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Cascade Radical Reactions via α-(Arylsulfanyl)imidoyl Radicals: Competitive [4 + 2] and [4 + 1] Radical Annulations of Alkynyl Isothiocyanates with Aryl Radicals§

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Aryl radicals react with 2-(2-phenylethynyl)phenyl isothiocyanate through a novel radical cascade reaction entailing formation of α-(arylsulfanyl)imidoyl radicals and affording a new class of compounds, i.e. thiochromeno[2,3-*b*]indoles. These derivatives are formed as mixtures of substituted analogues arising from competitive [4 + 2] and [4 + 1] radical annulations. The isomer ratio is strongly dependent on the aryl substituent and is correlated to its capability to delocalize spin density. The presence of a methylsulfanyl group in the ortho-position of the initial aryl radical results in complete regioselectivity and better yields, as the consequence of both strong spin-delocalization effect, which promotes exclusive [4 + 1] annulation, and good radical leaving-group ability, which facilitates aromatization of the final cyclohexadienyl radical. Theoretical calculations support the hypothesis of competitive, independent [4 + 2] and [4 + 1] annulation pathways. They also suggest that rearrangement onto the sulfur atom of the [4 + 1] intermediate does not occur via a sulfuranyl radical but rather through either a transition state or a sulfur-centered (thioamidyl) radical; the latter is possibly the preferred route in the presence of an *o*-methylsulfanyl moiety that can act as a leaving group in the final *ipso*-cyclization process.

Introduction

Within the great outbreak of kinetic, mechanistic, and synthetic work carried out on radical reactions in the past decades, our group has drawn a special attention to imidoyl radicals. These species are very attractive intermediates that can be readily produced by addition of carbon- and heteroatom-centered radicals to isonitriles,[1] by hydrogen atom abstraction from imines,[2] and by homolytic fragmentation of certain imidoylic precursors.[3] As far as their synthetic potential is concerned, they have been shown to perform smooth intra- and intermolecular additions to double and triple carbon−carbon bonds, as well as cyclizations onto aromatic rings, sulfur atoms, and cyano groups. They have been therefore widely, efficiently employed in cyclizations, annulations, and cascade reactions leading to the construction of various heterocyclic nitrogen-containing compounds, including phenanthridines,[2e] quinolines,[2d,f,g,4] indoles,[5] benzotriazines,[2h] and quinoxalines.[4c,6]

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§ Dedicated to Prof. Antonio Tundo on the occasion of the 1st anniversary of his death.

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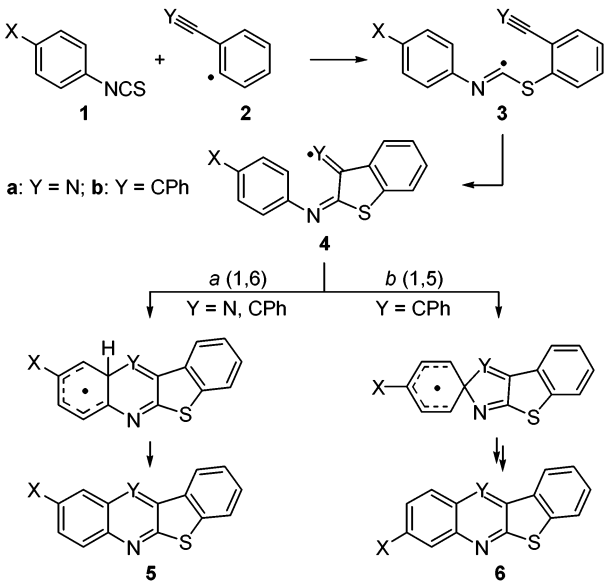
A further way to generate imidoyl radicals has involved the addition of carbon[7] and, especially, tin or silicon[8] radicals to the sulfur atom of isothiocyanates. Although known for a few decades, the resulting α-sulfanyl-substituted species have so far found only little use in organic synthesis. Indeed, only since the late eighties have they showed their synthetic appeal, first with the conversion of glycosyl isothiocyanates into glycosyl isonitriles and/or alditols,[8d] then with the Bachi synthesis of thiolactams and thiopyroglutamates from alkenyl isothiocyanates,[8e−g] and finally with the practicable alkyl-radical-mediated isomerization of the isothiocyanate moiety to the thiocyanate group reported by Barton in 1992.[7] Until 1997, Bachi's reaction has been the only example concerning the synthesis of heterocyclic compounds by radical addition to isothiocyanates, whereas Barton's work has been the only instance of addition of carbon-centered radicals to the sulfur atom of isothiocyanates.

In 1997 we reported a novel radical cascade reaction that involved carbon-centered radicals and aryl isothiocyanates and led to heterocycles containing both nitrogen and sulfur.[9] That reaction proceeded by 5-*exo*-*dig* cyclization onto the cyano group of α-[(2-cyanoaryl)sulfanyl]-imidoyl radicals **3a**, in turn obtained by addition of 2-cyanoaryl radicals **2a** to aryl isothiocyanates **1**; subsequent six-membered cyclization of the ensuing iminyl radical **4a** onto the aromatic ring of the original isothiocyanate allowed the one-pot synthesis of substituted benzothienoquinoxalines **5a** from commercially available or easily accessible materials (Scheme 1, path a). That paper was followed by the synthesis of benzothienoquinolines by a radical cascade reaction entailing, as in the previous work,[9] another rare [3 + 2] annulation[10] initiated by addition of 2-alkynylaryl radicals **2b** to aryl isothiocyanates.[11] However, unlike before,[9] this reaction yielded two isomeric quinoline derivatives, viz. **5b** and **6b**, arising through competitive six- and five-membered cyclizations of the final vinyl radical **4b** onto the aromatic ring of the isothiocyanate (Scheme 1, paths a and b).

The isomer ratio was found to depend on the nature of the X-substituent, with the "rearranged" isomer **6b** becoming more and more favored by increasing the electron-withdrawing capability of the substituent; this has been explained in terms of a SOMO/LUMO-controlled 1,5-cyclization of the slightly nucleophilic vinyl radical **4b** competing with a highly exothermic 1,6-cyclization dominated by enthalpic factors.[11]

SCHEME 1



To further explore the synthetic usefulness of isothiocyanate radical reactions and to get some more information on the stabilization and/or polar effects affecting the tandem cyclizations of the intermediate α-sulfanyl-substituted imidoyl radicals, we were next prompted to study the reaction of aryl radicals with 2-alkynyl-substituted aryl isothiocyanates. In particular, besides the access to a totally new class of heterocyclic compounds, we aimed at investigating the possible effects of both the aryl radical substituents and the isothiocyanate sulfur atom on the 1,5 and 1,6 competing cyclizations of the intermediate vinyl radicals. Herein we therefore report a new cascade radical reaction of 2-(phenylethynyl)-phenyl isothiocyanate with some aryl radicals that allows the one-pot synthesis of the polycondensed framework of substituted thiochromeno[2,3-*b*]indoles.

Results and Discussion

As before,[9,11] aryl radicals **8** were generated from the corresponding diazonium tetrafluoroborates **7** by reaction with potassium acetate in ethyl acetate at room temperature in the presence of [18-crown-6].[12] When isothiocyanate **9** was allowed to react with **7**, the 2-X- and 3-X-substituted 11-phenylthiochromeno[2,3-*b*]indoles **10** and **11** were obtained in 40−50% overall yield (Scheme 2 and Table 1).

None of the compounds **10** and **11** were previously reported in the literature and the general thiochromeno-[2,3-*b*]indole framework is completely unprecedented as well. The structures of **10** and **11** were confirmed by X-ray crystallographic analysis of derivatives **10b**,**c** and **11b**−**d**, and then by spectral analogies with the other congeners. In particular, a crucial support to structural assignment was brought by the peculiar ^{1}H NMR signal of the H-4 proton. Indeed, in almost all the examined

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SCHEME 2

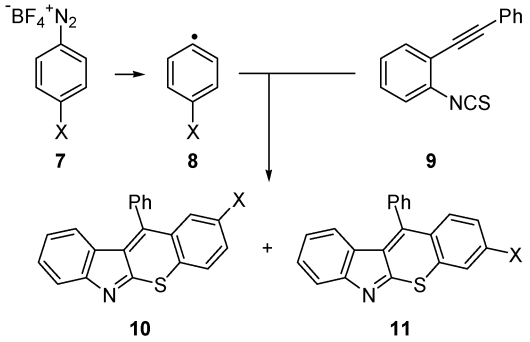


TABLE 1. Yields of Products 10 and 11 in the Reactions of Diazonium Salts 7 with Isothiocyanate 9

series	X	**10** (%)	**11** (%)	**10/11**
a	H	50		
b	CF_3	27	23	1.17
c	Cl	27	23	1.17
d	OMe	20	20	1.00
e	SMe	8	32	0.25
f	N_3	4	40	0.10
g	C(O)Me	2	43	0.05

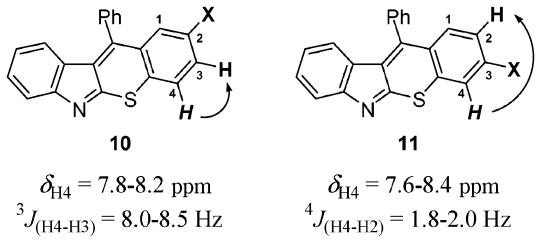


FIGURE 1. Structural assignment to **10** and **11** on the basis of their ^{1}H NMR spectra.

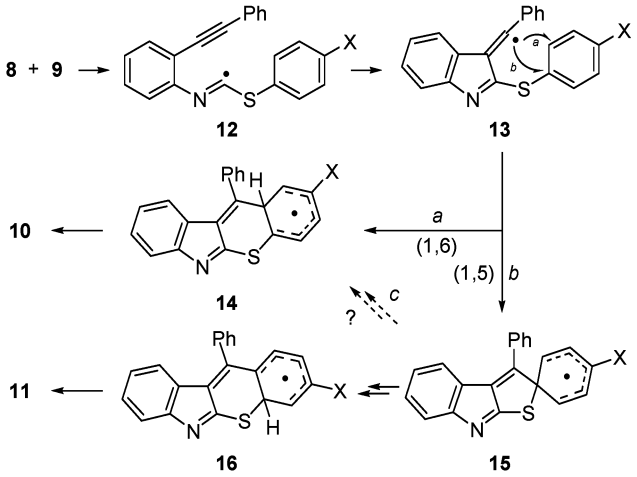
compounds, and mostly independently of the type of substituent, H-4 appeared as a doublet at the downfield limit of the spectrum: the magnitude of its coupling constant with H-3 (ortho-coupling, compounds **10**) or H-2 (meta-coupling, compounds **11**) was therefore diagnostic of the position of the X-substituent (Figure 1).

The reaction outcome can be accounted for through initial addition of the aryl radical to the sulfur atom of the isothiocyanate to give imidoyl radical **12**; subsequent cyclization of **12** onto the C−C triple bond leads to the vinyl radical **13**, which eventually undergoes two competitive 1,5- and 1,6-cyclizations onto the aromatic ring of the starting aryl radical (Scheme 3).

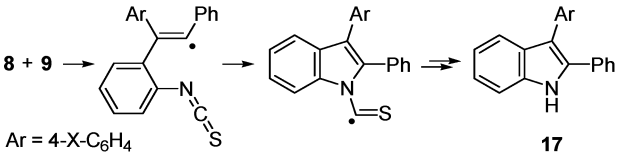
On one hand, 1,6-ring closure leads directly to the formation of the thiochromeno ring, whose sulfurated part can thus be seen as arising from a [4 + 2] radical annulation between radical **8** and isothiocyanate **9**; aromatization of cyclohexadienyl **14** eventually affords compound **10**. On the other hand, 1,5-cyclization produces the spirocyclohexadienyl radical **15**, whose thiophene ring is hence the result of a [4 + 1] annulation between **8** and **9**; ring expansion of radical **15** onto the sulfur atom followed by aromatization yields the isomeric compound **11**. The mechanism of such a ring expansion process will be discussed below.

The only identifiable reaction byproducts were indoles **17**. These compounds were isolated in very low (or even

SCHEME 3



SCHEME 4



nil) yields (<5%) and presumably arose from competing attack of the aryl radical **8** to the C−C triple bond of **9**, followed by cyclization of the ensuing vinyl radical onto the nitrogen atom of the isothiocyanate moiety, loss of CS, and eventual hydrogen atom abstraction (Scheme 4).

As can be seen in Table 1, the **10**/**11** yield ratio is strongly dependent on the X-substituent. On the assumption (suitably supported below) that indole **10** is exclusively the result of the [4 + 2] annulation (Scheme 3, path a), whereas the isomer **11** totally arises from the [4 + 1] route (Scheme 3, path b), the 1,5-cyclization of vinyl radical **13** would become more and more favored by moving rightward in Figure 2 from the trifluoromethyl to the acetyl group. It is also evident that, unlike our previous results,[11] there is no correlation between the **10**/**11** ratio and the electronic character of X, since two substituents such as the trifluoromethyl and the acetyl group, with very similar electron-withdrawing capabilities, gave very different isomer ratios. It can therefore be inferred that the sulfur atom linked to the aromatic ring target of the cyclization exerts very different effects with respect to the nitrogen atom of the related vinyl radical **4b**.

Ring strain could be a trivial explanation of the considerable occurrence of rearranged products obtained with radical **13**. Indeed, with respect to the formation of the pyrrole ring from radical **4b**, in the case of **13** the larger size of the sulfur atom could let the 1,5-cyclization to the thiophene ring compete to a greater extent with the 1,6-ring closure; this would in general favor the formation of the rearranged isomers.[13] However, this possibility would not explain the observed dependence of the **10**/**11** ratio on the X-substituent, thus we believe

(13) Ring strain can probably be one of the reasons accounting for the larger 1,6/1,5-cyclization ratios observed with radicals **4b** with respect to analogous vinyl radicals obtained by addition of α-phenyl-*N*-arylimidoyl radicals to phenylacetylene (ref 2f).

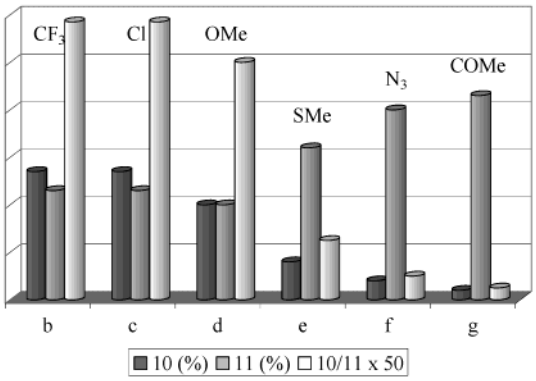


FIGURE 2. Effect of the substituents on the yields of **10** and **11** and the **10**/**11** ratio (the **10**/**11** ratio has been multiplied by 50 for better legibility).

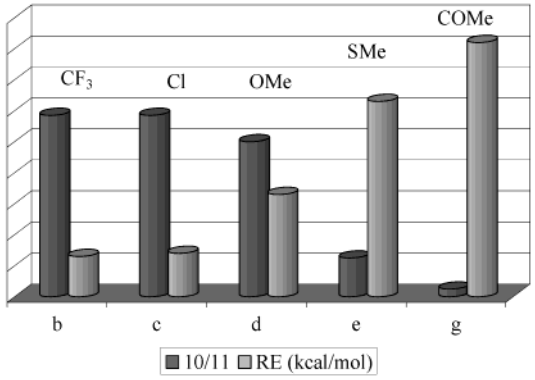


FIGURE 3. Variation of the **10**/**11** ratio with the substituent radical effect (RE).[15]

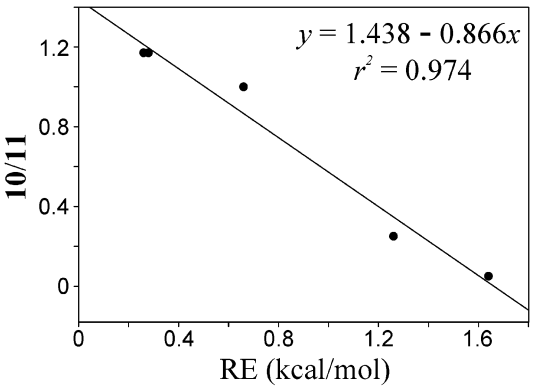


FIGURE 4. Correlation plot of the substituent radical effect (RE)[15] against the **10**/**11** ratio.

that ring strain could only marginally influence the reaction outcome.

Therefore, we turned our attention to the stabilization role played by the substituent, believing that the [4 + 2]/[4 + 1] competition should be mainly influenced by the capability of the X-group to delocalize spin density in radicals **15**. Usually, in the absence of sizable steric interactions, the description of the substituent effect on carbon radical systems needs both polar and radical stabilization parameters.[14] To better understand the nature of the substituent effect, a great deal of work has been carried out in recent years trying to set up Hammett-type radical spin delocalization $\sigma^{\bullet}$ parameters and to theoretically study the substituent effect on the C−H BDE of suitable hydrocarbons. Very recently, Wu et al. have reported a density functional study that attempts to separate the polar contribution from the radical spin delocalization effect.[15] In that paper, the radical effect (RE) on the BDE of the benzylic C−H bond of *p*-substituted toluenes has been calculated and correlated with spin density (to represent the spin delocalization effect) and charge variations (to represent the polar effect) at the benzylic radical center. Scattered points were obtained by plotting RE against charge variations, whereas good correlations were observed by plotting RE against spin density and even when both spin density and charge distribution were used as variables; this fact denotes a very small contribution of the polar effect to RE, which is therefore mainly the result of the spin delocalization effect.

Since our intermediates **15** are basically cyclohexadienyl radicals with the unpaired electron conjugated with the X-group, hence essentially comparable to the radical species studied by Wu et al., we thought that the substituents could have played very similar roles. Therefore, we tried to correlate the results of our reactions with the literature theoretical data. At a first sight (Figure 3), one can see that the **10**/**11** ratio, which is a measure of the relative occurrence of the [4 + 2] and [4 + 1] pathways, is strongly dependent on Wu's radical effect (RE): isomer **10** is strongly preferred over **11** with the trifluoromethyl- and chloro-substituent, which have the lowest RE values (0.26 and 0.28 kcal/mol, respectively), whereas isomer **11** becomes dramatically favored with the acetyl group, which is one of the best radical-stabilizing (spin-density delocalizing) substituents (RE = 1.64 kcal/mol). The RE value of the azido group is not available, hence this substituent was not included in this discussion; however, on the basis of the **10**/**11** ratio obtained with X = N_3 (see Figure 2 and Table 1, entry **f**), it can be assumed that its effect as a radical-stabilizing substituent is quite strong, being comparable to that of the acetyl group.

A good linear correlation ($r^2 = 0.974$) was observed by plotting the **10**/**11** ratio against RE (Figure 4), thus showing that the relationship between the isomer ratio and RE is not simply established on a qualitative basis, but it rather indicates a close interconnection between the reaction outcome and the radical substituent effect. Since the RE values are almost completely the result of spin delocalization ability, we can reasonably assume that, contrary to our previous results (Scheme 1),[11] the present reaction is only negligibly affected by polar effects. Therefore, the [4 + 2]/[4 + 1] competing annulations occur to an extent mostly dependent on the spin delocalization degree of the resulting cyclohexadienyl radicals.[16]

Remarkable results were obtained by inserting in the ortho-position of the attacking aryl radical a substituent that can function as both a radical-stabilizing moiety and

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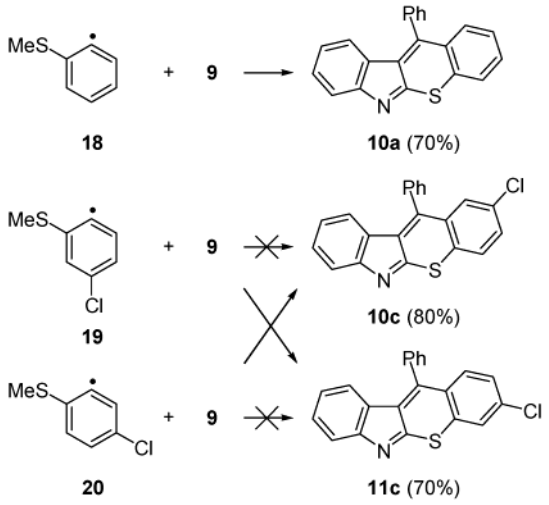
SCHEME 5



a radical-leaving group. When 2-(methylsulfanyl)phenyl radical **18** was allowed to react with isothiocyanate **9** under the usual conditions, compound **10a** was obtained in a yield significantly higher than that obtained in the case of the unsubstituted radical **8a** (70% instead of 50%) (Scheme 5). No traces of any methylsulfanyl-substituted thiochromenoindoles (i.e. **24** or **28**, X = H, Scheme 6) were detected. At first sight, this result might be explained by assuming that vinyl radical **21** (X = H) prefers to undergo (reversible) 1,6-cyclization onto the aromatic ring to give the cyclohexadienyl intermediates **22** and **23** (X = H, Scheme 6, paths a and b).[17] Due to the presence of the good sulfanyl radical leaving group, under our nonoxidative conditions the intermediate **22** (X = H) might be much proner to aromatize than the isomeric species **23** (X = H), and thence able to afford product **10a** in fairly good yield.

However, the real mechanism is instead that depicted in path d of Scheme 6 (framed structures), and this was proved by carrying out the reaction with aryl radicals **19** and **20** (Scheme 5). With **19**, the reaction did not afford compound **10c**, i.e. the expected product of direct *ipso*-substitution of the sulfanyl moiety by vinyl radical **21** (X = Cl), but it rather furnished the isomer **11c**, ascribable to spiro-cyclization of **21** to **25** (X = Cl), followed by ring expansion to cyclohexadienyl **27** (X = Cl) and eventual release of the sulfanyl group (Scheme 6). Likewise, radical **20** exclusively afforded compound **10c** instead of **11c**, with a mechanism wholly comparable to that shown in Scheme 6 for radical **19**.

We can conclude that, in the presence of the *o*-sulfide moiety, the reaction proceeds by exclusive [4 + 1] annulation via the spirocyclohexadienyl radical **25**, furnishing a single isomer whose structure depends on the relative positions of the methylsulfanyl and X groups. This fact has an important consequence from a synthetic point of view, since we can avoid lack of selectivity and obtain either thiochromenoindole pure isomer simply by using suitably *o*-sulfanyl-substituted aryl radicals. From a mechanistic standpoint, the effect of the methylsulfanyl group in pointing the reaction in a unique direction is most likely the result of *both* its leaving group ability *and* spin delocalization aptitude. Indeed, analogous reactions carried out with phenyl radicals bearing an *o*-iodine atom, which is another very good radical-leaving group, gave, besides product **10a**, minor amounts of a thiochromenoindole still containing the iodine atom (see Experimental Section). The strong effect of the *o*-sulfanyl group on both selectivity and yields could also suggest some degree of reversibility in vinyl radical cyclizations, at least when, in the absence of good leaving groups, oxidation of cyclohexadienyl radicals may not be very fast.

To verify the latter hypothesis and, in general, to get some more insight into the overall reaction mechanism, we carried out some theoretical calculations. Particularly, we aimed at estimating the endo-/exothermicity and activation barrier of the various steps, with the crucial target to get some information about a possible rearrangement of the spirocyclohexadienyl radical onto the C−C double bond and vis-à-vis the actual mechanism of its ring-expansion onto the sulfur atom.

As a matter of fact, spirocyclohexadienyl radical **15** could be in principle the unique reaction intermediate, affording **16** by rearrangement onto the sulfur atom and **14** by ring-expansion onto the C−C double bond; the latter route would occur via formation of intermediate **31** followed by fragmentation of the C−C intraannular bond (Scheme 7, path a). This would also mean that, in Scheme 3, path a should not operate, while route b should be the only reaction pathway. Ring expansions of 5-exo to 6-endo radicals, similar to the postulated conversion of **15** into **14**, are well documented in cyclizations of β-multiply bonded alkyl or vinyl radicals.[18] Unfortunately, no experimental procedures can be envisaged to establish, in Scheme 3, the possible occurrence of path a instead of path (b + c).

As far as the conversion of **15** into **16** is concerned, at least three distinct routes can be envisaged, viz. (i) concerted ring enlargement with concomitant C−S bond-making and bond-breaking through a transition state, (ii) formation of the intermediate sulfuranyl radical **29** followed by scission of the C−S intraannular bond, and (iii) fragmentation to the thioamidyl radical **30** followed by recyclization (Scheme 7, paths b, c, and d, respectively). Actually, S_Hi processes at sulfide moieties are known to entail either transition states or sulfuranyl radicals; the former were suggested to be involved with alkyl sulfides,[19] whereas the latter were assumed to be true intermediates when electronegative atoms are linked to the sulfur or intramolecular cyclizations onto diarylsulfides occur.[20] However, to the best of our knowledge, no references to such strained intermediates as **29** have been reported. On the other hand, the possibility that

(16) Correlation of the RE values with the [**14**]/[**15**] ratio would be more correct than that with the **10**/**11** yield ratio. However, since products **10** and **11** are the only fate of intermediates **14** and **15**, respectively, we think that the **10**/**11** yield ratio should completely mirror the [**14**]/[**15**] ratio, independent of the number of steps required for the formation of the final products. We are considering the possibility of performing ESR experiments to estimate the concentrations of radicals **14** and **15**.

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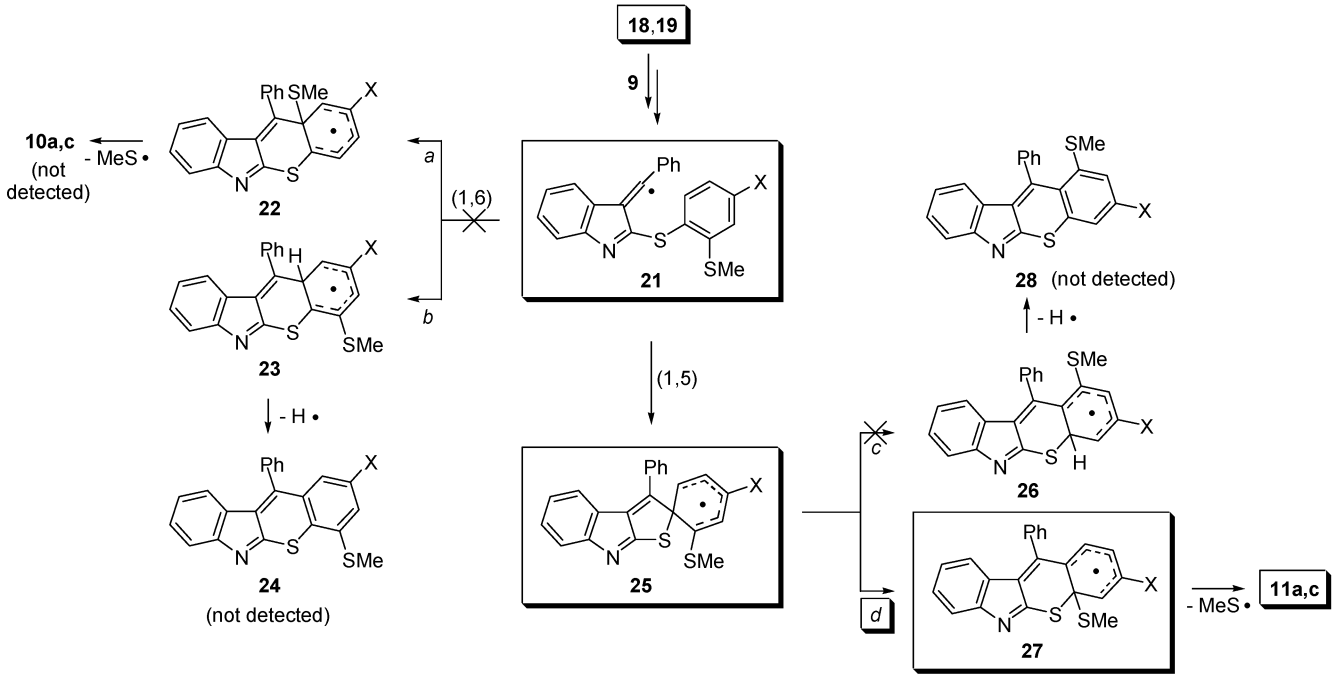
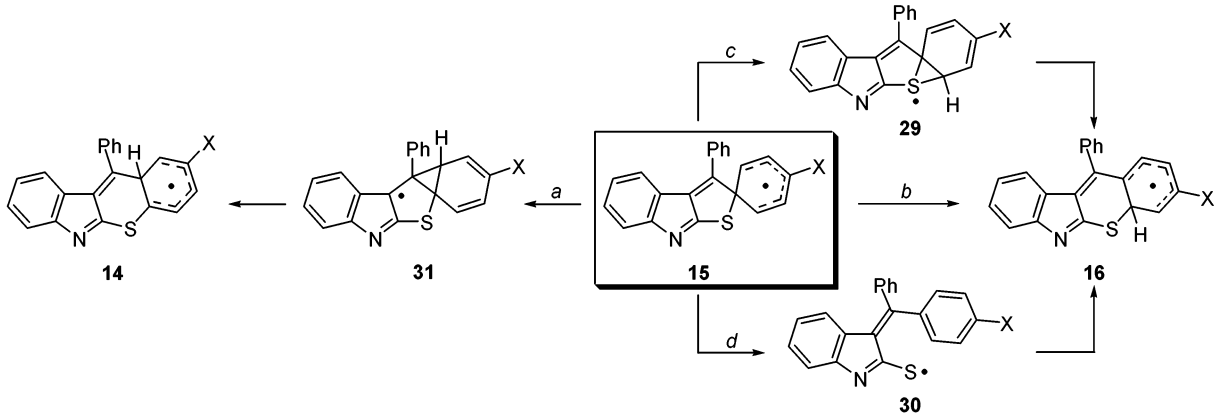
SCHEME 6



SCHEME 7



radical **15** could fragment to the fairly stable radical **30** cannot be in principle excluded. Indeed, ring openings of sulfur-substituted spirocyclohexadienyl radicals have been previously observed, although without concomitant recyclization of the resulting sulfanyl radical onto the aromatic ring.[18] Homolytic aromatic substitution by sulfur-centered radicals, although well-known (at least with sulfanyl radicals), is in fact supposed to be a reversible process,[21] substitution products being formed only in the presence of either good radical leaving groups, e.g. halogen atoms[22] or arylthio moieties,[23] or in highly oxidizing media able to oxidize the intermediate cyclohexadienyl radicals.[24] Very recently, the Mn(III)-mediated oxidation of *N,N′*-diarylthioureas has been reported to furnish, besides other major compounds, homolytic substitution products of **30**-like thioureidyl radicals, whose yield increased in the presence of an *o*-methylsulfanyl radical leaving group.[25]

First we examined the cyclization of vinyl radical **13**. DFT calculations found for **13** two conformational minima separated by 4 kcal/mol; only the high-energy conformer has the appropriate geometry for cyclization onto the S-phenyl ring, therefore all the subsequent steps were studied starting from this conformation (Figure 5 and Figure S1, Supporting Information). Both the 1,5- ([4 + 1] annulation) and the 1,6-cyclization ([4 + 2] annulation) were estimated to be exothermic ($\Delta H = -10.5$ and -8.7

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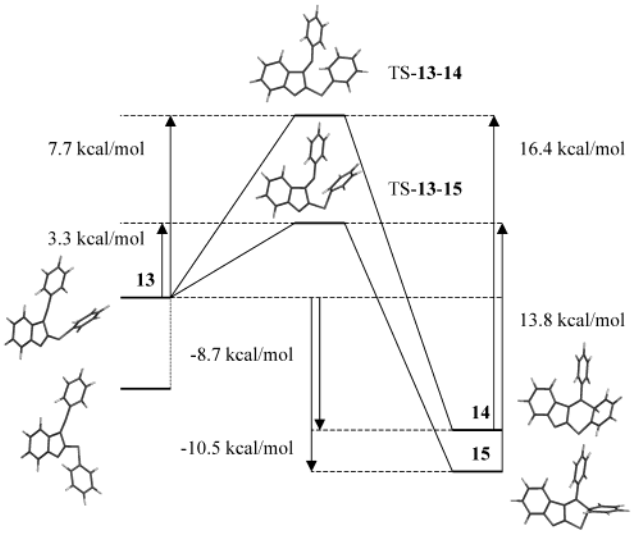

FIGURE 5. Cyclization pathways of radical **13**, with optimized structures, ΔHs, and activation barriers as obtained by DFT calculations ([4 + 2] annulation, top path; [4 + 1] annulation, bottom path).

kcal/mol, respectively). The transition states for the two cyclizations were optimized, giving activation barriers of 3.3 and 7.7 kcal/mol for the formation of **15** and **14**, respectively. The 1,5-cyclization seems therefore both enthalpically and, above all, kinetically preferred over the 1,6-ring closure. Nevertheless, the major distinction between the activation barriers of **14** and **15** ($\Delta E_a = 4.4$ kcal/mol), associated with the low enthalpy difference ($\Delta\Delta H = 1.8$ kcal/mol), suggests that the cyclization of **13** is not likely to be under complete kinetic control. Some equilibration between the two cyclized species may probably occur, especially in the absence of fast aromatization pathways for **14**, also due to the acceptable activation barriers for the reverse reactions (13.8 and 16.4 kcal/mol for the ring-opening of **15** and **16**, respectively). This is consistent with the proposed stabilizing substituent effect discussed above.

The evolution pathways of radical **15** are more uncertain, due to the difficulties in optimizing both the transition state (or intermediate **29**) for ring-enlargement (Scheme 7, path b or c) and the thioamidyl radical **30** (Scheme 7, path d). Route a of Scheme 7 was nevertheless fully optimized; besides being of course altogether endothermic by 1.8 kcal/mol, this path is characterized by another quite strongly endothermic step, i.e. formation of intermediate **31**, which was located 14.6 kcal/mol above **15** (Figure 6 and Figure S2, Supporting Information). The activation barrier for the conversion of **15** into **31** was estimated at 16.6 kcal/mol, and the second barrier, that for the transformation of **31** into **14**, albeit quite low (3.3 kcal/mol), was however found to be higher than that of the reconversion of **31** into **15** (2.0 kcal/mol).

To fully establish that this path is very unlikely we needed to estimate the ΔH and activation barrier(s) for the competitive one, i.e. the transformation of **15** into **16**. Although a full optimization of routes b, c, and d (Scheme 7) could not be obtained, nonetheless we think that enough data were acquired at least to prove that **15** cannot rearrange into **14** and hence that the latter radical, i.e. the [4 + 2] annulation intermediate, is the result of a direct 1,6-cyclization of vinyl radical **13**.

The rearrangement of **15** into **16** was calculated to be exothermic by 9.5 kcal/mol (Figure 6 and Figure S2, Supporting Information): this means that cyclohexadienyl **16** is much more stable than its congener **14**,

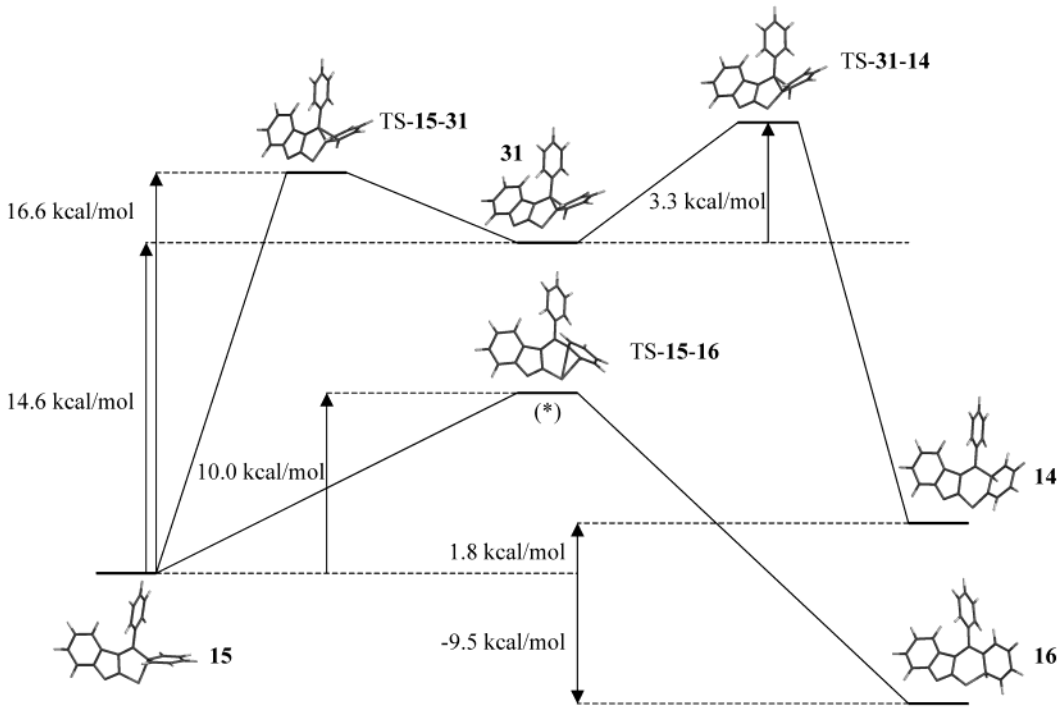

FIGURE 6. Rearrangement pathways of radical **15** into **14** and **16** according to routes *a* and *b* of Scheme 7, with optimized structures, ΔHs, and activation barriers as obtained by DFT calculations (* not fully optimized) (route *a*, top path; route *b*, bottom path).

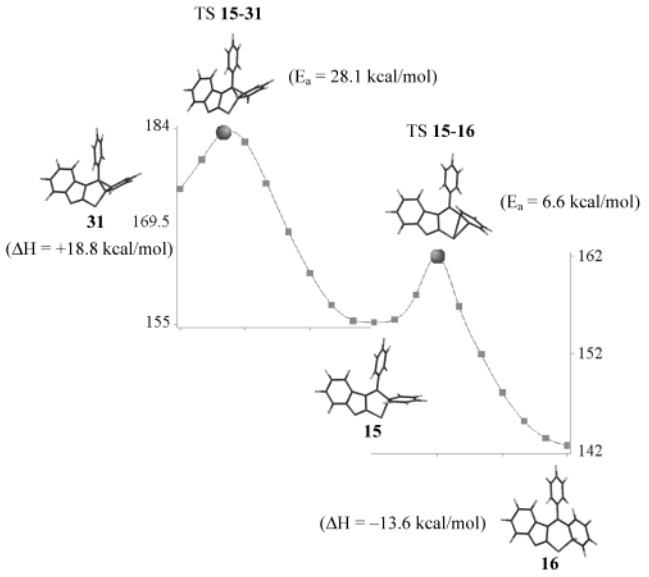

FIGURE 7. Energy profiles for the rearrangements of radical **15** into **31** and **16**, with optimized structures, Δ*H*s, and activation barriers as obtained by PM3 calculations.

probably as a result of direct conjugation of the unpaired electron with the whole π-system of the chromenoindole structure (in **14**, substantial stabilization is probably provided by the sulfur atom alone). The transition state for the **15**−**16** conversion could not be fully optmized by DFT methods; therefore, we tried to compare paths a and b (Scheme 7) by calculating an energy profile, on a PM3 semiempirical basis, for the two competitive routes (Figure 7 and Figure S3, Supporting Information). The profiles clearly suggest that both enthalpic and kinetic factors strongly favor ring expansion of **15** into **16** (Figure 7, right profile) rather than formation of the strained intermediate **31** (Figure 7, left profile). DFT single-point energy and vibrational frequency calculation of the structure found with PM3 methods for the maximum of the **15**−**16** profile gave a structure with a single, physically consistent imaginary vibrational frequency that can be assumed very close to the true transition state for the process.

This structure entails an activation barrier of 10.0 kcal/mol (Figure 6), much lower than that for the formation of intermediate **31**. Therefore, it can be reasonably inferred that path a of Scheme 7 cannot efficiently compete with path b, and hence spirocyclohexadienyl **15** is not on the reaction pathway leading to **14**.

It remains to be established which path is actually followed by spiro-radical **15** in its rearrangement into **16**, that is to distinguish between routes b, c, and d (Scheme 7). We already showed (Figures 6 and 7) that path b, i.e. direct conversion through a transition state, is a viable process with a reasonable activation barrier. The alternative formation of intermediate **29** (path c) should be excluded. Indeed, both PM3 and DFT calculations did not ever converge to any minima when trying to optimize structure **29**, affording instead either the starting radical **15** or the final cyclohexadienyl **16**.

As for the possible formation of the sulfur-centered radical **30**, it could not be optimized by DFT calculations, but its enthalpy and activation barriers for both 1,5- (recyclization into **15**) and 1,6-ring closure (cyclization to **16**) were estimated by PM3 methods (Figure 8 and Figure S4, Supporting Information).

Although fragmentation of **15** into **30** is endothermic by 4.4 kcal/mol, the activation energy for the scission is quite low (8.2 kcal/mol) and the corresponding transition state lies very close in energy to the transition state for the direct conversion of **15** into **16** (ΔE_a = 1.6 kcal/mol). Moreover, the barrier for the subsequent step, i.e. cyclization of **30** into **16**, is very low (2.9 kcal/mol), and however lower than the activation barrier for the reverse

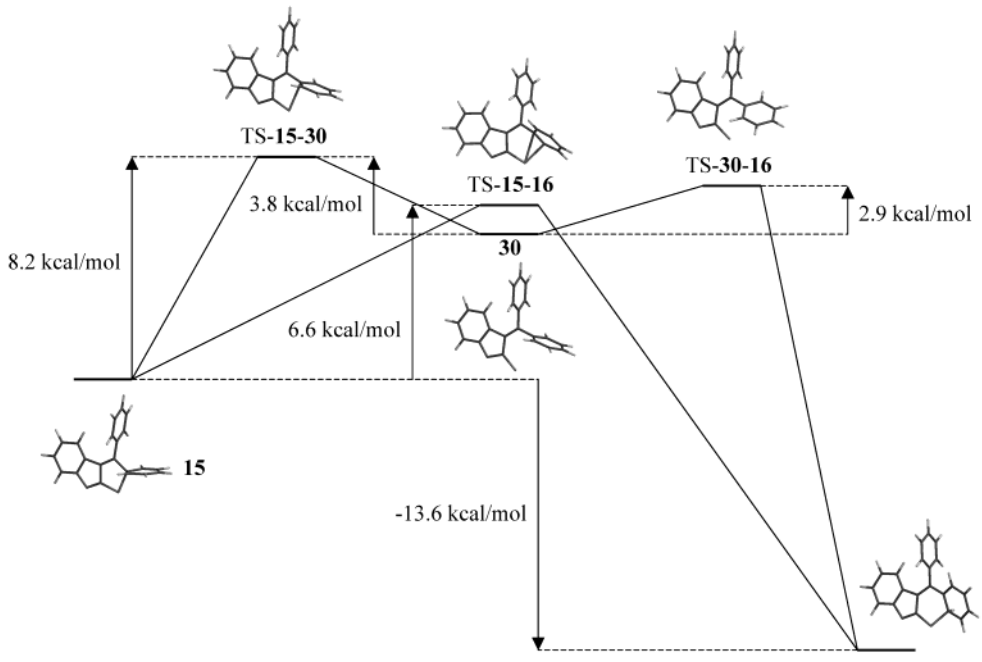

FIGURE 8. Rearrangements of radical **15** into **16** (routes *b* and *d* of Scheme 7), with optimized structures, Δ*H*s, and activation barriers as obtained by PM3 calculations (path *b*, bottom path; path *d*, top path).

reaction (3.8 kcal/mol). These data do not allow an unambiguous determination of the real rearrangement pathway, but rather suggest that paths b and d of Scheme 7 can be competitive, and both of them are however clearly favored with respect to path a. On the basis of the previous evidence that thioamidyl radicals can actually perform homolytic aromatic substitution,[25] it also might be concluded that path d may actually be the main rearrangement route, at least when a proper radical leaving group is present on the aromatic ring of the original aryl radical, as in the case of the methylsulfanyl-substituted radicals reported in Schemes 5 and 6.

Conclusions

Aryl radicals **8** react with isothiocyanate **9** through a novel radical cascade reaction affording a new class of 2-X- and 3-X-substituted thiochromeno[2,3-*b*]indoles (**10** and **11**). These isomeric compounds arise from competitive [4 + 2] and [4 + 1] radical annulations; the [4 + 2] pathway yields directly compound **10**, whereas the [4 + 1] ring closure is followed by ring-enlargement onto the sulfur atom to yield isomer **11**.

The **10**/**11** ratio is strongly dependent on the X-substituent. Contrary to analogous ring closures of vinyl radicals onto nitrogen-substituted aromatic rings,[11] the ratio is not correlated to the electron-withdrawing (or releasing) ability of the substituent, but it is instead associated with its capability to delocalize spin density.

The presence of a methylsulfanyl group in the ortho-position of the initial aryl radical results in complete regioselectivity and better yields, as the consequence of both strong spin-delocalization effect, which promotes exclusive [4 + 1] annulation, and good radical leaving-group ability, which facilitates aromatization of the final cyclohexadienyl radical. It is therefore possible to obtain a single thiochromenoindole derivative, bearing the X-substituent in a specific position, starting from a properly substituted aryl radical.

Semiempirical and DFT theoretical calculations suggest that spirocyclohexadienyl radicals **15** do not rearrange by ring closure onto the C−C double bond but by expansion onto the sulfur atom exclusively, and thence isomeric indoles **10** and **11** are formed by two distinct, competitive annulation routes. As far as the expansion onto sulfur is concerned, formation of a sulfuranyl radical seems very unlikely. The rearrangement through a transition state and that via a sulfur-centered (thioamidyl) radical appear instead to be competitive; the latter is probably favored in the presence of an *o*-methylsulfanyl moiety that can act as a leaving group in the final *ipso*-cyclization process.

Experimental Section

General Procedures. ^{1}H and ^{13}C NMR spectra were recorded in deuteriochloroform, unless otherwise stated, using tetramethylsilane as an internal standard. Mass spectra (MS) were performed by electron impact with a beam energy of 70 eV: relative intensities are given in parentheses. IR spectra were recorded in $CHCl_3$ solutions. Column chromatography was carried out on silica gel (63-200, 60 Å) or basic aluminum oxide (activity grade III) by gradual elution with light petroleum (40−70 °C) and light petroleum/diethyl ether/dichloromethane mixtures (up to 100% dichloromethane).

Starting Materials. Aniline and 4-(trifluoromethyl)-, 4-chloro-, 4-methoxy-, 4-(methylsulfanyl)-, 4-acetyl-, 2-(methylsulfanyl)-, and 2-iodoaniline were commercially available; 4-azidoaniline,[26] 4-chloro-2-(methylsulfanyl)aniline,[27] 5-chloro-2-(methylsulfanyl)aniline,[28] and 2-(2-phenylethynyl)aniline[29] were synthesized according to the literature. The corresponding diazonium tetrafluoroborates **7a**−**g** were prepared following usual procedures.[30]

2-(2-Phenylethynyl)phenyl isothiocyanate (9). A dichloromethane (10 mL) solution of 2-(2-phenylethynyl)aniline (7.64 g, 40 mmol) was added dropwise at 20 °C to a stirred solution of thiophosgene (5.70 g, 50 mmol) in a dichloromethane (6 mL)/water (14 mL) mixture. After 3 h, the organic layer was separated and dried (sodium sulfate). The solvent was evaporated and the residue was crystallized from ligroin (bp 80−95 °C) to give the title compound (60%), mp 50−51 °C: IR ν_{max} 2217 (C≡C), 2071 (NCS) cm^{-1}; ^{1}H NMR (300 MHz) δ 7.10−7.15 (1 H, m), 7.18−7.29 (2 H, m), 7.33−7.39 (3 H, m), 7.49−7.54 (1 H, m), 7.62−7.69 (2 H, m); ^{13}C NMR (75 MHz) δ 85.61 (C), 97.59 (C), 123.14 (C), 123.47 (C), 125.28, 127.57, 129.03, 129.55, 129.58, 132.33, 133.14 (C), 133.22, 138.62 (C, N=C=S); MS *m*/*z* (rel intensity) 235 (M$^+$, 100), 203 (6), 190 (15), 176 (6). Anal. Calcd for $C_{15}H_9NS$: C, 76.56; H, 3.86; N, 5.95. Found: C, 76.30; H, 3.87; N, 5.97.

General Procedure for the Reactions of Isothiocyanate 9 with the Tetrafluoroborates 7.[9,11,12] [18-Crown-6] (0.25 mmol), potassium acetate (10 mmol), and the tetrafluoroborate (5 mmol) were added to a solution of isothiocyanate (15 mmol) in 20 mL of ethyl acetate. The reaction mixture was kept at room temperature for ca. 1 h under vigorous stirring, the solvent was then evaporated, and the residue was chromatographed (silica gel, 3.5 cm ϕ × 40 cm h column, unless otherwise stated) eluting with petroleum ether to remove excess isothiocyanate and to separate indoles **17**. Subsequent elution with light petroleum/diethyl ether/dichloromethane mixtures furnished thiochromenoindoles **10** and **11**. Yields of **10** and **11**, as obtained by this method, are shown in Table 1. The following reactions were carried out according to this general procedure.

Reaction of 9 with 1-Phenyldiazonium Tetrafluoroborate (7a). Elution with light petroleum gave 2,3-diphenyl-1*H*-indole (**17a**) (5%), mp 113−116 °C (lit.[31] mp 114−116 °C) [IR ν_{max} 3463 (NH), 1601, 1494, 1457 cm^{-1}; ^{1}H NMR (300 MHz) δ 7.25−7.60 (12 H, m), 7.68 (1 H, br d, J = 7.8 Hz), 7.76 (1 H, br d, J = 7.6 Hz), 8.36 (1 H, br s); MS *m*/*z* (rel intensity) 269 (M$^+$, 100), 268 (17), 267 (25), 165 (26), 163 (11), 77 (20)]; further elution with light petroleum/diethyl ether/dichloromethane 60:20:20 v/v/v afforded 11-phenylthiochromeno[2,3-*b*]indole (**10a**) (50%) as a red solid, mp 214−215 °C (from light petroleum/benzene) [^{1}H NMR (200 MHz) δ 6.40 (1 H, d, J = 8.0 Hz), 6.93 (1 H, br t, J = 8.0 Hz), 7.30−7.72 (10 H, m), 7.82 (1 H, d, J = 8.0 Hz); ^{13}C NMR (50 MHz) δ 118.98, 122.74, 124.07, 126.54, 126.78 (C), 127.36, 128.91, 129.60, 129.68, 129.86, 130.06, 131.61, 133.93 (C), 136.86 (C), 146.53 (C), 155.69 (C), 162.09 (C) (2 quaternary signals not visible); MS *m*/*z* (rel intensity) 311 (M$^+$, 100), 310 (24). Anal. Calcd for $C_{21}H_{13}NS$: C, 81.00; H, 4.21; N, 4.50. Found: C, 81.30; H, 4.22; N, 4.49].

Reaction of 9 with 1-[4-(Trifluoromethyl)phenyl]diazonium Tetrafluoroborate (7b). Elution with light petro-

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leum gave 2-phenyl-3-[4-(trifluoromethyl)phenyl]-1*H*-indole (**17b**) (3%) as an oil [IR ν_{max} 3461 (NH), 1616, 1449, 1325 cm^{-1}; ^{1}H NMR (300 MHz) δ 7.10−7.80 (13 H, m), 8.38 (1 H, br s); ^{13}C NMR (75 MHz) δ 111.80, 119.94, 121.51, 123.68, 126.11 (q, J = 3.6 Hz), 128.82, 129.03, 129.56, 130.84 (due to the small amounts of this compound, only the CH signals are quoted); MS *m*/*z* (rel intensity) 337 (M$^+$, 100), 318 (6), 267 (19); HRMS calcd for $C_{21}H_{14}F_3N$ 337.1078, found 337.1080]; further elution with light petroleum/diethyl ether/dichloromethane 70:10:20 v/v/v yielded 11-phenyl-3-(trifluoromethyl)thiochromeno[2,3-*b*]indole (**11b**) (23%) as a red solid, mp 250−251 °C (from ethanol/benzene) [^{1}H NMR (200 MHz) δ 6.42 (1 H, br d, J = 8.0 Hz), 6.98 (1 H, td, J_t = 8.0 Hz, J_d = 1.0 Hz), 7.39−7.75 (9 H, m), 8.14 (1 H, br s); ^{13}C NMR (50 MHz) δ 119.10, 122.73 (q, J = 4.0 Hz), 123.16, 123.57 (C, q, J = 280 Hz), 124.30 (q, J = 4.0 Hz), 124.41, 126.32 (C), 128.81, 129.90, 130.24, 130.38, 131.33 (C), 131.39 (C, q, J = 36 Hz), 131.96, 133.97 (C), 136.11 (C), 144.92 (C), 155.70 (C), 161.15 (C) (2 quaternary signals overlapped); MS *m*/*z* (rel intensity) 379 (M$^+$, 100), 378 (25). Anal. Calcd for $C_{22}H_{12}F_3NS$: C, 69.65; H, 3.19; N, 3.69. Found: C, 69.47; H, 3.19; N, 3.70. The structure of **11b** was confirmed by X-ray diffraction (see Supporting Information)], and some impure 11-phenyl-2-(trifluoromethyl)thiochromeno-[2,3-*b*]indole (**10b**), which was purified by chromatography on aluminum oxide (1.5 cm ϕ × 20 cm h column) eluting with light petroleum/diethyl ether/dichloromethane 80:10:10 v/v/v, yield 27%, was also obtained as a red solid, mp 197−198 °C (from ethanol/benzene) [^{1}H NMR (200 MHz) δ 6.42 (1 H, br d, J = 7.7 Hz), 6.99 (1 H, td, J_t = 7.7 Hz, J_d = 1.0 Hz), 7.39−7.46 (2 H, m), 7.49 (1 H, dd, J_1 = 7.8 Hz, J_2 = 1.2 Hz), 7.67−7.83 (6 H, m), 7.99 (1 H, br d, J = 8.5 Hz); ^{13}C NMR (50 MHz) δ 119.21, 123.25, 124.20 (C, q, J = 275 Hz), 124.32, 125.63 (q, J = 4.0 Hz), 126.05 (C), 127.90, 128.02 (C), 128.70, 128.78 (q, J = 4.0 Hz), 129.90, 130.08, 130.32 (C), 135.73 (C), 137.41 (C), 145.32 (C), 155.64 (C), 161.27 (C) (2 CH signals overlapped, quaternary C-2 signal not visible); MS *m*/*z* (rel intensity) 379 (M$^+$, 100), 378 (18). Anal. Calcd for $C_{22}H_{12}F_3NS$: C, 69.65; H, 3.19; N, 3.69. Found: C, 69.45; H, 3.19; N, 3.70. The structure of **10b** was confirmed by X-ray diffraction (see Supporting Information)].

Reaction of 9 with 1-(4-Chlorophenyl)diazonium Tetrafluoroborate (7c). Elution with light petroleum gave 3-[4-chlorophenyl]-2-phenyl-1*H*-indole (**17c**)[32] (5%) as an oil [IR ν_{max} 3461 (NH), 1599, 1486 cm^{-1}; ^{1}H NMR (200 MHz) δ 7.04−7.40 (12 H, m), 7.57 (1 H, bd, J = 7.4 Hz), 8.20 (1 H, br s); MS *m*/*z* (rel intensity) 305 (M$^+$ + 2, 29), 303 (M$^+$, 100), 267 (28). HRMS calcd for $C_{20}H_{14}ClN$ 303.0815, found 303.0819]; further elution with light petroleum/diethyl ether/dichloromethane 70:15:15 v/v/v yielded 3-chloro-11-phenylthiochromeno[2,3-*b*]indole (**11c**) (23%) as a red solid, mp 244−245 °C (from ethanol/benzene) [^{1}H NMR (200 MHz) δ 6.41 (1 H, d, J = 8.0 Hz), 6.97 (1 H, td, J_t = 8.0 Hz, J_d = 1.2 Hz), 7.31−7.53 (5 H, m), 7.64−7.74 (4 H, m), 7.88 (1 H, d, J = 1.8 Hz); ^{13}C NMR (50 MHz) δ 118.53, 122.41, 123.46, 126.09, 126.45, 126.82 (C), 128.25, 128.91 (C), 129.19, 129.28, 129.57, 132.00, 134.73 (C), 135.68 (C), 135.83 (C), 155.03 (C), 160.90 (C) (2 quaternary signals not visible); MS *m*/*z* (rel intensity) 347 (M$^+$ + 2, 40), 345 (M$^+$, 100), 344 (18), 309 (14). Anal. Calcd for $C_{21}H_{12}ClNS$: C, 72.93; H, 3.50; N, 4.05. Found: C, 73.12; H, 3.49; N, 4.07. The structure of **11c** was confirmed by X-ray diffraction (see Supporting Information)], and 2-chloro-11-phenylthiochromeno[2,3-*b*]-indole (**10c**) (27%) as a red solid, mp 160−162 °C (from ethanol/benzene) [^{1}H NMR (200 MHz) δ 6.39 (1 H, d, J = 7.8 Hz), 6.97 (1 H, td, J_t = 7.8 Hz, J_d = 1.0 Hz), 7.36−7.50 (3 H, m), 7.51−7.58 (2 H, m), 7.66−7.75 (4 H, m), 7.81 (1 H, br d, J = 7.8 Hz); ^{13}C NMR (50 MHz) δ 118.56, 122.43, 123.72, 125.95 (C), 127.90, 128.27, 129.36, 129.44, 129.59, 129.71, 130.12, 131.41 (C), 131.98 (C), 135.56 (C), 144.50 (C), 155.27 (C), 161.14 (C) (2 quaternary signals not visible); MS *m*/*z* (rel intensity) 347 (M$^+$ + 2, 37), 345 (M$^+$, 100), 344 (12), 309 (8). Anal. Calcd for $C_{21}H_{12}ClNS$: C, 72.93; H, 3.50; N, 4.05. Found: C, 73.15; H, 3.50; N, 4.06. The structure of **10c** was confirmed by X-ray diffraction (see Supporting Information)].

Reaction of 9 with 1-(4-Methoxyphenyl)diazonium Tetrafluoroborate (7d). Elution with light petroleum gave 3-[4-methoxyphenyl]-2-phenyl-1*H*-indole (**17d**)[33] (trace amounts) as an oil [IR ν_{max} 3466 (NH), 1602, 1513 cm^{-1}; ^{1}H NMR (300 MHz) δ 3.80 (3 H, s), 6.85−7.65 (13 H, m), 8.20 (1 H, br s); MS *m*/*z* (rel intensity) 299 (M$^+$, 100), 284 (36); HRMS calcd for $C_{21}H_{17}NO$ 299.1310, found 299.1317]; further elution with light petroleum/diethyl ether/dichloromethane 40:30:30 v/v/v yielded 2-methoxy-11-phenylthiochromeno[2,3-*b*]indole (**10d**) (20%) as a red solid, mp 156−157 °C (from ethanol/benzene) [^{1}H NMR (200 MHz) δ 3.70 (3 H, s), 6.40 (1 H, br d, J = 7.8 Hz), 6.93 (1 H, td, J_t = 8.0 Hz, J_d = 1.0 Hz), 7.15 (1 H, d, J = 2.6 Hz), 7.22 (1 H, dd, J_1 = 2.6 Hz, J_2 = 8.3 Hz), 7.37−7.47 (3 H, m), 7.62−7.72 (4 H, m), 7.79 (1 H, d, J = 8.3 Hz); ^{13}C NMR (50 MHz) δ 56.09, 115.06, 118.36, 118.96, 122.64, 124.22, 125.69 (C), 126.76 (C), 128.39, 128.95, 129.75, 129.84, 130.22, 137.01 (C), 146.27 (C), 155.94 (C), 158.43 (C), 162.68 (C) (2 quaternary signals not visible); MS *m*/*z* (rel intensity) 341 (M$^+$, 100), 326 (20), 298 (13), 297 (14). Anal. Calcd for $C_{22}H_{15}NOS$: C, 77.39; H, 4.43; N, 4.10. Found: C, 77.51; H, 4.45; N, 4.09], and 3-methoxy-11-phenylthiochromeno[2,3-*b*]indole (**11d**) (20%) as a yellow-orange solid, mp 234−236 °C (from ethanol/benzene) [^{1}H NMR (200 MHz) δ 3.93 (3 H, s), 6.38 (1 H, br d, J = 7.8 Hz), 6.88−6.99 (2 H, m), 7.32−7.51 (5 H, m), 7.61−7.71 (4 H, m); ^{13}C NMR (50 MHz) δ 56.35, 110.14, 115.28, 118.86, 122.48, 123.41, 126.99 (C), 128.82, 128.87, 129.49, 129.96, 133.09, 136.63 (C), 137.10 (C), 146.97 (C), 155.23 (C), 160.84 (C), 161.82 (C) (2 quaternary signals not visible); MS *m*/*z* (rel intensity) 341 (M$^+$, 100), 326 (3), 298 (23), 297 (17). Anal. Calcd for $C_{22}H_{15}NOS$: C, 77.39; H, 4.43; N, 4.10. Found: C, 77.53; H, 4.44; N, 4.10. The structure of **11d** was confirmed by X-ray diffraction (see Supporting Information)].

Reaction of 9 with 1-[4-(Methylsulfanyl)phenyl]diazonium Tetrafluoroborate (7e). Elution with light petroleum/diethyl ether/dichloromethane 50:25:25 v/v/v yielded a mixture of 2-(methylsulfanyl)-11-phenylthiochromeno[2,3-*b*]-indole (**10e**) and 3-(methylsulfanyl)-11-phenylthiochromeno-[2,3-*b*]indole (**11e**) (40% overall yield, 1:4 **10e**/**11e** ratio by ^{1}H NMR analysis). This mixture could not be separated by changing either the eluant or the stationary phase; however, by washing the solid mixture with diethyl ether several times, we obtained pure solid **11e** together with a solution containing **10e** and **11e** in a 2:1 ratio. **11e**: red solid, mp 227−230 °C (from benzene/ligroin); ^{1}H NMR (200 MHz) δ 2.55 (3 H, s), 6.38 (1 H, br d, J = 7.7 Hz), 6.92 (1 H, br t, J = 7.7 Hz), 7.18 (1 H, dd, J_1 = 2.0 Hz, J_2 = 8.6 Hz), 7.33−7.46 (4 H, m), 7.57 (1 H, d, J = 2.0 Hz), 7.59−7.70 (4H, m); ^{13}C NMR (50 MHz) δ 15.55, 119.01, 122.32, 122.72, 123.82, 124.25, 125.67 (C), 126.91 (C), 127.61 (C), 128.94, 129.36, 129.64, 130.08, 131.40, 135.19 (C), 136.87 (C), 143.24 (C), 146.60 (C), 155.58 (C), 161.53 (C); MS *m*/*z* (rel intensity) 357 (M$^+$, 100), 309 (20). Anal. Calcd for $C_{22}H_{15}NS_2$: C, 73.91; H, 4.23; N, 3.92. Found: C, 74.12; H, 4.25; N, 3.92. **10e**: ^{1}H NMR (200 MHz, obtained by subtracting the signals of **11e**) δ 2.37 (3 H, s), 6.40 (1 H, br d, J = 7.7 Hz), 6.95 (1 H, br t, J = 7.7 Hz), 7.18−7.23 (1 H, m), 7.34−7.51 (5 H, m), 7.60−7.73 (3 H, m), 7.78 (1 H, d, J = 8.4 Hz). Anal. Calcd for $C_{22}H_{15}NS_2$ (**10e**/**11e** mixture): C, 73.91; H, 4.23; N, 3.92. Found: C, 74.18; H, 4.26; N, 3.91.

Reaction of 9 with 1-(4-Azidophenyl)diazonium Tetrafluoroborate (7f). Elution with light petroleum/diethyl ether/dichloromethane 34:33:33 v/v/v yielded 3-azido-11-phenylthiochromeno[2,3-*b*]indole (**11f**) (40%) as a red solid that was recrystallized from dichloromethane/diethyl ether and melted between 210 and 250 °C with slow decomposition [IR ν_{max} 2118 (N_3) cm^{-1}; ^{1}H NMR (CD_2Cl_2, 300 MHz) δ 6.35 (1 H, br d, J = 7.7 Hz), 6.89 (1 H, td, J_t = 7.7 Hz, J_d = 1.0 Hz), 7.03 (1 H, dd,

(32) Arcadi, A.; Cacchi, S.; Marinelli, F. *Tetrahedron Lett.* **1992**, *33*, 3915−3918. Neither mp nor spectral data are reported.

(33) Mentzer, C.; Molho, D.; Berguer, Y. *Bull. Chem. Soc. Fr.* **1950**, 555−561.

J_1 = 8.8 Hz, J_2 = 2.4 Hz), 7.33−7.40 (3 H, m), 7.48−7.54 (2 H, m), 7.59 (1 H, br d, J = 7.9 Hz), 7.62−7.68 (3 H, m); MS m/z (rel intensity) 352 (M^+, 5), 324 (M^+ − 28, 100)] and 2-azido-11-phenylthiochromeno[2,3-*b*]indole (**10f**) (4%) as a red solid that was recrystallized from light petroleum/diethyl ether and melted between 160 and 190 °C with slow decomposition [IR ν_{max} 2120 (N_3) cm^{-1}; ^1H NMR (200 MHz) δ 6.42 (1 H, br d, J = 8.0 Hz), 6.95 (1 H, td, J_t = 8.0 Hz, J_d = 1.0 Hz), 7.15 (1 H, d, J = 2.2 Hz), 7.26−7.50 (5 H, m), 7.64−7.72 (3 H, m), 7.85 (1 H, d, J = 8.8 Hz); MS m/z (rel intensity) 352 (M^+, 3), 324 (M^+ − 28, 100)].

Reaction of 9 with 1-(4-Acetylphenyl)diazonium Tetrafluoroborate (7g). Elution with light petroleum/diethyl ether/dichloromethane 34:33:33 v/v/v yielded 1-(11-phenylthiochromeno[2,3-*b*]indol-3-yl)-1-ethanone (**11g**) (43%) as a red solid, mp 239−241 °C (from ethanol/benzene) [IR ν_{max} 1686 (CO) cm^{-1}; ^1H NMR (200 MHz) δ 2.62 (3 H, s), 6.37 (1 H, br d, J = 7.7 Hz), 6.90 (1 H, td, J_t = 7.7 Hz, J_d = 1.0 Hz), 7.32−7.42 (3 H, m), 7.56−7.69 (5 H, m), 7.84 (1 H, dd, J_1 = 2.0 Hz, J_2 = 8.7 Hz), 8.38 (1 H, d, J = 2.0 Hz); ^{13}C NMR (50 MHz) δ 27.52, 119.29, 123.26, 124.60, 125.63, 126.60 (C), 127.68, 128.97, 129.99, 130.36, 130.57, 131.81 (C), 131.89, 132.20 (C), 133.98 (C), 136.47 (C), 136.99 (C), 145.37 (C), 155.94 (C), 162.14 (C), 197.22 (CO); MS m/z (rel intensity) 353 (M^+, 100), 310 (65), 43 (99). Anal. Calcd for $C_{23}H_{15}NOS$: C, 78.16; H, 4.28; N, 3.96. Found: C, 78.31; H, 4.30; N, 3.97], and 1-(11-phenylthiochromeno[2,3-*b*]indol-2-yl)-1-ethanone (**10g**) (2%) as a red-orange solid, mp 201−203 °C (from ethanol) [IR ν_{max} 1685 (CO) cm^{-1}; ^1H NMR (200 MHz) δ 2.71 (3 H, s), 6.33 (1 H, br d, J = 7.8 Hz), 6.89 (1 H, td, J_t = 7.8 Hz, J_d = 1.1 Hz), 7.32−7.68 (8 H, m), 7.85 (1 H, br d, J = 7.8 Hz), 8.22 (1 H, br d, J = 8.8 Hz); MS m/z (rel intensity) 353 (M^+, 100), 310 (24), 43 (66); HRMS calcd for $C_{23}H_{15}NOS$ 353.0874, found 353.0877].

Reaction of 9 with 1-[2-(Methylsulfanyl)phenyl]diazonium Tetrafluoroborate. Elution with light petroleum/diethyl ether/dichloromethane 60:20:20 v/v/v yielded **10a** (70%), with mp and spectral data identical to those reported for **10a** in the above reaction of **9** with **7a**.

Reaction of 9 with 1-[4-Chloro-2-(methylsulfanyl)-phenyl]diazonium Tetrafluoroborate. Elution with light petroleum/diethyl ether/dichloromethane 70:15:15 v/v/v yielded **11c** exclusively (70%), with mp and spectral data identical to those reported for **11c** in the above reaction of **9** with **7c**.

Reaction of 9 with 1-[5-Chloro-2-(methylsulfanyl)-phenyl]diazonium Tetrafluoroborate. Elution with light petroleum/diethyl ether/dichloromethane 70:15:15 v/v/v yielded **10c** exclusively (80%), with mp and spectral data identical to those reported for **10c** in the above reaction of **9** with **7c**.

Reaction of 9 with 1-(2-Iodophenyl)diazonium Tetrafluoroborate. Elution with light petroleum/diethyl ether/dichloromethane 70:15:15 v/v/v afforded **10a** (30%), with mp and spectral data identical to those reported for **10a** in the above reaction of **9** with **7a**, and 4-iodo-11-phenylthiochromeno-[2,3-*b*]indole (8%) as a red solid, mp 233−234 °C (from light petroleum/benzene) [^1H NMR (200 MHz) δ 6.37 (1 H, br d, J = 8.1 Hz), 6.97 (1 H, td, J_t = 8.1 Hz, J_d = 1.2 Hz), 7.14 (1 H, dd, J_1 = 8.1 Hz, J_2 = 7.6 Hz), 7.36−7.49 (3 H, m), 7.58−7.75 (5 H, m), 8.09 (1 H, dd, J_1 = 7.6 Hz, J_2 = 1.3 Hz); ^{13}C NMR (50 MHz) δ 96.50 (C), 118.65, 122.44, 123.53, 125.62 (C), 126.68, 128.33, 129.10, 129.40, 129.50, 130.79 (C), 131.26, 135.88 (C), 137.19 (C), 140.34, 145.38 (C), 155.28 (C), 163.31 (C) (1 quaternary signal not visible); MS m/z (rel intensity) 437 (M^+, 100), 310 (20); HRMS calcd for $C_{21}H_{12}INS$ 436.9735, found 436.9740. The structure was confirmed by X-ray diffraction (data not reported in the Supporting Information)].

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Supporting Information Available: Calculated reaction pathways, calculation details, and *Z*-matrices of radicals **13**, **14**, **15**, **16**, **30**, and **31** and the transition states connecting **13**−**14**, **13**−**15**, **15**−**31**, **31**−**14**, **15**−**16**, **15**−**30**, and **30**−**16** as obtained by DFT and/or PM3 methods; X-ray molecular structures, crystal data, and structure refinements of compounds **10b**,**c** and **11b**,**c**,**d**; CIF file for compounds **10b**,**c** and **11b**,**c**,**d**. This material is available free of charge via the Internet at http://pubs.acs.org.

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