JOC The Journal of Organic Chemistry

ARTICLE

pubs.acs.org/joc

Asymmetric Synthesis of Ethoxydienamines in Superbasic Medium Mediated by Chiral Sulfinyl Group

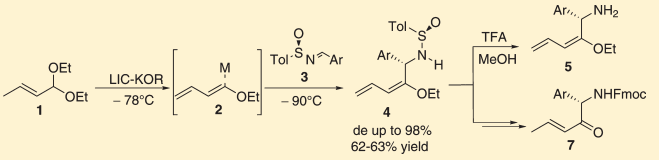
Marco Blangetti, Gianluca Croce,[†] Annamaria Deagostino, Eleonora Mussano, Cristina Prandi,* and Paolo Venturello

Dipartimento di Chimica Generale e Chimica Organica, Università degli Studi di Torino, Via P. Giuria, 7-10125 Torino, Italy

[†]Dipartimento di Scienze e Tecnologie Avanzate, Università degli Studi del Piemonte Orientale "Amedeo Avogadro", Viale Teresa Michel, 11-15121 Alessandria, Italy

Supporting Information

ABSTRACT: The direct addition of metalated alkoxydiene **2**, obtained from α,β-unsaturated acetal **1** through a LIC-KOR-promoted conjugated elimination reaction, to enantiopure sulfinimines **3** (both *R* and *S* *N*-sulfinyl imines) afforded *N*-sulfinyl alkoxydienyl amines **4** with high diastereoselectivity. Functionalized enantiopure alkoxydienyl amines **5** were then easily obtained upon the selective removal of the chiral auxiliary under mild conditions. Moreover, the further hydrolysis of the alkoxydienyl moiety gave access to protected enantiopure β-keto amines **7**.



INTRODUCTION

The role of the sulfinyl group in enantioselective syntheses is well documented in the literature, and in particular, sulfinyl imines represent a versatile class of prochiral electrophiles in which the presence of the electron-withdrawing sulfinyl group activates the C═N bond to nucleophilic attack and, at the same time, exerts powerful stereodirecting effects.[1−4] Due to the presence of the *N*-sulfinyl group, sulfinimines are particularly reactive toward a variety of nucleophiles; of these, carbon nucleophiles have been widely investigated. Hence, Grignard reagents,[5−8] cuprates,[9−11] organolithium,[2,12−14] cyanides,[15−17] and organozincates[18,19] all add to sulfinimines in a 1,2-addition fashion to give sulfinamides. In addition, sodium, potassium, and lithium enolates[3,4] react with chiral sulfinimines to afford β-amino esters with high yield and diastereoselectivity. Recently, β-amino acid derivatives have been successfully obtained by the addition of prochiral Weinreb amides to sulfinimines.[20−22] The metal seems to play a crucial role in determining the diastereoselectivity of the reaction, and a six-membered chairlike transition state where the metal is coordinated to the sulfinyl oxygen atom has been evoked to explain the sense of the induction. Moreover, a reversal of the diastereoselectivity has been realized by replacing potassium enolates with the corresponding lithium enolates.[6] These results are in agreement with the chelation-control transition-state hypothesis.

Within the context of our work on the study of the reactivity of metalated alkoxydienes with electrophiles in superbasic medium,[23−25] we recently reported the synthesis of stereodefined alkoxy dienamines by reaction of 1-metalated-1-alkoxybutadienes, these in turn obtained from α,β-unsaturated acetals in the presence of the LIC-KOR superbase and *N*-protected aldimines.[26] The current challenge is to control, in the superbasic medium, the stereochemistry of the new stereogenic center that is created upon addition of prochiral electrophiles. In this paper, we report the results we obtained when metalated alkoxydienes **2** have been reacted with sulfinyl imines **3** in superbasic medium. As far as we know, there are no references in the literature to the diastereoselective induction effect of the sulfinyl chiral auxiliary group in the presence of superbases.

RESULTS AND DISCUSSION

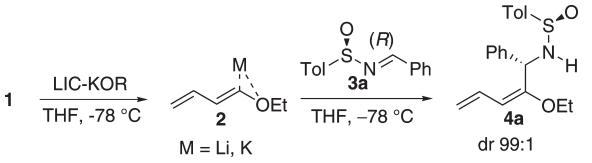
The metalated alkoxydiene **2** was generated from crotonaldehyde diethyl acetal **1** in the presence of 2.2 equiv of the superbase LIC-KOR, which is an equimolecular mixture of butyllithium (LIC) and potassium *tert*-butoxide (KOR), at −78 °C as previously reported.[26] After 2 h, sulfinyl imine **3a** (R_S) was added to the formed nucleophile, and the reaction was monitored by TLC until complete consumption of the electrophile was observed (Scheme 1). The reaction was then repeated using sulfinyl imine **3a** (S_S) as the electrophile. In both cases, the corresponding dienyl amines **4a** (*S*, R_S) or **4a** (*R*, S_S) were obtained with a surprisingly high dr, thus indicating the excellent level of stereoinduction occurring in superbasic medium.

The diastereomeric mixtures were then purified by flash column chromatography, and the absolute configuration of both enantiomers was determined by single-crystal X-ray analysis (see the Supporting Information).

Hence, in the case of a sulfinyl imine with an *R* configuration on the sulfur the major diastereoisomer formed in the nucleophilic addition pathway shows a *S* configuration on the new formed stereogenic carbon, while the sulfinyl imine S_S afforded

Received: December 16, 2010
Published: February 14, 2011

Scheme 1. Addition of Metalated Alkoxydiene 2 to *N*-Benzylidene-*p*-toluenesulfinamide 3a (R_S)



the *R*, S_S diastereoisomer as the major product. The sense of this asymmetric induction can be understood if a highly coordinated transition state is hypothesized where both the sulfoxide oxygen atom and the iminic nitrogen atom could coordinate one of the metal counterions of the superbasic mixed aggregate.[2,4] As a consequence, the alkoxydienyl anion will be locked above, or below, the plane containing the electrophile. In particular, with an R_S imine as electrophile the metalated diene appears stuck below the imine, and the addition to the *Re* face becomes the only possible pathway to afford the (*S*) diastereoisomer. On the other hand, considering an S_S imine, the alkoxydienyl anion would be locked above the imine's plane, and the addition proceeded to the *Si* face, giving the *R*, S_S diastereoisomer as the major product.

Encouraged by these results, we decided to extend the scope of the reaction and to evaluate both the diastereoselectivity and the yield of the addition reaction with differently substituted sulfinyl imines. To this purpose, different enantiopure sulfinamines were synthesized using the Andersen reagent,[27] by treatment with LHMDS in the presence of the appropriate aldehyde,[28] or alternatively according to the DAG procedure.[29,30] At first, we performed the reaction under standard conditions for this kind of LIC-KOR-promoted eliminations, i.e., 1 equiv of **1**, 2 equiv of LIC-KOR, and 1 equiv of **3** at −78 °C, but we soon realized that the weak point of this approach was the unsatisfactory yield of **4** in the addition reaction. Although TLC monitoring of the reaction indicated a rapid disappearance of sulfinyl imine **3**, the ^{1}H NMR spectrum of the crude product provided evidence of some unreacted imines **3**, thioester **C**, and a low amount of the desired product **4**. Puzzled by these data and on the grounds that sulfinyl imines are reported to be as electrophilic as tosyl imines are, we tried to understand what was happening in the reaction mixture. Supported by a recent publication,[31] we considered that the excess of superbasic reagent LIC-KOR could induce a β-elimination reaction on the newly formed ethoxydienyl amine **4** and the generation of the sulfenate anion **A** (Scheme 2). This species could act as a nucleophile and add to the sulfinyl imine **3** still present in the reaction mixture.[32] A further β-elimination on **B** regenerates **3** and the sulfenate anion **A**, which dimerizes to the corresponding thioester **C** upon quenching.[33]

On these bases, we realized that good conversions to the desired product **4** could be achieved by assuring an excess of metalated diene **2** during the whole reaction advancement, and we consequently changed the experimental conditions, namely 3 equiv of the starting α,β-unsaturated acetal **1**, very slow addition of the electrophile (over 1.5 h) and temperatures as low as −90 °C. Under these conditions, the yields of dienyl amines significantly increased, ranging from 52 to 63%, while the diastereoselectivity remained high (Table 1).

Aromatic (**4a**−**c**), heteroaromatic (**4d**), vinylic (**4e**), and aliphatic (**4f**) sulfinyl imines, as the *R* or *S* stereoisomer, have been used as electrophiles in the addition reaction, and in all of the cases examined the addition reaction takes place with very high diasteromeric ratio and with satisfactory yields of purified products.

Scheme 2. Decomposition of Dienyl Amines 4 to Thioester C via Sulfenate Anion A in Superbasic Medium

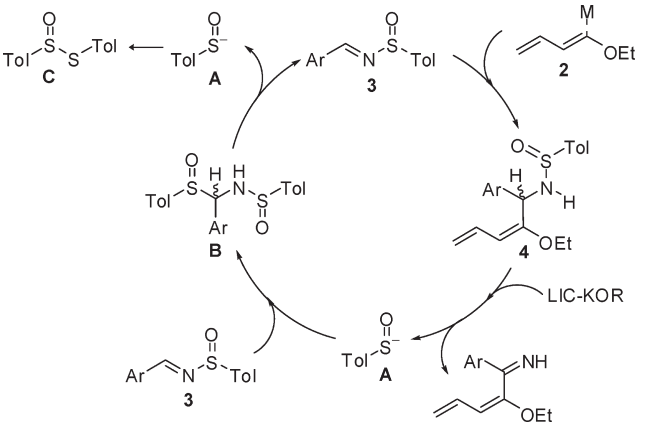
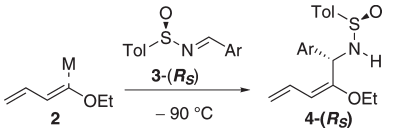


Table 1. Synthesis of Alkoxydienyl Sulfinyl Amines at −90 °C[a]



entry	Ar	imine	product	yield[b] (%)	dr[c] (%)
1	Ph	R_S	**4a**	52	99:1
2	*p*-Tol	R_S	**4b**	59	99:1
3	PMP	R_S	**4c**	55	99:1
4	2-thienyl	R_S	**4d**	55	99:1
5	cinnamyl	R_S	**4e**	55	99:1
6	Piv	R_S	**4f**	53	99:1

[a] The enantiomer of each of the products has been also prepared (see the Experimental Section). Reaction conditions: **1** (3 equiv), LIC-KOR (7.5 equiv), **3** (1 equiv), −90 °C. [b] Yield refers to major diastereoisomer separated by column chromatography. [c] Determined by ^{1}H NMR on the crude reaction mixture by comparison with the ^{1}H spectra of each diasteroisomer as pure compound (see the Experimental Section and Supporting Information).

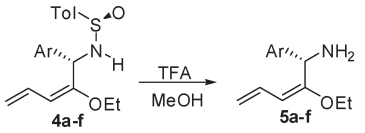
In view of further developments, *N*-sulfinyl amines **4** were then treated with TFA in MeOH: under these conditions only the removal of the chiral auxiliary occurred so that enantiopure alkoxydienylamines **5** were isolated in almost quantitative yields (Table 2).[34]

The conversion of **5** into α,β-unsaturated ketones proved to be troublesome. In this case, the alkoxydienyl function is in fact resistant to acidic hydrolysis. It could be assumed that the fast protonation of the amino group to the ammonium intermediate (**A**) prevents the formation of the cationic species (**B**) that is involved in the deprotection process (Scheme 3).

A series of attempts under different experimental conditions led to the recovery of the unreacted starting material.[35] Nevertheless, the vinyl ether function underwent hydrolysis when

dx.doi.org/10.1021/jo1024943 |*J. Org. Chem.* 2011, 76, 1814–1820

Table 2. Synthesis of Enantiopure Ethoxydienyl Amines 5[a]



entry	reactant	product	Ar	yield[b] (%)
1	**4a**	**5a**	Ph	91
2	**4b**	**5b**	*p*-Tol	92
3	**4c**	**5c**	PMP	93
4	**4d**	**5d**	2-thienyl	94
5	**4e**	**5e**	cinnamyl	87
6	**4f**	**5f**	Piv	92

[a] The enantiomer of each of the products has been also prepared (see the Experimental Section). Reaction conditions: **4** (0.5 mmol), MeOH (3 mL), 0 °C, then TFA (1.75 mmol, 3.5 equiv). Stirred for 10 min at 0 °C and then 1 h at rt. [b] Yields refer to isolated products. The enantiomer of each of the products has been also prepared (see the Experimental Section).

Fmoc was used as a protecting function of the newly formed amino group. In this case, Fmoc-protected dienyl amines **6** can be easily converted to the corresponding Fmoc-protected α,β-unsaturated ketones **7**. Remarkably, all of the synthetic transformations leading to derivatives **7** occur without epimerization at the chiral center.[34]

CONCLUSIONS

In summary, in this work we have exploited the high potential of chiral sulfinyl imines (Davis imines) as electrophiles to obtain enantiopure products in superbasic medium. We have demonstrated that the addition reaction of metalated alkoxydienes to enantiopure sulfinyl imines leads to alkoxydienyl amines with high diastereomeric excesses, thus proving that the reactions proceed through a highly coordinated transition state in which both the metals of the superbasic complex can be involved. The results we obtained are in agreement with the "chelation-control" transition-state hypothesis,[2,4] the current theory to explain the high diastereoselective level for monometallic species (Na, Li, K, Zn, Mn). Moreover, the chiral auxiliary can be selectively removed to afford enantiopure alkoxy dienyl amines. The change in protecting group to Fmoc allows the hydrolysis of the vinyl ether moiety without the loss of enantiopurity and gives ready access to keto-amino derivatives.

EXPERIMENTAL SECTION

Synthesis of Chiral Sulfinimines 3. Chiral sulfinimines were synthesized according to the literature procedure described by Davis and co-workers,[28] starting either from Andersen reagents or DAG-*p*-toluenesulfinates. The spectral data were in agreement with reported values.

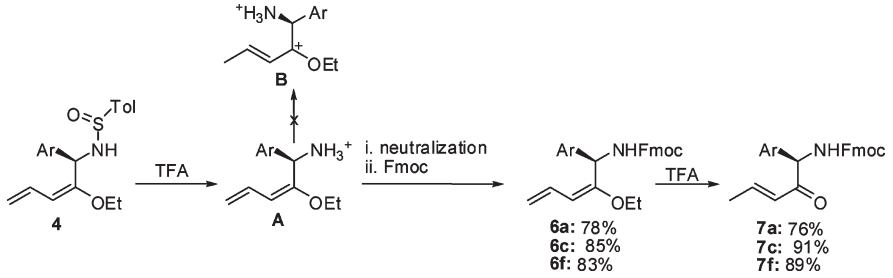
Typical procedure for the synthesis of *p*-toluenesulfinimines: In a 500 mL three-necked, round-bottomed flask equipped with a magnetic stir bar, rubber septum, and argon inlet was placed (1*R*,2*S*,5*R*)-(−)-menthyl (*S*)-*p*-toluenesulfinate (14.0 g, 47.5 mmol) dissolved in 225 mL of freshly distilled THF, and the mixture was cooled to −78 °C. A solution of 62.0 mL of LiHMDS (62.0 mmol, 1.0 M solution in THF, 1.3 equiv) was added dropwise via syringe, and the reaction mixture was allowed to warm to rt with stirring. After 5 h, the reaction mixture was cooled to −78 °C, and benzaldehyde (53.0 mmol, 5.0 mL, 1.1 equiv) was added dropwise. After being stirred for 2 h at −78 °C, the reaction mixture was quenched with water (50 mL) and extracted with Et_2O (3 × 30 mL). The organic layer was washed with water (2 × 100 mL) and brine (100 mL), dried (Na_2SO_4), and concentrated to give an oil that was purified by flash column chromatography (petroleum ether/EtOAc 9/1 + 1% Et_3N, yield 73%). (*S*)-(+)-*N*-Benzylidene-*p*-toluenesulfinamide **3a**: ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.76 (s, 1H), 7.89−7.22 (m, 9H), 2.38 (s, 3H); $[\alpha]^{20}_D$ = +117.1 (*c* 1.5, $CHCl_3$).

General Procedure for the Syntheses of *N*-Sulfinyl Alkoxydienyl Amines 4. A solution of freshly sublimated *t*-BuOK (4.5 mmol, 504 mg, 7.5 equiv) in THF (10 mL) was cooled to −78 °C. 1,1-Diethoxybut-2-ene (1.8 mmol, 259 mg, 3 equiv) in THF (2 mL) and *n*-BuLi (1.6 M in hexanes, 4.5 mmol, 2.81 mL) were added in quick succession, and the mixture was stirred for 2 h during which time the temperature was raised to −40 °C. Afterward the reaction was cooled to −90 °C, and a 0.20 M solution of the appropriate sulfinimine (0.6 mmol) in THF was added dropwise over about 1.5 h. Once the addition was completed, a saturated NH_4Cl solution (10 mL) was added. The resulting mixture was extracted with Et_2O (3 × 10 mL), washed with water (10 mL) and brine (2 × 10 mL), and dried with anhydrous K_2CO_3. After filtration and evaporation of the solvent, the crude products were purified by flash column chromatography.

***N*-((*S*,*R*$_S$,*E*)-2-Ethoxy-1-phenylpenta-2,4-dienyl)-4-methylbenzenesulfinamide (4a).** Purified by flash chromatography (alumina, Et_2O/petroleum ether 1:1, R_f 0.40) to give **4a** (106 mg, 52%) as a white solid: ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.57−7.45 (m, 2H), 7.20−7.09 (m, 7H), 6.39 (dt, *J* = 16.5, 10.5 Hz, 1H), 5.32 (d, *J* = 10.5 Hz, 1H) superimposed to 5.39 (d, *J* = 8.0 Hz, 1H), 5.07 (d, *J* = 8.0 Hz, 1H) superimposed to 5.00 (dd, *J* = 16.5, 1.9 Hz, 1H), 4.82 (dd, *J* = 10.5, 1.9 Hz, 1H), 3.84 (qd, *J* = 7.0, 2.4 Hz, 2H), 2.29 (s, 3H), 1.21 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (50.2 MHz, $CDCl_3$) δ 154.9 (s), 140.3 (s), 140.2 (s), 139.0 (s), 129.9 (d), 128.4 (d), 127.2 (d), 126.3 (d), 125.8 (d), 124.9 (d), 112.6 (t), 101.4 (d), 62.1 (t), 52.4 (d), 20.4 (q), 13.4 (q); MS *m*/*z* 341 (M^+, 9), 244 (16), 202 (84), 172 (88), 139 (100), 91 (89), 77 (80); $[\alpha]^{21}_D$ = −68.1 (*c* 0.9, CH_2Cl_2); mp 116 °C. Anal. Calcd for $C_{20}H_{23}NO_2S$: C, 70.35; H, 6.79. Found: C, 70.03; H, 6.47. ***N*-((*R*,*S*$_S$,*E*)-2-Ethoxy-1-phenylpenta-2,4-dienyl)-4-methylbenzenesulfinamide** was prepared by the above procedure using the corresponding S_S sulfinimine. Purified by flash chromatography (alumina, Et_2O/petroleum ether 1:1, R_f 0.40, 129 mg, 63% yield) as a white solid: $[\alpha]^{21}_D$ = +68.1 (*c* 1.0, CH_2Cl_2); mp 116 °C. Spectral data identical to those of **4a**.

***N*-((*S*,*R*$_S$,*E*)-2-ethoxy-1-*p*-tolylpenta-2,4-dienyl)-4-methylbenzenesulfinamide (4b).** Purified by flash chromatography (alumina, Et_2O/petroleum ether 1:1, R_f 0.35) to give **4b** (127 mg, 59%) as a white solid: ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.52 (d, *J* = 8.2 Hz, 2H), 7.17 (d, *J* = 8.2 Hz, 2H), 7.06−6.90 (m, 4H), 6.38 (dt, *J* = 16.5, 10.4 Hz, 1H), 5.32 (d, *J* = 10.4 Hz, 1H) superimposed to 5.27 (d, *J* = 7.9 Hz, 1H), 5.01 (d, *J* = 7.9 Hz, 1H) superimposed to 4.96 (dd, *J* = 16.5, 1.9 Hz, 1H), 4.81 (dd, *J* = 10.4, 1.9 Hz, 1H), 3.76 (qd, *J* = 7.0, 2.3 Hz, 2H), 2.31 (s, 3H), 2.22 (s, 3H), 1.22 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (50.2 MHz, $CDCl_3$) δ 155.1 (s), 140.2 (s, 2C), 135.9 (s, 2C), 129.9 (d), 128.4 (d), 127.9 (d), 125.7 (d), 124.9 (d), 112.5 (t), 101.3 (d), 62.1 (t), 52.4 (d), 20.3 (q), 20.0 (q), 13.4 (q); MS *m*/*z* 355 (M^+, 29), 258 (18), 216 (98), 186 (89), 149 (100), 91 (89), 77 (49); $[\alpha]^{25}_D$ = −64.6 (*c* 1.4, CH_2Cl_2); mp 121 °C. Anal. Calcd for $C_{21}H_{25}NO_2S$: C, 70.95; H, 7.09. Found: C, 70.83; H, 6.89. ***N*-((*R*,*S*$_S$,*E*)-2-Ethoxy-1-*p*-tolylpenta-2,4-dienyl)-4-methylbenzenesulfinamide** was prepared by the above procedure using the corresponding S_S sulfinimine. Purified by flash chromatography (alumina, Et_2O/petroleum ether 1:1, R_f 0.35, 121 mg, 57% as a white solid: $[\alpha]^{25}_D$ = +64.6 (*c* 1.2, CH_2Cl_2); mp 121 °C. Spectral data identical to those of **4b**.

Scheme 3. Removal of the Chiral Auxiliary and Hydrolysis of the Vinyl Ether Function



***N*-((*S*,R_S,*E*)-2-Ethoxy-1-(4-methoxyphenyl)penta-2,4-dienyl)-4-methylbenzenesulfinamide (4c).** Purified by flash chromatography (alumina, Et_2O/petroleum ether 3:2, R_f 0.30) to give **4c** (122 mg, 55%) as a pale yellow solid: ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.52 (d, J = 8.2 Hz, 2H), 7.17 (d, J = 8.2 Hz, 2H), 7.05 (d, J = 8.8 Hz, 2H), 6.67 (d, J = 8.8 Hz, 2H), 6.39 (dt, J = 16.5, 10.5 Hz, 1H), 5.31 (d, J = 10.5 Hz, 1H) superimposed to 5.25 (d, J = 7.9 Hz, 1H), 5.02 (d, J = 7.9 Hz, 1H) superimposed to 4.95 (dd, J = 16.5, 1.8 Hz, 1H), 4.82 (dd, J = 10.5, 1.8 Hz, 1H), 3.78 (qd, J = 7.0, 2.3 Hz, 2H) superimposed to 3.68 (s, 3H), 2.31 (s, 3H), 1.23 (t, J = 7.0 Hz, 3H); ^{13}C NMR (50.2 MHz, $CDCl_3$) δ 158.6 (s), 155.9 (s), 141.1 (s), 141.0 (s), 131.9 (s), 130.7 (d), 129.2 (d), 127.8 (d), 125.7 (d), 113.4 (t), 113.3 (d), 102.0 (d), 62.9 (t), 55.0 (q), 52.9 (d), 21.1 (q), 14.2 (q); MS m/z 371 (M^+, 8), 274 (44), 232 (100), 202 (68), 187 (98), 91 (88), 77 (97); $[\alpha]^{25}_D$ = −44.0 (c 0.8, CH_2Cl_2); mp 123 °C. Anal. Calcd for $C_{21}H_{25}NO_3S$: C, 67.89; H, 6.78. Found: C, 67.80; H, 6.55. ***N*-((*R*,S_S,*E*)-2-Ethoxy-1-(4-methoxyphenyl)penta-2,4-dienyl)-4-methylbenzenesulfinamide** was prepared by the above procedure using the corresponding S_S sulfinimine.. Purified by flash chromatography (alumina, Et_2O/petroleum ether 3:2, R_f 0.30, 134 mg, 60% as a pale yellow solid: $[\alpha]^{25}_D$ = +44.0 (c 1.6, CH_2Cl_2); mp 123 °C. Spectral data identical to those of **4c**. ***N*-((*R*,R_S,*E*)-2-Ethoxy-1-*p*-tolylpenta-2,4-dienyl)-4-methylbenzenesulfinamide (minor diastereoisomer).** Purified by flash chromatography (alumina, Et_2O/petroleum ether 1:1, R_f 0.32) to give **4c′** as a pale yellow solid: ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.59 (d, J = 8.1 Hz, 2H), 7.27−7.08 (m, 4H), 7.00 (d, J = 8.1 Hz, 2H), 6.28 (dt, J = 16.6, 10.5 Hz, 1H), 5.47 (d, J = 10.0 Hz, 1H), 5.29 (d, J = 10.0 Hz, 1H), 5.02 (d, J = 10.5 Hz, 1H), 4.91 (dd, J = 16.6, 1.2 Hz, 1H), 4.81 (dd, J = 10.5, 1.2 Hz, 1H), 3.47 (dq, J = 9.2, 7.0 Hz, 1H), 3.13 (dq, J = 9.2, 7.0 Hz, 1H), 2.32 (s, 3H), 2.23 (s, 3H), 1.04 (t, J = 7.0 Hz, 3H).

N*-((*R*,R_S,*E*)-2-Ethoxy-1-(thiophene-2-yl)penta-2,4-dienyl)-4-methylbenzenesulfinamide (4d).** Purified by flash chromatography (alumina, Et_2O/petroleum ether 3:2, R_f 0.40) to give **4d** (114 mg, 55%) as a yellow solid: ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.57 (d, J = 8.2 Hz, 2H), 7.22 (d, J = 8.2 Hz, 2H), 7.07 (dd, J = 5.1, 1.3 Hz, 1H), 6.75 (dd, J = 5.1, 3.5 Hz, 1H), 6.64 (dt, J = 3.5, 1.3 Hz, 1H), 6.27 (dt, J = 16.5, 10.6 Hz, 1H), 5.43 (d, J = 7.8 Hz, 1H), 5.32 (d, J = 10.6 Hz, 1H), 5.20 (d, J = 7.8 Hz, 1H), 5.02 (dd, J = 16.5, 1.8 Hz, 1H), 4.83 (dd, J = 10.6, 1.8 Hz, 1H), 3.78 (qd, J = 7.0, 2.3 Hz, 2H), 2.33 (s, 3H), 1.23 (t, J = 7.0 Hz, 3H); ^{13}C NMR (50.2 MHz, $CDCl_3$) δ 155.2 (s), 143.7 (s), 141.2 (s), 140.4 (s), 130.4 (d), 129.3 (d), 126.3 (d), 125.9 (d), 124.9 (d), 124.7 (d), 113.7 (t), 101.8 (d), 63.2 (t), 49.7 (d), 21.2 (q), 14.2 (q); MS m/z 347 (M^+, 21), 250 (63), 208 (100), 91 (73), 55 (82); $[\alpha]^{21}_D$ = −45.7 (c 1.3, CH_2Cl_2); mp 104 °C. Anal. Calcd for $C_{18}H_{21}NO_2S_2$: C, 62.21; H, 6.09. Found: C, 62.09; H, 5.88.N*-((*S*,S_S,*E*)-2-Ethoxy-1-(thiophene-2-yl)penta-2,4-dienyl)-4-methylbenzenesulfinamide** was prepared by the above procedure using the corresponding S_S sulfinimine. Purified by flash chromatography (alumina, Et_2O/petroleum ether 3:2, R_f 0.40, 122 mg, 58%) as a yellow solid: $[\alpha]^{21}_D$ = +45.7 (c 0.8, CH_2Cl_2); mp 104 °C. Spectral data identical to those of **4d**.

***N*-((*S*,R_S,1*E*,4*E*)-4-Ethoxy-1-phenylhepta-1,4,6-trien-3-yl)-4-methylbenzenesulfinamide (4e).** Purified by flash chromatography (alumina, Et_2O/petroleum ether 1:1, R_f 0.30) to give **4e** (120 mg, 55%) as a white solid: ^{1}H NMR (200 MHz, $CDCl_3$) δ δ 7.70−7.47 (m, 2H), 7.28−7.11 (m, 7H), 6.44 (dt, J = 16.6, 10.5 Hz, 1H), 6.19 (d, J = 15.9 Hz, 1H), 6.01 (dd, J = 15.9, 6.3 Hz, 1H), 5.30 (d, J = 10.8 Hz, 1H), 5.03 (dd, J = 16.6, 2.0 Hz, 1H) superimposed to 4.94 (d, J = 6.3 Hz, 1H), 4.87 (dd, J = 10.5, 2.0 Hz, 1H) superimposed to 4.80 (d, J = 10.8 Hz, 1H), 3.78 (qd, J = 7.0, 2.5 Hz, 2H), 2.30 (s, 3H), 1.27 (t, J = 7.0 Hz, 3H); ^{13}C NMR (50.2 MHz, $CDCl_3$) δ 155.4 (s), 141.2 (s), 141.1 (s), 136.3 (s), 131.2 (d), 130.6 (d), 129.3 (d), 128.2 (d), 127.7 (d), 127.4 (d), 126.3 (d), 125.8 (d), 113.4 (t), 101.9 (d), 62.9 (t), 52.4 (d), 21.1 (q), 14.2 (q); MS m/z 367 (M^+, 15), 270 (25), 229 (83), 198 (100), 139 (85), 91 (90), 77 (85); $[\alpha]^{20}_D$ = −78.9 (c 1.0, CH_2Cl_2); mp 111 °C. Anal. Calcd for $C_{22}H_{25}NO_2S$: C, 71.90; H, 6.86. Found: C, 71.64; H, 6.73. ***N*-((*R*,S_S,1*E*,4*E*)-4-Ethoxy-1-phenylhepta-1,4,6-trien-3-yl)-4-methylbenzenesulfinamide** was prepared by the above procedure using the corresponding S_S sulfinimine. Purified by flash chromatography (alumina, Et_2O/petroleum ether 1:1, R_f 0.30, 123 mg, 56%) as a white solid: $[\alpha]^{20}_D$ = +78.9 (c 1.0, CH_2Cl_2); mp 111 °C. Spectral data identical to those of **4e**.

***N*-((*S*,R_S,*E*)-4-Ethoxy-2,2-dimethylhepta-4,6-dien-3-yl)-4-methylbenzenesulfinamide (4f).** Purified by flash chromatography (alumina, Et_2O/petroleum ether 1:1, R_f 0.20) to give **4f** (101 mg, 53%) as a pale yellow solid: ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.47 (d, J = 8.2 Hz, 2H), 7.21 (d, J = 8.2 Hz, 2H), 6.24 (dt, J = 16.6, 10.4 Hz, 1H), 5.27 (d, J = 10.4 Hz, 1H), 4.94 (dd, J = 16.6, 1.9 Hz, 1H), 4.76 (dd, J = 10.4, 1.9 Hz, 1H) superimposed to 4.71 (d, J = 9.8 Hz, 1H), 3.79 (d, J = 9.8 Hz, 1H) superimposed to 3.68 (q, J = 7.0 Hz, 2H), 2.33 (s, 3H), 1.21 (t, J = 7.0 Hz, 3H), 0.73 (s, 9H); ^{13}C NMR (50.2 MHz, $CDCl_3$) δ 156.6 (s), 141.6 (s), 140.9 (s), 131.6 (d), 129.1 (d), 125.6 (d), 112.2 (t), 102.5 (d), 62.3 (t), 58.8 (t), 34.9 (s), 26.9 (q), 21.1 (q), 14.3 (q); MS m/z 321 (M^+, 1), 264 (13), 182 (13), 139 (100), 124 (86), 96 (46), 80 (13); $[\alpha]^{21}_D$ = −66.3 (c 1.8, CH_2Cl_2); mp 79 °C. Anal. Calcd for $C_{18}H_{27}NO_2S$: C, 67.25; H, 8.47. Found: C, 67.10; H, 8.12. ***N*-((*R*,S_S,*E*)-4-Ethoxy-2,2-dimethylhepta-4,6-dien-3-yl)-4-methylbenzenesulfinamide** was prepared by the above procedure using the corresponding S_S sulfinimine. Purified by flash chromatography (alumina, Et_2O/petroleum ether 1:1, R_f 0.20, 111 mg, 58%) as a pale yellow solid: $[\alpha]^{21}_D$ = +66.3 (c 2.2, CH_2Cl_2); mp 79 °C. Spectral data identical to **4f**.

General Procedure for the Syntheses of Alkoxydienyl Amines 5. A solution of the appropriate *N*-sulfinyl alkoxydienyl amine (0.5 mmol) in MeOH (3 mL) was cooled to 0 °C using an ice/water bath, and TFA (1.75 mmol, 130 μL, 3.5 equiv) was added dropwise. After 10 min, the solution was warmed to rt and stirred for an additional time of 1 h. When the reaction was complete, the mixture was quenched with a NaOH solution (10%). After extraction with Et_2O (3 × 10 mL), the organic layers were washed with water (10 mL) and brine (2 × 10 mL), and dried with anhydrous K_2CO_3. After filtration and evaporation

dx.doi.org/10.1021/jo1024943 |*J. Org. Chem.* 2011, 76, 1814–1820

of the solvent, the crude products were purified by flash column chromatography.

(*S*,*E*)-2-Ethoxy-1-phenylpenta-2,4-dien-1-amine (5a). Purified by flash chromatography (Et_2O/petroleum ether 7:3, 1% Et_3N, R_f 0.30) to give **5a** (92 mg, 91%) as a yellow oil: ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.49−7.03 (m, 5H), 6.56 (dt, J = 16.6, 10.5 Hz, 1H), 5.27 (d, J = 10.5 Hz, 1H), 4.98 (dd, J = 16.6, 1.9 Hz, 1H) superimposed to 4.97 (s, 1H), 4.79 (dd, J = 10.5, 1.9 Hz, 1H), 3.69 (qd, J = 7.0, 2.5 Hz, 2H), 1.83 (br, 2H), 1.18 (t, J = 7.0 Hz, 3H); ^{13}C NMR (50.2 MHz, $CDCl_3$). δ 158.1 (s), 142.2 (s), 130.5 (d), 127.2 (d), 125.8 (d), 125.3 (d), 111.5 (t), 100.3 (d), 61.8 (t), 52.5 (d), 13.3 (q). MS m/z 203 (M^+, 57), 174 (53), 158 (52), 129 (40), 106 (100), 77 (64); $[\alpha]^{20}_D$ = −159.0 (c 1.1, CH_2Cl_2). Anal. Calcd for $C_{13}H_{17}NO$: C, 76.81; H, 8.43. Found: C, 76.79; H, 8.26. **(*R*,*E*)-2-Ethoxy-1-phenylpenta-2,4-dien-1-amine** was obtained by the above procedure starting from *N*-((*R*,S_S,*E*)-2-ethoxy-1-phenylpenta-2,4-dienyl)-4-methylbenzenesulfinamide. Purified by flash chromatography (Et_2O/petroleum ether 7:3, 1% Et_3N, R_f 0.30, 100 mg, 99%) as a yellow oil: $[\alpha]^{20}_D$ = +159.0 (c 0.5, CH_2Cl_2). Spectral data identical to those of **5a**.

(*S*,*E*)-2-Ethoxy-1-*p*-tolylpenta-2,4-dien-1-amine (5b). Purified by flash chromatography (CH_2Cl_2/petroleum ether 4:1, 1% Et_3N, R_f 0.70) to give **5b** (99 mg, 92%) as a red oil: ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.24 (d, J = 7.9 Hz, 2H), 7.06 (d, J = 7.9 Hz, 2H), 6.58 (dt, J = 16.6, 10.4 Hz, 1H), 5.29 (d, J = 10.4 Hz, 1H), 4.99 (ddd, J = 16.6, 2.0, 0.7 Hz, 1H) superimposed to 4.97 (s, 1H), 4.81 (ddd, J = 10.4, 2.0, 0.4 Hz, 1H), 3.73 (qd, J = 7.0, 2.5 Hz, 2H), 2.27 (s, 3H), 1.90 (br, 2H), 1.22 (t, J = 7.0 Hz, 3H); ^{13}C NMR (50.2 MHz, $CDCl_3$) δ 159.0 (s), 140.2 (s), 136.3 (s), 131.4 (d, 2C), 128.7 (d, 2C), 126.0 (d), 112.2 (t), 101.0 (d), 62.6 (t), 53.1 (d), 20.8 (q), 14.2 (q); MS m/z 217 (M^+, 100), 188 (65), 172 (54), 120 (74), 96 (31), 77 (15); $[\alpha]^{22}_D$ = −37.5 (c 1.0, CH_2Cl_2). Anal. Calcd for $C_{14}H_{19}NO$: C, 77.38; H, 8.81. Found: C, 77.26; H, 8.79. **(*R*,*E*)-2-Ethoxy-1-*p*-tolylpenta-2,4-dien-1-amine** was obtained by the above procedure starting from (*R*,S_S,*E*)-2-ethoxy-1-*p*-tolylpenta-2,4-dienyl)-4-methylbenzenesulfinamide. Purified by flash chromatography (CH_2Cl_2/petroleum ether 4:1, 1% Et_3N, R_f 0.70, 104 mg, 96%) as a red oil: $[\alpha]^{22}_D$ = +37.5 (c 1.2, CH_2Cl_2). Spectral data identical to those of **5b**.

(*S*,*E*)-2-Ethoxy-1-(4-methoxyphenyl)penta-2,4-dien-1-amine (5c). Purified by flash chromatography (CH_2Cl_2, 1% Et_3N, R_f 0.85) to give **5c** (108 mg, 93%) as a yellow oil: ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.23 (d, J = 8.8 Hz, 2H), 6.75 (d, J = 8.8 Hz, 2H), 6.54 (dt, J = 16.6, 10.5 Hz, 1H), 5.24 (d, J = 10.8 Hz, 1H), 4.96 (dd, J = 16.6, 2.0 Hz, 1H) superimposed to 4.95 (s, 1H), 4.77 (dd, J = 10.5, 2.0 Hz, 1H), 3.73 (qd, J = 7.0, 2.5 Hz, 2H) superimposed to 3.68 (s, 3H), 1.75 (br, 2H), 1.18 (t, J = 7.0 Hz, 3H); ^{13}C NMR (50.2 MHz, $CDCl_3$) δ 159.2 (s), 158.3 (s), 135.3 (s), 131.4 (d), 127.2 (d), 113.4 (d), 112.2 (t), 100.9 (d), 62.6 (t), 55.0 (q), 52.8 (d), 14.2 (q); MS m/z 233 (M^+, 96), 204 (38), 188 (45), 136 (100), 121 (38), 109 (20), 96 (29); $[\alpha]^{21}_D$ = −68.9 (c 1.0, CH_2Cl_2). Anal. Calcd for $C_{14}H_{19}NO_2$: C, 72.07; H, 8.21. Found: C, 71.94; H, 8.09. **(*R*,*E*)-2-Ethoxy-1-(4-methoxyphenyl)penta-2,4-dien-1-amine was** obtained by the above procedure starting from *N*-((*R*,S_S,*E*)-2-ethoxy-1-(4-methoxyphenyl)penta-2,4-dienyl)-4-methylbenzenesulfinamide. Purified by flash chromatography (CH_2Cl_2, 1% Et_3N, R_f 0.85,104 mg, 89%) as a yellow oil: $[\alpha]^{21}_D$ = +68.9 (c 0.4, CH_2Cl_2). Spectral data identical to those of **5c**.

(*R*,*E*)-2-Ethoxy-1-(thiophen-2-yl)penta-2,4-dien-1-amine (5d). Purified by flash chromatography (CH_2Cl_2, 1% Et_3N, R_f 0.75) to give **5d** (98 mg, 94%) as a brown oil: ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.18 (dd, J = 4.5, 1.8 Hz, 1H), 6.94 (d, J = 4.5 Hz, 1H) superimposed to 6.91 (d, J = 1.8 Hz, 1H), 6.56 (dt, J = 16.6, 10.5 Hz, 1H), 5.37 (d, J = 10.5 Hz, 1H), 5.25 (s, 1H), 5.08 (dd, J = 16.6, 1.8 Hz, 1H), 4.89 (dd, J = 10.5, 1.8 Hz, 1H), 3.74 (qd, J = 7.0, 2.4 Hz, 2H), 1.93 (br, 2H), 1.31 (t, J = 7.0 Hz, 3H); ^{13}C NMR (50.2 MHz, $CDCl_3$) δ 157.9 (s), 147.6 (s), 131.0 (d), 126.4 (d), 124.1 (d), 123.5 (d), 112.8 (t), 101.1 (d), 62.8 (t), 50.2 (d), 29.5 (q), 14.2 (q); MS m/z 209 (M^+, 46), 180 (25), 162 (38), 135 (35), 112 (100), 97 (29), 85 (44); $[\alpha]_D^{21}$ = −65.8 (c 1.0, CH_2Cl_2). Anal. Calcd for $C_{11}H_{15}NOS$: C, 63.12; H, 7.22. Found: C, 63.01; H, 7.16. **(*S*,*E*)-2-Ethoxy-1-(thiophene-2-yl)penta-2,4-dien-1-amine** was obtained by the above procedure starting from *N*-((*S*,S_S,*E*)-2-ethoxy-1-(thiophene-2-yl)penta-2,4-dienyl)-4-methylbenzenesulfinamide. Purified by flash chromatography (CH_2Cl_2, 1% Et_3N, R_f 0.75, 100 mg, 96%) as a brown oil: $[\alpha]^{21}_D$ = +65.8 (c 1.3, CH_2Cl_2). Spectral data identical to those of **5d.**

(*S*,1*E*,4*E*)-4-Ethoxy-1-phenylhepta-1,4,6-trien-3-amine (5e). Purified by flash chromatography (CH_2Cl_2, 1% Et_3N, R_f 0.70) to give **5e** (99 mg, 87%) as a yellow oil: ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.38−7.09 (m, 5H), 6.51 (dt, J = 16.6, 10.1 Hz, 1H) superimposed to 6.47 (dd, J = 16.0, 2.0 Hz, 1H), 6.24 (dd, J = 16.0, 6.3 Hz, 1H), 5.26 (d, J = 10.1 Hz, 1H), 4.99 (dd, J = 16.6, 2.1 Hz, 1H), 4.81 (dd, J = 10.1, 2.1 Hz, 1H), 4.53 (d, J = 6.3 Hz, 1H), 3.75 (q, J = 7.0 Hz, 2H), 1.73 (br, 2H), 1.26 (t, J = 7.0 Hz, 3H); ^{13}C NMR (50.2 MHz, $CDCl_3$) δ 158.6 (s), 136.8 (s), 131.2 (d), 129.4 (d), 128.3 (d), 127.2 (d), 126.2 (d), 112.2 (t), 100.7 (d), 62.6 (t), 52.3 (d), 14.2 (q); MS m/z 229 (M^+, 48), 214 (60), 200 (62), 117 (100), 84 (61), 69 (36); $[\alpha]^{21}_D$ = −40.4 (c 1.0, CH_2Cl_2). Anal. Calcd for $C_{15}H_{19}NO$: C, 78.56; H, 8.35. Found: C, 78.37; H, 8.28. **(*R*,1*E*,4*E*)-4-Ethoxy-1-phenylhepta-1,4,6-trien-3-amine** was obtained by the above procedure starting from *N*-((*S*,S_S,*E*)-2-ethoxy-1-(thiophene-2-yl)penta-2,4-dienyl)-4-methylbenzenesulfinamide. Purified by flash chromatography (CH_2Cl_2, 1% Et_3N, R_f 0.70,96 mg, 84%) as a yellow oil: $[\alpha]^{21}_D$ = +40.4 (c 1.0, CH_2Cl_2). Spectral data identical to those of **5e**

(*S*,*E*)-4-Ethoxy-2,2-dimethylhepta-4,6-dien-3-amine (5f). Purified by flash chromatography (CH_2Cl_2, 1% Et_3N, R_f 0.60) to give **5f** (84 mg, 92%) as a yellow oil: ^{1}H NMR (200 MHz, $CDCl_3$) δ 6.36 (dt, J = 16.6, 10.4 Hz, 1H), 5.18 (d, J = 10.4 Hz, 1H), 4.85 (ddd, J = 16.6, 2.0, 0.7 Hz, 1H), 4.66 (ddd, J = 10.4, 2.0, 0.7 Hz, 1H), 3.63 (q, J = 7.0 Hz, 2H), 3.39 (s, 1H), 1.47 (br, 2H), 1.17 (t, J = 7.0 Hz, 3H), 0.81 (s, 9H); ^{13}C NMR (50.2 MHz, $CDCl_3$) δ 159.5 (s), 132.3 (d), 111.0 (t), 101.7 (d), 62.0 (t), 57.9 (d), 34.9 (s), 27.1 (q), 14.2 (q); MS m/z 183 (M^+, 5), 126 (56), 80 (100); $[\alpha]^{21}_D$ = +30.4 (c 1.0, CH_2Cl_2). Anal. Calcd for $C_{11}H_{21}NO$: C, 72.08; H, 11.55. Found: C, 71.94; H, 11.39. **(*R*,*E*)-4-Ethoxy-2,2-dimethylhepta-4,6-dien-3-amine** obtained by the above procedure starting from *N*-((*R*,S_S,*E*)-4-ethoxy-2,2-dimethylhepta-4,6-dien-3-yl)-4-methylbenzenesulfinamide. Purified by flash chromatography (CH_2Cl_2, 1% Et_3N, R_f 0.60, 83 mg, 91%) as a yellow oil: $[\alpha]^{21}_D$ = −30.4 (c 1.1, CH_2Cl_2). Spectral data identical to those of **5f.**

General Procedure for the Syntheses of *N*-Fmoc Alkoxydienyl Amines 6. A solution of 9-fluorenylmethoxycarbonyl chloride (Fmoc-Cl, 129 mg, 0.5 mmol, 1 equiv) in anhydrous Et_2O (5 mL) was cooled to 0 °C, and the appropriate alkoxydienyl amine (0.5 mmol) was slowly added. After 10 min, the solution was warmed to rt and stirred for 1 h, and the reaction progress was monitored by TLC. Then water (1 mL) was added, and the reaction mixture was stirred for an additional time of 5 min. The resulting mixture was then extracted with Et_2O (3 × 10 mL), washed with brine, and dried with anhydrous Na_2SO_4. After filtration and evaporation of the solvent, crude products were purified by column flash chromatography.

(*S*,*E*)-(9*H*-Fluoren-9-yl)methyl 2-ethoxy-1-phenylpenta-2,4-dienylcarbamate (6a). Purified by flash chromatography (alumina, EtOAc/petroleum ether 1:4, R_f 0.65) to give **6a** (165 mg, 78%) as a white solid: ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.73 (d, J = 7.2 Hz, 2H), 7.58 (d, J = 7.2 Hz, 2H), 7.43−7.14 (m, 9H), 6.67 (dt, J = 16.6, 10.4 Hz, 1H), 5.97 (d, J = 9.0 Hz, 1H), 5.75 (d, J = 9.0 Hz, 1H), 5.42 (d, J = 10.4 Hz, 1H), 5.09 (dd, J = 16.6, 1.5 Hz, 1H), 4.92 (dd, J = 10.4, 1.5 Hz, 1H), 4.44 (d, J = 6.7 Hz, 2H), 4.21 (t, J = 6.7 Hz, 1H), 3.78 (qd, J = 7.1, 2.4 Hz, 2H), 1.22 (t, J = 7.1 Hz, 3H); ^{13}C NMR (50.2 MHz, $CDCl_3$) δ 155.6 (s), 154.7 (s), 143.8 (s, 2C), 143.7 (s), 141.1 (s, 2C), 130.9 (d), 128.3 (d, 2C), 127.5 (d, 2C), 127.2 (d, 2C), 126.8 (d), 126.2 (d, 2C),

124.9 (d, 2C), 119.8 (d, 2C), 113.7 (t), 102.7 (d), 66.6 (t), 62.9 (t), 52.6 (d), 47.2 (d), 14.2 (q); MS *m/z* 425 (M^+, 6), 328 (14), 238 (35), 223 (26), 195 (100), 179 (23), 165 (46), 77 (68), 51 (52); $[\alpha]^{20}_D$ = −36.6 (*c* 1.3, CH_2Cl_2); mp 86 °C. Anal. Calcd for $C_{28}H_{27}NO_3$: C, 79.03; H, 6.40. Found: C, 78.88; H, 6.29.

(*R,E*)-(9*H*-Fluoren-9-yl)methyl 2-Ethoxy-1-(4-methoxyphenyl)penta-2,4-dienylcarbamate (6c). Purified by flash chromatography (alumina, EtOAc/petroleum ether 3:7, R_f 0.60) to give **6c** (193 mg, 85%) as a pale pink solid: ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.72 (d, *J* = 7.3 Hz, 2H), 7.56 (d, *J* = 7.2 Hz, 2H), 7.44−7−07 (m, 6H), 6.80 (d, *J* = 8.6 Hz, 2H), 6.63 (dt, *J* = 16.6, 10.3 Hz, 1H), 5.90 (d, *J* = 9.0 Hz, 1H), 5.70 (d, *J* = 9.0 Hz, 1H), 5.38 (d, *J* = 10.3 Hz, 1H), 5.06 (dd, *J* = 16.6, 1.8 Hz, 1H), 4.90 (dd, *J* = 10.3, 1.8 Hz, 1H), 4.41 (d, *J* = 7.2 Hz, 2H), 4.19 (t, *J* = 7.2 Hz, 1H), 3.76 (q, *J* = 7.0 Hz, 2H) superimposed to 3.74 (s, 3H), 1.26 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (50.2 MHz, $CDCl_3$) δ 158.7 (s), 155.6 (s), 154.9 (s), 143.8 (s), 143.7 (s, 2C), 141.1 (s, 2C), 131.8 (d, 2C), 130.9 (d, 2C), 127.4 (d, 2C), 126.8 (d), 124.8 (d, 2C), 119.8 (d, 2C), 114.1 (d, 2C), 113.6 (t), 102.4 (d), 66.6 (t), 62.9 (t), 55.1 (q), 47.1 (d), 14.2 (q); MS *m/z* 455 (M^+, 3), 358 (11), 238 (39), 223 (31), 217 (19), 195 (100), 165 (44), 91 (53), 77 (61), 51 (39); $[\alpha]^{21}_D$ = +52.5 (*c* 1.0, CH_2Cl_2); mp 98 °C. Anal. Calcd for $C_{29}H_{29}NO_4$: C, 76.46; H, 6.42. Found: C, 76.35; H, 6.37.

(*R,E*)-(9*H*-Fluoren-9-yl)methyl 4-Ethoxy-2,2-dimethylhepta-4,6-dien-3-ylcarbamate (6f). Purified by flash chromatography (alumina, EtOAc/petroleum ether 1:9, R_f 0.40) to give **6f** (168 mg, 83%) as a pale yellow solid: ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.71 (d, *J* = 7.0 Hz, 2H), 7.54 (d, *J* = 7.2 Hz, 2H), 7.42−7.14 (m, 4H), 6.54 (dt, *J* = 16.5, 10.4 Hz, 1H), 5.32 (d, *J* = 10.4 Hz, 1H), 4.98 (dd, *J* = 16.5, 1.7 Hz, 1H), 4.82 (dd, *J* = 10.4, 1.7 Hz, 1H), 4.55 (d, J = 10.1 Hz, 1H), 4.40, (d, *J* = 10.1 Hz, 1H), 4.23 (t, *J* = 7.2 Hz, 1H), 4.07 (d, *J* = 7.2 Hz, 2H), 3.73 (q, *J* = 7.0 Hz, 2H), 1.26 (t, *J* = 7.0 Hz, 3H), 0.90 (s, 9H); ^{13}C NMR (50.2 MHz, $CDCl_3$). δ 155.9 (s), 155.3 (s), 143.8 (s, 2C), 141.1 (s, 2C), 131.9 (d, 2C), 127.4 (d, 2C), 126.8 (d), 124.8 (d, 2C), 119.7 (d, 2C), 112.5 (t), 103.1 (d), 66.4 (t), 62.3 (t), 47.1 (d), 35.5 (s), 26.9 (q), 14.3 (q); MS *m/z* 405 (M^+, 9), 308 (21), 238 (46), 223 (31), 195 (100), 182 (22) 165 (39), 57 (44); $[\alpha]^{21}_D$ = −25.4 (*c* 1.0, CH_2Cl_2); mp 78 °C. Anal. Calcd for $C_{26}H_{31}NO_3$: C, 77.01; H, 7.71. Found: C, 76.89; H, 7.62.

General Procedure for the Syntheses of *N*-Fmoc Aminopentenones 7. A solution of *N*-Fmoc alkoxydienyl amine (0.5 mmol) in CH_2Cl_2 (2 mL) was stirred in the presence of Amberlyst-15 and the reaction monitored by TLC. When the reaction was complete, a small amount of anhydrous K_2CO_3 was added, and after filtration and evaporation of the solvent, crude products were purified by column flash chromatography.

(*S,E*)-(9*H*-Fluoren-9-yl)methyl 2-oxo-1-phenylpent-3-enylcarbamate (7a). Purified by flash chromatography (alumina, EtOAc/petroleum ether 1:4, R_f 0.40) to give **7a** (151 mg, 76%) as a white solid: ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.74 (d, *J* = 7.5 Hz, 2H), 7.56 (d, *J* = 5.9 Hz, 2H), 7.46−7.16 (m, 9H), 7.04 (dq, *J* = 16.9, 6.9 Hz, 1H), 6.37 (d, *J* = 6.2 Hz, 1H), 6.12 (dd, *J* = 16.9, 1.5 Hz, 1H), 5.50 (d, *J* = 6.2 Hz, 1H), 4.32 (d, *J* = 6.6 Hz, 2H), 4.19 (t, *J* = 6.6 Hz, 1H), 1.81 (dd, *J* = 6.9, 1.5 Hz, 3H); ^{13}C NMR (50.2 MHz, $CDCl_3$) δ 192.6 (s), 154.4 (s), 144.7 (d), 142.8 (s), 142.7 (s), 140.2 (s, 2C), 135.7 (s), 128.1 (d), 127.5 (d), 127.1 (d), 126.7 (d), 126.6 (d), 126.0 (d), 124.0 (d), 118.9 (d), 65.9 (t), 61.9 (d), 46.1 (d), 17.4 (q); MS *m/z* 397 (M^+, 5), 328 (9), 238 (22), 223 (100), 174 (61), 77 (78), 51 (31); $[\alpha]_D^{20}$ = +48.2 (*c* 1.0, CH_2Cl_2); mp 81 °C. Anal. Calcd for $C_{26}H_{23}NO_3$: C, 78.57; H, 5.83. Found: C, 78.39; H, 5.71.

(*R,E*)-(9*H*-Fluoren-9-yl)methyl 1-(4-Methoxyphenyl)-2-oxopent-3-enylcarbamate (7c). Purified by flash chromatography (alumina, EtOAc/petroleum ether 3:7, R_f 0.40) to give **7c** (194 mg, 91%) as a white solid: ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.67 (d, *J* = 7.4 Hz, 2H), 7.49 (d, *J* = 6.9 Hz, 2H), 7.37−7.13 (m, 6H), 6.96 (dq, *J* = 16.0, 6.9 Hz, 1H) superimposed to 6.81 (d, *J* = 8.4 Hz, 2H), 6.24 (d, *J* = 6.2 Hz, 1H), 6.03 (dd, *J* = 16.0, 1.2 Hz, 1H), 5.36 (d, *J* = 6.2 Hz, 1H), 4.25 (d, *J* = 6.6 Hz, 2H), 4.11 (t, *J* = 6.6 Hz, 1H), 3.71 (s, 3H), 1.74 (dd, *J* = 6.9, 1.2 Hz, 3H); ^{13}C NMR (50.2 MHz, $CDCl_3$) δ 192.7 (s), 158.6 (s), 154.4 (s), 144.4 (d), 142.8 (s, 2C), 140.2 (s, 2C), 130.9 (d, 2C), 128.4 (s), 126.6 (d), 126.0 (d, 2C), 124.1 (d, 2C), 118.9 (d, 2C), 113.5 (d, 2C), 113.3 (d, 2C), 65.9 (t), 61.2 (d), 54.3 (q), 46.1 (d), 17.4 (q). MS *m/z* 427 (M^+, 8), 328 (11), 238 (41), 223 (100), 189 (48), 77 (62), 51 (34); $[\alpha]^{20}_D$ = −62.8 (*c* 1.2, CH_2Cl_2); mp 80 °C. Anal. Calcd for $C_{27}H_{25}NO_4$: C, 75.86; H, 5.89. Found: C, 75.79; H, 5.82.

(*R,E*)-(9*H*-Fluoren-9-yl)methyl 2,2-Dimethyl-4-oxohept-5-en-3-ylcarbamate (7f). Purified by flash chromatography (alumina, EtOAc/petroleum ether 3:7, R_f 0.70) to give **7f** (168 mg, 89%) as a white solid: ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.68 (d, *J* = 7.0 Hz, 2H), 7.51 (d, *J* = 7.2 Hz, 2H), 7.41−7.13 (m, 4H), 6.92 (dq, *J* = 15.6, 6.9 Hz, 1H), 6.18 (dd, *J* = 15.6, 1.1 Hz, 1H), 5.54 (d, *J* = 9.4 Hz, 1H), 4.43 (d, *J* = 9.4 Hz, 1H), 4.27 (d, *J* = 6.7 Hz, 2H), 4.15 (t, *J* = 6.7 Hz, 1H), 1.84 (dd, *J* = 6.9, 1.1 Hz, 3H), 0.90 (s, 9H); ^{13}C NMR (50.2 MHz, $CDCl_3$) δ 197.9 (s), 155.2 (s), 143.4 (s), 142.9 (d), 142.8 (s), 140.3 (s, 2C), 130.5 (d), 126.6 (d, 2C), 126.0 (d, 2C), 124.1 (d, 2C), 118.9 (d, 2C), 65.9 (t), 63.2 (d), 46.2 (d), 34.4 (s), 25.8 (q), 17.4 (q); MS *m/z* 377 (M^+, 11), 308 (12), 238 (38), 223 (100), 57 (40); $[\alpha]^{20}_D$ = −22.5 (*c* 1.0, CH_2Cl_2); mp 77 °C. Anal. Calcd for $C_{24}H_{27}NO_3$: C, 76.36; H, 7.21. Found: C, 76.15; H, 7.08.

■ ASSOCIATED CONTENT

Supporting Information. Detailed experimental procedures and copies of ^{1}H NMR and ^{13}C NMR spectra and X-ray crystallographic data (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author
*E-mail: cristina.prandi@unito.it.

■ ACKNOWLEDGMENT

We thank Regione Piemonte for financial support. We are grateful to Prof. Ernesto G. Occhiato for helpful discussions.

■ REFERENCES

(1) Davis, F. A. *J. Org.. Chem.* **2006**, *71* (24), 8993–9003.
(2) Ellman, J. A.; Owens, T. D.; Tang, T. P. *Acc. Chem. Res.* **2002**, *35* (11), 984–995.
(3) Robak, M. T.; Herbage, M. A.; Ellman, J. A. *Chem. Rev.* **2010**, *110* (6), 3600–3740.
(4) Zhou, P.; Chen, B. C.; Davis, F. A. *Tetrahedron* **2004**, *60* (37), 8003–8030.
(5) Asensio, A.; Bravo, P.; Crucianelli, M.; Farina, A.; Fustero, S.; Soler, J. G.; Meille, S. V.; Panzeri, W.; Viani, F.; Volonterio, A.; Zanda, M. *Eur. J. Org. Chem.* **2001**, 1449.
(6) Koriyama, Y.; Nozawa, A.; Hayakawa, R.; Shimizu, M. *Tetrahedron* **2002**, 58.
(7) Chan, W. H.; Lee, A. W. M.; Xia, P. F.; Wong, W. Y. *Tetrahedron Lett.* **2000**, *41*, 5725.
(8) Dragoli, D. R.; Burdett, M. T.; Ellman, J. A. *J. Am. Chem. Soc.* **2001**, *123*, 10127–10128.
(9) Li, G.; Kim, S. H.; Wei, H.-X. *Tetrahedron* **2000**, *56*, 719.
(10) Evans, D. A.; Miller, S. J.; Lectka, T.; von Matt, P. *J. Am. Chem. Soc.* **1999**, *121*, 7559–7573.
(11) Evans, D. A.; Barnes, D. M.; Johnson, J. S.; Lectka, R.; von Matt, P.; Miller, S. J.; Murry, J. A.; Norcross, R. D.; Shaughnessy, E. A.; Campos, K. R. *J. Am. Chem. Soc.* **1999**, *121* (33), 7582–7594.
(12) Cogan, D. A.; Ellman, J. A. *J. Am. Chem. Soc.* **1999**, *121*, 268.

(13) Plobeck, N.; Powell, D. *Tetrahedron: Asymmetry* **2002**, *13*, 303.
(14) Pflum, D. A.; Krishnamurthy, D.; Han, Z.; Wald, S. A.; Senanayake, C. H. *Tetrahedron Lett.* **2002**, *43*, 923.
(15) Mabic, S.; Cordi, A. A. *Tetrahedron* **2001**, *57*, 8861.
(16) Davis, F. A.; Srirajan, V.; Fanelli, D. L.; Portonovo, P. *J. Org. Chem.* **2000**, *65*, 7663.
(17) Davis, F. A.; Zhang, H.; Lee, S. H. *Org. Lett.* **2001**, 759.
(18) Louvel, J.; Botuha, C.; Chemla, F.; Demont, E.; Ferreira, F.; Perez-Luna, A. *Eur. J. Org. Chem.* **2010**, *15*, 2921–2926.
(19) Fandrick, D. R.; Johnson, C. S.; Fandrick, K. R.; Reeves, J. T.; Tan, Z.; Lee, H.; Song, J. J.; Yee, N. K.; Senanayake, C. H. *Org. Lett.* **2010**, *12*, 748–751.
(20) Davis, F. A.; Theddu, N. *J. Org. Chem.* **2010**, *75*, 3814–3820.
(21) Davis, F. A.; M., S. *Org. Lett.* **2007**, *9* (12), 2413–2416.
(22) Davis, F. A.; Nolt, M. B.; Wu, Y.; Prasad, K. R.; Li, D.; Yang, B.; Bowen, K.; Lee, S. H.; Eardley, J. H. *J. Org. Chem.* **2004**, *70*, 2184–2190.
(23) Schlosser, M. *J. Organomet. Chem.* **1967**, *8*, 9.
(24) Mordini, A.; Snieckus, V. *Adv. Carbanion Chem.* **1992**, 1.
(25) Lochmann, L. *Eur. J. Inorg. Chem.* **2000**, *6*, 1115–1126.
(26) Blangetti, M.; Deagostino, A.; Prandi, C.; Tabasso, S.; Venturello, P. *Org. Lett.* **2009**, *11*, 3914–3917 and references cited therein.
(27) Solladie, G.; Hutt, J.; Girardin, A. *Synthesis* **1987**, 173.
(28) Davis, F. A.; Reddy, R. E.; Szewczyk, J. M.; Reddy, G. V.; Portonovo, P. S.; Zhang, H.; Fanelli, D.; Thimma Reddy, R.; Zhou, P.; Carroll, P. J. *J. Org. Chem.* **1997**, *62*, 2555.
(29) Fernandez, I.; Khiar, N.; M., L. J.; Alcudia, F. *J. Org. Chem.* **1992**, 6789.
(30) Cogan, D. A.; Liu, G.; Kim, K.; Backes, B. J.; Ellman, J. A. *J. Am. Chem. Soc.* **1998**, *120*, 8011.
(31) Bernoud, E.; Le Duc, G.; Bantreil, X.; Prestat, G.; Madec, D.; Poli, G. *Org. Lett.* **2010**, *12* (2), 320–323.
(32) Kanazawa, A. M.; Denis, J. N.; Greene, A. E. *J. Org. Chem.* **1994**, *59*, 1234.
(33) Thioester **C** has been recovered in 42% yield under these reaction conditions. An alternative explanation could be the attack of the nucleophile at sulfur; to this purpose we tried *tert*-butansulfinylimine (*E*)-*N*-benzylidene-2-methylpropane-2-sulfinamide under the same reaction conditions but the yield remained low.
(34) Enantiomeric purity has been verified using $Eu(hfc)_3$ as chiral shift reagent.
(35) HCl, TFA, triflic acid, and chloromethanesulfonic acid were used as acidic catalysts under various conditions, but in every case the unreacted alkoxydienylamine **5** was recovered.