Diastereoselective Cycloadditions of 1,3-Thiazolium-4-olates with Chiral 1,2-Diaza-1,3-butadienes

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A series of 2-(*N*-methyl)benzylamino-1,3-thiazolium-4-olates (2-aminothioisomünchnones) react with chiral 1,2-diaza-1,3-butadienes derived from carbohydrates to afford a diastereomeric mixture of (4*R*,5*S*)- and (4*R*,5*R*)-4,5-dihydrothiophenes. These substrate-controlled cycloadditions are chemoselective, regiospecific, and proceed with a high facial diastereoselection. A theoretical rationale at semiempirical level does justify the stereochemical outcome observed in the experiments.

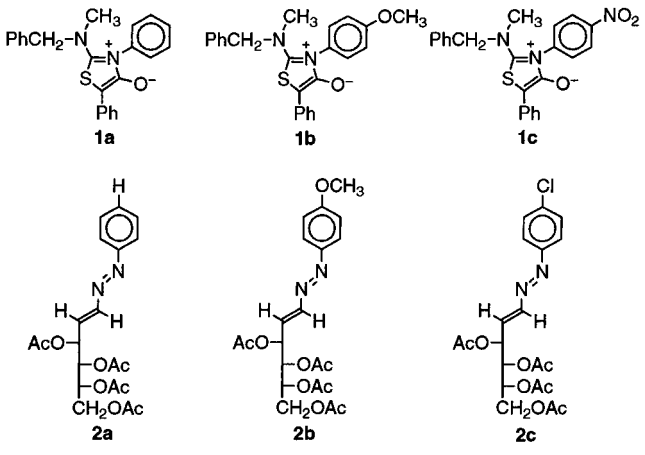
Introduction

1,3-Dipolar cycloaddition chemistry with mesoionic rings has proved to be a useful and versatile methodology in synthetic organic chemistry.[1] During the past decade our research group has explored the reactivity and synthetic utility of a large family of type I mesoionics, 1,3-thiazolium-4-olates, colloquially denoted as thioisomünchnones.[2] Although these five-membered heterocycles exhibit an inherent aromaticity, they also contain a masked azomethine ylide dipole and are therefore willing partners in [3 + 2] cycloadditions. Gratifyingly, in the course of our quest for novel heterocyclic systems, we came across the unusual range of three-,[2c] four-,[2f] five-,[2d,e] and six-membered[2g] rings supplied by reaction of 2-aminothioisomünchnones and hitherto inaccessible by conventional dipolar cycloadditions.[3] With these premises in mind, we were also interested in the study of asymmetric processes using either thioisomünchnones on a chiral template or chiral unsaturated dipolarophiles. As far as we know the condensation of mesoionic compounds with 1,2-diazoalkenes has not yet been reported. The latter substances contain an attractive heterodiene unit whose cycloaddition with other heteroatom-containing compounds would afford densely functionalized nitrogenated heterocycles. 1,2-Diazadienes derived from carbohydrates can easily be prepared from unprotected sugars in a few steps.[4] Their Diels−Alder reactions either with homo- or heterodienophiles have also been described by our group, disclosing that the facial selectivity provided by these inductors is largely dependent on the relative configurations of the chiral chain.[5]

The aim of the work described herein was to study the facial stereoselection provided by a series of carbohydrate-based 1,2-diaza-1,3-butadienes when coupled with simple 2-aminothioisomünchnones. Since the mechanism of dipolar cycloadditions continues to elicit interest, especially the question of whether these reactions proceed in a stepwise manner involving zwitterionic or diradical intermediates, or via a concerted pericyclic path,[3b] this manuscript also describes a semiempirical study of the above-mentioned processes. These results are consistent with reaction stereochemistry which is considered to be a crucial probe for the nature of cycloadditions. It is hoped that our timely exploration will expand the scope of cycloaddition chemistry with mesoionics.

Results and Discussion

Asymmetric Reactions. Thioisomünchnones **1a**−**c** were utilized as starting dipoles to be reacted with three homochiral 1,2-diaza-1,3-butadienes (**2a**−**c**) bearing an acyclic side chain of definite D-*arabino* configuration.



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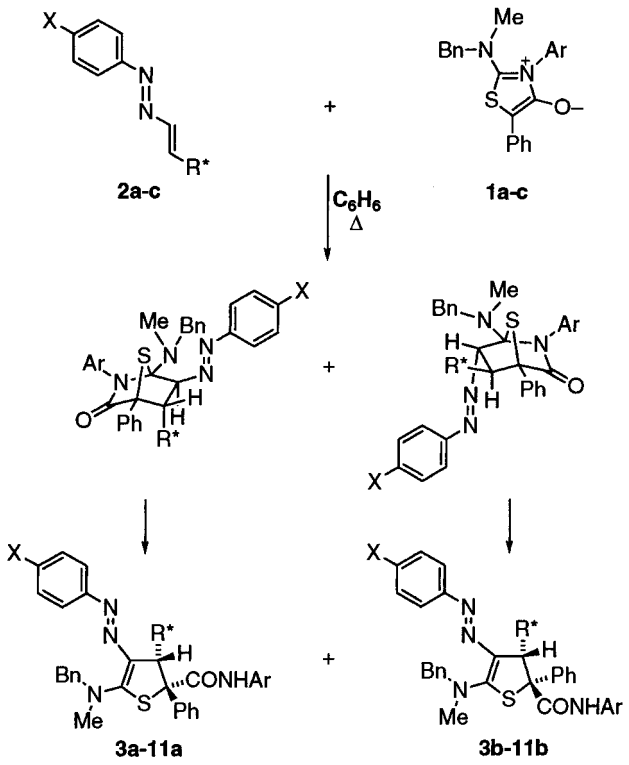
Scheme 1



R* = D-*arabino*-$(CHOAc)_3CH_2OAc$

3a	Ar = C_6H_5	X = H	**3b**
4a	Ar = 4-$MeOC_6H_4$	X = H	**4b**
5a	Ar = 4-$NO_2C_6H_4$	X = H	**5b**
6a	Ar = C_6H_5	X = OMe	**6b**
7a	Ar = 4-$MeOC_6H_4$	X = OMe	**7b**
8a	Ar = 4-$NO_2C_6H_4$	X = OMe	**8b**
9a	Ar = C_6H_5	X = Cl	**9b**
10a	Ar = 4-$MeOC_6H_4$	X = Cl	**10b**
11a	Ar = 4-$NO_2C_6H_4$	X = Cl	**11b**

Cycloadditions were conducted in benzene solution at reflux and are essentially complete within 2 h under such conditions. TLC analysis (diethyl ether−petroleum ether, 3:1) revealed the formation of two new products, which could be separated by flash chromatography. Moreover, inspection of crude samples by ^{1}H NMR spectroscopy at 400 MHz also evidenced high diastereomeric ratios in all cases. Spectroscopic and analytical data of such products are inconsistent with the existence of cycloadducts, pyridones or thiophenes, which can be obtained by reaction of thioisomünchnones with alkenes.[1a] Instead, they quite agree with a dihydrothiophene nucleus, which was obtained for the first time in the cycloadditions of these mesoionics with nitroalkenes.[2e] On the basis of these results, especially in the fact that the structures of diastereomers were solved by single-crystal X-ray analysis, structures **3**−**11** were equally attributed to reaction products (Scheme 1).

Diastereomers **3a**−**11a** were always prevalent and showed ^{1}H and ^{13}C NMR chemical shifts different from those of **3b**−**11b**. It is noteworthy that both diastereomers exhibited a pattern similar to those obtained in the cycloadditions of **1a**−**c** with nitroalkenes,[2e] thereby facilitating our assignments. In addition, an examination of such resonances revealed that the cycloaddition was chemoselective to the C=C bond. The only proton at the heterocyclic nucleus, H-4, appears in the range δ 5.07−5.27 and this signal is more shielded in diastereomers of series **a** ($\Delta\delta$ ∼0.1−0.2 ppm). Due to the influence of the chiral moiety, benzylic protons of the dialkylamino group appear as diastereomeric signals (NCH_aCH_bPh) between δ 4.60−5.02. Carbon resonances also offer a valuable identification of the dihydrothiophene ring. The carbon attached to the sugar fragment, C-4, is the more shielded resonance at δ ∼44.7−47.2, whereas the olefinic protons (C-2 and C-3) are largely deshielded and showed distinctive resonances consistent with their substitution patterns. It should be pointed out that C-4 of **3a**−**11a** appear at upper field than in **3b**−**11b**, while signals for C-2, C-3, and C-5 of the former diastereomers were shifted downfield with respect to those of **3b**−**11b**.

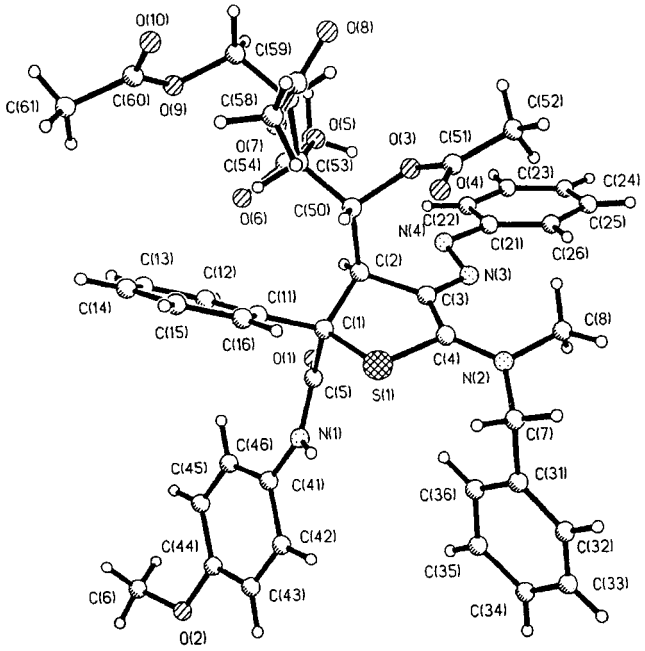


Figure 1. X-ray molecular structure of **4b** with the atom numbering system used in the crystallographic analysis.

These assignments were fully confirmed by the crystal structure of **4b** as determined by X-ray diffraction (Figure 1).[6] This unequivocal analysis also supported our surmise that the carbon−carbon double bond of the azadiene was involved in the cycloadditive process, while the nitrogenated double bond remained unaffected. Notably, this fact does generate a novel conjugated heterodiene whose reactivity will be examined in future studies.

Our attempts to isolate or detect by NMR the transient diastereomeric cycloadducts failed. At room temperature, cycloadditions proceeded slowly and decomposition of the starting mesoionic ring was observed at a large extent.

A few comments are necessary concerning the stereochemical outcome of the above-mentioned cycloadditions

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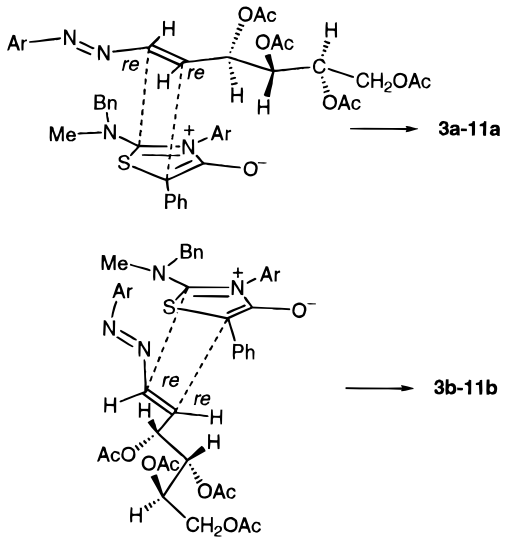
(6) The authors have deposited X-ray crystallographic data, a description of the structure determination, and tables of atomic coordinates, anisotropic displacement coefficients, bond lengths and angles for this structure with the Cambridge Crystallographic Data Centre (registry number CCDC-135482), and are available on request from the Director of the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK.

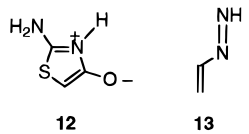
Scheme 2



with respect to our earlier work on the reactions of 2-aminothioisomünchnones with a series of nitroalkenes containing different carbohydrate side chains.[2e] Chiral nitroalkenes having an acyclic side chain of D-*galacto* configuration afford diastereomeric dihydrothiophenes with (4*S*,5*R*) and (4*S*,5*S*) configurations at the newly created stereogenic centers, while a D-mannose-based template produces (4*R*,5*S*) and (4*R*,5*R*)-configured dihydrothiophenes. In both cases, modest levels of diastereoselection with respect to the mesoionic ring were observed, albeit the heterocycle attacks to one face of the nitroalkene. In contrast, these chiral azabutadienes with D-*arabino* configuration give rise to dihydrothiophenes having (4*R*,5*R*) and (4*R*,5*S*) configurations. Again, facial selectivity results from the attack of the mesoionic ring to one face of the chiral butadiene, and remarkably, the heterocycle exposes preferentially one of its faces.

Theoretical Rationale. A theoretical study is now required to account for our experimental observations. At first glance, three issues should be considered: (a) the exclusive chemoselectivity (C=C versus N=N bonds); (b) complete regiocontrol because regioisomers are invariably formed according to the interactions involving C-2 and C-5 of the thioisomünchnones with C-3 and C-4 respectively, of parent azoalkenes; and (c) a high stereoselectivity—formation of two diastereomers, assuming that four new stereocenters are created in the cycloaddition, albeit removal of two takes place during cycloadduct cleavage thereby reducing the number of possible dihydrothiophenes to four. Our experimental results would be consistent with the approach of either face of the dipole to the *re*,*re* face of the dipolarophile (Scheme 2).

(a) Chemoselectivity. The reaction between **12** and **13** represents a simplified model for compounds **1** and **2**, respectively. Owing to the number of heavy heteroatoms, high-level ab initio methods could not be utilized at a reasonable computational cost. Instead, we have



12 **13**

used semiempirical calculations with full optimization at the PM3 level[7] with GAUSSIAN94,[8] which has proved to be one of the most robust methodologies for computing cycloaddition reactions.[9] Table 1 shows the energies and coefficients of the frontier orbitals and we can see that the interaction $HOMO_{dipole}-LUMO_{dipolarophile}$ ($\Delta E = 5.99$ eV) has a smaller energy gap than the opposite $HOMO_{dipolarophile}-LUMO_{dipole}$ interaction ($\Delta E = 8.16$ eV). This fact agrees with a Sustmann's type I cycloaddition,[10] also called *dipole−HOMO controlled* reactions.

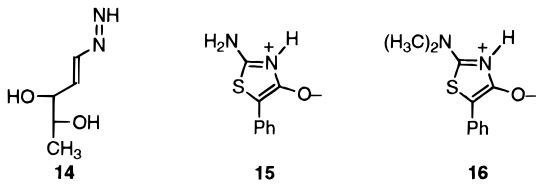
Table 1. Energies and Coefficients of the Frontier Orbitals for Compounds 12 and 13

compound	MO	E (eV)[a]	c_1[b]	c_2	c_3	c_4	c_5
12	HOMO	−7.89		−0.32			0.70
	LUMO	−1.36		0.75			0.38
13	HOMO	−9.52	0.56	−0.57	0.18	−0.04	
	LUMO	−1.90	0.61	−0.50	−0.41	0.59	

[a] At PM3 level. [b] Numbering refers to the positions of atoms.

On the other hand, the largest coefficient of the thioisomünchnone HOMO is on C-5, but the coefficients of the azoalkene LUMO at C-3 and C-4 are relatively similar. The scarce polarization in the LUMO impedes a rationalization of the regiochemical outcome and hence the enhanced reactivity of the carbon−carbon double bond.

A fundamental difference in these simplified systems compared to the real situation is that there are no large substituents in both the dipole and the dipolarophile, which will affect the relative size of the coefficients in the frontier orbitals, but not their signs. Unfortunately, a model incorporating a 1-(1,2-dihydroxypropyl) group of D-*threo* configuration on the azoalkene C-4 atom (**14**) and a phenyl group on the dipole C-5 atom (**15**) did not alter either the polarization of the LUMO in a significant manner.



14 **15** **16**

To better understand the nature of this particular [3 + 2] cycloaddition, systematic thermodynamic and kinetic studies, employing models **12** and **13** again, were undertaken. Scheme 3 depicts the eight possible cycloadditive processes arising from the participation of the nitrogen−nitrogen double bond (**a**−**d**) or the carbon−carbon double bond (**e**−**h**) of the azoalkene, either with *exo* or *endo*

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Scheme 3

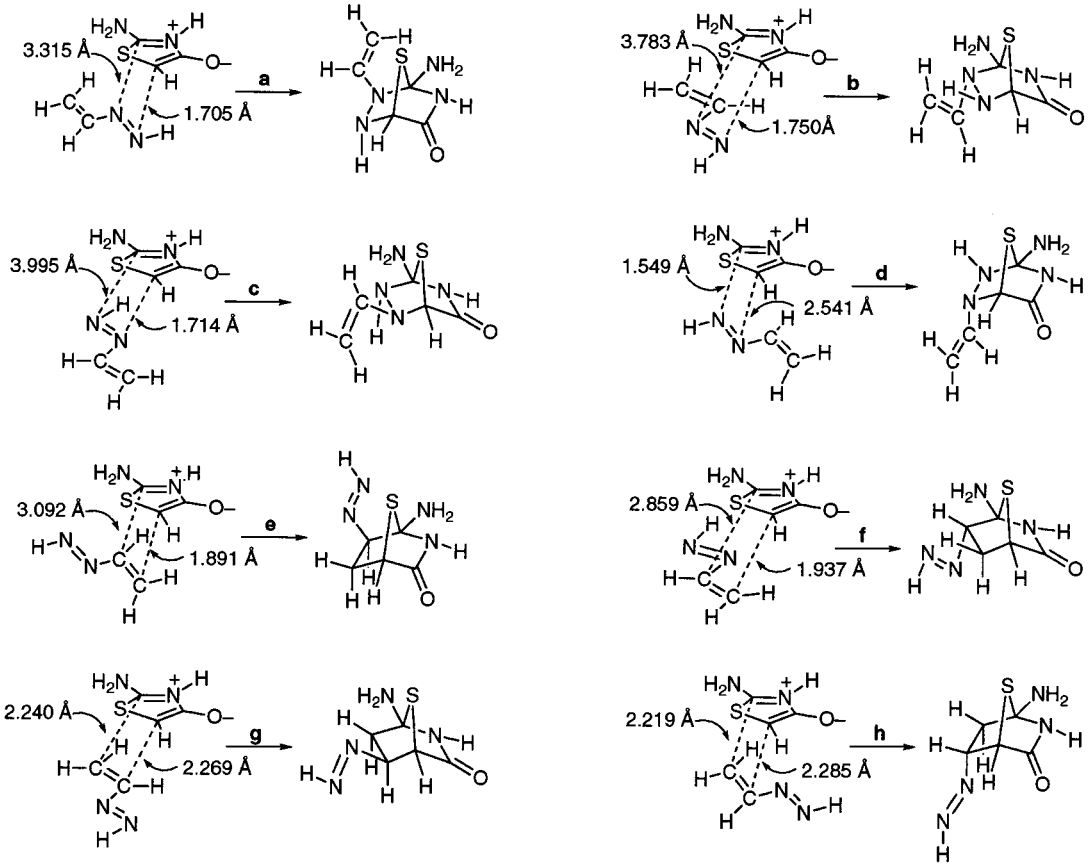


Table 2. Predicted Energies (in kcal/mol, PM3 level) for Cycloadditions a−h (Scheme 3)

	PM3 Energies[a]			
cycloaddition	TS	cycloadducts	$\Delta E^{\ddagger}$	ΔE_R
a	96.8	53.0	32.7	−11.0
b	94.6	53.2	30.5	−10.9
c	102.4	50.6	38.3	−13.5
d	105.7	50.9	41.6	−13.2
e	90.8	36.9	26.7	−27.2
f	90.4	34.0	26.3	−30.1
g	94.3	35.4	30.2	−28.7
h	97.2	34.5	33.1	−32.0

[a] In all cases the energy of the ground state is 64.1 kcal/mol, which corresponds to the energies of 2-amino-1,3-thiazolium-4-olate (8.0 kcal/mol) and 1,2-diaza-1,3-butadiene (56.1 kcal/mol).

orientation.[11] For these reactions, the reactants and transition structures were fully optimized at the PM3 level. Each of the transition structures gave only one imaginary harmonic vibrational frequency, corresponding to the formation of the C−N or C−C bonds. The predicted energies for cycloadducts and transition states as well as activation energies and reaction heats are listed below in Table 2. Clearly the calculations produce results which corroborate the available experimental data, since cycloadditions involving the carbon−carbon double bond are either kinetically (**e**−**f** with lower $\Delta E^{\ddagger}$ values) or thermodynamically favored (**e**−**h** with lower ΔE_R values).

Remarkably, a look at bond lengths in the calculated transition structures evidences that the simulated processes **e** and **f** are concerted but asynchronous. Thus, atom distances representing the forming bonds C-5 and C-4 (1.89−1.94 Å) are significantly shorter than those of C-2 and C-3 (2.86−3.09 Å). In other words the dipolar cycloaddition is reminiscent of a Michael-type addition, which is otherwise consistent with the strong nucleophilic character exhibited by the dipole at C-5 with an electrostatic atomic charge of −0.79.

(b) Regioselectivity. Having demonstrated the selective participation of the carbon moiety of the dipolarophile, our next target was to examine the regioselective approach of the azoalkene. Because the LUMO of model azoalkenes is highly symmetric having similar coefficients on C-3 and C-4, a switch in regioselectivity cannot properly be explained by FMO theory; as a consequence, any electronic contribution needs another rationale. Data from Table 2 suggest that the kinetically controlled processes (**e** and **f**) have the observed regiochemistry (C-3 and C-4 linked to C-2 and C-5 of the dipole respectively), albeit differing in the orientation of the nitrogen−nitrogen double bond which arises from *endo*/*exo* pathways. Nevertheless, our calculations reflect the high preference of that approach due to the large difference among **TSe**/**TSf** and **TSg**/**TSh** (in the range 3.6−6.7 kcal/mol), which renders in practice a regiospecific process.

(c) Facial Selectivity. As with other asymmetric cycloadditions, the key stereochemical issue is facial diastereoselectivity. The enhanced stereodifferentiation exhibited by azoalkenes **2a**−**c** should be a consequence of the C-4 polyacetoxy substituent. Assuming that an acyclic carbohydrate moiety has a conformational flexibility, it is clear that the bulky alkoxy group is not solely responsible for the facial bias but that it does augment it. This surmise could further be confirmed by computing the energetics of the transition states arising from the

(11) To clarify the discussion, the terms *endo* and *exo* refer to the orientation of the dipolarophile substituent with respect to the heterodiene fragment of the dipole during the approach of both reactants.

Scheme 4

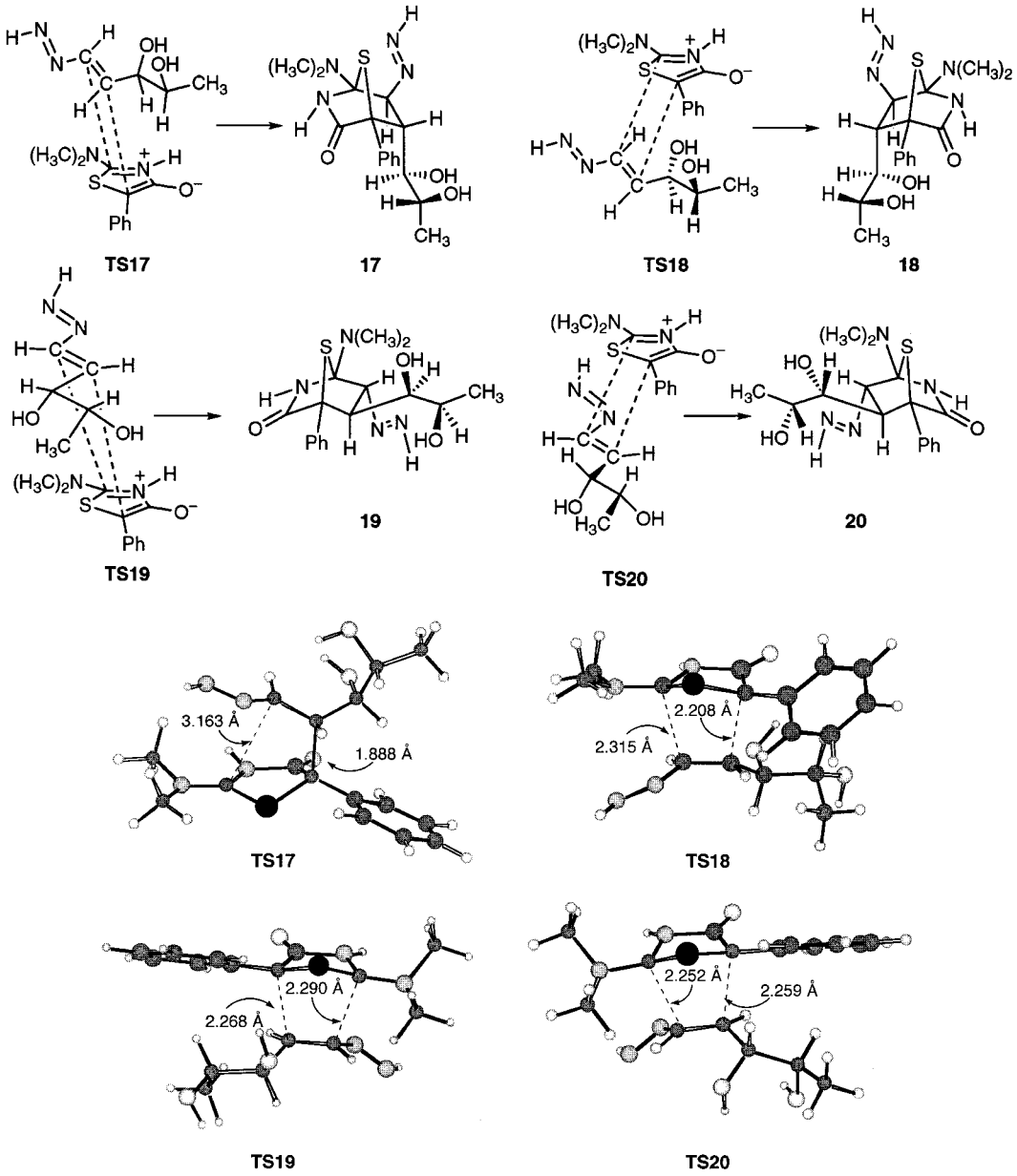


Figure 2. Computed (PM3 Level) transition structures 17−20.

cycloaddition between **12** and **14**, the latter having a side chain which resembles closely the configuration of azoalkenes **2a**−**c** at their stereogenic centers C-1′ and C-2′. The calculated transition structures show that the double bond N═N adopts an *endo* orientation regardless of the face of approach of the dipolarophile (either *re,re* or *si,si* faces of the carbon−carbon double bond) as well as a facial indiscrimination provided by the chiral substituent.

Next, a better imitation of dipoles **1a**−**c** would be thioisomünchnone **15** since a phenyl group at C-5 could discriminate the approach of the dipole to the diastereotopic faces of the dipolarophile **14**. Even though the computation of the corresponding transition structures reveals the preferential attack to the *re,re* face, the stabilizing *endo* orientation of the activating group (N═N) of the dipolarophile with respect to the dipole decreases. Moreover, a phenyl group at C-5 diminishes markedly the nucleophilicity on that carbon, and as a result, the process becomes more synchronous.

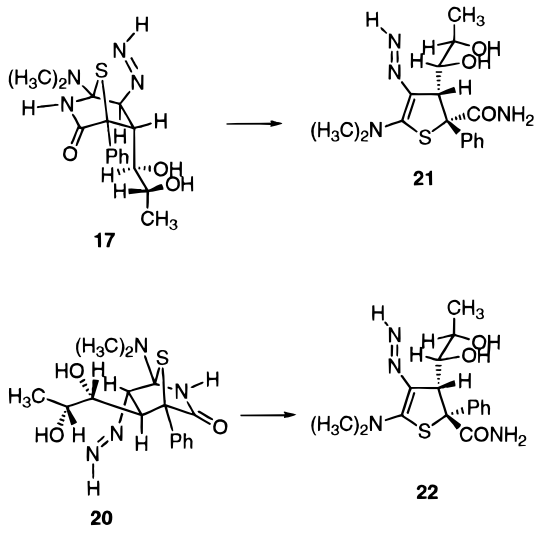
We then reasoned that a better mimicry of experiment would result from a model reaction combining **14** with dipole **16** bearing a dialkylamino group at the exocyclic nitrogen atom. It was also expected that the cycloadditions would be regiospecific, which would halve the number of possible cycloadducts. Accordingly, Scheme 4 shows the transition structures leading to four diastereomeric cycloadducts involving the approach of either face of the dipole to *re,re* and *si,si* faces of the chiral dipolarophile. Figure 2 shows the transition structures **17**−**20** for such cycloadditions.

Table 3 also lists the predicted energies for cycloadducts and transition structures together with distances between forming bonds. The greater stability of **TS17** and **TS20**, arising from the approach of the dipole to the *re,re* face is consistent with experiment and offers a general predictive tool. Ring cleavage of cycloadducts **17** and **20** would afford two diastereomeric dihydrothiophenes (**21** and **22**), whose configurations at the newly created

Table 3. Calculated (PM3) Energies (kcal/mol) and Distances (Å) of Forming Bonds for Transitions Structures and Cycloadducts 17−20

	TS17	TS18	TS19	TS20	**17**	**18**	**19**	**20**
energy	26.1	30.8	30.4	27.6	−21.7	−25.6	−24.1	−21.7
C_2-C_3	3.163	2.315	2.290	2.252	1.568	1.570	1.572	1.570
C_4-C_5	1.888	2.208	2.268	2.259	1.560	1.559	1.560	1.557

Scheme 5



stereocenters are coincident with those of compounds **3a**−**11a** and **3b**−**11b**, respectively (Scheme 5).

Although the latter study is consistent with the experiment, it is still unclear if similar predictions could be attained with the real situation of **1a** plus **2a** assuming that calculations can be performed at the PM3 semiempirical level without excessive cost.[12] Accordingly, Scheme 6 and Figure 3 illustrate the four possible TSs that describe the facial attack of the mesoionic dipole to both faces of the chiral azabutadiene.

As expected, **TS3a** and **TS3b** are energetically favored (−124.8 and −122.9 kcal/mol, respectively, Table 4). Furthermore, the ∼2 kcal/mol difference between both transition structures also accounts for the preference for a particular diastereomer. This result fully agrees with those obtained with the simplified model that highlights a ∼1.5 kcal/mol difference between **TS17** and **TS20**, thereby confirming the validity of our approach. In conclusion, these [3 + 2] dipolar cycloadditions of thioisomünchnones with carbohydrate-appended 1,2-diazabutadienes will be *endo* selective and highly facially selective as a result of the high steric interactions between bulky substituents in the transition structures.

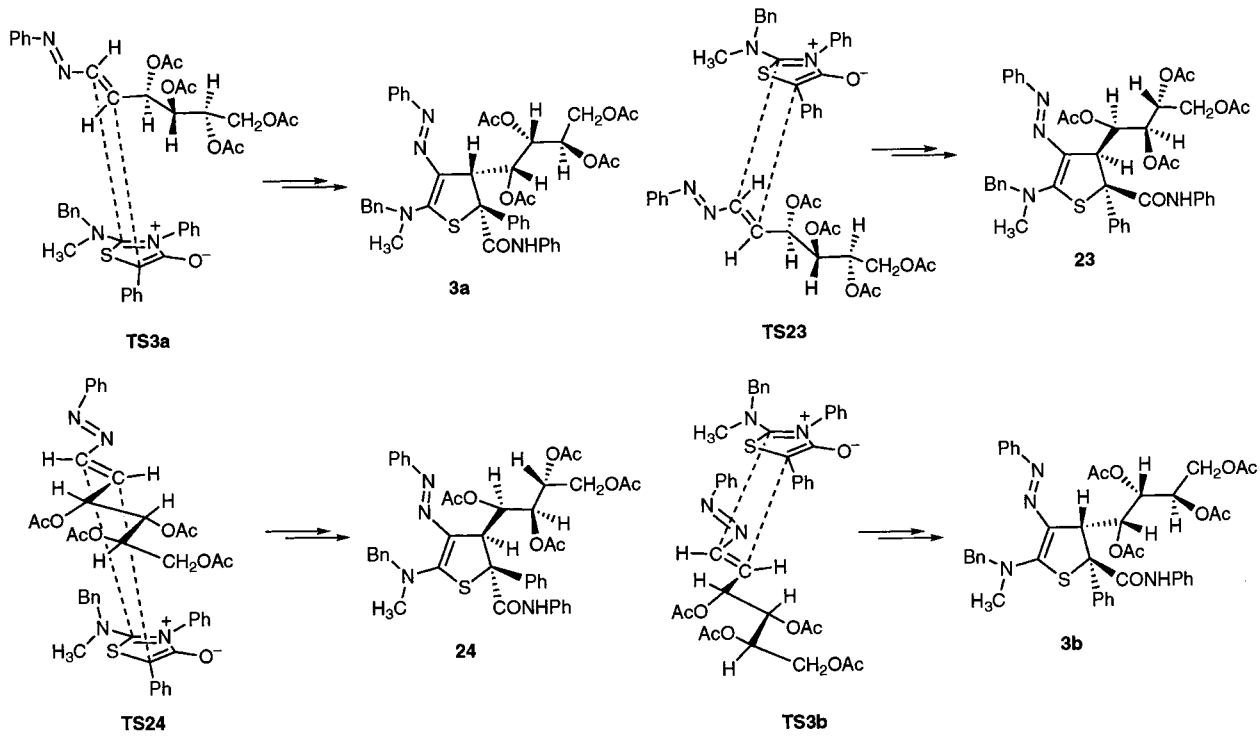
Conclusions

Intermolecular [3 + 2] cycloadditions between three *N*,*N*-dialkylamino-1,3-thiazolium-4-olates (**1a**−**c**) with three homochiral 1,2-diaza-1,3-butadienes (**2a**−**c**) as dipolarophiles were studied. This study represents the first example of a cycloaddition involving such reaction partners, which afforded tetrasubstituted 4,5-dihydrothiophene derivatives containing a new 1,2-diaza-1,3-butadiene moiety. Structures attributed to the resulting diastereomers were consistent with their spectroscopic and analytical data and further corroborated by X-ray diffraction analysis of **4b**. The process was regiospecific, and remarkably high facial selectivity was observed. This was attributed to a combination of steric shielding from dipole substituents and an inherent facial bias provided by the polyacetoxy C-4 substituent.

Experimental Section

General Methods. Melting points were determined on a capillary apparatus and are uncorrected. Optical rotations were measured at the sodium line at 18 ± 2 °C. Analytical and preparative TLC were performed on silica gel with monitoring by means of UV at 254 and 360 nm and iodine vapors. Flash chromatography[13] was performed with silica gel (400−230 mesh). IR spectra were recorded on KBr pellets. ^{1}H and ^{13}C NMR spectra were obtained at 400 and 100 MHz

Scheme 6



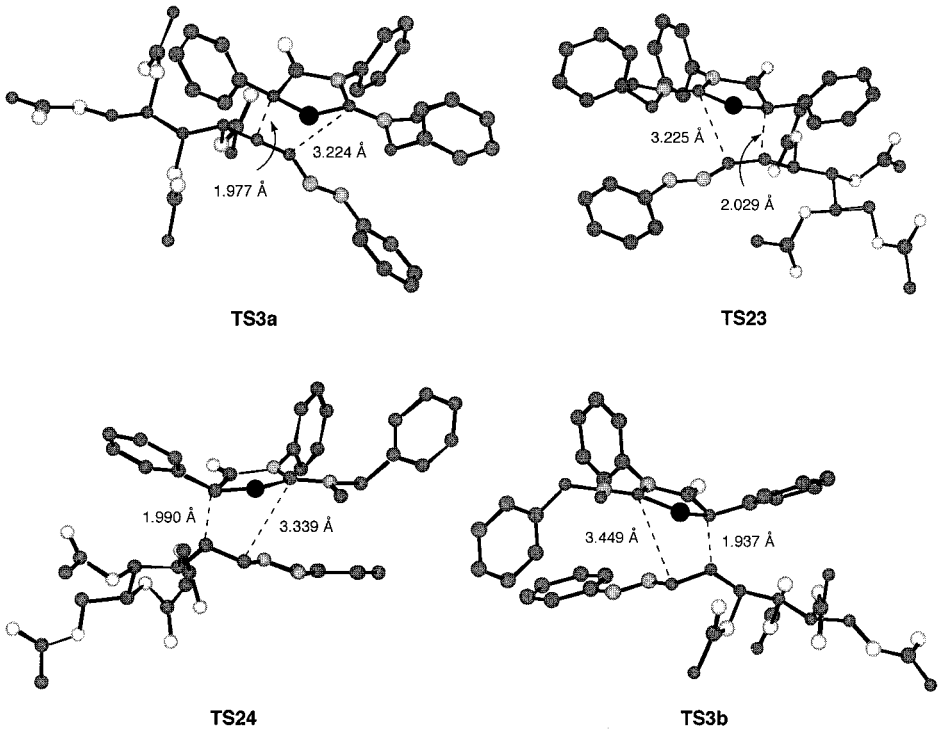


Figure 3. Computer-generated transition structures **3a**, **3b**, **23**, and **24**.

Table 4. Calculated (PM3) Energies (kcal/mol) and Distances (Å) of Forming Bonds for TS3a, TS3b, TS23, and TS24

	TS3a	TS23	TS24	TS3b
energy	−124.8	−120.4	−117.1	−122.9
C_2-C_3	3.224	3.225	3.339	3.449
C_4-C_5	1.977	2.029	1.990	1.937

respectively, in $CDCl_3$ (Me_4Si as internal standard) unless otherwise specified. Elemental analyses were recorded at the Universidad de Extremadura and by the Servei de Microanàlisi del CSIC at Barcelona. High-resolution mass spectra (HRMS/FAB$^+$) were obtained by the Servicio de Espectrometría de Masas at the Universidad de Córdoba, Spain. Compounds **1a**−**c**[2e] and **2a**−**c**[4] were prepared according to literature procedures. Petroleum ether refers to a boiling range of 40−60 °C.

Cycloadditions of Mesoionics with Azadienes. General Procedure for the Synthesis of (4*R*,5*R*)- and (4*R*,5*S*)-4-(1′,2′,3′,4′-Tetra-*O*-acetyl-D-*arabino*-tetritol-1-yl)-2-(*N*-methyl)benzylamino-5-phenyl-3-phenylazo-5-phenylcarbamoyl-4,5-dihydrothiophenes (3a and 3b). To a suspension of **1a** (1.00 g, 2.7 mmol) in benzene (50 mL) was added **2a** (0.75 g, 1.8 mmol). The reaction mixture was refluxed until the complete disappearance of **2a** (1−2 h, TLC analysis: diethyl ether−petroleum ether 3:1) and the appearance of two new products **3a** (R_f 0.4) and **3b** (R_f 0.2). An analysis by ^{1}H NMR of the crude mixture revealed that these substances were formed in a diastereomeric ratio 7:1. The solvent was evaporated, and the resulting residue was crystallized from diethyl ether affording **3a** as an orange solid (1.00 g, 71%). The mother liquors were concentrated, and the residue was flash-chromatographed using a gradient from diethyl ether−petroleum ether 1:2 at the beginning to diethyl ether at the end, to give an additional crop of **3a** (0.24 g, 17%; 88% overall yield) along with **3b** (0.08 g, 6%).

Compound **3a**: mp 165 °C; $[\alpha]_D$ +1214.7° (*c* 0.5, $CHCl_3$); IR (KBr) ν_{max} 3280, 1745, 1685 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (s, 1H), 7.52−7.00 (m, 20H), 6.03 (dd, J = 7.4 Hz, J = 2.3 Hz, 1H), 5.42 (dd, J = 8.7 Hz, 1H), 5.16 (m, 2H), 4.87 (d, J = 15.5 Hz, 1H), 4.70 (d, 1H), 4.17 (dd, J = 1.9 Hz, J = 12.7 Hz, 1H), 4.00 (dd, J = 4.0 1H), 3.22 (s, 3H), 2.37 (s, 3H), 2.10 (s, 3H), 1.85 (s, 3H), 1.45 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.2, 170.9, 170.0, 169.2, 166.6, 160.2, 155.2, 141.7, 137.2, 135.8, 128.9, 128.7, 128.6, 128.3, 127.7, 127.6, 127.1, 126.5, 125.8, 124.7, 120.9, 120.0, 74.5, 71.5, 68.5, 67.1, 61.9, 60.9, 44.9, 42.6, 21.4, 20.8, 19.8. Anal. Calcd for $C_{43}H_{44}N_4O_9S$: C, 65.14; H, 5.59; N, 7.06; S, 4.04. Found: C, 65.21; H, 5.86; N, 6.82; S, 3.98.

Compound **3b**: mp 90 °C; $[\alpha]_D$ +420.0° (*c* 0.1, $CHCl_3$); IR (KBr) ν_{max} 3400, 1740, 1675 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (s, 1H), 7.81−7.06 (m, 20H), 5.45 (dd, J = 7.6 Hz, J = 1.9 Hz, 1H), 5.27 (d, 1H), 5.02 (d, J = 15.9 Hz, 1H), 4.88 (m, 1H), 4.81 (d, 1H), 4.31 (dd, J = 8.5 Hz, 1H), 3.93 (dd, J = 2.3 Hz, J = 12.5 Hz, 1H), 3.79 (dd, J = 5.1 Hz, 1H), 3.39 (s, 3H), 2.27 (s, 3H), 2.00 (s, 3H), 1.95 (s, 3H), 1.79 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4, 170.1, 169.7, 169.5, 169.2, 156.8, 154.7, 137.6, 136.1, 133.2, 129.7, 129.1, 128.9, 128.8, 128.6, 128.5, 128.4, 128.2, 128.1, 127.7, 127.3, 126.8, 126.5, 125.4, 124.4, 121.2, 119.2, 118.3, 70.7, 70.1, 68.3, 67.3, 61.8, 61.1, 47.1, 43.1, 21.1, 20.9, 20.8, 20.7. Anal. Calcd for $C_{43}H_{44}N_4O_9S$: C, 65.14; H, 5.59; N, 7.06; S, 4.04. Found: C, 65.01; H, 5.41; N, 6.99; S, 4.15.

Synthesis of (4*R*,5*R*)- and (4*R*,5*S*)-4-(1′,2′,3′,4′-Tetra-*O*-acetyl-D-*arabino*-tetritol-1-yl)-5-(4-methoxyphenyl)carbamoyl-2-(*N*-methyl)benzylamino-5-phenyl-3-phenylazo-4,5-dihydrothiophenes (4a and 4b). These substances were obtained from **1b** and **2a** according to the general procedure described above: **4a** (R_f 0.5) and **4b** (R_f 0.2) in a diastereomeric ratio of 11:1 (^{1}H NMR). They were purified by flash chromatography (using a gradient from diethyl ether−hexane 2:1 to diethyl ether) to give **4a** (90%) and **4b** (6%) as orange solids.

Compound **4a**: mp 79 °C; $[\alpha]_D$ +986.3° (*c* 0.2, $CHCl_3$); IR (KBr) ν_{max} 3380, 1740, 1680 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (s, 1H), 7.43−6.81 (m, 19 H), 6.02 (dd, J = 2.4 Hz, J = 7.1 Hz, 1H), 5.40 (dd, J = 8.4 Hz, 1H), 5.19 (m, 1H), 5.13 (d, 1H), 4.90 (d, J = 15.5 Hz, 1H), 4.70 (d, 1H), 4.20 (dd, J = 1.8 Hz, J = 12.6 Hz, 1H), 4.00 (dd, J = 4.3 Hz, 1H), 3.76 (s, 3H), 3.22 (s, 3H), 2.36 (s, 3H), 2.09 (s, 3H), 1.85 (s, 3H), 1.54 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.1, 170.9, 170.0, 169.3, 166.4, 160.4, 156.6, 155.2, 141.9, 135.8, 130.3, 128.8, 128.7,

(12) One of the reviewers has pointed out the possibility that the PM3 results on reduced models might not fully establish the concertedness of their reactions, as well as the steric effects controlling the facial diastereoselection.

(13) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923−2925.

128.6, 128.2, 127.7, 127.6, 127.1, 126.5, 125.7, 121.7, 120.9, 114.0, 74.3, 71.6, 68.5, 67.2, 62.1, 60.9, 55.4, 44.9, 42.6, 21.4, 20.8, 19.9. Anal. Calcd for $C_{44}H_{46}N_4O_{10}S$: C, 64.22; H, 5.63; N, 6.81; S, 3.81. Found: C, 64.04; H, 5.90; N, 6.76; S, 3.67.

Compound **4b**: mp 92 °C; $[\alpha]_D$ +592.4° (*c* 0.5, $CHCl_3$); IR (KBr) ν_{max} 3320, 1745, 1675 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.05 (s, 1H), 7.81−6.75 (m, 19 H), 5.44 (dd, J = 7.6 Hz, J = 2.2 Hz, 1H), 5.26 (d, 1H), 5.01 (d, J = 15.9 Hz, 1H), 4.88 (m, 1H), 4.82 (d, 1H), 4.30 (dd, J = 8.5 Hz, 1H), 3.94 (dd, J = 2.3 Hz, J = 12.5 Hz, 1H), 3.78 (dd, J = 5.6 Hz, 1H), 3.74 (s, 3H), 3.39 (s, 3H), 2.26 (s, 3H), 1.99 (s, 3H), 1.95 (s, 3H), 1.79 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.5, 170.2, 169.8, 169.6, 169.0, 157.0, 156.5, 154.7, 136.2, 133.5, 130.7, 129.1, 128.9, 128.6, 128.5, 128.4, 127.7, 126.9, 126.5, 121.5, 121.2, 113.9, 70.7, 70.1, 68.3, 67.3, 61.8, 61.1, 55.5, 47.2, 43.1, 21.1, 20.9, 20.8, 20.7. Anal. Calcd for $C_{44}H_{46}N_4O_{10}S$: C, 64.22; H, 5.63; N, 6.81; S, 3.81. Found: C, 64.09; H, 5.60; N, 6.51; S, 4.18.

Synthesis of (4*R*,5*R*)- and (4*R*,5*S*)-4-(1′,2′,3′,4′-Tetra-*O*-acetyl-D-*arabino*-tetritol-1-yl)-2-(*N*-methyl)benzylamino-5-(4-nitrophenyl)carbamoyl-5-phenyl-3-phenylazo-4,5-dihydrothiophenes (5a and 5b). These substances were obtained from **1c** and **2a** according to the general procedure described above: **5a** (R_f 0.8, diethyl ether) and **5b** (R_f 0.3, diethyl ether) in a diastereomeric ratio > 32:1 (^1H NMR). They were purified by flash chromatography (using a gradient from diethyl ether−petroleum ether 2:1 to diethyl ether) to give **5a** (63%) and **5b** which could not be isolated in pure form. A homogeneous sample of **5b** was obtained by preparative TLC (using diethyl ether as eluent).

Compound **5a**: mp 85 °C; $[\alpha]_D$ +870.0° (*c* 0.2, $CHCl_3$); IR (KBr) ν_{max} 3320, 1740, 1680 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.21 (s, 1H), 8.19−7.01 (m, 19 H), 5.97 (dd, J = 2.9 Hz, J = 6.6 Hz, 1H), 5.26 (m, 2H), 5.16 (d, 1H), 4.92 (d, J = 15.5 Hz, 1H), 4.70 (d, 1H), 4.22 (dd, J = 1.1 Hz, J = 12.5 Hz, 1H), 3.92 (dd, J = 4.3 Hz, 1H), 3.25 (s, 3H), 2.34 (s, 3H), 2.02 (s, 3H), 1.88 (s, 3H), 1.62 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.2, 170.9, 169.9, 169.4, 167.5, 160.1, 155.0, 143.8, 142.9, 141.0, 135.7, 129.1, 128.8, 128.7, 128.6, 127.7, 127.1, 127.0, 126.4, 126.0, 124.9, 121.0, 119.7, 118.4, 74.1, 71.8, 68.6, 67.3, 62.5, 60.9, 44.7, 42.7, 21.3, 20.8, 20.8, 20.1. Anal. Calcd for $C_{43}H_{43}N_5O_{11}S$: C, 61.34; H, 5.17; N, 8.36; S, 3.83. Found: C, 61.42; H, 5.07; N, 8.45; S, 3.98.

Compound **5b**: ^1H NMR (400 MHz, $CDCl_3$) δ 8.35 (s, 1H), 8.11−7.05 (m, 19 H), 5.43 (dd, J = 7.6 Hz, J = 2.3 Hz, 1H), 5.26 (d, 1H), 5.02 (d, J = 16.1 Hz, 1H), 4.89 (m, 1H), 4.79 (d, 1H), 4.30 (dd, J = 8.4 Hz, 1H), 3.94 (dd, 1H, J = 3.9 Hz, J = 12.5 Hz, 1H), 3.80 (dd, J = 4.9 Hz, 1H), 3.42 (s, 3H), 2.32 (s, 3H), 1.99 (s, 3H), 1.96 (s, 3H), 1.79 (s, 3H).

Synthesis of (4*R*,5*R*)- and (4*R*,5*S*)-4-(1′,2′,3′,4′-Tetra-*O*-acetyl-D-*arabino*-tetritol-1-yl)-3-(4-methoxy)phenylazo-2-(*N*-methyl)benzylamino-5-phenyl-4,5-dihydrothiophenes (6a and 6b). These substances were obtained from **1a** and **2b** according to the general procedure described above: **6a** (R_f 0.5) and **6b** (R_f 0.2) in a diastereomeric ratio of 5:1 (^1H NMR). They were purified by flash chromatography (using a gradient from diethyl ether−hexane 1:2 to diethyl ether) to give **6a** (66%) and **6b** (9%) as orange solids.

Compound **6a**: mp 105 °C; $[\alpha]_D$ +967.1° (*c* 0.3, $CHCl_3$); IR (KBr) ν_{max} 3370, 1745, 1685 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.77 (s, 1H), 7.52−6.85 (m, 19 H), 6.03 (dd, J = 2.3 Hz, J = 7.4 Hz, 1H), 5.41 (dd, J = 8.5 Hz, 1H), 5.16 (m, 1H), 5.11 (d, 1H), 4.68 (d, J = 15.6 Hz, 1H), 4.60 (d, 1H), 4.17 (dd, J = 2.0 Hz, J = 12.7 Hz, 1H), 4.00 (dd, J = 4.1 Hz, 1H), 3.81 (s, 3H), 3.20 (s, 3H), 2.36 (s, 3H), 2.10 (s, 3H), 1.85 (s, 3H), 1.45 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.1, 170.9, 170.1, 169.2, 166.7, 158.5, 158.2, 149.4, 141.8, 137.2, 136.1, 128.9, 128.8, 128.6, 128.2, 127.5, 127.1, 127.0, 126.6, 124.6, 122.0, 120.1, 114.0, 74.3, 71.5, 68.5, 67.0, 61.9, 60.8, 55.5, 44.9, 42.5, 21.4, 20.9, 19.8. Anal. Calcd for $C_{44}H_{46}N_4O_{10}S$: C, 64.22; H, 5.63; N, 6.81; S, 3.89. Found: C, 64.15; H, 5.81; N, 6.74; S, 3.68.

Compound **6b**: mp 107 °C; $[\alpha]_D$ +740.0° (*c* 0.2, $CHCl_3$); IR (KBr) ν_{max} 3300, 1745, 1680 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.19 (s, 1H), 7.81−6.82 (m, 19 H), 5.45 (dd, J = 7.6 Hz, J = 2.4 Hz, 1H), 5.24 (d, 1H), 4.99 (d, J = 15.9 Hz, 1H), 4.89 (m, 1H), 4.79 (d, 1H), 4.31 (dd, J = 8.5 H, 1H), 3.93 (dd, J = 2.5 Hz, J = 12.4 Hz, 1H), 3.78 (m, 4H), 3.36 (s, 3H), 2.26 (s, 3H), 2.00 (s, 3H), 1.96 (s, 3H), 1.77 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.5, 170.1, 169.8, 169.6, 169.3, 158.7, 155.1, 149.0, 137.6, 136.4, 134.0, 129.1, 128.9, 128.8, 128.6, 128.0, 127.7, 126.9, 124.4, 122.5, 119.8, 113.9, 70.8, 70.2, 68.4, 67.3, 61.9, 61.0, 55.4, 47.2, 43.0, 21.2, 20.9, 20.8, 20.7. Anal. Calcd for $C_{44}H_{46}N_4O_{10}S$: C, 64.22; H, 5.63; N, 6.81; S, 3.89. Found: C, 63.88; H, 5.60; N, 6.79; S, 3.88.

Synthesis of (4*R*,5*R*)- and (4*R*,5*S*)-4-(1′,2′,3′,4′-Tetra-*O*-acetyl-D-*arabino*-tetritol-1-yl)-3-(4-methoxy)phenylazo-5-(4-methoxyphenyl)carbamoyl-2-(*N*-methyl)benzylamino-5-phenyl-4,5-dihydrothiophenes (7a and 7b). These compounds were obtained from **1b** and **2b** according to the general procedure described above: **7a** (R_f 0.4) and **7b** (R_f 0.2) in a diastereomeric ratio of 9:1 (^1H NMR). They were purified by flash chromatography (using a gradient from diethyl ether−hexane 1:2 to diethyl ether) to give **7a** (65%) and **7b** (10%) as orange solids.

Compound **7a**: mp 80 °C; $[\alpha]_D$ +904.0° (*c* 0.2, $CHCl_3$); IR (KBr) ν_{max} 3370, 1745, 1685 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.68 (s, 1H), 7.43−6.81 (m, 18H), 6.03 (dd, J = 2.0 Hz, J = 7.0 Hz, 1H), 5.41 (dd, J = 8.3 Hz, 1H), 5.18 (m, 1H), 5.07 (d, 1H), 4.85 (d, J = 15.5 Hz, 1H), 4.67 (d, 1H), 4.18 (dd, J < 1.0 Hz, J = 12.6 Hz, 1H), 4.01 (dd, J = 4.3 Hz, 1H), 3.81 (s, 3H), 3.75 (s, 3H), 3.20 (s, 3H), 2.35 (s, 3H), 2.10 (s, 3H), 1.85 (s, 3H), 1.54 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.0, 170.9, 170.1, 169.3, 166.5, 158.7, 158.2, 156.6, 149.4, 142.0, 136.1, 130.4, 128.8, 128.6, 128.1, 127.5, 127.1, 127.0, 126.5, 122.0, 121.7, 114.0, 74.1, 71.6, 68.6, 67.1, 62.1, 60.8, 55.4, 44.9, 42.5, 21.4, 20.9, 20.0. Anal. Calcd for $C_{45}H_{48}N_4O_{11}S$: C, 63.37; H, 5.67; N, 6.57; S, 3.76. Found: C, 63.05; H, 5.47; N, 6.51; S, 3.74.

Compound **7b**: mp 86 °C; $[\alpha]_D$ +653.7° (*c* 0.1, $CHCl_3$); IR (KBr) ν_{max} 3340, 1745, 1675 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.12 (s, 1H), 7.80−6.75 (m, 18H), 5.45 (dd, J = 7.5 Hz, J = 2.3 Hz, 1H), 5.23 (d, 1H), 4.99 (d, J = 15.9 Hz, 1H), 4.88 (m, 1H), 4.79 (d, 1H), 4.31 (dd, J = 8.4 Hz, 1H), 3.93 (dd, J = 2.4 Hz, J′ = 12.4 Hz, 1H), 3.79 (m, 7H), 3.36 (s, 3H), 2.25 (s, 3H), 2.01 (s, 3H), 1.98 (s, 3H), 1.79 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.5, 170.1, 169.8, 169.6, 169.2, 158.7, 156.5, 155.2, 149.0, 136.5, 133.5, 130.8, 129.1, 128.9, 128.6, 128.0, 127.7, 126.9, 122.5, 121.5, 113.9, 113.9, 70.7, 70.2, 68.4, 67.3, 61.9, 61.0, 55.5, 47.2, 43.0, 21.2, 20.9, 20.8, 20.7. Anal. Calcd for $C_{45}H_{48}N_4O_{11}S$: C, 63.37; H, 5.67; N, 6.57; S, 3.76. Found: C, 63.33; H, 5.34; N, 6.90; S, 3.91.

Synthesis of (4*R*,5*R*)- and (4*R*,5*S*)-4-(1′,2′,3′,4′-Tetra-*O*-acetyl-D-*arabino*-tetritol-1-yl)-3-(4-methoxy)phenylazo-2-(*N*-methyl)benzylamino-5-(4-nitrophenyl)carbamoyl-5-phenyl-4,5-dihydrothiophenes (8a and 8b). These substances were obtained from **1c** and **2b** according to the general procedure described above: **8a** (R_f 0.5, diethyl ether−petroleum ether 4:1) and **8b** (R_f 0.2, diethyl ether−petroleum ether 4:1) in a diastereomeric ratio > 30:1 (^1H NMR). They were purified by flash chromatography (using a gradient from diethyl ether−hexane 3:1 to diethyl ether) to give **8a** (58%) and **8b** (5%) as orange solids.

Compound **8a**: mp 91 °C; $[\alpha]_D$ +887.2° (*c* 0.2, $CHCl_3$); IR (KBr) ν_{max} 3320, 1745, 1690 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.19 (s, 1H), 8.19−6.85 (m, 18H), 5.98 (dd, J = 2.9 Hz, J = 6.5 Hz, 1H), 5.26 (m, 2H), 5.12 (d, 1H), 4.89 (d, J = 15.6 Hz, 1H), 4.67 (d, 1H), 4.22 (dd, J < 1.0 Hz, J = 12.7 Hz, 1H), 3.93 (dd, J = 4.4 Hz, 1H), 3.81 (s, 3H), 3.75, 3.22 (s, 3H), 2.33 (s, 3H), 2.03 (s, 3H), 1.88 (s, 3H), 1.62 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.1, 170.9, 169.9, 169.3, 167.6, 158.4, 149.2, 143.8, 142.9, 141.2, 136.0, 129.1, 129.0, 128.6, 128.6, 127.6, 127.1, 126.4, 124.9, 122.1, 119.6, 114.1, 73.9, 71.9, 68.7, 67.3, 62.5, 60.8, 55.5, 44.8, 42.6, 21.3, 20.8, 20.7, 20.1. Anal. Calcd for $C_{44}H_{46}N_5O_{12}S$: C, 60.89; H, 5.23; N, 8.07; S, 3.61. Found: C, 60.71; H, 4.97; N, 7.92; S, 4.06.

Compound **8b**: mp 100 °C; $[\alpha]_D$ +875.1° (*c* 0.2, $CHCl_3$); IR (KBr) ν_{max} 3320, 1735, 1690 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.41 (s, 1H), 8.11−6.85 (m, 18H), 5.43 (dd, J = 7.4 Hz, J = 2.3 Hz, 1H), 5.23 (d, 1H), 4.99 (d, J = 16.1 Hz, 1H), 4.88 (m, 1H), 4.76 (d, 1H), 4.31 (dd, J = 8.5 Hz, 1H), 3.93 (dd, J = 2.3 Hz, J = 12.4 Hz, 1H), 3.79 (m, 4H), 3.40 (s, 3H), 2.27 (s, 3H),

2.00 (s, 3H), 1.96 (s, 3H), 1.80 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4, 170.2, 170.0, 169.7, 169.6, 159.0, 154.6, 148.8, 143.6, 143.4, 136.4, 132.6, 129.5, 129.1, 128.9, 128.6, 127.9, 127.8, 126.6, 124.8, 122.5, 119.2, 114.0, 70.9, 70.2, 68.3, 67.1, 61.8, 61.1, 55.5, 47.1, 43.3, 21.2, 20.9, 20.8, 20.7. HRMS (FAB^+) found: 868.283006 ($C_{44}H_{46}N_5O_{12}S$ requires 868.286369), Δ = 3.9 ppm.

Synthesis of (4*R*,5*R*)- and (4*R*,5*S*)-4-(1′,2′,3′,4′-Tetra-*O*-acetyl-D-*arabino*-tetritol-1-yl)-3-(4-chloro)phenylazo-2-(*N*-methyl)benzylamino-5-phenyl-5-phenylcarbamoyl-4,5-dihydrothiophenes (9a and 9b). These substances were obtained from **1a** and **2c** according to the general procedure described above: **9a** (R_f 0.4) and **9b** (R_f 0.2) in a diastereomeric ratio of 8:1 (^{1}H NMR). They were purified by flash chromatography (using a gradient from diethyl ether−petroleum ether 1:2 to diethyl ether) to give **9a** (75%) and **9b** (4%) as orange solids.

Compound **9a**: mp 152 °C; $[\alpha]_D$ +1083.2° (*c* 0.2, $CHCl_3$); IR (KBr) ν_{max} 3280, 1745, 1685 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (s, 1H), 7.5−7.01 (m, 19H), 6.01 (dd, *J* = 7.1 Hz, *J* = 2.6 Hz, 1H), 5.39 (dd, *J* = 8.3, 1H), 5.19 (m, 1H), 5.12 (d, 1H), 4.87 (d, *J* = 15.5 Hz, 1H), 4.75 (d, 1H), 4.18 (dd, *J* = 1.8 Hz, *J* = 12.7 Hz, 1H), 3.99 (dd, *J* = 4.2 Hz, 1H), 3.22 (s, 3H), 2.34 (s, 3H), 2.09 (s, 3H), 1.85 (s, 3H), 1.47 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.0, 170.9, 170.0, 169.2, 166.5, 161.2, 153.7, 141.6, 137.1, 135.6, 130.7, 128.9, 128.7, 128.6, 128.3, 127.8, 127.7, 127.0, 126.4, 124.7, 121.9, 120.1, 74.5, 71.5, 68.5, 67.2, 62.0, 60.9, 44.9, 42.7, 21.3, 20.8, 19.8. Anal. Calcd for $C_{43}H_{43}ClN_4O_9S$: C, 62.42; H, 5.24; N, 6.77; S, 3.87. Found: C, 62.32; H, 5.23; N, 6.76; S, 3.81.

Compound **9b**: mp 109 °C; $[\alpha]_D$ +848.7° (*c* 0.2, $CHCl_3$); IR (KBr) ν_{max} 3310, 1745, 1675 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (s, 1H), 7.79−7.07 (m, 19H), 5.42 (dd, *J* = 7.2 Hz, *J* = 1.5 Hz, 1H), 5.25 (d, 1H), 5.00 (d, *J* = 15.9 Hz, 1H), 4.89 (m, 1H), 4.84 (d, 1H), 4.31 (dd, *J* = 8.3 Hz, 1H), 3.94 (dd, *J* = 2.9 Hz, *J* = 12.3 Hz, 1H), 3.78 (dd, *J* = 5.2 Hz, 1H), 3.38 (s, 3H), 2.00 (s, 3H), 1.99 (s, 3H), 1.96 (s, 3H), 1.78 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4, 170.0, 169.7, 169.5, 169.1, 157.5, 153.2, 137.5, 135.9, 133.1, 131.6, 129.3, 129.0, 128.8, 128.7, 128.6, 128.5, 127.8, 126.8, 124.5, 122.3, 119.8, 70.7, 70.1, 68.3, 67.3, 61.8, 61.2, 47.2, 43.2, 21.1, 20.8, 20.8, 20.7. Anal. Calcd for $C_{43}H_{43}ClN_4O_9S$: C, 62.42; H, 5.24; N, 6.77; S, 3.87. Found: C, 62.20; H, 5.31; N, 6.77; S, 4.01.

Synthesis of (4*R*,5*R*)- and (4*R*,5*S*)-4-(1′,2′,3′,4′-Tetra-*O*-acetyl-D-*arabino*-tetritol-1-yl)-3-(4-chloro)phenylazo-5-(4-methoxyphenyl)carbamoyl-2-(*N*-methyl)benzylamino-5-phenyl-4,5-dihydrothiophenes (10a and 10b). These substances were obtained from **1b** and **2c** according to the general procedure described above: **10a** (R_f 0.3) and **10b** (R_f 0.1) in a diastereomeric ratio of 6:1 (^{1}H NMR). They were purified by flash-chromatography (using a gradient from diethyl ether−hexane 3:2 to diethyl ether) to give **10a** (77%) and **10b** (3%) as orange solids.

Compound **10a**: mp 77 °C; $[\alpha]_D$ +976.9° (*c* 0.2, $CHCl_3$); IR (KBr) ν_{max} 3330, 1740, 1675 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (s, 1H), 7.42−6.81 (m, 18H), 6.02 (dd, *J* = 2.7 Hz, *J* = 6.8 Hz, 1H), 5.40 (dd, *J* = 8.1 Hz, 1H), 5.23 (m, 1H), 5.09 (d, 1H), 4.88 (d, *J* = 15.5 Hz, 1H), 4.75 (d, 1H), 4.21 (dd, *J* < 1.0 Hz, *J* = 12.6 Hz, 1H), 4.01 (dd, *J* = 4.5 Hz, 1H), 3.76 (s, 3H), 3.22 (s, 3H), 2.32 (s, 3H), 2.09 (s, 3H), 1.85 (s, 3H), 1.56 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.9, 171.0, 170.0, 169.2, 166.3, 161.4, 156.7, 153.7, 141.7, 135.6, 130.7, 130.2, 128.9, 128.7, 128.7, 128.3, 127.8, 127.7, 127.0, 126.4, 121.9, 121.8, 114.0, 74.4, 71.6, 68.6, 67.3, 62.2, 60.9, 55.4, 45.0, 42.7, 21.3, 20.8, 20.8. Anal. Calcd for $C_{44}H_{45}ClN_4O_{10}S$: C, 61.64; H, 5.29; N, 6.53; S, 3.74. Found: C, 61.70; H, 5.03; N, 6.64; S, 3.91.

Compound **10b**: mp 90 °C; $[\alpha]_D$ +728.6° (*c* 0.1, $CHCl_3$); IR (KBr) ν_{max} 3325, 1740, 1675 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (s, 1H), 7.79−6.76 (m, 18H), 5.42 (dd, *J* = 7.5 Hz, *J* = 2.4 Hz, 1H), 5.24 (d, 1H), 5.00 (d, *J* = 15.8 Hz, 1H), 4.90 (m, 1H), 4.86 (d, 1H), 4.32 (dd, *J* = 8.3 Hz, 1H), 3.94 (dd, *J* = 2.3 Hz, *J* = 12.4 Hz, 1H), 3.78 (dd, *J* = 5.2 Hz, 4H), 3.75 (s, 1H), 3.38 (s, 3H), 2.23 (s, 3H), 1.99 (s, 3H), 1.96 (s, 3H), 1.78 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4, 170.0, 169.7, 169.5, 169.0, 157.7, 156.5, 153.3, 136.0, 133.3, 131.5, 130.6, 129.2, 129.0, 128.7, 128.6, 128.5, 127.8, 126.8, 122.3, 121.5, 114.0, 70.6, 70.1, 68.3, 67.4, 61.8, 61.2, 55.5, 47.2, 43.2, 21.1, 20.9, 20.8, 20.7. HRMS (FAB^+) found 857.261274 ($C_{44}H_{45}ClN_4O_{10}S$ + H^+ requires 857.262319), Δ = 1.2 ppm.

Synthesis of (4*R*,5*R*)- and (4*R*,5*S*)-4-(1′,2′,3′,4′-Tetra-*O*-acetyl-D-*arabino*-tetritol-1-yl)-3-(4-chloro)phenylazo-2-(*N*-methyl)benzylamino-5-(4-nitrophenyl)carbamoyl-5-phenyl-4,5-dihydrothiophenes (11a and 11b). These compounds were obtained from **1c** and **2c** according to the general procedure described above: **11a** (R_f 0.5, diethyl ether−petroleum ether 4:1) and **11b** (R_f 0.1, diethyl ether−petroleum ether 4:1) in a diastereomeric ratio > 60:1 (^{1}H NMR). They were purified by flash chromatography (using a gradient from diethyl ether−petroleum ether 1:1 to diethyl ether) to give **11a** (77%) and **11b** (2%) as orange solids.

Compound **11a**: mp 90 °C; $[\alpha]_D$ +985.4° (*c* 0.2, $CHCl_3$); IR (KBr) ν_{max} 3320, 1740, 1690 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (s, 1H), 8.19−7.03 (m, 18H), 5.96 (dd, *J* = 3.7 Hz, *J* = 6.1 Hz, 1H), 5.31 (m, 1H), 5.23 (dd, *J* = 7.3 Hz, 1H), 5.13 (d, 1H), 4.91 (d, *J* = 15.5 Hz, 1H), 4.75 (d, 1H), 4.24 (dd, *J* = 1.6 Hz, *J* = 12.8 Hz, 1H), 3.91 (dd, *J* = 5.1 Hz, 1H), 3.25 (s, 3H), 2.29 (s, 3H), 2.01 (s, 3H), 1.88 (s, 3H), 1.65 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.9, 171.1, 169.9, 169.4, 167.4, 161.2, 153.6, 143.9, 142.9, 141.0, 135.5, 131.0, 129.2, 128.8, 127.8, 127.1, 126.3, 124.9, 122.0, 119.7, 74.2, 71.9, 68.7, 67.5, 62.7, 60.9, 44.9, 42.9, 21.2, 20.8, 20.2. Anal. Calcd for $C_{43}H_{42}ClN_5O_{11}S$: C, 59.20; H, 4.85; N, 8.03; S, 3.67. Found: C, 58.99; H, 4.93; N, 7.98; S, 3.73.

Compound **11b**: mp 105 °C; $[\alpha]_D$ +667.7° (*c* 0.3, $CHCl_3$); IR (KBr) ν_{max} 3320, 1740, 1670 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 (s, 1H), 8.13−8.21 (m, 18H), 5.40 (dd, *J* = 7.4 Hz, *J* = 2.5 Hz, 1H), 5.23 (d, 1H), 5.00 (d, *J* = 15.9 Hz, 1H), 4.90 (m, 1H), 4.81 (d, 1H), 4.31 (dd, *J* = 8.2 Hz, 1H), 3.94 (dd, *J* <1 Hz, *J* = 12.4 Hz, 1H), 3.78 (dd, *J* = 5.0 Hz, 4H), 3.41 (s, 3H), 2.25 (s, 3H), 1.99 (s, 3H), 1.96 (s, 3H), 1.79 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4, 170.2, 169.7, 169.5, 157.7, 153.2, 156.2, 143.8, 143.3, 135.9, 132.4, 132.0, 129.6, 129.2, 129.0, 128.9, 128.5, 128.3, 128.0, 127.0, 126.7, 124.9, 122.3, 119.27, 70.9, 70.2, 68.3, 67.2, 61.8, 61.2, 47.1, 43.5, 21.1, 20.9, 20.7. Anal. Calcd for $C_{43}H_{42}ClN_5O_{11}S$: C, 59.20; H, 4.85; N, 8.03; S, 3.67. Found: C, 59.35; H, 5.05; N, 7.82; S, 3.92.

X-ray Crystallographic Data for Compound 4b.[6] Data and diffraction parameters were obtained for a crystal with dimensions 0.45 × 0.40 × 0.25 mm^3 using a wavelength λ = 0.71069 Å at 180(2) K. Crystal system: monoclinic. Space group: $P2_1$. Unit cell dimensions: *a* = 12.802(5) Å, *b* = 26.832(5) Å, *c* = 13.317(5) Å, α = 90.000(5)°, β = 97.210(5)°, γ = 90.000(5)°, *V* = 4538(3) Å^3, *Z* (molecules/unit cell) = 2. Density (calcd): 1.231 Mg/m^3. μ (abs coefficient): 0.131 mm^{-1}. *F*(000) = 1778. θ range for data collection: 3.55 to 21.50°. Index ranges: −13 = *h* = 13, −3 = *k* = 27, −13 = *l* = 13. Collected reflections: 6216. Independent reflections: 5942 [R_{int} = 0.0806]. Maximum and minimum transmission: 0.9680 and 0.9434. Data/restraints/parameters: 5942/25/1095. GOF (goodness-of-fit on F^2): 1.101. Final *R* indices [$I > 2\sigma(I)$]: *R1* = 0.0795, *wR2* = 0.1758. Final *R* indices (all data): *R1* = 0.1504, *wR2* = 0.2130. $\Delta\rho_{max}$ and $\Delta\rho_{min}$ (largest diff. peak and hole): 0.380 and −0.296 eÅ^{-3}. Refinement method: full-matrix least-squares on F^2.

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Supporting Information Available: Tables of complete crystallographic data and a full list of IR absorbances, ^{1}H NMR and ^{13}C NMR listings with assignments for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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