New Synthetic Applications of Aryllead Triacetates. *N*-Arylation of Amides

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p-Tolyllead triacetate efficiently arylates the nitrogen atom of carboxamide, sulfonamide, imide, and hydantoin anions under mild conditions. This reaction did not interfere with the arylation of amino and *β*-dicarbonyl groups.

N-Aryl derivatives of amides and other compounds bearing amide-like nitrogen atoms (*e.g.* imides, hydantoins, etc.) are important from the point of view of their biological activity. The antidepressant almoxantone,[1] the sedative amphenidone,[2] the anticonvulsant arfendazam,[3] and the anthelmintic clioxanide[4,5] (Figure 1), among others, may serve as examples. From a synthetic point of view, *N*-arylamides and related compounds are precursors to diarylamines[6] and different types of heterocycles.[7]

The Goldberg reaction[8] is the classical method for the *N*-arylation of amides and is closely related to the Ullmann arylation of amines. This reaction consists of treating anilides with aryl halides at high temperature, in the presence of potassium carbonate and copper(I) iodide. Other related conditions allow the *N*-arylation of other carboxamides,[9] imides,[10] hydantoins[11] and also sulfonamides,[12] although in the latter case the reaction could not be controlled to give monoarylation products. In spite of the recent development of phase-transfer conditions,[13] the Goldberg reaction remains unsuitable for many applications due to the very high temperatures required, the limited range of aryl halides and amides that can be employed, and the moderate yields often obtained (Scheme 1). Diaryliodonium reagents[14,15] have been employed as an alternative in some cases, such as the arylation of sulfonamides, with moderate success. The Heck palladium-catalyzed reaction between aryl halides and primary or secondary amines under a CO atmosphere[16] is also of relevance in this context. Due to the limitations of known reactions, the development of a milder, more general method for the *N*-arylation of amides and related compounds would be synthetically useful.

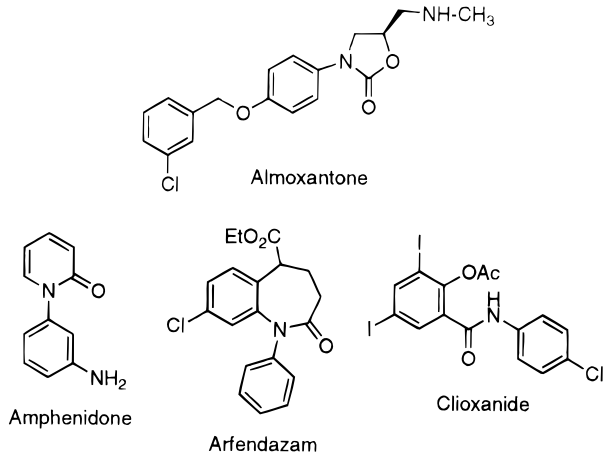

Figure 1.

Arylation is a traditional synthetic operation that has attracted renewed interest in recent years,[17] particularly in connection with the use of organometallic compounds such as arylpalladium species,[18] arylbismuth pentavalent derivatives,[19] and aryllead triacetates. However, most laboratories have focused their efforts on *C*-arylation reactions and *N*-arylation has received little attention. Aryllead triacetates[20,21] have been successfully employed for the arylation of several types of nucleophillic carbon atoms, including those found in enamines,[22] phenols,[23]

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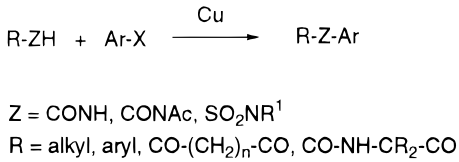
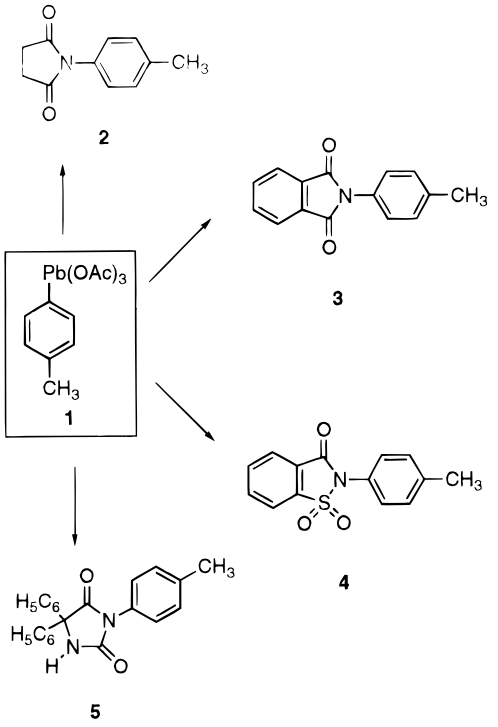
Scheme 1



silyl enol ethers,[24] nitroalkanes,[25] β-dicarbonyl compounds[26] and other active methylene compounds,[27] among others. Some inorganic nucleophiles, such as iodide and azide anions,[28] have also been efficiently arylated by these reagents. Although amines did not react under comparable conditions, the well-known similarity between the chemistries of lead and bismuth and the fact that copper species catalyze the arylation of amines by organobismuth reagents[29] prompted the discovery of a similar behaviour for the reaction between amines[30] or azoles[31] and aryllead triacetates in the presence of copper(II) acetate. In this paper we report in full[32] our studies on the *N*-arylation of amides by *p*-tolyllead triacetate (**1**) as a model reagent.

In our first experiments (Scheme 2), we used as substrates compounds containing relatively acidic NH−CO bonds, like carboxylic acid imides, mixed carboxylic-sulfonic imides, and hydantoins. Treatment of the starting material with a slight excess of sodium hydride at room temperature in CH_2Cl_2−DMF mixtures, followed by addition of **1** and a catalytic amount of copper(II) acetate and heating at 60−80 °C, afforded the desired *N*-aryl derivatives **2**−**5** in excellent yields (Table 1, entries 1−5). The presence of base was not essential with phthalimide as a substrate (see entries 2 and 3 of Table 1), but slightly longer reaction times were required in its absence. All reactions were clean and reproducible, and the only limitation we found was due to the lack of solubility of certain substrates (*e.g.* cyclohexanespirohydantoin) in our reaction conditions.[33] The mechanism of this arylation is apparently similar to the one proposed for the *N*-arylation of amines.[30] As in that instance, the reaction did not proceed in the absence of copper(II) catalyst, and also, the use of 1,1-diphenylethylene, a well-known free radical trapping agent, did not lower the yield of the reaction significantly.

Scheme 2



Simple carboxamides and sulfonamides were also efficiently arylated (Scheme 3 and Table 1, entries 6−10), although carboxamides required longer reaction times. Unlike other arylating reagents, compound **1** allowed mono- or diarylation in substrates bearing two N−H bonds simply by using 1 or 2 equiv of base and arylating reagent.

In order to gain some knowledge on the applicability of our method to polyfunctional substrates, we undertook a study of the chemoselectivity of amide arylation in the presence of two of the most important functional groups that are known to react with aryllead triacetates, namely the amino and β-dicarbonyl units. To this end, we studied in the first place the arylation of 4-aminoacetanilide and 4-aminobenzenesulfonamide with compound **1**, and the results are shown in Scheme 4. It was possible to achieve chemoselective arylation of the amino group in 4-aminoacetanilide to yield derivative **11**, either under neutral conditions or in the presence of sodium hydride (Table 1, entries 11 and 12). This behavior was anticipated, bearing in mind the very mild conditions under

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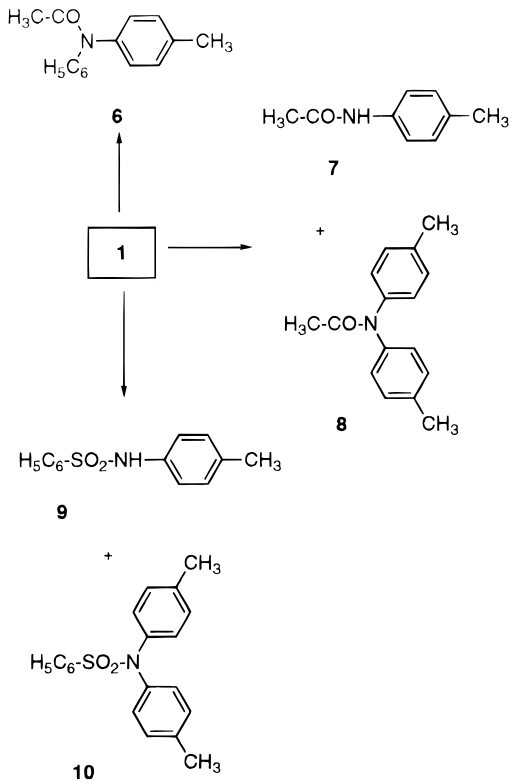
Table 1. Conditions and Yields of the *N*-Arylation Reactions of Amide Anions

entry	substrate	product(s)	yield/%[a]	equiv of **1**	equiv of NaH	conditions: time/h	conditions: temp/°C	conditions: solvent
1	succinimide	**2**	86	1.1	0	7	70	CH_2Cl_2−DMF (4:1)
2	phthalimide	**3**	82	1.2	1.2	1	70	CH_2Cl_2−DMF (6:1)
3	phthalimide	**3**	82	1.2	0	6	70	CH_2Cl_2−DMF (6:1)
4	sodium saccharin[b]	**4**	98	1.1	–	5	60	CH_2Cl_2−DMF (2:3)
5	5,5-diphenylhydantoin	**5**	75	1.1	1.2	7	80	CH_2Cl_2−DMF (3:1)
6	acetanilide	**6**	75 (89)[c]	1.2	2.0	48	80	CH_2Cl_2
7	acetamide	**7**	76	1.1	1.1	16	80	CH_2Cl_2
		8	10					
8	acetamide	**7**	10	2.1	2.1	48	80	CH_2Cl_2
		8	60					
9	benzenesulfonamide	**9**	73	1.1	1.1	5	90	CH_2Cl_2−DMF (3:1)
		10	9					
10	benzenesulfonamide	**9**	0	2.4	2.4	6	90	CH_2Cl_2−DMF (3:1)
		10	85					
11	4-aminoacetanilide	**11**	79	1.2	0	1	25	CH_2Cl_2
12	4-aminoacetanilide	**11**	53	1.1	1.1	20	90	CH_2Cl_2
13	sulfanilamide	**13**	70	1.1	1.1	16	40	CH_2Cl_2−Et_3N
14	**14a**	**15a**	31	1.1	1.1	8	90	CH_2Cl_2
		16a	19					
15	**14a**	**15a**	33	1.1	2.2	8	90	CH_2Cl_2
		16a	18					
16	**14b**	**15b**	11 (22)[c]	1.1	1.1	4	90	CH_2Cl_2
		16b	8 (16)[c]					

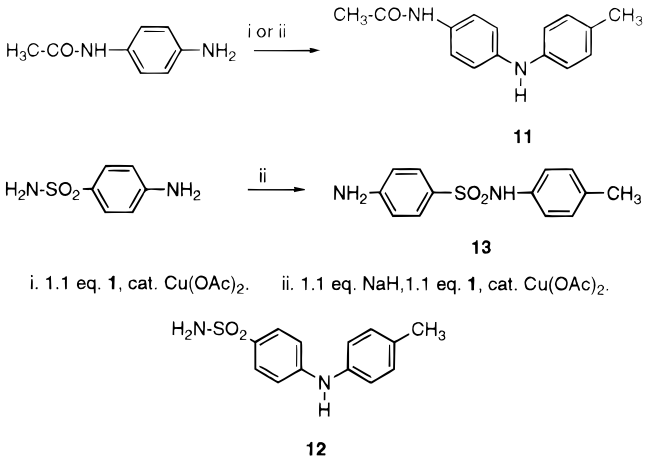
[a] Yields are given for isolated, purified compounds. [b] Purchased as a sodium salt. [c] The yields in parentheses are based on recovered starting material.

Scheme 3



which arylamines react with aryllead triacetates and the slow reaction of carboxamide anions. Sulfanilamide, on the other hand, gave only a trace of N^4-(*p*-tolylamino)-benzenesulfonamide (**12**)[34] in the absence of base, due to its very low solubility in the reaction medium, even in the presence of DMF, and was selectively arylated on the amide nitrogen when sodium hydride was added to yield compound **13** (Table 1, entry 13).

Scheme 4



Treatment of *β*-ketoanilides with compound **1** was next undertaken in order to examine the arylation of an amide nitrogen in the presence of a *β*-dicarbonyl system. Heating *N*-(2′,5′dimethoxyphenyl)-3-oxobutanamide (**14a**)[35] with **1** in the presence of 1.1 equiv of sodium hydride and a catalytic amount of copper(II) acetate gave a mixture of the C_2-monoarylated derivative **15a** and the α-ketoanilide **16a** (see below). This preference toward *C*-arylation cannot be attributed to a higher acidity of C-2 with respect to the nitrogen atom since the NH of *β*-ketoanilides is known to be more acidic than their methylene group.[36] Steric hindrance on the nitrogen atom caused by the nearby $C_{2'}$-OCH_3 group might be an alternative explanation, but it was ruled out by the results obtained in a similar reaction of the monomethoxy derivative **14b**, prepared from *m*-anisidine and 2,2,6-trimethyl-1,3-dioxin-4-one.[37] Its reaction with **1** under

(34) ^{1}H-NMR ($CDCl_3$, 250 MHz) δ 7.79 (d, 2H, J = 8.1 Hz); 7.41 (d, 2H, J = 7.9 Hz.); 7.01 (d, 2H, J = 8.4 Hz); 6.95 (br s, 1H); 671 (d, 2H, J = 8.4 Hz); 4.85 (br s, 2H); 2.39 (s, 3H) ppm.

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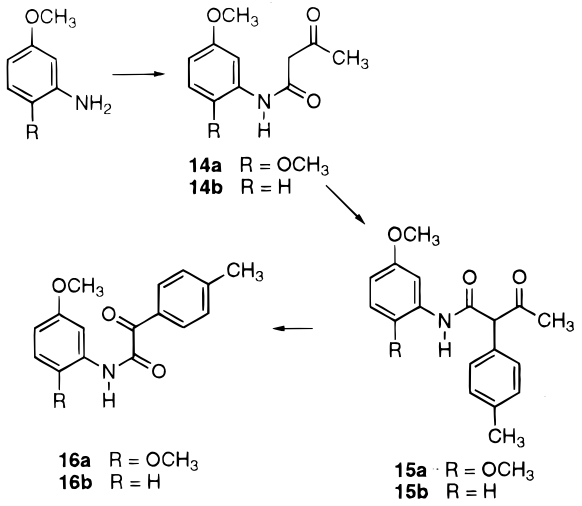
Scheme 5



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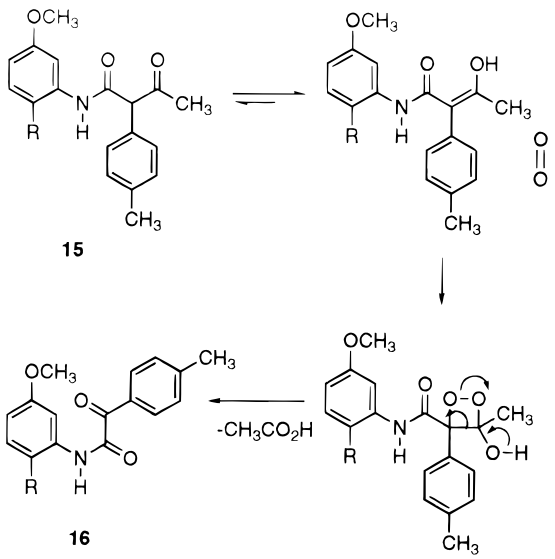

the conditions used for **14a** led to a mixture of **15b** and **16b**, without isolation of any *N*-arylated derivative. Use of 2.4 equiv of base did not alter these results (Scheme 5). This negative evidence points toward an explanation for the observed chemoselectivity based on the HSAB principle, since aryllead triacetates are "soft" electrophiles[20] which must give easier reactions with "soft" nucleophiles like enolate anions than with the "harder" nitrogen nucleophiles.

Compounds **15** are unstable in solution and are transformed into derivatives **16**. This is an interesting reaction since, to our knowledge, it is the first example of an oxidative deacylation of a β-ketoanilide.[38] This transformation is apparently associated with the existence of a high proportion of the enol tautomer in solutions of compounds **15**,[39] probably as a consequence of the extended conjugation of this structure. On the basis of the known ability of molecular oxygen to add to enols,[40] we propose the mechanism outlined in Scheme 6 to rationalize the isolation of compounds **16**.

In conclusion, *p*-tolyllead triacetate is an excellent reagent for the arylation of amidic nitrogen atoms, allowing also the chemoselective arylation of other functional groups in their presence. The reaction is superior to traditional methods for *N*-arylation in that the conditions required are mild and its scope is wider, in terms both of the substrate and the arylating reagent.

Experimental Section

General. Melting points are uncorrected. IR spectra were recorded with all solid compounds compressed into KBr pellets, and liquid compounds placed neat between NaCl plates. NMR spectra were obtained at 250 or 300 MHz for ^{1}H and 75.4 or 62.9 MHz for ^{13}C with $CDCl_3$ and DMSO-d_6 as solvents. Combustion elemental analyses were determined by the Servicio de Microanálisis, Universidad Complutense. Reactions were monitored by thin layer chromatography, on aluminum plates coated with silica gel with fluorescent indicator. Solutions were dried with anhydrous Na_2SO_4 and evaporated under reduced pressure (water aspirator) in a rotary evaporator. Separations by flash chromatography were performed on silica gel (230−400 mesh). All reagents were of commercial quality and were used as received. The expression "petroleum ether" refers to the fraction boiling at 40−60 °C. *p*-Tolyllead triacetate was prepared according to reference 26a (*warning:* organolead compounds are very toxic and should be handled with due caution).

***N*-Arylation of Amides. General Methods. Method A.** *p*-Tolyllead triacetate (1.1−2.4 equiv) and copper(II) acetate (10 mg) were added to a solution of the starting amide in CH_2Cl_2 (5 mL) containing the minimum amount of DMF. The green solution was added to a suspension of sodium hydride (equimolecular to *p*-tolyllead triacetate) in CH_2Cl_2 (3 mL), except in the synthesis of compound **3**, which started from a commercial sodium salt. The suspension thus obtained was heated in an oil bath at 70−90 °C for 1−7 h, cooled, and treated with 10 mL of dilute aqueous hydrogen sulfide. The black biphasic system was filtered through Celite, and the aqueous layer was extracted with chloroform (3 × 20 mL). The combined organic layers were dried (Na_2SO_4) and evaporated, and the residue was purified by column chromatography.

Method B. Sodium hydride (1.1−2 equiv) was added to a hot (80 °C) solution of the starting amide, *p*-tolyllead triacetate (1.1−1.2 equiv), and copper(II) acetate (10 mg) in CH_2Cl_2 (7 mL). The suspension was heated in an oil bath at 80 °C for 16 to 48 h, with partial evaporation of the solvent. Workup was the same as in method A.

Method C. *p*-Tolyllead triacetate (1.2) and copper(II) acetate (10 mg) were added to a solution of the starting amide in CH_2Cl_2 (7 mL) containing the minimum amount of DMF. The green solution was heated in an oil bath at 70 °C for 6−7 h and worked up as in method A.

1-(*p*-Tolyl)pyrrolidine-2,5-dione (2). Starting from succinimide (50 mg, 0.51 mmol) and *p*-tolyllead triacetate (287 mg, 0.61 mmol) in 4:1 CH_2Cl_2−DMF, method C was followed at 70 °C for 7 h. A yield of 82 mg (86%) of **2** was obtained after column chromatography on silica gel, eluting with 8:2 petroleum ether−ethyl ether. Mp 155−156 °C (EtOH). IR (KBr): 1700 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 7.28 (d, 2H, J = 8.1 Hz); 7.15 (d, 2H, J = 8.1 Hz); 2.88 (s, 4H); 2.38 (s, 3H). ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 176.2; 138.6; 126.1; 129.7; 129.1; 28.3; 21.1. Anal. Calcd for $C_{11}H_{11}NO_2$: C, 69.82; H, 5.86; N, 7.40. Found: C, 69.49; H, 5.88; N, 7.37.

2-(*p*-Tolyl)benzo[*c*]pyrrole-1,3-dione (3). Starting from phthalimide (100 mg, 0.68 mmol) and *p*-tolyllead triacetate (387 mg, 0.82 mmol) in 6:1 CH_2Cl_2−DMF, method A was followed at 70 °C for 1 h. A yield of 130 mg (82%) of **3** was obtained after chromatography on silica gel, eluting with 9:1

(38) The main degradation pathway previously known for β-ketoanilides was photochemical decomposition to ketones and aryl isocyanates. See: (a) Mukaiyama, T.; Tozikawa, M.; Nohira, H.; Takai, H. *J. Org. Chem.* **1961**, *26*, 4381. (b) Reisch, J.; Niemeyer, D. *Tetrahedron* **1971**, *27*, 4637. (c) Fahmy, A. F. M.; Badday, H. A.; Alkhateeb, A. N. *Indian J. Chem. Sect. B* **1981**, *20B*, 489.

(39) Compounds very similar to **15**, but existing as dioxo tautomers, are stable in solution. P. López-Alvarado, Ph. D. Thesis. Universidad Complutense, Madrid, 1995.

(40) Jones, A. B. In *Comprenhensive Organic Synthesis*; Ley, S. V., Ed.; Trost, B. M., Fleming, I., Gen Eds.; Pergamon Press: New York, 1991; Vol. 7, p 151.

petroleum ether−CH_2Cl_2. The same yield was obtained following method C at 70 °C for 6 h. Mp 201−203 °C (EtOH). IR (KBr): 1720 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 7.94 (m, 2H); 7.78 (m, 2H); 7.31 (s, 4H); 2.41 (s, 3H). ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 167.4; 138.2; 134.3; 131.8; 129.8; 128.9; 126.4; 123.7; 21.2. Anal. Calcd for $C_{15}H_{11}NO_2$: C, 75.93; H, 4.67; N, 5.90. Found: C, 75.56; H, 4.94; N, 5.76.

1,1-Dioxo-2-(*p*-tolyl)benzo[*c*]1,2-thiazol-3-one (4). Starting from sodium saccharine (100 mg, 0.49 mmol) and *p*-tolyllead triacetate (255 mg, 0.54 mmol) in 1:1.5 CH_2Cl_2−DMF, method A was used at 60 °C for 5 h. A yield of 129 mg (98%) of **4** was obtained after chromatography on silica gel, eluting with 95:5 petroleum ether−ethyl ether. Mp 198−200 °C (EtOH). IR (KBr): 1718, 1308, 1192 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 8.15 (dd, 1H, J = 7.5 and 1.8 Hz); 7.99 (dd, 1H, J = 7.5 and 1.8 Hz); 7.92 (td, 1H, J = 7.5 and 1.8 Hz); 7.88 (td, 1H, J = 7.5 and 1.8 Hz); 7.41 (d, 2H, J = 8.1 Hz); 7.35 (d, 2H, J = 8.1 Hz); 2.43 (s, 3H). ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 158.5; 140.5; 137.6; 135.0; 134.4; 130.6; 128.7; 127.2; 125.7; 125.6; 121.2; 21.4. Anal. Calcd for $C_{14}H_{11}NO_3S$: C, 61.53; H, 4.05; N, 5.12. Found: C, 61.14; H, 4.25; N, 5.07.

5,5-Diphenyl-3-(*p*-tolyl)imidazolidine-2,4-dione (5). Starting from diphenylhydantoin (100 mg, 0.39 mmol) and *p*-tolyllead triacetate (222 mg, 0.47 mmol) in 3:1 CH_2Cl_2−DMF, method A was used at 80 °C for 7 h. A yield of 101 mg (75%) of **5** was obtained after chromatography on silica gel, eluting with CH_2Cl_2. Mp 202−204 °C (EtOH). IR (KBr): 3230, 1725 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 7.88 (br s, 1H); 7.44−7.41 and 7.34−7.32 (2 m, 10H); 7.23 (s, 4H); 2.35 (s, 3H). ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 172.2; 155.9; 139.1; 138.4; 129.6; 128.8; 128.5; 126.8; 126.1; 69.9; 21.1. Anal. Calcd for $C_{22}H_{18}N_2O_2$: C, 77.17; H, 5.30; N, 8.18. Found: C, 76.62; H, 5.19; N, 7.97.

***N*-Phenyl-*N*-(*p*-tolyl)acetamide (6).** Starting from acetanilide (50 mg, 0.37 mmol), *p*-tolyllead triacetate (211 mg, 0.44 mmol), and NaH (17 mg of a 60% dispersion in mineral oil, followed by 14 mg 24 h later, totaling 0.78 mmol), method B was used for 48 h at 80 °C. A yield of 62 mg of **6** was obtained (75%, 91% based on recovered acetanilide), after column chromatography on silica gel, using a gradient of 98:2 hexane−CH_2Cl_2 to neat CH_2Cl_2. IR (NaCl): 1670 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 250 MHz) δ 7.26−7.14 (m, 9H); 2.32 (br s, 3H); 2.03 (s, 3H). Anal. Calcd for $C_{15}H_{15}NO$: C, 79.97; H, 6.71; N, 6.22. Found: C, 79.52; H, 7.06; N, 6.16.

***N*-(*p*-Tolyl)acetamide (7) and *N*,*N*-Bis(*p*-tolyl)acetamide (8).** Starting from acetamide (25 mg, 0.43 mmol), *p*-tolyllead triacetate (221 mg, 0.47 mmol), and NaH (18 mg of a 60% dispersion in mineral oil, 0.47 mmol), method B was used at 80 °C for 16 h. A yield of 48 mg (76%) of **7** and 10 mg (10%) of **8**, after column chromatography on silica gel eluting with 7:3 petroleum ether-ethyl ether was obtained.

Data for **7**: Mp 129−130 °C. IR (KBr): 3260, 1672 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 250 MHz) δ 7.34 (d, 2H, J = 8.1 Hz); 7.18 (br s, 1H); 7.09 (d, 2H, J = 8.1 Hz); 2.29 (s, 3H); 2.14 (s, 3H). ^{13}C-NMR ($CDCl_3$, 63 MHz) δ 168.2; 135.2; 135.2; 133.9; 129.5; 120.0; 24.6; 20.9. Anal. Calcd for $C_9H_{11}NO$: C, 72.45; H, 7.43; N, 9.38. Found: C, 72.14; H, 7.54; N, 8.98.

Data for **8**: IR (NaCl): 1671 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 250 MHz) δ 7.15 (br s, 8H); 2.35 (br s, 6H); 2.05 (s, 3H). Anal. Calcd for $C_{16}H_{17}NO$: C, 80.30; H, 7.16; N, 5.85. Found: C, 80.38; H, 7.42; N, 5.74.

***N*-(*p*-Tolyl)benzenesulfonamide (9) and *N*,*N*-Bis(*p*-tolyl)benzenesulfonamide (10).** Starting from benzenesulfonamide (60 mg, 0.38 mmol), *p*-tolyllead triacetate (199 mg, 0.42 mmol) in 3:1 CH_2Cl_2−DMF, and NaH (17 mg of a 60% dispersion in mineral oil, 0.42 mmol), method A was used at 90 °C for 5 h. A yield of 69 mg (73%) of **9** and 11 mg (9%) of **10**, after column chromatography on silica gel eluting with 1:1 CH_2Cl_2−hexane, was obtained.

Data for **9**: Mp 117−119 °C (EtOH). IR (KBr): 3310, 1316, 1172, 740 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 250 MHz) δ 7.75 (d, 2H, J = 7.2 Hz); 7.53 (tt, 1H, J = 7.3 and 2.0 Hz); 7.43 (t, 2H, J = 7.1 Hz); 7.03 (d, 2H, J = 8.3 Hz); 6.95 (d, 2H, J = 8.4 Hz); 6.74 (br s, 1H); 2.27 (s, 3H). ^{13}C-NMR ($CDCl_3$, 63 MHz) δ 139.1; 135.7; 133.6; 133.0; 130.0; 129.1; 127.3; 122.6; 22.0. Anal. Calcd for $C_{13}H_{13}NO_2S$: C, 63.13; H, 5.30; N, 5.66. Found: C, 62.85; H, 5.25; N, 5.28.

Data for **10**: Mp 158−159 °C (EtOH). IR (KBr): 1348, 1156, 710 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 250 MHz) δ 7.70 (dd, 2H, J = 8.1 and 1.6 Hz); 7.58 (tt, 1H, J = 7.8 and 2.0 Hz); 7.47 (td, 2H, J = 7.9 and 1.2 Hz); 7.14 (d, 4H, J = 8.8 Hz); 7.02 (d, 4H, J = 8.5 Hz); 2.30 (s, 6H). ^{13}C-NMR ($CDCl_3$, 63 MHz) δ 140.6; 138.9; 137.4; 132.6; 129.9; 128.8; 128.1; 127.7; 21.0. Anal. Calcd for $C_{20}H_{19}NO_2S$: C, 71.19; H, 5.67; N, 4.15. Found: C, 71.07; H, 5.63; N, 4.04.

4-[*N*-(*p*-Tolyl)amino]acetanilide (11). Starting from 4-aminoacetanilide (50 mg, 0.21 mmol) and *p*-tolyllead triacetate (174 mg, 0.37 mmol) in CH_2Cl_2 (2 mL), method C was followed at 25 °C for 1 h. A yield of 75 mg (97%) of **11** was obtained after chromatography on silica gel, eluting with ethyl ether. The same yield was obtained following method C at 70 °C for 6 h. Mp 141−143 °C ($CDCl_3$). IR (KBr): 3320, 1650 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 250 MHz) δ 7.66 (br s, 1H); 7.34 (d, 2H, J = 8.8 Hz); 7.06 (d, 2H, J = 8.2 Hz); 6.95 (d, 2H, J = 8.8 Hz); 6.94 (d, 2H, J = 8.3 Hz); 5.63 (br s, 1H); 2.29 (s, 3H); 2.13 (s, 3H). ^{13}C-NMR ($CDCl_3$, 63 MHz) δ 168.5; 140.5; 140.4; 130.8; 130.4; 129.8; 121.8; 118.0; 117.7; 24.2; 20.6. Anal. Calcd for $C_{15}H_{16}N_2O$: C, 74.97; H, 6.71; N, 11.65. Found: C, 74.74; H, 6.70; N, 11.49.

***N*^{1}-(*p*-Tolyl)sulfanilamide (13).** A solution of *p*-tolyllead triacetate (152 mg, 0.319 mmol) and copper(II) acetate (10 mg) in CH_2Cl_2 (3 mL) containing pyridine or triethylamine (1.1 equiv) was added to a suspension of sulfanilamide (50 mg, 0.29 mmol) in CH_2Cl_2 (5 mL) at 40 °C. The green suspension was heated in an oil bath at 40 °C for 16 h and worked up as in method A. The crude reaction product was purified by chromatography on silica gel, eluting with $CHCl_3$, yielding 53 mg (70%) of **13**. IR (NaCl): 3410, 3250, 3330, 1340, 1160 cm^{-1}. ^{1}H-NMR (acetone-d_6, 250 MHz) δ 7.86 (br s, 1H); 7.73 (d, 2H, J = 7.6 Hz); 7.18 (br s, 4H); 7.12 (d, 2H, J = 7.6 Hz); 6.36 (br s, 1H); 2.33 (s, 3H). ^{13}C-NMR (acetone-d_6, 63 MHz) δ 149.2; 139.7; 134.1; 132.8; 130.6; 128.7; 121.3; 114.6; 20.7. Anal. Calcd for $C_{13}H_{14}N_2O_2S$: C, 59.52; H, 5.38; N, 10.68. Found: C, 59.33; H, 5.33; N, 10.49.

***N*-(3′-Methoxyphenyl)-3-oxobutanamide (14b).** A solution of *m*-anisidine (3 g, 24.35 mmol) and 2,2,6-trimethyl-4*H*-1,3-dioxin-3-one (3.63 g; 25.57 mmol) in xylene (20 mL) was heated in an open flask at 120 °C for 1 h. The solvent was evaporated under reduced pressure, and the crude reaction product was purified by chromatography on silica gel, eluting with CH_2Cl_2, yielding 3.63 g (72%) of anilide **14b**. Mp 76−77 °C (acetone/petroleum ether). IR (KBr): 3150, 1676, 1624 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 300 MHz) δ: 9.22 (br s, 1H); 7.27 (m, 1H); 7.18 (t, 1H, J = 8.1 Hz); 7.03 (d, 1H, J = 7.5 Hz); 6.66 (d, 1H, J = 8.4 Hz); 3.75 (s, 3H); 3.54 (s, 2H); 2.26 (s, 3H) ppm. ^{13}C-NMR ($CDCl_3$, 75 MHz) δ: 204.2; 161.9; 159.6; 138.3; 129.2; 111.9; 109.8; 105.5; 54.8; 49.9; 30.6 ppm. Anal. Calcd for $C_{11}H_{13}NO_3$: C, 63.75; H, 6.32; N, 6.76. Found: C, 63.84; H, 6.20; N, 6.82.

2-(*p*-Tolyl)-*N*-(2′,5′-dimethoxyphenyl)-3-oxobutanamide (15a) and 2-(*p*-tolyl)-*N*-(2′,5′-dimethoxyphenyl)-2-oxoacetamide (16a). Starting from *N*-(2′,5′-dimethoxyphenyl)-3-oxobutanamide (100 mg, 0.42 mmol), *p*-tolyllead triacetate (220 mg, 0.46 mmol) in CH_2Cl_2 (5 mL), and sodium hydride (18 mg of a 60% dispersion in mineral oil, 0.46 mmol), method A was used at 90 °C for 4 h. A yield of 15 mg (11%, 22% based on recovered starting material) of **15a** and 10 mg (8%, 16% based on recovered starting material) of **16a** was obtained after column chromatography on silica gel eluting with 9:1 petroleum ether−CH_2Cl_2.

Data for **15a**: ^{1}H-NMR ($CDCl_3$, 250 MHz, 67% oxo tautomer, 33% enol tautomer) δ: 14.46 (s, 1H); 9.32 (br s, 1H); 7.98 (d, 1H, J = 3.0 Hz); 7.93 (d, 1H, J = 3.0 Hz); 7.52 (br s, 1H); 7.25−7.15 (m, 6H); 7.11 (d, 2H, J = 7.9 Hz); 6.71 (d, 1H, J = 8.9 Hz); 6.60 (d, 1H, J = 7.6 Hz); 6.49 (dd, 1H, J = 9.0 and 3.0 Hz); 6.44 (dd, 1H, J = 8.8 and 2.9 Hz); 4.67 (s, 1H); 3.75 (s, 3H); 3.71 (s, 3H); 3.67 (s, 3H); 3.46 (s, 3H); 2.35 (s, 3H); 2.28 (s, 3H); 2.21 (s, 3H); 1.76 (s, 3H).

Data for **16a**: Mp 101−102 °C (acetone/petroleum ether). IR (KBr): 3456, 3375, 1700, 1656, 1290 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 250 MHz) δ 9.48 (br s, 1H); 8.25 (d, 2H, J = 8.2 Hz); 8.14 (d, 1H, J = 3.0 Hz); 7.23 (d, 2H, J = 8.2 Hz); 6.77 (d, 1H, J = 8.9 Hz); 6.58 (dd, 1H, J = 8.9 and 3.0 Hz); 3.81(s, 3H);

3.74 (s, 3H); 2.37 (s, 3H, CH_3). ^{13}C-NMR ($CDCl_3$, 63 MHz) δ 186.7; 159.2; 153.7; 145.7; 143.0; 131.5; 130.2; 129.3; 127.0; 110.9; 109.9; 105.9; 56.2; 55.8; 21.9. Anal. Calcd for $C_{17}H_{17}NO_4$: C, 68.21; H, 5.72; N, 4.68. Found: C, 68.42; H, 6.09; N, 4.36.

2-(*p*-Tolyl)-*N*-(3′-methoxyphenyl)-3-oxobutanamide (15b) and 2-(*p*-Tolyl)-*N*-(3′-methoxyphenyl)-2-oxoacetamide (16b). Starting from *N*-(3′-methoxyphenyl)-3-oxobutanamide (100 mg, 0.48 mmol), *p*-tolyllead triacetate (252 mg, 0.53 mmol) in CH_2Cl_2 (5 mL), and NaH (21 mg of a 60% dispersion in mineral oil, 0.53 mmol), method A was used at 90 °C for 8 h. A yield of 45 mg (31%) of **15b** and 25 mg (19%) of **16b** was obtained after column chromatography on silica gel eluting with 8:2 petroleum ether−CH_2Cl_2.

Data for **15b**: IR (NaCl): 3281, 1722, 1668, 1292 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 250 MHz, 58% oxo tautomer, 42% enol tautomer[41]) δ 14.54 (s, 1H); 9.09 (br s, 1H); 7.28 (d, 1H, J = 2.5 Hz); 7.25 (d, 1H, J = 1.8 Hz); 7.21−7.14 (m, 8H); 7.11−7.08 and 6.99−6.96 (2 m, 2H); 6.79−6.75 (m, 2H); 6.66−6.59 (m, 2H); 4.70 (s, 1H); 3.77 (2 s, 6H); 2.41 (s, 3H); 2.34 (s, 3H); 2.26 (s, 3H); 1.81 (s, 3H). ^{13}C-NMR ($CDCl_3$, 63 MHz) δ 206.3; 172.7; 170.6; 166.0; 160.0; 160.0; 138.7; 138.5; 138.4; 138.1; 131.7; 131.5; 130.4; 130.2; 129.5; 129.5; 128.7; 128.3; 112.5; 112.1; 110.6; 110.00; 106.1; 105.5; 104.9; 65.1; 55.3; 55.2; 30.2; 21.2; 21.1; 20.1. Anal. Calcd for $C_{18}H_{19}NO_3$: C, 72.71; H, 6.44; N, 4.71. Found: C, 72.51; H, 6.63; N, 4.38.

Data for **16b**: Mp 106−107 °C (EtOH). IR (KBr): 3446, 3342, 1685, 1660, 1274 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 250 MHz) δ 8.97 (br s, 1H); 8.34 (d, 2H, J = 8.3 Hz); 7.46 (t, 1H, J = 2.2 Hz); 7.33−7.29 (m, 3H); 7.14 (t, 1H, J = 8.5 Hz); 6.75 (dd, 1H, J = 7.9 and 2.4 Hz); 3.85 (s, 3H); 2.45 (s, 3H). ^{13}C-NMR ($CDCl_3$, 63 MHz) δ 186.6; 160.1; 159.0; 145.9; 137.8; 131.6; 130.4; 129.8; 129.2; 112.0; 111.1; 105.3; 55.3; 21.8. Anal. Calcd for $C_{16}H_{15}NO_3$: C, 71.36; H, 5.61; N, 5.20. Found: C, 71.24; H, 5.23; N, 5.26.

(41) This enol content corresponds to a freshly prepared solution and quickly rose to 67% before decomposition to **16a**.

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