JOC The Journal of Organic Chemistry

Note

pubs.acs.org/joc

Stepwise Formation of 1,3-Diazolium-4-thiolates by Münchnone Cycloadditions: Promising Candidates for Nonlinear Optics

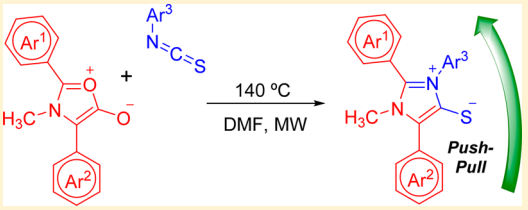
David Cantillo,*[†,§] Martín Ávalos,[†] Reyes Babiano,[†] Pedro Cintas,[†] José L. Jiménez,[†] Mark E. Light,[‡] Juan C. Palacios,[†] and Rocío Porro[†]

[†]Departamento de Química Orgánica e Inorgánica, QUOREX Research Group, Facultad de Ciencias, Universidad de Extremadura, E-06006, Badajoz, Spain

[‡]Department of Chemistry, University of Southampton, Highfield, Southampton, U.K., SO17 1BJ

Supporting Information

ABSTRACT: An improved preparation of mesoionic heterocycles 1,3-diazolium-4-thiolates by [3 + 2] cycloadditions of münchnones with aryl isothiocyanates is reported. The process takes place with high or complete regioselectivity, and fast and clean transformations are observed under microwave heating in DMF. DFT calculations support that this cycloaddition proceeds preferably through a stepwise mechanism. Given the pattern substitution around the mesoionic ring resulting in a push−pull system, theoretical estimations predict large hyperpolarizabilities in some cases, which is typical of molecules exhibiting nonlinear optical responses.



Mesoionic rings, by virtue of their dipolar nature, are not only suitable partners in cycloaddition reactions but also promising candidates for optoelectronic applications combining donor and acceptor moieties. In the course of our studies directed toward the preparation of stable mesoionic heterocycles that could be regarded as precursors of new NLO materials, we have described recently the synthesis of 2-amino-1,3-thiazolium-4-thiolate systems by stepwise thionation of 2-aminothioisomünchnones with aryl isothiocyanates.[1] In this context, the reaction of münchnones (1,3-oxazolium-5-olates) with other heterocumulenes (CS_2) leading to 1,3-thiazolium-5-thiolate derivatives has also been revisited.[2] In this case, however, it was found that both the concerted cycloaddition and the retrocycloaddition tandem reactions compete favorably with the stepwise thionation. It is noteworthy that, within mesoionic heterocycles, münchnones still attract considerable attention as their regio- and stereochemical outcome cannot easily be predicted, and recent theoretical studies provide further insight into the actual mechanistic pathway.[3,4]

Herein, we report an experimental and theoretical study aimed at designing a new series of 1,3-diazolium-4-thiolates from the corresponding münchnones and aryl isothiocyanates. Although an example of this transformation was first reported by Huisgen and co-workers more than four decades ago,[5] neither has the procedure in question been synthetically explored in detail nor has its rationale been assessed.

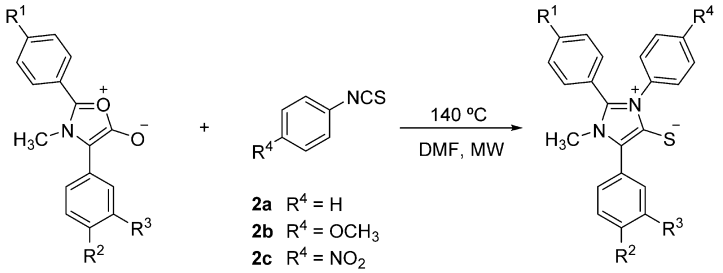
Syntheses of 1,3-diazolium-4-thiolates (**3a**−**3i**) were carried out by reaction of the corresponding münchnones (**1a**−**1c**)[2,6] with an excess of the corresponding *para*-substituted aryl isothiocyanate (**2a**−**2c**) (Scheme 1). In agreement with the seminal protocol,[5] reactions were first attempted in refluxing toluene, but most reactions were sluggish, often low yielding, and required at least 6 h for completion. Under prolonged heating, decomposition of the starting münchnone was a common drawback, partly accounting for poor yields of the isolated products. Thus, we decided to move to a polar solvent such as DMF, susceptible of dielectric heating, at higher temperatures to enhance the reaction and minimize decomposition of the starting material. Gratifyingly, when DMF was used as solvent in combination with rapid heating at 140 °C in a microwave (MW) oven, clean reactions were obtained in very short times (<10 min) (see the Experimental Section for details).

The results obtained for the reactions of münchnones **1a**−**1c** with aryl isothiocyanates (**2a**−**2c**) are collected in Table 1. Reactions of **1a** with either **2a** or **2c** led to mixtures of two isomeric products (**3a** + **3a′** and **3c** + **3c′**), although **3b** was the only product isolated from the reaction of **1a** with **2b**. However, the corresponding reactions of münchnones **1b** and **1c** with the same isothiocyanates (**2a**−**2c**) occurred in a regiospecific manner, and only one mesoionic product (**3d**−**3i**) could be detected and isolated. The structure of **3e** could be confirmed by X-ray diffraction (see Figure S1a, Supporting Information). Likewise, the solid-state structure of **3a′**, which corresponds to the regioisomer of the expected 1,3-diazolium-4-thiolate **3a**, was also unequivocally assigned by single-crystal X-ray diffraction (Figure S1b, Supporting Information). In compound **3a′**, the aryl group linked to carbon atoms adopts a coplanar arrangement with the mesoionic core, thereby favoring electron delocalization, while the aryl group joined to the nitrogen atom shows a perpendicular disposition with the heterocyclic ring. Such structural features are also shared by

Received: February 24, 2014
Published: April 10, 2014

 © 2014 American Chemical Society dx.doi.org/10.1021/jo500349g | J. Org. Chem. 2014, 79, 4201−4205

Scheme 1



1a $R^1 = NO_2$; $R^2 = OCH_3$; $R^3 = H$
1b $R^1 = OCH_3$; $R^2 = H$; $R^3 = NO_2$
1c $R^1 = R^2 = H$; $R^3 = NO_2$

3a $R^1 = NO_2$; $R^2 = OCH_3$; $R^3 = R^4 = H$
3a' $R^1 = OCH_3$; $R^2 = NO_2$; $R^3 = R^4 = H$
3b $R^1 = NO_2$; $R^2 = R^4 = OCH_3$; $R^3 = H$
3c $R^1 = R^4 = NO_2$; $R^2 = OCH_3$; $R^3 = H$
3c' $R^1 = OCH_3$; $R^2 = R^4 = NO_2$; $R^3 = H$
3d $R^1 = OCH_3$; $R^2 = R^4 = H$; $R^3 = NO_2$
3e $R^1 = R^4 = OCH_3$; $R^2 = H$; $R^3 = NO_2$
3f $R^1 = OCH_3$; $R^2 = H$; $R^3 = R^4 = NO_2$
3g $R^1 = R^2 = R^4 = H$; $R^3 = NO_2$
3h $R^1 = R^2 = H$; $R^3 = NO_2$; $R^4 = OCH_3$
3i $R^1 = R^2 = H$; $R^3 = R^4 = NO_2$

Table 1. Reactions of Münchnones 1a−1c with Isothiocyanates 2a−2c[a]

reactants	time (min)	product	yield (%)[b]
1a + **2a**	10	**3a** + **3a′**	30 + 42
1a + **2b**	10	**3b**	58
1a + **2c**	6	**3c** + **3c′**	39 + 55
1b + **2a**	10	**3d**	57
1b + **2b**	10	**3e**	23
1b + **2c**	5	**3f**	48
1c + **2a**	3	**3g**	49
1c + **2b**	2.5	**3h**	24
1c + **2c**	1	**3i**	80

[a]Conditions: 0.8 mmol of **1**, 1 mL of DMF, 4.0 mmol of **2**. MW irradiation at 140 °C. [b]Isolated yield.

3e, which shows the expected regiochemistry for these cycloadditions.

From a mechanistic standpoint, the formation of 1,3-diazolium-4-thiolates **3** and **3′** may be rationalized by two possible approaches of the aryl isothiocyanate to the mesoionic heterocycle (Figure 1). The first approach (a) involves binding of the nucleophilic carbon atom (C-4) of **1** to the thiocarbonyl carbon of **2** to yield cycloadduct **4**, whereas the second approach (b) would lead to **4′** through the linkage of electrophilic C-2 and C═S carbon atoms of **1** and **2**, respectively. Both pathways would afford, after the loss of carbon dioxide, the regioisomeric heterocycles **3** and **3′** that can only be differentiated by the relative position of the thiolate group with respect to the two *para*-substituted aryl groups at the mesoionic ring. To shed light into the origin of the regioselectivity, we optimized at the M06-2X/6-311+G(d,p) level[7]/basis set[8] the structures of all stationary states involved in the two reaction channels (a) and (b) of münchnones **1a** and **1b** with aryl isothiocyanates **2a−2c**. Solvent effects were included in all geometry optimizations and frequency analyses, using the SMD method[9] and either toluene or DMF (vide infra) as solvents.[10]

Figure 1 shows the free energy profiles for the reaction of **1a** and **1b** with **2a**. In both cases, pathway (a) involves a stepwise process for which we have located two transition states and the corresponding zwitterionic intermediate. The cycloadduct formation is slightly exergonic, although the retrocycloaddition of carbon dioxide is very exergonic and releases more than 30 kcal mol^{-1} relative to the starting materials (see Table S1, Supporting Information). Remarkably, the formation of cycloadduct **4a′** derived from **1a** and **2a** through pathway (b) proceeds by a concerted process characterized by an energy barrier similar to that found for route (a) ($\Delta\Delta G^{\ddagger} < 3$ kcal mol^{-1}). This fact suggests that, in such a case, and presumably others with a similar substitution pattern, both routes might coexist, in agreement with the experimental results (see Table 1). However, for the reaction of **1b** with **2a**, route (b) would only be feasible after overcoming an energy barrier of ∼10 kcal mol^{-1} higher than that estimated for route (a). This energy difference accounts for the regiospecificity observed experimentally in the reactions of dipoles **1b** and **1c** with **2a−2c**. The presence of NO_2 and MeO substituents at the C-2 and C-4 positions of the parent münchnone **1a** most likely enhances its reactivity toward the concerted pathway, thereby decreasing the corresponding energy barrier. The cycloadditions of **1a** and **1b** with **2a** were also computationally assessed using DMF as solvent in the calculations. Notably, this solvent switching had no effect on the concertedness, and analogous energy profiles were obtained for both reactions (see Figure S2, Supporting Information). Data collected in Table S1 (Supporting Information) summarize the energy landscape for the cycloaddition of münchnones **1a** and **1b** with aryl isothiocyanates **2a−2c**. 4-Nitrophenyl isothiocyanate **2c** exhibits the highest reactivity with the münchnones, in close agreement with Sustmann's type I dipolar cycloaddtions (i.e., HOMO(dipole)-LUMO(dipolarophile)-controlled reactions).[11] Moreover, the computational data are also in agreement with the experimental results, as the reactions of the münchnones with **2c** proceeded faster than those of electron-rich aryl isothiocyanates **2a** and **2b** (cf. Table 1) and adequately predict the regioselectivity in all cases except for the reaction of **1a** with **2b**. In this case, the calculated barriers point to a nonregioselective reaction, albeit only a product could be experimentally observed. Alternative concerted or stepwise mechanisms for pathways (a) and (b)

dx.doi.org/10.1021/jo500349g | J. Org. Chem. 2014, 79, 4201−4205

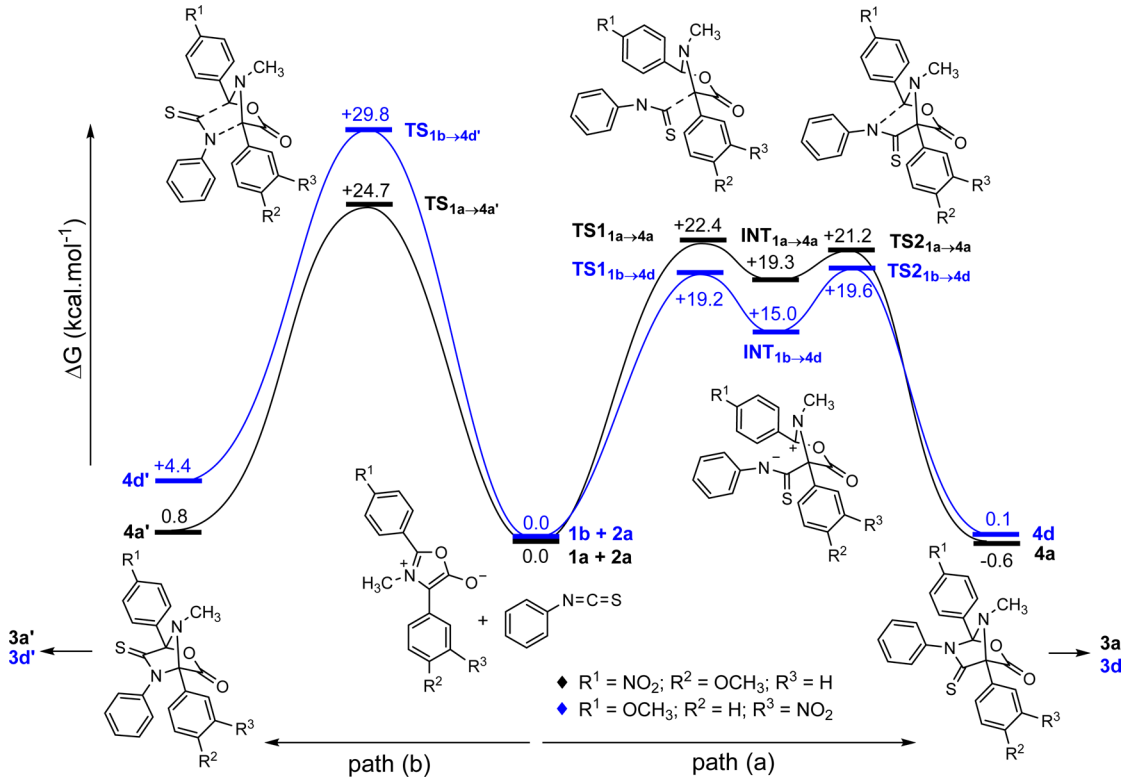


Figure 1. Free energy profiles for the formation of regioisomeric cycloadducts in the 1,3-dipolar cycloaddition of **1a** (black) and **1b** (blue) with **2a**. For the sake of clarity, the saddle points show the corresponding bond-forming processes only (dashed lines).

Table 2. $\beta(0)_{tot}$ and $\beta(\omega)_{tot}$[a] ($\times 10^{-30}$ esu) Calculated for 3a−3i by the FF and CPHF Methods

	FF[b]	CPHF[c]			FF[b]	CPHF[c]	
compound	$\beta(0)_{tot}$	$\beta(0)_{tot}$	$\beta(\omega)_{tot}$	compound	$\beta(0)_{tot}$	$\beta(0)_{tot}$	$\beta(\omega)_{tot}$
3a	366.8	112.6	149.7	**3e**	35.3	8.9	13.0
3a′	114.4	29.3	36.0	**3f**	23.0	10.4	12.4
3b	363.8	109.9	146.5	**3g**	39.4	17.6	21.6
3c	355.8	106.9	141.8	**3h**	34.6	11.1	21.5
3c′	88.8	21.4	26.4	**3i**	34.0	15.8	22.9
3d	29.1	9.2	11.7	**3j**[d]	52.3	21.0	27.1

[a] ω = 1064 nm. [b] B3LYP/6-31+G(d). [c] HF/6-31+G(d). [d] **3j**: $R^1 = R^2 = R^3 = R^4$ = H.

were also explored. However, in both cases, stationary points accounting for a single reaction channel could be located. To further rationalize the concerted vs stepwise mechanisms for the cycloadditions of münchnones with isothiocynates, we constructed the potential energy surfaces for the approaches (a) and (b). A simple mathematical analysis[12] of theoretical data demonstrated the stepwise character leading to cycloadduct formation through pathway (a), and a concerted, yet a very asynchronous mechanism, for pathway (b) (see the Supporting Information for a more detailed discussion on other plausible reaction channels and PES analyses).

In contrast with their parent münchnones, which are relatively unstable and decompose when stored for long periods, 1,3-diazolium-4-thiolates (**3a−3i**) are very stable as solid materials or in solution. Furthermore, the presence of electron-donating and electron-withdrawing groups at the ends of the 1,3-diazolium-4-thiolate ring with extended π-conjugation suggests that such substances could be a new family of nonlinear optical materials. Second-order NLO properties of the aforementioned mesoionic compounds were estimated by calculating their molecular hyperpolarizabilities using the coupled perturbed Hartree−Fock (CPHF) and the finite-field (FF) methods implemented in the Gaussian 09 software package.[13] To establish an adequate level of theory for the estimation of the NLO properties, we performed a series of calculations for the hyperpolarizabilities of two model compounds, 4-nitroaniline (pNA) and 4-dimethylamino-4′-nitrostilbene (DANS), known for their good NLO properties (see Table S2 in the Supporting Information). Using the finite-field (FF) method, good results, close to the experimental values, were obtained when the B3LYP density functional was employed in conjunction with a basis set containing diffuse functions. Also, the CPHF method worked well when diffuse functions were added. Thus, we decided to calculate the hyperpolarizabilities of compounds **3a−3i** using both the FF and the CPHF methods at the B3LYP/6-31+G(d) and HF/6-31+G(d) levels, respectively. High hyperpolarizabilities (Table 2) were obtained for 1,3-diazolium-4-thiolates (regioisomers **3**) possessing an electron-withdrawing group attached to the C-2 atom and an electron-releasing group at the C-5 carbon atom. This effect is particularly relevant when the electron-deficient substituent is a nitro group. In contrast, the nature of the

dx.doi.org/10.1021/jo500349g | J. Org. Chem. 2014, 79, 4201−4205

substituent linked to the N-3 position, which comes from the isothiocyanate moiety, has little or no influence on the magnitude of the hyperpolarizability. However, the β value of **3d** is remarkably smaller than that calculated for **3a′**, thus reflecting the importance of the position occupied by the electron-withdrawing substituent. Although the 1,3-diazolium-4-thiolate ring substituted with simple phenyl groups (**3j**) also exhibits a certain hyperpolarizability, the push−pull character of the mesoionic system is greatly enhanced by the introduction of electron-withdrawing and electron-donating groups. Analysis of the frontier molecular orbitals for **3c** (Figure S4, Supporting Information), one of the three 1,3-diazolium-4-thiolates showing a high hyperpolarizability, revealed that the HOMO is formerly located on the ring fragment where the negative charge (MeO-C_6H_4-C═C-S^-) exists, whereas the LUMO orbital is located on the acceptor fragment of the push−pull system (O_2N-C_6H_4-C═N^+−). This spatial separation of frontier orbitals unveils the charge transfer of the HOMO−LUMO transition as well as the required overlapping through the C-2 carbon atom to obtain large nonlinear responses.[14] It is worth pointing out that some β values collected in Table 2 for mesoionic compounds **3** are significantly higher than those of standard compounds taken as NLO references, pNA and DANS, calculated at the same levels of theory (see Table S2, Supporting Information).

In summary, the experimental results show that 1,3-diazolium-4-thiolates, described for the first time several decades ago, can advantageously be obtained with high regioselectivity using a polar solvent such as DMF at high temperatures. DFT calculations suggest that the cycloaddition of münchnones **1a** or **1b** with phenyl isothiocyanate (**2a**) proceeds through a stepwise mechanism involving two transition states plus a zwitterionic intermediate. A competing concerted process may still occur for the cycloaddition of **1a** and **2a**, consistent with the experimental detection of both regioisomers. Reactions of münchnones **1b** and **1c** with aryl isothiocyanates follow apparently stepwise mechanisms based on energy considerations and supported by the stereochemical outcome. As inferred from theoretical calculations too, compounds **3a−3i** possess high hyperpolarizabilities that depend on the nature and position of electron-withdrawing substituents at the heterocyclic ring. These and previous results suggest that mesoionic systems constitute a promising, yet underestimated, family of molecules with large NLO responses waiting for practical applications.

EXPERIMENTAL SECTION

General Remarks. Solvents and reagents were purchased from standard commercial suppliers and used without further purification. 1,3-Oxazolium-5-olates (münchnones) **1a−1c** were prepared in a three-step sequence as reported previously.[6] The identity of the unknown compounds **3a−3i** was confirmed by their elemental analyses, mp's, and NMR data (Supporting Information).

Computational Details. All of the calculations reported in this work were carried out using the Gaussian 09 package.[13] The M06-2X[7] density functional method in conjunction with the 6-311+G(d,p) basis set was selected for all the geometry optimizations and frequency analysis. The geometries were optimized including solvation effects. For this purpose, the SMD[9] solvation method was employed, using toluene as solvent. Frequency calculations at 298.15 K on all the stationary points were carried out at the same level of theory as the geometry optimizations to ascertain the nature of the stationary points. Ground and transition states were characterized by none and one imaginary frequency, respectively. All of the presented relative energies are free energies at 298.15 K with respect to the reactants.

Reactions of 1,3-Oxazolium-5-olates with Aryl Isothiocyanates. A mixture of münchnone (0.8 mmol), aryl isothiocyanate (4.0 mmol), and DMF (1 mL) was placed in a pyrex 10 mL flask and heated in a MW oven (max. 500 W) (Milestone Ethos) at 140 °C (open vessel, internal probe temperature measurement) until the disappearance of the starting heterocycle (TLC analysis, benzene:acetonitrile, 2:1). The reaction mixture was cooled to room temperature, the solvent was evaporated to dryness, and the resulting residue was purified by column chromatography (benzene/acetonitrile).

1-Methyl-5-(4-methoxyphenyl)-2-(4-nitrophenyl)-3-phenyl-1,3-diazolium-4-thiolate (3a). This compound was hardly soluble in typical deuterated solvents, and as a result, a suitable ^{13}C NMR spectrum could not be recorded; (100 mg, 30%); mp 228−231 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.27 (d, J = 8.0 Hz, 2H), 8.11 (s, 2H), 7.32−7.14 (m, 7H), 6.83 (d, J = 8.0 Hz, 2H), 3.75 (s, 3H), 3.62 (s, 3H); IR (KBr, cm^{-1}) 1525, 1345, 1248. Anal. Calcd for $C_{23}H_{19}N_3O_3S$: C, 66.17; H, 4.59; N, 10.07; S, 7.68. Found: C, 65.87; H, 4.68; N, 9.90; S, 7.75.

1-Methyl-2-(4-methoxyphenyl)-5-(4-nitrophenyl)-3-phenyl-1,3-diazolium-4-thiolate (3a′). (140 mg, 42%); mp 192−194 °C; ^1H NMR (400 MHz, DMSO-d_6) δ 8.31 (s, 4H), 7.47−7.30 (m, 7H), 6.99 (d, J = 8.0 Hz, 2H), 3.76 (s, 3H), 3.60 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.4, 152.7, 145.2, 142.8, 137.7, 136.2, 132.8, 130.0, 129.6, 129.1, 124.7, 123.6, 116.1, 114.7, 55.8, 36.4; IR (KBr, cm^{-1}) 1531, 1348, 1230. Anal. Calcd for $C_{23}H_{19}N_3O_3S$: C, 66.17; H, 4.59; N, 10.07; S, 7.68. Found: C, 65.76; H, 4.81; N, 9.83; S, 7.70.

1-Methyl-3,5-bis(4-methoxyphenyl)-2-(4-nitrophenyl)-1,3-diazolium-4-thiolate (3b). (207 mg, 58%); mp 230−231 °C; ^1H NMR (400 MHz, DMSO-d_6) δ 8.30 (s, 4H), 7.47 (d, J = 8.0 Hz, 2H), 7.22 (d, J = 8.0 Hz, 2H), 7.01 (d, J = 8.0 Hz, 2H), 6.93 (d, J = 8.0 Hz, 2H), 3.78 (s, 3H), 3.76 (s, 3H), 3.60 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.4, 159.5, 145.2, 143.0, 137.8, 132.8, 130.7, 129.9, 128.8, 124.6, 123.5, 116.3, 114.7, 114.2, 55.8, 55.8, 36.3; IR (KBr, cm^{-1}) 1516, 1333, 1251. Anal. Calcd for $C_{24}H_{21}N_3O_4S$: C, 64.41; H, 4.73; N, 9.39; S, 7.17. Found: C, 64.03; H, 4.97; N, 9.31; S, 7.19.

1-Methyl-5-(4-methoxyphenyl)-2,3-bis(4-nitrophenyl)-1,3-diazolium-4-thiolate (3c). (144 mg, 39%); mp 206−207 °C; ^1H NMR (400 MHz, DMSO-d_6) δ 8.34−8.26 (m, 6H), 7.66 (d, J = 12.0 Hz, 2H), 7.50 (d, J = 8.0 Hz, 2H), 7.02 (d, J = 8.0 Hz, 2H), 3.77 (s, 3H), 3.63 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.7, 147.6, 145.4, 142.7, 141.8, 137.3, 132.9, 131.4, 130.1, 128.8, 125.0, 124.3, 123.7, 115.6, 114.9, 55.9, 36.4; IR (KBr, cm^{-1}) 1522, 1344, 1251. Anal. Calcd for $C_{23}H_{18}N_4O_5S$: C, 59.73; H, 3.92; N, 12.11; S, 6.93. Found: C, 59.45; H, 4.13; N, 12.02; S, 6.99.

1-Methyl-2-(4-methoxyphenyl)-3,5-bis(4-nitrophenyl)-1,3-diazolium-4-thiolate (3c′). (203 mg, 55%); mp 221−223 °C; ^1H NMR (400 MHz, DMSO-d_6) δ 8.27 (dd, J = 4.0 Hz, 12.0 Hz, 4H), 7.79 (t, J = 8.0 Hz, 4H), 7.68 (d, J = 8.0 Hz, 2H), 7.09 (d, J = 8.0 Hz, 2H), 3.83 (s, 3H), 3.58 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) 159.2, 159.2, 148.7, 147.7, 147.6, 132.8, 132.8, 132.2, 131.2, 124.3, 114.1, 55.7; IR (KBr, cm^{-1}) 1349, 1265. Anal. Calcd for $C_{23}H_{18}N_4O_5S$: C, 59.73; H, 3.92; N, 12.11; S, 6.93. Found: C, 59.67; H, 4.02; N, 12.23; S, 6.94.

1-Methyl-2-(4-methoxyphenyl)-5-(4-nitrophenyl)-3-phenyl-1,3-diazolium-4-thiolate (3d). (190 mg, 57%); mp 112−115 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.59 (s, 1H), 8.42 (d, J = 8.0 Hz, 1H), 8.19 (d, J = 8.0 Hz, 1H), 7.58 (t, J = 8.0 Hz, 1H), 7.40−7.28 (m, 5H), 7.22 (d, J = 8.0 Hz, 2H), 6.89 (d, J = 8.0 Hz, 2H), 3.81 (s, 3H), 3.66 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.7, 148.2, 136.8, 135.3, 131.8, 129.7, 129.3, 129.1, 128.7, 128.3, 124.6, 122.5, 115.2, 114.8, 113.7, 55.5, 35.5; IR (KBr, cm^{-1}) 1505, 1346, 1255. Anal. Calcd for $C_{23}H_{19}N_3O_3S$: C, 66.17; H, 4.59; N, 10.07; S, 7.68. Found: C, 66.09; H, 4.71; N, 10.19; S, 7.55.

1-Methyl-2,3-bis(4-methoxyphenyl)-5-(4-nitrophenyl)-1,3-diazolium-4-thiolate (3e). (83 mg, 23%); mp 209−211 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.59 (s, 1H), 8.44 (d, J = 8.0 Hz, 1H), 8.17 (t, J = 4.0 Hz, 1H), 7.21 (d, J = 8.0 Hz, 4H), 6.90 (t, J = 8.0 Hz,

dx.doi.org/10.1021/jo500349g | J. Org. Chem. 2014, 79, 4201−4205

4H), 3.82 (s, 3H), 3.78 (s, 3H), 3.65 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.6, 159.8, 148.2, 141.5, 136.8, 131.8, 131.4, 129.7, 129.6, 127.9, 124.6, 122.4, 115.3, 114.8, 114.4, 55.5, 55.5, 35.6; IR (KBr, cm^{-1}) 1513, 1344, 1252. Anal. Calcd for $C_{24}H_{21}N_3O_4S$: C, 64.41; H, 4.73; N, 9.39; S, 7.17. Found: C, 64.20; H, 4.85; N, 9.55; S, 6.71

1-Methyl-2-(4-methoxyphenyl)-3,5-bis(4-nitrophenyl)-1,3-diazolium-4-thiolate (3f). (177 mg, 48%); mp 139−141 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.94 (d, 1H), 8.32−8.17 (m, 4H), 7.79 (t, J = 8.0 Hz, 1H), 7.66 (d, J = 12.0 Hz, 2H), 7.50 (d, J = 8.0 Hz, 2H), 7.02 (d, J = 8.0 Hz, 2H), 3.77 (s, 3H), 3.61 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.6, 148.0, 147.6, 141.7, 136.1, 132.9, 131.3, 129.9, 129.3, 124.7, 124.3, 121.9, 115.6, 114.9, 113.9, 55.9, 35.9; IR (KBr, cm^{-1}) 1509, 1346, 1253. Anal. Calcd for $C_{23}H_{18}N_4O_5S$: C, 59.73; H, 3.92; N, 12.11; S, 6.93. Found: C, 59.63; H, 4.03; N, 12.08; S, 7.03.

1-Methyl-5-(4-nitrophenyl)-2,3-diphenyl-1,3-diazolium-4-thiolate (3g). (152 mg, 49%); mp 230−231 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62 (s, 1H), 8.42 (d, J = 8.0 Hz, 1H), 8.19 (d, J = 8.0 Hz, 1H), 7.68 (t, J = 8.0 Hz, 1H), 7.46−7.28 (m, 10H), 3.67 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13C NMR (101 MHz, CDCl3) δ 148.2, 140.9, 136.9, 135.1, 131.4, 131.2, 130.2, 129.7, 129.4, 129.3, 129.1, 128.7, 124.8, 123.5, 122.6, 35.5; IR (KBr, cm^{-1}) 1525, 1343. Anal. Calcd for $C_{22}H_{17}N_3O_2S$: C, 68.20; H, 4.42; N, 10.85; S, 8.28. Found: C, 67.90; H, 4.38; N, 10.85; S, 8.24.

1-Methyl-3-(4-methoxyphenyl)-5-(4-nitrophenyl)-2-phenyl-1,3-diazolium-4-thiolate (3h). (80 mg, 24%); mp 119−120 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (s, 1H), 8.45 (d, J = 8.0 Hz, 1H), 8.20 (d, J = 8.0 Hz, 1H), 7.68 (t, J = 8.0 Hz, 1H), 7.48−7.41 (m, 3H), 7.31 (d, J = 4.0 Hz, 2H), 7.23 (d, J = 8.0 Hz, 2H), 6.88 (d, J = 8.0 Hz, 2H), 3.78 (s, 3H), 3.67 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.9, 148.2, 141.1, 136.9, 131.4, 131.2, 130.2, 129.7, 129.7, 129.3, 127.7, 124.7, 123.6, 122.6, 114.4, 55.4, 35.5; IR (KBr, cm^{-1}) 1515, 1342, 1253. Anal. Calcd for $C_{23}H_{19}N_3O_3S$: C, 66.17; H, 4.59; N, 10.07; S, 7.68. Found: C, 66.39; H, 4.81; N, 10.38; S, 7.63.

1-Methyl-3,5-bis(4-nitrophenyl)-2-phenyl-1,3-diazolium-4-thiolate (3i). (275 mg, 80%); mp 135−136 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.64 (s, 1H), 8.30 (d, J = 8.0 Hz, 1H), 8.23−8.19 (m, 3H), 7.68 (t, J = 8.0 Hz, 1H), 7.59 (d, J = 8.0 Hz, 2H), 7.50 (t, J = 8.0 Hz, 1H), 8.45 (t, J = 8.0 Hz, 2H), 7.33 (d, J = 8.0 Hz, 2H), 3.69 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.2, 147.7, 140.5, 136.6, 131.9, 130.7, 130.2, 130.1, 129.8, 129.7, 126.2, 124.9, 124.3, 122.9, 35.6; IR (KBr, cm^{-1}) 1527, 1347. Anal. Calcd for $C_{22}H_{16}N_4O_4S$: C, 61.10; H, 3.73; N, 12.96; S, 7.41. Found: C, 61.02; H, 3.72; N, 13.13; S, 7.57.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Supplementary figures and tables, copies of ^{1}H and ^{13}C NMR spectra for all new compounds, crystallographic data for **3e** and **3a′**, and Cartesian coordinates and electronic energies for all calculated structures. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: david.cantillo@uni-graz.at.

Present Address

[§]Institute of Chemistry, Karl-Franzens-University Graz, Heinrichstrasse 28, A-8010 Graz, Austria.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This research was supported by the Ministry of Science and Innovation (Grant CTQ2010-18938/BQU), the Junta de Extremadura (Ayuda a Grupos Consolidados, Grant GRU10049) and FEDER. We are also grateful to CénitS and COMPUTAEX for allowing us the use of supercomputing facilities (LUSITANIA).

■ REFERENCES

(1) (a) Cantillo, D.; Ávalos, M.; Babiano, R.; Cintas, P.; Jiménez, J. L.; Light, M. E.; Palacios, J. C. *Org. Lett.* **2008**, *10*, 1079−1082. (b) Cantillo, D.; Ávalos, M.; Babiano, R.; Cintas, P.; Jiménez, J. L.; Light, M. E.; Palacios, J. C. *J. Org. Chem.* **2009**, *74*, 3698−3705. (c) Cantillo, D.; Ávalos, M.; Babiano, R.; Cintas, P.; Jiménez, J. L.; Light, M. E.; Palacios, J. C. *J. Org. Chem.* **2009**, *74*, 7644−7650.

(2) Cantillo, D.; Ávalos, M.; Babiano, R.; Cintas, P.; Jiménez, J. L.; Light, M. E.; Palacios, J. C.; Rodríguez, V. *Org. Biomol. Chem.* **2010**, *8*, 5367−5374.

(3) Lopchuk, J. M.; Hughes, R. P.; Gribble, G. W. *Org. Lett.* **2013**, *15*, 5218−5221.

(4) Morin, M. S. T.; St-Cyr, D. J.; Arndtsen, B. A.; Krenske, E. H.; Houk, K. N. *J. Am. Chem. Soc.* **2013**, *135*, 17349−17358.

(5) Huisgen, R.; Funke, E.; Schaefer, F. C.; Gotthardt, H.; Brunn, E. *Tetrahedron Lett.* **1967**, *8*, 1809−1814.

(6) Bayer, H. O.; Huisgen, R.; Knorr, R.; Schaefer, F. C. *Chem. Ber.* **1970**, *103*, 2581−2597.

(7) (a) Zhao, Y.; Truhlar, D. G. *J. Chem. Theory Comput.* **2006**, *3*, 289−300. (b) Zhao, Y.; Truhlar, D. G. *Acc. Chem. Res.* **2008**, *41*, 157−167. (c) Jissy, A. K.; Ashik, U. P. M.; Datta, A. *J. Phys. Chem. C* **2011**, *115*, 12530−12546.

(8) Sherrill, C. D.; Takatani, T.; Hohenstein, E. G. *J. Phys. Chem. A* **2009**, *113*, 10146−10159.

(9) Marenich, A. V.; Cramer, C. J.; Truhlar, D. G. *J. Phys. Chem. B* **2009**, *113*, 6378−6396.

(10) Regioselection remains essentially unchanged by solvent effects (either toluene or DMF). Since early thermal studies were conducted in toluene, the latter was employed in theoretical modeling.

(11) Sustmann, R. *Pure Appl. Chem.* **1974**, *40*, 569−593.

(12) Cantillo, D.; Ávalos, M.; Babiano, R.; Cintas, P.; Jiménez, J. L.; Palacios, J. C. *J. Phys. Org. Chem.* **2012**, *25*, 77−82.

(13) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, J. A., Jr.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, J. M.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, Ö; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. *Gaussian 09*, Revision D.01; Gaussian, Inc.: Wallingford, CT, 2009.

(14) Kanis, D. R.; Ratner, M. A.; Marks, T. J. *Chem. Rev.* **1994**, *94*, 195−242.