH), 43.2 (CH_2), 39.2 (CH_2), 13.6 (CH_3), 12.2 (CH_3). IR (neat): 3000−2500 (br), 2967, 1687, 1631, 1421, 1287, 773, 691 cm^{-1}. HRMS (TOF MS FD) $C_{18}H_{19}N_3O_3$, $[M]^+$ calcd 325.1426; found, 325.1445.

*2-Fluoro-3-(phenyldiazenyl)benzoic Acid (**30**) and 3-((2-Carboxyphenyl)diazenyl)-2-fluorobenzoic Acid (**31**) (Entry 8).* According to the general procedure, 1-(2-fluorophenyl)-2-phenyldiazene (**20**) (200 mg, 1 mmol) in THF (10 mL) was added to a THF solution of LTMP (3 mmol) at −78 °C. Standard workup followed by chromatography (cyclohexane/ethylacetate 9:1 → 0:10) afforded **30** (164 mg, 67%) as a red solid and **31** (46 mg, 16%) as an orange solid.

*2-Fluoro-3-(phenyldiazenyl)benzoic Acid (**30**).* Mp 178−179 °C. ^{1}H NMR (400 MHz) δ: 8.16 (ddd, J = 7.9 Hz, J_{H-F} = 6.7 Hz, J = 1.6 Hz, 1H), 8.02−7.98 (m, 3H), 7.57−7.51 (m, 3H), 7.34 (t, J = 7.9 Hz, 1H). ^{13}C NMR (100 MHz) δ: 168.6 (d, J_{C-F} = 2.6 Hz, C), 160.0 (d, J_{C-F} = 271.9 Hz, C), 152.8 (C), 141.8 (d, J_{C-F} = 7.1 Hz, C), 135.0 (CH), 132.1 (CH), 129.4 (2CH), 124.0 (d, J_{C-F} = 4.9 Hz, CH), 123.5 (2CH), 123.2 (CH), 119.3 (d, J_{C-F} = 8.2 Hz, C). ^{19}F (376 MHz) δ: −121.51 (t, J_{F-H} = 6.7 Hz). IR (neat): 3000−2500 (br), 2817, 1688, 1608, 1577, 1461, 1409, 1278, 1232, 768, 681 cm^{-1}. HRMS (CI) calcd for $C_{13}H_{10}FN_2O_2$, $[M+H]^+$ 245.0726; found, 245.0729.

*3-((2-Carboxyphenyl)diazenyl)-2-fluorobenzoic Acid (**31**).* Mp 237−239 °C (degradation). ^{1}H NMR (400 MHz, CD_3OD) δ: 8.10 (ddd, J = 8.0 Hz, J_{H-F} = 6.6 Hz, J = 1.8 Hz, 1H), 7.92 (ddd, J = 8.2 Hz, J_{H-F} = 6.6 Hz, J = 1.8 Hz, 1H), 7.88 (d, J = 8.0 Hz, 1H), 7.69−7.65 (m, 2H), 7.62−7.58 (m, 1H), 7.36 (td, J = 8.0 Hz, J = 1.0 Hz, 1H). ^{13}C NMR (100 MHz, CD_3OD) δ: 170.5 (C), 166.6 (d, J_{C-F} = 2.5 Hz, C), 160.7 (d, J_{C-F} = 276.2 Hz, C), 152.8 (C), 142.7 (d, J_{C-F} = 7.4 Hz, C), 136.2 (CH), 133.1 (CH), 132.0 (CH), 131.6 (C), 130.9 (CH), 125.2 (d, J_{C-F} = 5.0 Hz, CH), 123.4 (CH), 122.4 (d, J_{C-F} = 8.9 Hz, C), 119.2 (CH). ^{19}F (376 MHz, CD_3OD) δ: −123.57 (t, J_{F-H} = 6.6 Hz). IR (neat): 3100−2500 (br), 2817, 1712, 1692, 1607, 1578, 1457, 1413, 1285, 1230, 757, 682 cm^{-1}. HRMS (FI) calcd for $C_{14}H_9FN_2O_4$, $[M]^+$ 288.0546; found, 288.0559.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Details of compound characterization. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*Fax: +33 243 83 39 02. E-mail: jacques.mortier@univ-lemans.fr.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This research was supported by CNRS and Université du Maine. E.B. would like to thank CNRS for a postdoctoral fellowship and T.T.T.N. a grant from the Ministry of Education and Training of the Socialist Republic of Viêt Nam. We also express appreciation to Amélie Durand, Patricia Gangnery, and Frédéric Legros (Université du Maine) for technical assistance.

■ REFERENCES

(1) *The Chemistry of the Hydrazo, Azo and Azoxy Groups*, Vol. 2; Patai, S., Ed.; John Wiley & Sons Ltd.: Chichester, U.K., 1997.

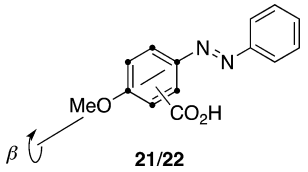
(2) Merino, E. *Chem. Soc. Rev.* **2011**, *40*, 3835−3853.

(3) (a) *Smart Light-Responsive Materials. Azobenzene-Containing Polymers and Liquid Crystals*; Zao, Y., Ikeda, T., Eds.; John Wiley & Sons Inc.: Hoboken, NJ, 2009. (b) Beharry, A. A.; Woolley, G. A. *Chem. Soc. Rev.* **2011**, *40*, 4422−4437.

(4) Lithiated azobenzene derivatives were applied to the synthesis of azobenzenes bearing silyl, germyl, stannyl, and phosphinyl groups. See, *inter alia*: (a) Kozlecki, T.; Syper, L.; Wilk, K. A. *Synthesis* **1997**, 681−684. (b) Segarra-Maset, M. D.; van Leeuwen, P. W. N. M.; Freixa, Z. *Eur. J. Inorg. Chem.* **2010**, 2075−2078.

(5) Katritzky, A. R.; Wu, J.; Verin, S. V. *Synthesis* **1995**, *6*, 651−653.

(6) (a) Carpino, L. A.; Terry, R. H.; Crowley, P. J. *J. Org. Chem.* **1961**, *26*, 4336−4340. (b) Kaiser, E. M.; Bartling, G. J. *J. Org. Chem.* **1972**, *37*, 490−494.
(7) (a) Hartung, C. G.; Snieckus, V. The Directed ortho Metalation Reaction − A Point of Departure for New Synthetic Aromatic Chemistry. In *Modern Arene Chemistry*; Astruc, D., Ed.; Wiley-VCH: Weinheim, Germany, 2002; pp 330−367. (b) Clayden, J. Directed Metallation of Aromatic Compounds. In *Chemistry of Organolithium Compounds*; Rappoport, Z., Marek, I., Eds.; Wiley: Chichester, U.K., 2004; Vol. *1*, pp 495−646.
(8) Majewski, M.; Gleave, D. M. *J. Organomet. Chem.* **1994**, *470*, 1−16 and references cited therein.
(9) Lithiation occuring by a single electron transfer (SET) to initially generate a radical anion cannot be excluded: Newcomb, M.; Varick, T. R.; Goh, S.-H. *J. Am. Chem. Soc.* **1990**, *112*, 5186−5193.
(10) Krizan, T. D.; Martin, J. C. *J. Am. Chem. Soc.* **1983**, *105*, 6155−6157.
(11) Schlosser, M.; Guio, L.; Leroux, F. *J. Am. Chem. Soc.* **2001**, *123*, 3822−3823.
(12) Reviews: (a) Lochmann, L. *Eur. J. Inorg. Chem.* **2000**, 1115−1126. (b) Schlosser, M. *Mod. Synth. Methods* **1992**, *6*, 227−271.
(13) Dubbaka, S. R.; Kienle, M.; Mayr, H.; Knochel, P. *Angew. Chem., Int. Ed.* **2007**, *46*, 9093−9096.
(14) Hence, both ortho (C3) and remote (C2′) positions of 2-biphenyl carboxylic acid are metalated with LICKOR *in refluxing benzene* without the need to protect the carboxylate (CO_2M, M = Li, K). See: Tilly, D.; Samanta, S. S.; De, A.; Castanet, A.-S.; Mortier, J. *Org. Lett.* **2005**, *7*, 827−830.
(15) Recent studies on aromatic metalation mechanisms: (a) Nguyen, T. H.; Chau, N. T. T.; Castanet, A.-S.; Nguyen, K. P. P.; Mortier, J. *Org. Lett.* **2005**, *7*, 2445−2448. (b) Tilly, D.; Fu, J.-m.; Zhao, B.-p.; Alessi, M.; Castanet, A.-S.; Snieckus, V.; Mortier, J. *Org. Lett.* **2010**, *12*, 68−71. (c) Tilly, D.; Magollan, J.; Mortier, J. *Chem.—Eur. J.* **2012**, *18*, 3804−3820.
(16) Kauffmann, T.; Jordan, J.; Sander, J. *Chem. Ber.* **1992**, *125*, 153−155.
(17) Garlichs-Zschoche, F. A.; Dötz, K. H. *Organometallics* **2007**, *26*, 4535−4540 and references cited therein.
(18) For each product, there are in principle two distinct isomers corresponding to two possible alignments of the CO_2H group in the trans conformer. This rotation, indicated by the angle β, is usually ignored in gas phase or solution experiments because the rotation barrier is small: Henningsen, N.; Franke, K. J.; Torrente, I. F.; Schulze, G.; Priewisch, B.; Rück-Braun, K.; Dokic, J.; Klamroth, T.; Saalfrank, P.; Pascual, J. I. *J. Phys. Chem. C* **2007**, *111*, 14843−14848 .



21/22

(19) Lithiation attempts of **14** with *n*-BuLi and *s*-BuLi/TMEDA failed.
(20) Whisler, M. C.; MacNeil, S.; Snieckus, V.; Beak, P. *Angew. Chem., Int. Ed.* **2004**, *43*, 2206−2225.
(21) Recent references: (a) Ma, X.-T.; Tian, S.-K. *Adv. Synth. Catal.* **2013**, *355*, 337−340. (b) Li, H.; Li, P.; Wang, L. *Org. Lett.* **2013**, *15*, 620−623.
(22) (a) Delorme, N.; Bardeau, J.-F.; Bulou, A.; Poncin-Epaillard, F. *Langmuir* **2005**, *21*, 12278−12282. (b) Nguyen, T. B.; Castanet, A.-S.; Nguyen, T.-H.; Nguyen, K. P. P.; Bardeau, J.-F.; Gibaud, A.; Mortier, J. *Tetrahedron* **2006**, *62*, 647−651. (c) Banaszak, E.; Xu, L.-W.; Bardeau, J.-F.; Castanet, A.-S.; Mortier, J. *Tetrahedron* **2009**, *65*, 3961−3966.
(23) Schlosser, M. *Organometallics in Synthesis. A Manual*, 2nd ed.; Wiley: Chichester, U.K., 2002.
(24) Burchat, A. F.; Chong, J. M.; Nielsen, N. *J. Organomet. Chem.* **1997**, *542*, 281−283.
(25) (a) Leonard, N. J.; Nommensen, E. W. *J. Am. Chem. Soc.* **1949**, *71*, 2808−2813. See also: (b) Kampmann, D.; Stuhlmüller, G.; Simon, R.; Cottet, F.; Leroux, F.; Schlosser, M. *Synthesis* **2005**, 1028−1029.
(26) Prepared by mixing *n*-BuLi in hexanes (3 mmol) and *t*-BuOK (3 mmol) in THF (10 mL) at −40 °C. See: Schlosser, M. *Mod. Synth. Methods* **1992**, *6*, 227−271 and references cited therein..
(27) Kira, M.; Nagai, S.; Nishimura, M.; Sakurai, H. *Chem. Lett.* **1987**, 153−156.
(28) Zhang, Y.; Tang, Q.; Luo, M. *Org. Biomol. Chem.* **2011**, *9*, 4977−4982.
(29) Krageloh, K.; Anderson, G. H.; Stang, P. J. *J. Am. Chem. Soc.* **1984**, *106*, 6015−6021.
(30) Taft, R. W., Jr.; Price, E.; Fox, I. R.; Lewis, I. C.; Andersen, K. K.; Davis, G. T. *J. Am. Chem. Soc.* **1963**, *85*, 709−724.
(31) Leyva, E.; Sagredo, R.; Moctezuma, E. *J. Fluorine Chem.* **2004**, *125*, 741−747.
(32) Zhao, R.; Tan, C.; Xie, Y.; Gao, C.; Liu, H.; Jiang, Y. *Tetrahedron Lett.* **2011**, *52*, 3805−3809.
(33) Imai, Y.; Naka, K.; Chujo, Y. *Macromolecules* **1999**, *32*, 1013−1017.
(34) Anspon, H. D. In *Organic Synthesis*; John Wiley & Sons: New York, 1955; Collect. Vol. 3, pp 711−713.
(35) Fatas, P.; Longo, E.; Rastrelli, F.; Crisma, M.; Toniolo, C.; Jimenez, A. I.; Cativiela, C.; Moretto, A. *Chem.—Eur. J.* **2011**, *17*, 12606−12611.