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1,3-Dipolar Cycloadditions of Acetylenic Sulfones in Solution and on Solid Supports

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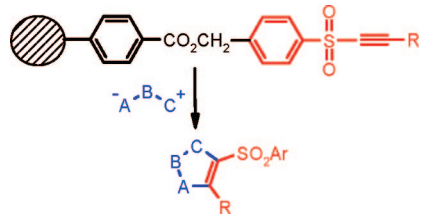

Several representative acetylenic sulfones were immobilized on a polymer support derived from Merrifield resin by means of ester linkers that were used to couple free carboxylic acid groups on the solid support with benzylic hydroxyl functions on the arylsulfonyl moieties of the acetylenes. Several examples of reversed ester linkers, using Merrifield resin directly, were also successfully prepared. The 1,3-dipolar cycloadditions of the solid-supported acetylenic sulfones were investigated with a series of 1,3-dipoles, including benzyl azide, ethyl diazoacetate, diazomethane, as well as representative nitrile oxides, nitrile imines, nitrile ylides, nitrones, azomethine imines, azomethine ylides, munchnones, and sydnones. In general, analogous cycloadditions were also performed with acetylenic sulfones in solution phase for comparison. The cycloadditions typically afforded good to excellent yields of the desired products in both solution and solid phase, although the latter reactions sometimes required more vigorous conditions. Except in the case of benzyl azide and diazo compounds, where mixtures of regioisomers were obtained, the other 1,3-dipoles reacted with high regioselectivity and afforded essentially unique regioisomers. Cleavage of the products from the resin was smoothly effected by alkaline hydrolysis, while several attempts at reductive desulfonylation with sodium amalgam or samarium diiodide-HMPA resulted in N−O or C−O scission, in addition to cleavage from the polymer. The method provides access to a number of important classes of heterocycles, including variously substituted and functionalized triazoles, pyrazoles, 1,2-oxazoles, pyrroles, as well as their dihydro and bicyclic analogues. The success of the cycloadditions on polymer supports paves the way to future investigations of sequential transformations leading to libraries of useful heterocycles.

Introduction

Acetylenic sulfones are a readily available class of compounds that provide the opportunity for a broad range of synthetically useful transformations.[1−3] The strongly electron-withdrawing sulfone group activates an adjacent alkyne moiety toward Diels−Alder and related cycloadditions,[4] as well as toward conjugate additions of various types of nucleophiles.[5] It also stabilizes adjacent carbanions,[6] thus making it possible to carry out combinations of conjugate additions and intramolecular

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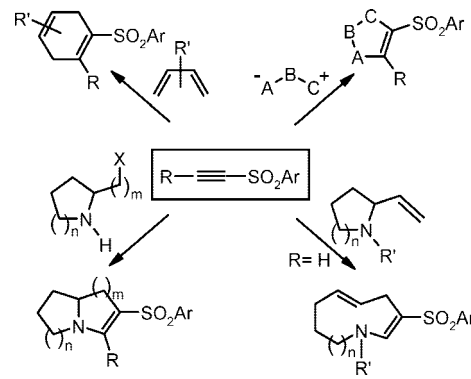
alkylations or acylations.[7] The removal of the sulfone group from the product can be achieved by several types of reductive, oxidative or alkylative desulfonylations.[8] The combination of conjugate addition, intramolecular alkylation or acylation and desulfonylation has been employed in the synthesis of a variety of alkaloids, including (−)-pumiliotoxin C,[7a] (−)-indolizidines 167B, 207A, 209B, and 209D,[7b] *ent*-(−)-julifloridine,[9] (−)-lasubine II,[10] (±)-myrtine,[10] and 4-quinolone alkaloids derived from the medicinal plant *Ruta chalepensis*.[11] The conjugate additions of cyclic tertiary α-vinyl amines to acetylenic sulfones afford zwitterions that undergo facile aza-Cope rearrangements, resulting in ring-expansions that have been utilized in the synthesis of the marine natural products motuporamine A and B.[12] Acetylenic sulfones also undergo cycloadditions with several types of 1,3-dipoles, including diazo compounds,[13] azides,[13b,14] nitrones,[15] pyridine *N*-oxides,[16] nitrile oxides,[13b,17] nitrile imines,[17a] certain mesoionic compounds,[17a,18a,b] and others.[18c,d] These general transformations are summarized in Scheme 1. We recently reported the first preparation of acetylenic sulfones on solid supports and a few of their representative reactions.[19] Several earlier examples of the reactions of vinyl sulfones on solid supports have also appeared.[20] The utility of 1,3-dipolar cycloadditions[21] in the preparation of diverse heterocyclic products and the special

SCHEME 1



advantages of solid phase organic synthesis[22] have prompted us to examine a wider range of 1,3-dipoles for this purpose. We now report the results of these cycloadditions both on solid supports and, for comparison, in solution.

Results and Discussion

Of several methods that were investigated for the preparation of acetylenic sulfones on solid supports,[19] the one shown in Scheme 2 proved the most generally applicable. Thus, sulfonylhydrazide **1** was converted into the corresponding selenosulfonate **2** by oxidation with benzeneseleninic acid.[23] Several representative acetylenes **3a**−**3c** were then subjected to free-radical selenosulfonation[24] with **2**, followed by esterification[25] of the resulting adducts **4** with the polymer-supported carboxylic acid **5** to afford the corresponding ester-linked products **6a-**

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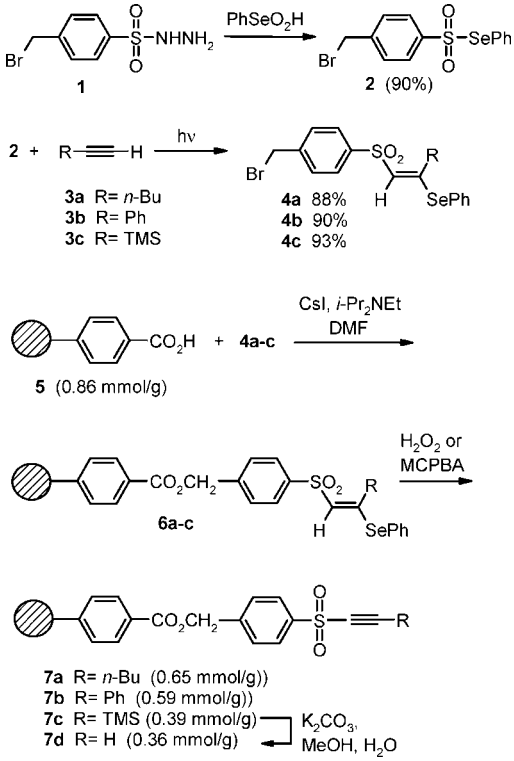
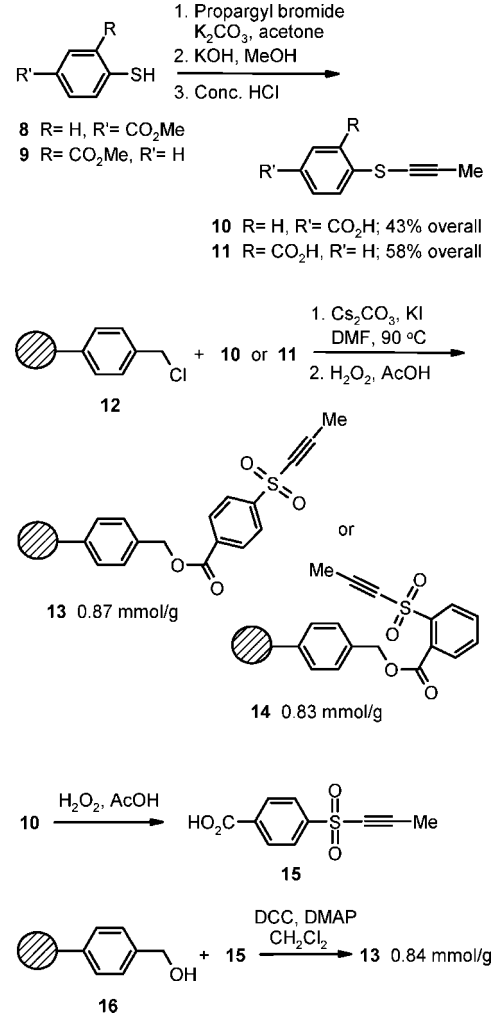
SCHEME 2



6c.[26] The carboxylic acid **5** was in turn obtained from Merrifield resin by the method of Kurth et al.[27] Finally, oxidation and selenoxide *syn*-elimination produced the desired acetylenic sulfones **7a**−**7c**, while hydrolysis of **7c** afforded the terminal acetylene **7d**. When the selenoxide elimination was performed in solution phase with adducts **4**, prior to attachment to the polymer-supported carboxylic acid **5**, the final products were generally less pure, with lower loadings. The loadings in **7a** and **7c** were determined gravimetrically, while those in **7b** and **7d** were determined by hydrolysis of the ester linkers with lithium hydroxide solution and isolation of 1-[(*p*-hydroxymethyl)benzenesulfonyl]-2-phenylethyne and (*p*-hydroxymethyl)phenyl methyl sulfone (formed by cleavage of the corresponding β-keto sulfone), respectively. The loading of **5** was determined gravimetrically after conversion into the corresponding cesium carboxylate. The presence of the acetylenic sulfone moieties on the polymer supports was confirmed by strong IR absorptions at ca. 2200 cm^{-1}.

A different approach to the preparation of solid-supported acetylenic sulfones by means of a reversed ester linker is shown in Scheme 3. Acetylenic sulfides **10** and **11** were obtained from the corresponding thiols **8** and **9**, respectively, via alkylation with propargyl bromide, followed by the base-catalyzed isomerization of the initially formed propargylic sulfides to their

SCHEME 3



thermodynamically favored acetylenic isomers, and acid-catalyzed hydrolysis of the methyl ester groups. The free carboxylic acid functions of **10** and **11** were then coupled with Merrifield resin **12** and oxidation of the sulfide products[28] afforded the corresponding solid-supported sulfones **13** and **14** respectively. Moreover, oxidation of **10** to the sulfone **15** and coupling of the latter with Wang resin **16** provided an alternative route to **13**.

Cleavage of the products from the supports was accomplished by alkaline hydrolysis of the ester linkers. When acetylenic sulfones **7** were employed in the cycloadditions, the polymer-supported carboxylic acid **5** could be recovered after the cleavage of the cycloadducts from the resin was complete. The recycled **5** was converted back to **7a** and **7b**, which were employed in several cycloadditions with comparable results to those obtained starting with fresh carboxylic acid **5**.

Alternatively, cleavage by reductive desulfonylation with either 5% sodium amalgam[29] or samarium(II) iodide in the presence of HMPA[30] proved less successful because of other competing reduction pathways.

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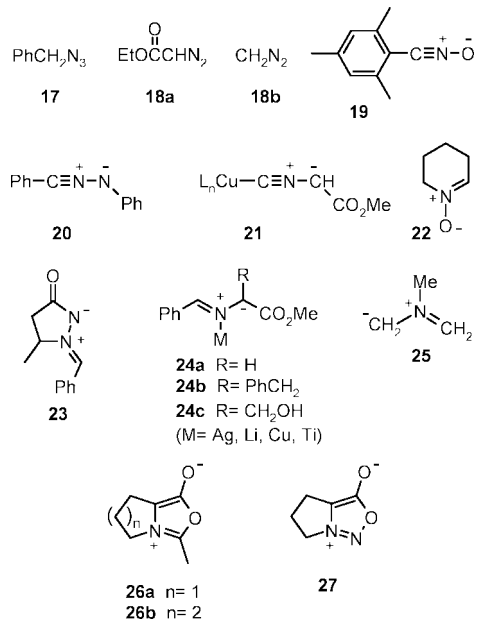
CHART 1

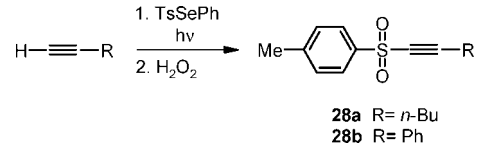


In general, an excess of the 1,3-dipole was employed in the cycloaddition step and the yields of the isolated products were calculated from their weights and the loadings of the solid-supported acetylenic sulfones. The representative dipoles that were investigated (Chart 1) include benzyl azide (**17**),[31] ethyl diazoacetate (**18a**), diazomethane (**18b**), nitrile oxide **19**,[32] nitrile imine **20**,[17a,33] nitrile ylide **21**,[34] nitrone **22**,[35] azomethine imine **23**,[36] azomethine ylides **24**[37] and **25**,[38] munchnones **26**,[39] and sydnone **27**.[40]

In most cases, we first investigated the reactions of dipoles **17**−**27** with representative acetylenic sulfones **28a** and/or **28b** in solution phase in order to compare them with analogous cycloadditions performed with the polymer-supported reagents **7a**, and **7b** or, in several instances, with the terminal acetylene **7d** or the reversed ester derivatives **13** and **14**. Compounds **28a** and **28b** are readily available from the selenosulfonation and selenoxide *syn*-elimination of 1-hexyne[7,41] and 1-phenylacetylene,[24a] respectively (Scheme 4). The results of the cycloadditions and the yields of products **29**−**71** are summarized in Table 1.

Thus, benzyl azide **17** and sulfone **28a** afforded the two regioisomeric triazoles **29** and **30** in 57 and 28% yield,

SCHEME 4



respectively, in refluxing toluene solution (Table 1, entry 1). Attempts were made to perform the reaction under Cu(I)-catalyzed conditions in order to improve the regioselectivity.[42] Unfortunately, decomposition of the acetylenic sulfone competed with cycloaddition in the presence of Cu(I) and neither **29** nor **30** was isolated in useful amounts. Azide **17** and the immobilized *n*-butyl-substituted acetylenic sulfone **7a** produced the analogous products **31** and **32** in similar yields (entry 2), after cleavage from the polymer by ester hydrolysis with lithium hydroxide, whereas the phenyl derivative **7b** afforded a slight excess of the opposite regioisomer **34**, along with **33** (entry 3). An X-ray structure of the minor product **32** made it possible to assign the regiochemistry of **31** and **32** unequivocally, while similar assignments to **29** and **30**, as well as to **33** and **34**, were based on a comparison of their spectroscopic properties with those of the solid phase analogues **31** and **32**.

The solution-phase reaction of ethyl diazoacetate (**18a**) with the *n*-butyl-substituted acetylenic sulfone **28a** afforded pyrazoles **35** and **36** in 55% yield in the ratio of 4:1 (entry 4). Surprisingly, when performed on solid phase under similar conditions, a highly regioselective cycloaddition of the *n*-butyl-substituted acetylenic sulfone **7a** with **18a** was observed, affording only pyrazole **37** in 53% yield (entry 5). In contrast, the analogous reaction of the phenyl derivative **7b** with **18a** failed under a variety of conditions. The structure of the major solution product **35** was confirmed by X-ray crystallography and the structures of the compounds **36** and **37** were assigned by comparison of their spectra with those of **35**. When the more nucleophilic diazomethane (**18b**) was employed, the opposite cycloaddition regiochemistry predominated and *N*-methylation was observed. Thus, diazomethane reacted with **7a** to afford **38** as the minor cycloaddition regioisomer, along with an inseparable mixture of **39a** and **39b**, produced by the further *N*-methylation of the two respective nitrogen atoms of the major cycloaddition regioisomer (entry 6). The phenyl derivative **7b** produced only the single cycloaddition regioisomer as a similar mixture of *N*-methylated isomers **40a** and **40b** (entry 7). The identification of individual isomers in entries 6 and 7 was based on NOE experiments, and is tentative. Thus, irradiation of the *N*-methyl group of **38** enhanced the signal of the allylic methylene protons of the *n*-butyl substituent. On the other hand, irradiation of the pyrazole C−H protons in **39a**,**b** and **40a**,**b** enhanced the signals of protons from the *n*-butyl and phenyl substituents, respectively.

The remaining dipoles **19**−**27** provided highly regioselective reactions, generally producing essentially unique (i.e., >95:5) regioisomers of the products. Thus, 1,2-oxazole **41** was obtained in 79% yield as a single regioisomer from the solution-phase reaction of nitrile oxide **19** with **28b** (entry 8). Similarly, 1,2-oxazoles **42**−**46** were obtained from the solid-phase reactions of **19** with acetylenic sulfones **7a**, **7b**, **7d**, **13** and **14**, respectively (entries 9−13). Cleavage of the products from their polymer supports was achieved by hydrolysis with aqueous lithium

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TABLE 1. 1,3-Dipolar Cycloadditions of Acetylenic Sulfones

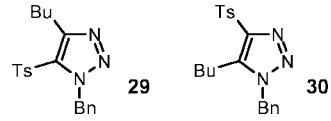
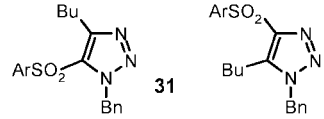
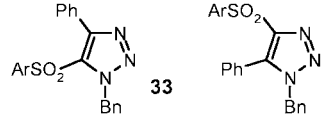
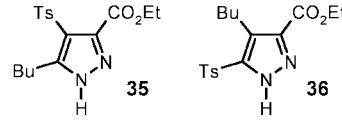
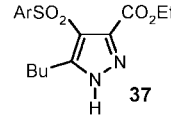
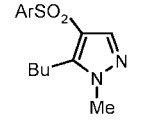
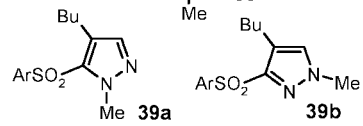
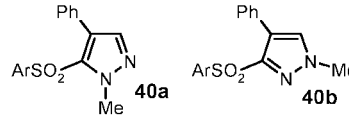
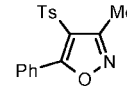
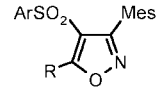
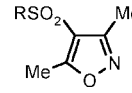
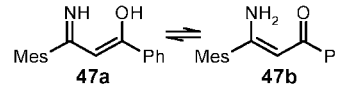
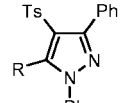
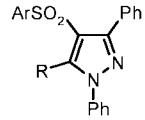
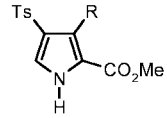
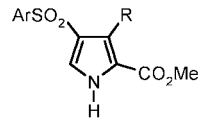
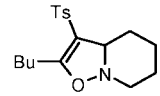
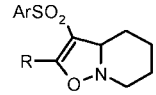
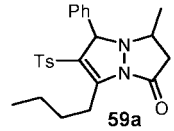
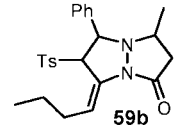
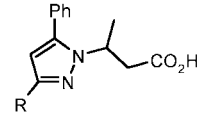
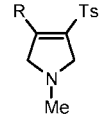
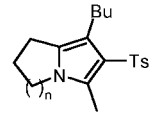
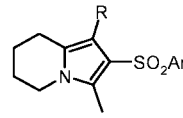
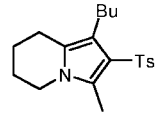
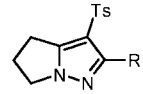
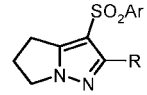
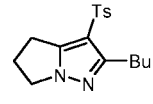
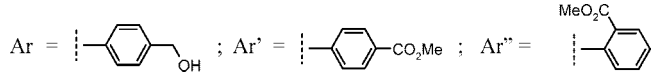
entry	dipole	sulfone	cycloaddition[a] conditions	cleavage conditions	product(s)[b]	yield (ratio)
1	**17**	**28a**	toluene, Δ, 3 d	*c*	 **29** **30**	**29** 57% **30** 28%
2	**17**	**7a**	toluene, Δ, 7 d	LiOH, THF	 **31** **32**	**31** 55% **32** 29%
3	**17**	**7b**	toluene, Δ, 4 d	LiOH, THF	 **33** **34**	**33** 40% **34** 46%
4	**18a**	**28a**	CH_2Cl_2, RT, 3 d	*c*	 **35** **36**	55% (4:1)[d]
5	**18a**	**7a**	CH_2Cl_2, RT, 4 d	LiOH, THF	 **37**	53%
6	**18b**	**7a**	Et_2O, RT, 26 h	LiOH, THF	 **38**  **39a** **39b**	**38** 14% **39** 42% (**39a**:**39b** = 2:1)[d]
7	**18b**	**7b**	Et_2O, RT, 3 h	LiOH, THF	 **40a** **40b**	56% (2:1)[d]
8	**19**	**28b**	CH_2Cl_2, RT, 20 h	*c*	 **41**	79%
9 10 11	**19**	**7a** **7b** **7d**	Et_2O, RT, 30 h	LiOH, THF	 **42** R= *n*-Bu **43** R= Ph **44** R= H	48% 69% 64%
12 13	**19**	**13** **14**	Et_2O, RT, 2 d	NaOMe, MeOH-THF	 **45** R= Ar' **46** R= Ar''	54% 68%
14	**19**	**7b**	Et_2O, RT, 2 d	5% Na-Hg, THF	 **47a** **47b**	34%
15 16	**20**	**28a** **28b**	$CHCl_3$, DIPEA, Δ, 6 h	*c*	 **48** R= *n*-Bu **49** R= Ph	67% 70%
17 18	**20**	**7a** **7b**	$CHCl_3$, DIPEA, Δ, 16 h	LiOH-THF	 **50** R= *n*-Bu **51** R= Ph	61% 67%
19 20	**21**	**28a** **28b**	DMF, 85 °C, 3 h	*c*	 **52** R= *n*-Bu **53** R= Ph	72% 70%

TABLE 1. Continued

entry	dipole	sulfone	cycloaddition[a] conditions	cleavage conditions	product(s)[b]		yield (ratio)
21	**21**	**7a**	DMF, 95 °C, 16 h	LiOH-THF		**54** R= *n*-Bu	57%
22		**7b**				**55** R= Ph	50%
23	**22**	**28a**	CH_2Cl_2, RT, 10 min	*c*		**56**	78%
24	**22**	**7a**	CH_2Cl_2, RT, 16 h	LiOH-THF		**57** R= *n*-Bu	67%
25		**7b**				**58** R= Ph	72%
26	**23**	**28a**	anisole, Δ, 15 min	*c*		**59a**	32%
27			anisole, Δ, 2 h			**59b**	57%
28	**23**	**28b**	anisole, Δ, 4 h	*c*		**60** R= Ph	88%
29		**7a**	anisole, Δ, 2 h	LiOH-THF		**61** R= *n*-Bu	37%
30		**7b**				**60** R= Ph	41%
31	**25**	**28a**	toluene, Δ, 24 h	*c*		**62** R= *n*-Bu	76%
32		**28b**				**63** R= Ph	73%
33	**26a**	**28a**	Ac_2O-DMF, Δ, 30 min	*c*		**64** n= 1	88%
34	**26b**					**65** n= 2	87%
35	**26b**	**7a**	Ac_2O-DMF, Δ, 30 min	LiOH-THF		**66** R= *n*-Bu	78%
36		**7b**				**67** R= Ph	83%
37	**26b**	**7a**	Ac_2O-DMF, Δ, 1 h	5% Na-Hg, DMF		**65**	67%
38	**27**	**28a**	xylenes, Δ, 30 min	*c*		**68** R= *n*-Bu	90%
39		**28b**				**69** R= Ph	89%
40	**27**	**7a**	xylenes, Δ, 3 h	LiOH-THF		**70** R= *n*-Bu	82%
41		**7b**	xylenes, Δ, 6 h			**71** R= Ph	78%
42	**27**	**7a**	xylenes Δ, 3 h	SmI_2,HMPA		**68**	77%

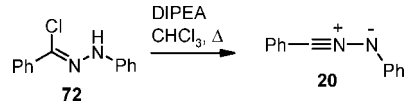
[a] Δ = reflux; RT = room temperature. [b] Ts = *p*-toluenesulfonyl; Mes = 2,4,6-trimethylphenyl (mesityl);



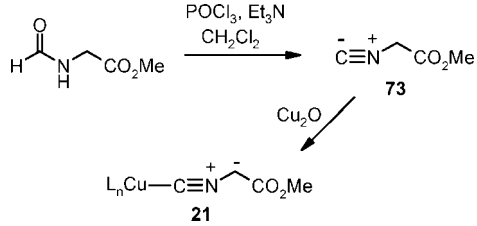
[c] Performed in solution; no cleavage step required. [d] Ratios were determined by NMR integration and refer to unseparated products.

hydroxide (entries 9−11) or by transesterification with sodium methoxide in methanol (entries 12−13). Alternatively, the product obtained from the cycloaddition of **19** and **7b** was cleaved from its support by reductive desulfonylation with 5% sodium amalgam, resulting in concomitant N−O cleavage to produce **47** as a mixture of equilibrating tautomers (entry 14).

SCHEME 5



SCHEME 6



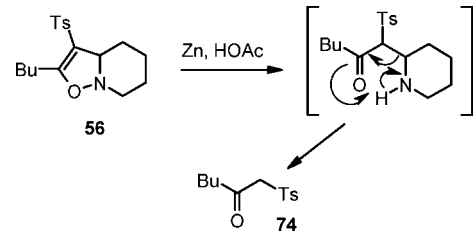
The formation of the latter confirms the regiochemistry of product **43** in entry 10, and by analogy that of the other cycloadducts obtained from nitrile oxide **19**.

The nitrile imine **20** was generated *in situ* by dehydrochlorination of hydrazonyl chloride **72**,[33] as shown in Scheme 5. Its solution phase cycloadditions with **28a** and **28b** afforded the pyrazoles **48** and **49** (entries 15 and 16), with the same regiochemistry (i.e., 4-sulfonyl) as the major isomers **35** and **37** obtained with ethyl diazoacetate (**18a**) in entries 4 and 5 and the minor isomer **38** formed with diazomethane (**18b**) in entry 6. Similar cycloadditions of **20** with 1-(phenylsulfonyl)-propyne and 1-phenyl-2-(phenylsulfonyl)ethyne were reported previously[17a] with the same regiochemistry corresponding to that of **48**−**49** in entries 15−16. The reaction of **20** with solid-supported acetylenic sulfones **7a** and **7b** produced the analogous products **50** and **51**, respectively. The structures of **48** and **51** were confirmed unequivocally by X-ray crystallography. Compound **49** has been prepared previously by a different method.[43]

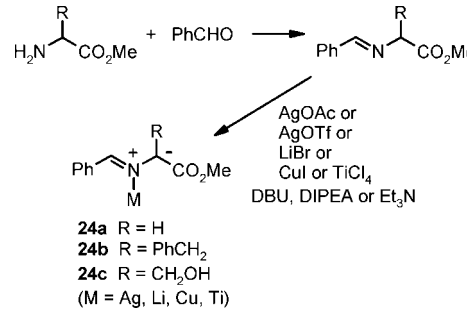
Nitrile ylide **21** was also generated *in situ*. Methyl *N*-formylglycinate was dehydrated to the corresponding isocyanide **73**,[34a] which was in turn treated with catalytic Cu_2O (10 mol %) to generate **21**,[34b,c] as shown in Scheme 6. Its cycloaddition with **28a** and **28b** proceeded smoothly to afford trisubstituted pyrrole products **52** and **53**, respectively (entries 19 and 20). The corresponding reactions with solid-supported sulfones **7a** and **7b** required harsher conditions, longer reaction times and excess Cu_2O, but again afforded unique regioisomers of pyrroles **54** and **55** after cleavage from the support by alkaline hydrolysis (entries 21 and 22). The structure of **54** was confirmed by X-ray crystallography and those of the other pyrrole products **52**, **53**, and **55** were inferred by analogy and from the similarity of their spectra.

Padwa et al.[15a,b] reported that the cycloadditions of several acyclic nitrones with 1-(benzenesulfonyl)propyne afforded the corresponding 4-sulfonyl-substituted dihydro-1,2-oxazoles as the principal or sole products. The solution-phase cycloaddition of nitrone **22**[35] with acetylenic sulfone **28a** proceeded rapidly in dichloromethane and similarly afforded dihydro-1,2-oxazole **56** as the only isolable product (entry 23). The solid-supported sulfones **7a** and **7b** also reacted regioselectively with **22**, but required a considerably longer reaction time. After cleavage by hydrolysis, products **57** and **58** were obtained in yields of 67% and 72% (entries 24 and 25). The regiochemistry was confirmed in **56** by an HMBC correlation between the α-carbon of the vinyl ether moiety at δ 169.2 ppm and the allylic protons of

SCHEME 7



SCHEME 8



the butyl substituent at δ 2.90 and 2.66 ppm. Moreover, reduction of **56** with zinc in acetic acid resulted in cleavage of the N−O bond, followed by fragmentation to the corresponding known[44] β-keto sulfone **74** (Scheme 7).

The solution phase cycloadditions of azomethine imine **23**[36]b with **28a** and **28b** proceeded slowly and afforded poor yields of cycloadducts in refluxing THF, toluene, xylenes or in DMF at 120 °C. The best results were obtained in refluxing anisole, affording the 1,5-diaza[3.3.0]bicyclooctane **59b** from the *n*-butyl derivative **28a**, after isomerization of the alkene double bond of the initial cycloadduct **59a** to the exocyclic position (entry 27). With shorter reaction times, **59a** could be isolated in low yield (entry 26). Single regio- and diastereoisomers of both **59a** and **59b** were isolated, but their exact stereochemistry could not be determined (the *E* isomer of **59b** is shown in the Table arbitrarily). In contrast, the phenyl-substituted acetylenic sulfone **28b** afforded pyrazole **60**, the product of lactam hydrolysis and elimination of *p*-toluenesulfinic acid from the initial cycloadduct corresponding to **59a** in the butyl series.[45] When the cycloaddition was performed on solid phase with either **7a** or **7b**, a similar hydrolysis and elimination afforded **61** and **60**, respectively (entries 29 and 30). The structure of **61** was confirmed by X-ray crystallography, while that of **60** was based on a comparison of its spectra with those of **61**. The structure assignment of **61** in turn verified the structure of the initial cycloadduct **59a**, obtained in solution phase.

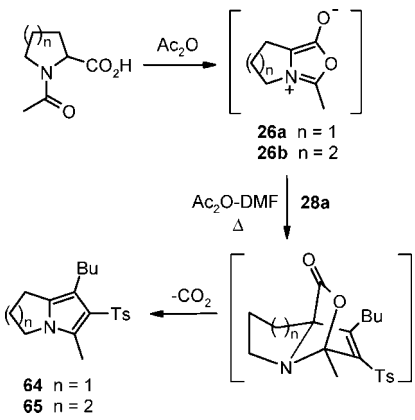
Azomethine ylides **24a**, **24b**, and **24c** were prepared by the condensation of the methyl esters of glycine, phenylalanine and serine with benzaldehyde, followed by treatment with the metal halides, acetates, or triflates shown in Scheme 8.[37] Unfortunately, attempts to react these stabilized ylides with acetylenic sulfones **28a** and **28b** in solution under a variety of conditions resulted either in the recovery of unreacted **28a** and **28b**, or in extensive decomposition. On the other hand, the nonstabilized

(43) Padmavathi, V.; Reddy, A. V. B.; Sumathi, R. P.; Padmaja, A.; Reddy, D. B. *Indian J. Chem.* **1998**, *37B*, 1286–1289.

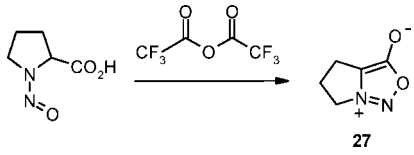
(44) Iwata, N.; Morioka, T.; Kobayashi, T.; Asada, T.; Kinoshita, H.; Inomata, K. *Bull. Chem. Soc. Jpn.* **1992**, *65*, 1379–1388.

(45) Under rigorously anhydrous conditions, the reaction of **23** with the phenyl-substituted acetylenic sulfone **28b** afforded the expected initial cycloadduct analogous to **59a**. It was formed in the ratio of 5:1, in a combined yield of 89%, with a minor regio- or diastereomer that could not be identified with certainty and could not be separated from the main product.

SCHEME 9



SCHEME 10



azomethine ylide **25**, which was generated in situ from sarcosine and paraformaldehyde,[38] reacted successfully with **28a** and **28b** in refluxing toluene to afford the corresponding dehydropyrrolidines **62** and **63** (entries 31 and 32). However, it failed to undergo cycloaddition with the solid-supported acetylenic sulfones **7a** and **7b**.

Mesoionic compounds such as munchnones and sydnones are also capable of undergoing 1,3-dipolar cycloadditions with activated acetylenes, followed by loss of carbon dioxide.[46] Thus, munchnones **26a** and **26b** were prepared in situ from proline and pipecolinic acid, respectively[39] and allowed to react with acetylenic sulfone **28a** in refluxing acetic anhydride (Scheme 9). Slightly better yields of products **64** and **65** were obtained with DMF as a cosolvent (entries 33 and 34). When munchnones **26a** and **26b** were similarly generated in the presence of solid-supported acetylenic sulfones **7a** and **7b**, the more strained analogue **26a** failed to undergo cycloaddition and appeared to decompose to unknown products. In complete contrast, the homologue **26b** afforded cycloadducts **66** and **67** smoothly and in high yield after the usual hydrolysis of the ester linker (entries 35 and 36). When an attempt was made to cleave the product obtained from **26b** and **7a** from the solid support by reductive desulfonylation instead of by alkaline hydrolysis,[47] reduction of the ester linker at the benzylic position occurred instead, affording the *p*-toluenesulfonyl derivative **65** (entry 37). The structure of product **66** was established unequivocally by X-ray crystallography, while the regiochemistry of **64**, **65**, and **67** was inferred by comparison of their spectra with those of **66**.

Sydnone **27**[40] was prepared from *N*-nitrosoproline via cyclodehydration with trifluoroacetic anhydride (Scheme 10). Its cycloaddition to acetylenic sulfones **28a** and **28b**, followed by decarboxylation, proceeded in an analogous fashion to that of munchnones **26a** and **26b**, affording **68** and **69**, respectively, in excellent yield (entries 38 and 39). The corresponding reactions with the solid-supported sulfones **7a** and **7b** provided cycloadducts **70** and **71** in slightly diminished yields after removal from the support by alkaline hydrolysis (entries 40 and 41). The reductive cleavage of the product obtained from **7a** with samarium diiodide in the presence of HMPA resulted in benzylic C−O fission, as observed previously in the munchnone series in entry 37, to afford **68** (entry 42). An X-ray crystal structure of cycloadduct **70** confirmed its regiochemistry and the structures of the other products **68**, **69**, and **71** were inferred by comparison of their spectra with those of **68**.

In general, the strongly electron-withdrawing sulfone group of acetylenic sulfones enhances dipole HOMO-dipolarophile LUMO interactions, leading to the high regioselectivities observed in most of the examples shown in Table 1, where only one regioisomer was isolated. Only in the case of azide **17** (entries 1−3 in Table 1) and diazo compounds **18a** (entry 4) and **18b** (entry 6) were significant amounts of both regioisomers formed. Moreover, a comparison of the relatively electrophilic diazo ester **18a** (entries 4 and 5) with that of the more nucleophilic diazomethane (**18b**) (entries 6 and 7) reveals a reversal of regioselectivity. This may be attributed to dipole HOMO control in the case of **18b**, as expected in reactions with electron-deficient dipolarophiles, while dipole LUMO control predominates with the ester-substituted dipole **18a**.

Summary and Conclusions

Only a few examples of 1,3-dipolar cycloadditions of acetylenic sulfones in solution have been investigated to date and, to our knowledge, there are no previous reports of such processes with nitrile ylides, azomethine imines and azomethine ylides. Furthermore, acetylenic sulfones immobilized on solid supports had not been reported until our preliminary communication,[19] in which only one type of dipolar cycloaddition, with nitrile oxide **19**, was described. The reactions listed in Table 1 indicate that diverse 1,3-dipolar cycloadditions of acetylenic sulfones can be carried out easily, both in solution and on polymer supports. The majority of the products are formed with high regioselectivity, often in good to excellent yield. The regiochemistry and yields of these processes in solution and on solid phase are generally similar, although reactions conducted on polymer supports often required longer reaction times. These cycloadditions provide facile access to a host of variously substituted and functionalized triazoles, pyrazoles, 1,2-oxazoles, pyrroles, as well as their dihydro and bicyclic analogues. These are common ring systems which are found in many types of natural products and medicinal compounds. Further transformations of the immobilized cycloadducts on polymer supports are under investigation, with the objective of ultimately producing small libraries of these important classes of nitrogen heterocycles.

Experimental Section

All NMR spectra were recorded in deuteriochloroform and all mass spectra were obtained by electron impact unless otherwise indicated. "Chromatography" refers to flash chromatography on silica-gel (230−400 mesh).

The following general procedure was used for the workup and alkaline cleavage of the products from the resin for cycloadditions performed on solid phase. After completion of the cycloaddition, the reaction mixture was filtered and the resulting resin was washed

(46) See the following and references cited therein: Coppola, B. P.; Noe, M. C.; Schwartz, D. J.; Abdon, R. L.; Trost, B. M. *Tetrahedron* **1994**, *50*, 93–116.

(47) It is doubtful that direct reductive cleavage of the polymer-supported cycloadduct occurred with sodium amalgam, as penetration of the polymer beads by the reagent under the two-phase conditions of the reaction is unlikely. However, it is possible that the relatively basic conditions resulted in prior hydrolysis of the ester linker, followed by reduction of the liberated benzyl alcohol moiety in a subsequent step. The same product **65** was obtained in 53% yield when samarium diiodide-HMPA was employed as the reductant.

three times alternatively with each of dichloromethane and methanol. The resin was air-dried and then dried under vacuum overnight. The resin (ca. 0.5 g) was stirred in THF (25 mL) for 30 min, followed by the addition of 5% aqueous LiOH solution (1.0 mL, 2.1 mmol). The reaction mixture was stirred at room temperature for 1−3 d, the resin was filtered and washed three times alternatively with each of THF and methanol. The combined filtrate was neutralized with 5% HCl, evaporated under reduced pressure and triturated with dichloromethane (20 mL). The mixture was filtered, the filtrate was concentrated under reduced pressure and the residue was separated by flash chromatography on silica gel.

The experimental details for the preparation of acetylenic sulfones on polymer supports (**7a**−**7d**) and for the preparation and characterization of compounds **42**−**44** and **47** were reported in the Supporting Information of our preliminary communication.[19] Representative procedures and characterization of products from Table 1 are provided below, while the preparation of solid-supported acetylenic sulfones **13** and **14**, as well as the remaining procedures and characterization data from Table 1 are given in the Supporting Information.

1-Benzyl-4-*n*-butyl-5-*p*-toluenesulfonyl-1H-1,2,3-triazole (29) and 1-Benzyl-5-*n*-butyl-4-*p*-toluenesulfonyl-1H-1,2,3-triazole (30). A solution of acetylenic sulfone **28a** (59 mg, 0.25 mmol) and benzyl azide (**17**) (50 mg, 0.38 mmol) in toluene (25 mL) was refluxed for 3 d. The solution was washed with water and brine. The organic phase was dried, filtered, and concentrated in vacuo. The crude mixture was chromatographed (25% ethyl acetate−hexanes) to afford 52 mg (57%) of triazole **29** as a pale-yellow oil: IR (film) 1343, 1161, 1087, 817 cm^{-1}; ^1H NMR (300 MHz) δ 7.32−6.94 (m, 9 H), 5.81 (s, 2 H), 2.84 (t, J = 7.6 Hz, 2 H), 2.27 (s, 3 H), 1.74−1.56 (m, 2 H), 1.44−1.25 (m, 2 H), 0.87 (t, J = 8.6 Hz, 3 H);^{13}C NMR (75 MHz) δ 151.6, 145.2, 137.3, 134.5, 131.9, 129.8, 128.7, 128.1, 127.6, 127.0, 53.6, 31.0, 25.5, 22.5, 21.5, 13.8; MS (CI, *m*/*z*, %) 370 (M^+ + 1, 100); HRMS calcd for $C_{13}H_{16}N_3$ (M^+-Ts): 214.1344; found: 214.1339.

Further elution (35% ethyl acetate−hexanes) provided 26 mg (28%) of cycloadduct **30** as a yellow oil that crystallized from ethyl acetate−hexanes: mp 102−103 °C; IR (film) 1330, 1152, 817 cm^{-1}; ^1H NMR (300 MHz) δ 7.93 (d, J = 8.3 Hz, 2 H), 7.37−7.28 (m, 5 H), 7.20−7.09 (m, 2 H), 5.47 (s, 2 H), 2.86 (t, J = 7.7 Hz, 2 H), 2.39 (s, 3 H), 1.40 − 1.11 (m, 4 H), 0.81 (t, J = 6.9 Hz, 3 H);^{13}C NMR (75 MHz) 145.0, 144.9, 140.2, 138.2, 134.0, 130.0, 129.3, 128.9, 128.0, 127.5, 52.6, 30.9, 22.8, 22.7, 21.8, 13.7; MS (*m*/*z*, %) 369 (M^+, 1), 263 (14), 234 (10), 91 (100); HRMS calcd for $C_{20}H_{23}N_3O_2S$ (M^+): 369.1511; found: 369.1492. Anal. Calcd for $C_{20}H_{23}N_3O_2S$: C, 65.01; H, 6.27; N, 11.38. Found: C, 64.88; H, 6.37; N, 11.27.

[4-(1-Benzyl-4-*n*-butyl-1H-1,2,3-triazol-5-ylsulfonyl)phenyl]-methanol (31) and [4-(1-Benzyl-5-*n*-butyl-1H-1,2,3-triazol-4-ylsulfonyl)phenyl]methanol (32). The solid-supported acetylenic sulfone **7a** (0.50 g, 0.67 mmol/g) was stirred in toluene for 0.5 h. Benzyl azide **17** (67 mg, 0.50 mmol) was added and the mixture was refluxed for 7 d. The cycloadduct was cleaved from the support with LiOH and chromatographed (ethyl acetate−hexanes, 2:1) to afford 71 mg (55%) of product **31** as a yellow oil that crystallized from ethyl acetate−hexanes: mp 82−84 °C; IR (film) 3391, 1330, 1148, 809 cm^{-1}; ^1H NMR (300 MHz) δ 7.36 (d, J = 8.5 Hz, 2 H), 7.32−7.22 (m, 5 H), 7.07 (d, J = 7.8 Hz, 2 H), 5.86 (s, 2 H), 4.68 (s, 2 H), 2.87 (t, J = 7.3 Hz, superimposed on br s, 3 H), 1.81−1.55 (m, 2 H), 1.38 (m, 2 H), 0.92 (t, J = 7.3 Hz, 3 H); ^{13}C NMR (75 MHz) 151.8, 147.9, 138.9, 134.4, 131.7, 128.8, 128.3, 127.6, 127.1, 127.0, 63.8, 53.8, 31.0, 25.5, 22.5, 13.8; MS (CI, *m*/*z*, %) 386 (M^+ + 1, 63); HRMS calcd for $C_{20}H_{23}N_3O_3S$ (M^+): 385.1460; found: 385.1451. Anal. Calcd for $C_{20}H_{23}N_3O_3S$: C, 62.31; H, 6.01; N, 10.90. Found C, 62.14; H, 6.11; N, 10.44.

Further elution with the same solvent provided 37 mg (29%) of **32** as a yellow oil that crystallized from ethyl acetate−hexanes: mp 111.5−112 °C; IR (KBr) 3365, 1335, 1148, 1061 cm^{-1}; ^1H NMR (300 MHz) δ 8.00 (d, J = 8.4 Hz, 2 H), 7.51 (d, J = 8.3 Hz, 2 H), 7.42−7.30 (m, 3 H), 7.23−7.05 (m, 2 H), 5.48 (s, 2 H), 4.78 (d, J = 4.9 Hz, 2 H), 2.87 (t, J = 7.7 Hz, 2 H), 2.40 (t, J = 5.4 Hz, 1 H), 1.39−1.21 (m, 4 H), 0.84 (t, J = 6.9 Hz, 3 H);^{13}C NMR (75 MHz) δ 147.4, 144.6, 140.21, 139.7, 133.7, 129.1, 128.8, 128.0, 127.3, 127.1, 64.1, 52.5, 30.8, 22.6, 22.55, 13.5; MS (*m*/*z*, %) 385 (M^+, 0.5), 279 (22), 91 (100); HRMS calcd for $C_{20}H_{23}N_3O_3S$ (M^+): 385.1460; found: 385.1427. Anal. Calcd for $C_{20}H_{23}N_3O_3S$: C, 62.31; H, 6.01; N, 10.90. Found C, 62.31; H, 6.20; N, 10.54. The ORTEP diagram and X-ray crystallographic data for structure **32** are provided in the Supporting Information.

Ethyl 5-*n*-Butyl-4-(*p*-toluenesulfonyl)-1H-pyrazole-3-carboxylate (35) and Ethyl 4-*n*-Butyl-5-(*p*-toluenesulfonyl)-1H-pyrazole-3-carboxylate (36). A solution of acetylenic sulfone **28a** (59 mg, 0.25 mmol) and ethyl diazoacetate **18a** (32 mg, 0.28 mmol) in dichloromethane (5 mL) was stirred in the dark for 3 d. The reaction mixture was concentrated in vacuum. The crude mixture was chromatographed (5% methanol-chloroform) to afford 48 mg (55%) of an unseparated 4:1 mixture of pyrazoles **35** and **36** as a pale-yellow oil that crystallized from ethyl acetate-hexanes to afford pure **35**: mp 104−105 °C; IR (KBr) 3204, 1743, 1700, 1322, 1230, 1161 cm^{-1}; ^1H NMR (300 MHz) δ 11.61 (s, 1 H), 7.91 (d, J = 8.4 Hz, 2 H) 7.32 (d, J = 8.2 Hz, 2 H), 4.39 (q, J = 7.1 Hz, 2 H), 2.95 (t, J = 7.6 Hz, 2 H), 2.42 (s, 3 H), 1.57−1.31 (m, 7 H), 0.91 (t, J = 7.0 Hz, 3 H); ^{13}C NMR (75 MHz) δ 159.3, 150.6, 144.9, 138.1, 133.2, 129.9, 128.2, 127.4, 62.0, 33.3, 23.2, 23.0, 21.8, 14.3, 13.9; MS (*m*/*z*, %) 350 (M^+, 18), 308 (60), 275 (72), 262 (86), 91 (100); HRMS calcd for $C_{17}H_{22}N_2O_4S$ (M^+): 350.1300; found: 350.1279. Anal. Calcd for $C_{17}H_{22}N_2O_4S$: C, 58.26; H, 6.33; N, 7.99. Found: C, 58.01; H, 6.07; N, 7.77. The ORTEP diagram and X-ray crystallographic data for structure **35** are provided in the Supporting Information.

The filtrate contained a mixture of **35** and **36**, from which **36** could not be separated completely free of **35**. Isomer **36** had distinct ^1H NMR signals at δ 4.28 (q, J = 7.1 Hz) and 3.07 (t, J = 7.8 Hz).

Ethyl 5-*n*-Butyl-4-[4-(hydroxymethyl)benzenesulfonyl]-1H-pyrazole-3-carboxylate (37). The solid-supported acetylenic sulfone **7a** (0.50 g, 0.67 mmol/g) was stirred in dichloromethane (50 mL) for 30 min. Ethyl diazoacetate (190 mg, 1.67 mmol) was added and the reaction mixture was stirred at room temperature for 4 days in the dark. The cycloadduct was cleaved from the support with LiOH. The resulting yellow oil was purified by chromatography (3% methanol-chloroform) to afford pyrazole **37** as a pale-yellow oil (65 mg, 53%): IR (film) 3274, 1713, 1309, 1148 cm^{-1}; ^1H NMR (300 MHz) δ 11.66 (s, 1 H), 7.99 (d, J = 8.2 Hz, 2 H), 7.54 (d, J = 8.1 Hz, 2 H), 4.84 (s, 2 H), 4.43 (q, J = 7.1 Hz, 2 H), 2.99 (t, J = 7.7 Hz, 2 H), 1.58−1.31 (m, 7 H), 0.95 (t, J = 7.1 Hz, 3 H); ^{13}C NMR (75 MHz) δ 158.9, 150.5, 147.2, 139.7, 133.0, 128.2, 127.4, 127.0, 64.2, 61.8, 33.2, 23.0, 22.8, 14.1, 13.8; MS (*m*/*z*, %) 366 (M^+, 16), 320 (45), 42 (100); HRMS calcd for $C_{17}H_{22}N_2O_5S$ (M^+): 366.1249; found: 366.1252.

5-*n*-Butyl-4-[(*p*-hydroxymethyl)benzenesulfonyl]-1-methylpyrazole (38), 4-*n*-Butyl-5-[(*p*-hydroxymethyl)benzenesulfonyl]-1-methylpyrazole (39a), and 4-*n*-Butyl-3-[(*p*-hydroxymethyl)benzenesulfonyl]-1-methylpyrazole (39b). A solution of diazomethane (2.0 mmol) in 6 mL of ether was added dropwise at 0 °C to a suspension of resin **7a** (400 mg, 0.65 mmol/g) in 10 mL of ether and the mixture was stirred at room temperature for 26 h. The excess diazomethane was quenched with acetic acid. The cycloadducts were cleaved from the resin with LiOH and the crude product was purified by chromatography (40% hexanes-ethyl acetate) to afford 11 mg (14%) of the less polar regioisomer **38** as a colorless oil: IR (film) 3399, 1312, 1156, 1119 cm^{-1}; ^1H NMR (300 MHz) δ 7.87 (d, J = 8.2 Hz, 2 H), 7.55 (d, J = 8.2 Hz, 2 H), 7.35 (s, 1 H), 4.81 (s, 2 H), 4.02 (s, 3 H), 2.77 (t, J = 7.2 Hz, 2 H), 1.90 (br, s, 1 H), 1.70−1.55 (m, 2 H), 1.50−1.35 (m, 2 H), 0.95 (t, J = 7.2 Hz, 3 H); ^{13}C NMR (75 MHz) δ 147.2, 140.3, 138.4, 134.8, 128.0, 127.3, 127.2, 64.1, 39.5, 32.6, 23.9, 22.5, 13.9; MS (*m*/*z*, %) 308 (M^+,

6), 266 (56), 95 (100); HRMS calcd for $C_{15}H_{20}N_2O_3S$: 308.1195; found 308.1196.

Further elution (25% hexanes-ethyl acetate) afforded 34 mg (42%) of the more polar regioisomer as an inseparable 2:1 mixture of **39a** and **39b**, obtained as a colorless oil, which solidified upon standing; IR (film) 3383, 1308, 1160, 1117 cm^{-1}; ^1H NMR (300 MHz, both isomers) δ 7.89 (d, $J = 8.2$ Hz, 2 H), 7.84 (s, 1 H, major isomer), 7.81 (s, 1 H, minor isomer), 7.50 (d, $J = 7.7$ Hz, 2 H), 4.79 (s, 2 H), 3.86 (s, 3 H, major isomer), 3.78 (s, 3 H, minor isomer), 2.82 (t, $J = 7.7$ Hz, 2 H, minor isomer), 2.67 (d, $J = 7.7$ Hz, 2 H, major isomer), 2.02 (br s, 1 H), 1.59−1.23 (m, 4 H), 0.91 (t, $J = 6.7$ Hz, 3 H, minor isomer), 0.88 (t, $J = 7.7$ Hz, 3 H, major isomer); ^{13}C NMR (75 MHz, both isomers) 152.3, 146.3, 146.2, 145.1, 142.2, 141.8, 139.3, 134.0, 127.8, 127.2, 127.1, 127.0, 126.9, 120.8, 64.2, 39.3, 36.7, 30.8, 30.5, 26.3, 24.0, 22.6, 22.5, 13.8, 13.7; MS (*m/z,* %) 308 (M^+, 9), 266 (52), 95 (100); HRMS calcd for $C_{15}H_{20}N_2O_3S$: 308.1195; found 308.1199.

5-[(*p*-Hydroxymethyl)benzenesulfonyl]-1-methyl-4-phenylpyrazole (40a) and 3-[(*p*-Hydroxymethyl)benzenesulfonyl]-1-methyl-4-phenylpyrazole (40b). The cycloaddition of diazomethane with **7b** was performed as with **7a**, followed by cleavage with LiOH in the usual manner. Chromatography (40% hexanes-ethyl acetate) afforded an inseparable 2:1 mixture of **40a** and **40b** as a colorless oil in 56% yield; IR (film) 3397, 1307, 1165, 1140 cm^{-1}; ^1H NMR (300 MHz) δ 8.01 (s 1 H, minor isomer), 7.99 (s, 1 H, major isomer), 7.64−7.15 (m, 9 H), 4.67 (s, 2 H, major isomer), 4.66 (s, 2 H, minor isomer), 3.94 (s, 3 H, minor isomer), 3.64 (s, 3 H, major isomer), 2.45 (br, s, 1 H); ^{13}C NMR (75 MHz, both isomers) δ 150.4, 146.4, 146.3, 143.9, 141.0, 140.7, 139.3, 135.3, 130.6, 130.2, 130.1, 129.2, 129.0, 128.5, 128.1, 127.21, 127.15, 126.6, 126.5, 122.3, 121.8, 64.00, 63.97, 39.5, 37.5; MS (*m/z,* %) 328 (M^+, 75), 105 (47), 89 (48), 77 (100); HRMS calcd for $C_{17}H_{16}N_2O_3S$: 328.0882; found: 328.0897.

3-Mesityl-4-(*p*-toluenesulfonyl-5-phenyl-1,2-oxazole (41). Acetylenic sulfone **28b** (102 mg, 0.400 mmol) and nitrile oxide **19** (161 mg, 1.00 mmol) were stirred in dichloromethane at room temperature for 20 h. The solvent was evaporated under vacuum and the resulting yellow oil was chromatographed (20% ethyl acetate−hexanes), to provide 132 mg (79%) of 1,2-oxazole **41** as a pale yellow oil. Recrystallization from ethyl acetate−hexanes afforded colorless needles: mp 167−168 °C; IR (film): 1380, 1161, 1124 cm^{-1}; 1H NMR (400 MHz) δ 8.01 (d, $J = 6.8$ Hz, 2 H), 7.68−7.51 (m, 3 H), 7.25 (d, $J = 8.3$ Hz, 2 H), 7.06 (d, $J = 8.1$ Hz, 2 H), 6.86 (s, 2 H), 2.367 (s, 3 H), 2.373 (s, 3 H), 1.87 (s, 6 H); ^{13}C NMR (100 MHz) δ 172.5, 160.6, 144.7, 139.7, 138.1, 137.4, 131.8, 130.1, 129.3, 128.4, 128.1, 127.9, 126.0, 123.1, 118.6, 21.6, 21.3, 20.0; MS (CI, *m/z*) 418 ($M^+ + 1$); HRMS calcd for $C_{25}H_{24}NO_3S$ ($M^+ + 1$), 418.1477; found, 418.1495. Anal. Calcd for: $C_{25}H_{23}NO_3S$: C, 71.92; H, 5.55; N, 3.35. Found: C, 71.56; H, 6.04; N, 3.12.

3-Mesityl-4-[(*p*-methoxycarbonyl)benzenesulfonyl]-5-methyl-1,2-oxazole (45). A suspension of nitrile oxide **19** (98 mg, 0.61 mmol) and resin **13** (400 mg, 0.87 mmol/g) in 10 mL of ether was stirred for 48 h and filtered. The resin was washed with ether and then with dichloromethane, methanol, and ether, followed by drying under reduced pressure. The product was cleaved from the resin by refluxing it in 10 mL of methanol−THF (1:2) containing sodium methoxide (81 mg, 1.5 mmol) overnight. The resin was removed by filtration and was washed with methanol−THF (1:1), THF, methanol, and ether. The filtrate was evaporated to dryness, triturated with dichloromethane, dried, filtered, evaporated, and chromatographed (25% hexanes-ethyl acetate) to give 74 mg (54%) of **45** as a white solid: mp 98−101 °C (from ethyl acetate−hexanes); IR (KBr) 1729, 1333, 1278, 1167 cm^{-1}; ^1H NMR (300 MHz) δ 7.98 (d, $J = 8.2$ Hz, 2 H), 7.46 (d, $J = 8.2$ Hz, 2 H), 6.84, (s, 2 H), 3.97 (s, 3 H), 2.93 (s, 3 H), 2.35 (s, 3 H), 1.69 (s, 6 H); ^{13}C NMR (75 MHz) δ 174.5, 165.4, 159.7, 144.2, 140.0, 137.9, 134.6, 129.9, 128.1, 127.8, 122.4, 117.5, 52.7, 21.2, 19.6, 13.3; MS (*m/z,* %) 399 (M^+, 4), 104 (48), 43 (100); HRMS calcd for $C_{21}H_{21}NO_5S$: 399.1140; found: 399.1161. Anal. Calcd for $C_{21}H_{21}NO_5S$: C, 63.14; H, 5.30; N, 3.51. Found: C, 62.70; H, 5.17; N, 3.40.

5-*n*-Butyl-1,3-diphenyl-4-(*p*-toluenesulfonyl)-1H-pyrazole (48). Hydrazonyl chloride **72**[33] (87 mg, 0.38 mol) and diisopropylethylamine (245 mg, 1.9 mmol were added to a solution of acetylenic sulfone **28a** (59 mg, 0.25 mmol) in chloroform (20 mL) and the mixture was refluxed for 6 h. The solution was washed with water and brine. The organic phase was dried, filtered and concentrated. The crude product was purified by chromatography (30% chloroform-hexanes to 3% methanol-chloroform) to afford 72 mg (67%) of pyrazole **48** as a pale-yellow oil that crystallized from ethyl acetate−hexanes: mp 128−129 °C; IR (film) 1313, 1148, 761 cm^{-1}; ^1H NMR (300 MHz) δ 7.90−7.21 (m, 12 H), 7.09 (d, $J = 8.1$ Hz, 2 H), 3.06 (t, $J = 7.9$ Hz, 2 H), 2.34 (s, 3 H), 1.86−1.50 (m, 2 H), 1.46−1.10 (m, 2 H), 0.84 (t, $J = 7.3$ Hz, 3 H);^{13}C NMR (75 MHz) δ 151.5, 147.8, 143.4, 140.0, 138.5, 131.4, 130.1, 129.4, 129.3, 129.1, 128.8, 127.7, 127.0, 126.4, 118.4, 32.0, 25.0, 22.6, 21.5, 13.5; MS (*m/z*, %) 430 (M^+, 7), 275 (25), 233 (100); HRMS calcd for $C_{26}H_{26}N_2O_2S$ (M^+): 430.1715; found: 430.1714. Anal. Calcd for $C_{26}N_2H_{26}O_2S$: C, 72.53; H, 6.09; N, 6.51. Found: C, 72.47; H, 6.09; N, 6.33. The ORTEP diagram and X-ray crystallographic data for structure **48** are provided in the Supporting Information.

5-*n*-Butyl-4-[*p*-(hydroxymethyl)benzenesulfonyl]-1,3-diphenyl-1H-pyrazole (50). Polymer resin **7a** (0.50 g, 0.67 mmol/g) was stirred in chloroform (50 mL) for 30 min, followed by the addition of hydrazonyl chloride **72** (117 mg, 0.507 mmol) and diisopropylethylamine (328 mg, 2.54 mmol). The reaction mixture was refluxed 16 h. The resulting solid-supported cycloadduct was cleaved by LiOH in the usual manner. The resulting yellow oil was purified by chromatography (4% methanol-chloroform) to afford 91 mg (61%) of pyrazole **50** as a pale-yellow oil that crystallized from ethyl acetate−hexanes: mp 114−115 °C; IR (film) 3422, 1317, 1143 cm^{-1}; ^1H NMR (300 MHz,) δ 7.73−7.04 (m, 14 H), 4.61 (s, 2 H), 3.04 (t, $J = 7.9$ Hz, 2 H), 2.33 (s, 1 H), 1.79−1.50 (m, 2 H), 1.40−1.20 (m, 2 H), 0.83 (t, $J = 7.3$ Hz, 3 H); ^{13}C NMR (75 MHz) δ 151.9, 148.2, 146.2, 141.5, 138.4, 131.3, 130.1, 129.5, 129.4, 128.9, 127.7, 127.1, 126.4, 118.1, 64.0, 32.0, 25.0, 22.6, 13.5; MS (*m/z*, %) 446 (M^+, 5), 275 (24), 233 (100); HRMS calcd for $C_{26}H_{26}N_2O_3S$ (M^+): 446.1664; found: 446.1646. Anal. Calcd for $C_{26}H_{26}N_2O_3S$: C, 69.93; H, 5.87; N, 6.27; Found: C, 69.90; H, 6.08; N, 6.14.

Methyl 3-*n*-Butyl-4-(*p*-toluenesulfonyl)-1H-pyrrole-2-carboxylate (52). Isocyanide **73**[34a] (99 mg, 1.0 mmol) and cuprous oxide (9 mg, 0.06 mmol) were added successively to a solution of acetylenic sulfone **28a** (59 mg, 0.25 mmol) in DMF (20 mL). The mixture was heated at 85 °C for 3 h. The solution was filtered, diluted with water and extracted with ethyl acetate. The organic phase was washed with 5% ammonium hydroxide solution, water and brine. It was dried, filtered, concentrated in vacuo and purified by chromatography (35% ethyl acetate−hexanes) to afford 60 mg (72%) of pyrrole **52** as a pale-yellow oil that crystallized from ethyl acetate−hexanes: mp 149−150 °C; IR (film) 3300, 1713, 1257, 1157, 1096 cm^{-1}; ^1H NMR (300 MHz) δ 9.79 (br s, 1 H), 7.81 (d, $J = 8.2$ Hz, 2 H), 7.58 (d, $J = 3.4$ Hz, 1 H), 7.30 (d, $J = 8.3$ Hz, 2 H), 3.86 (s, 3 H), 2.81 (t, $J = 7.5$ Hz, 2 H), 2.44 (s, 3 H), 1.36−1.17 (m, 4 H), 0.85 (t, $J = 7.0$ Hz, 3 H); ^{13}C NMR (75 MHz); 161.2, 143.8, 140.0, 132.1, 129.8, 127.4, 126.2, 125.7, 121.4, 51.9, 33.0, 24.6, 23.1, 21.6, 13.9; MS (*m/z*, %) 335 (M^+, 42), 293 (100); HRMS calcd for $C_{17}H_{21}NO_4S$ (M^+): 335.1191; found: 335.1178. Anal. Calcd for $C_{17}H_{21}NO_4S$: C, 60.87; H, 6.31; N, 4.18. Found: C, 60.90; H, 6.79; N, 3.85.

Methyl 3-*n*-Butyl-4-[*p*-(hydroxymethyl)benzenesulfonyl)]-1H-pyrrole-2-carboxylate (54). Resin **7a** (0.50 g, 0.67 mmol/g) was stirred in DMF (40 mL) for 30 min. Isocyanide **73** (280 mg, 2.85 mmol) and cuprous oxide (75 mg, 0.50 mmol) were added and the reaction mixture was heated at 95 °C for 16 h. Cleavage of the product from the support was effected with LiOH in the usual manner, followed by chromatography (65% ethyl acetate−hexanes) to afford 67 mg (57%) of pyrrole **54** as a pale-yellow oil: IR (film)

3304, 1717, 1304, 1139 cm^{-1}; ^1H NMR (300 MHz) δ 9.58 (br s, 1 H), 7.86 (d, $J = 8.3$ Hz, 2 H), 7.53 (d, $J = 3.5$ Hz, 1 H), 7.48 (d, $J = 8.2$ Hz, 2 H), 4.77 (s, 2 H), 3.85 (s, 3 H), 2.78 (t, $J = 7.6$ Hz, 2 H), 2.19 (s, 1 H), 1.46−1.06 (m, 4 H), 0.83 (t, $J = 7.0$ Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$-DMSO-d_6) δ 161.1, 147.4, 141.4, 131.5, 126.8, 126.62, 126.57, 123.9, 121.2, 63.3, 51.2, 32.8, 24.3, 22.8, 13.7; MS (*m*/*z*, %) 351 (M^+, 35), 309 (100), 246 (30); HRMS calcd for $C_{17}H_{21}NO_5S$ (M^+): 351.1140; found: 351.1144. Anal. Calcd for $C_{17}H_{21}NO_5S$: C, 58.10; H, 6.02; N, 3.99. Found: C, 58.04; H, 6.18; N, 3.56. The ORTEP diagram and X-ray crystallographic data for structure **54** are provided in the Supporting Information.

2-*n*-Butyl-3-(*p*-toluenesulfonyl)-4,5,6,7-tetrahydro-3aH-isoxazolo[2,3-a] pyridine (56). Acetylenic sulfone **28a** (59 mg, 0.25 mmol) was added to a solution of nitrone **22** (10 mL, 0.5 M) in dichloromethane at room temperature and the reaction mixture was stirred for 10 min. The solvent was evaporated and the product was chromatographed (25% ethyl acetate−hexanes) to give 65 mg (78%) of cycloadduct **56** as a pale-yellow oil: IR (film) 1617, 1317, 1161, 1148 cm^{-1};^1H NMR (300 MHz) δ 7.77 (d, $J = 8.3$ Hz, 2 H), 7.35 (d, $J = 8.0$ Hz, 2 H), 4.26 (br s, 1 H), 3.15 (br s, 1 H), 3.06−2.82 (m, 2 H), 2.66 (dt, $J = 13.8$, 7.0 Hz, 1 H), 2.46 (s, 3 H), 2.21−1.75 (m, 2 H), 1.73−1.20 (m, 8 H), 0.99 (t, $J = 7.3$ Hz, 3 H); ^{13}C NMR (75 MHz) δ 169.2, 143.4, 139.5, 129.9, 126.4, 109.8, 64.3, 51.6, 28.9, 25.8, 22.7, 21.5, 19.5, 13.9; MS (*m*/*z*, %) 335 (M^+, 40), 334 (100); HRMS Calcd for $C_{18}H_{25}NO_3S$ (M^+): 335.1555; found: 335.1524. Anal. Calcd for $C_{18}H_{25}NO_3S$: C, 64.44; H, 7.51; N, 4.18. Found: C, 64.31; H, 7.60; N, 4.62.

Cycloadduct **56** (100 mg, 0.30 mmol) was treated with 0.5 g of zinc powder in 5 mL of acetic acid at 65 °C until TLC analysis indicated consumption of the starting material. The mixture was filtered and the resulting solution was diluted with water and extracted with ethyl acetate. The organic solution was washed with saturated sodium bicarbonate solution, water and brine, and then dried. The solvent was evaporated and the residue was purified by chromatography (25% ethyl acetate−hexanes) to afford 36 mg (43%) of β-keto sulfone **74**.[44]

2-*n*-Butyl-3-[(*p*-hydroxymethyl)benzenesulfonyl]-4,5,6,7-tetrahydro-3aH-isoxazolo[2,3-a]pyridine (57). The resin **7a** (0.50 g, 0.67 mmol/g) was stirred in dichloromethane (50 mL) for 30 min. Nitrone **22** in dichloromethane (20 mL, 0.5 M) was added and the reaction mixture was stirred at room temperature for 16 h. The resulting solid-supported cycloadduct was cleaved with LiOH in the usual manner and the crude product was purified by chromatography (50% ethyl acetate−hexanes) to afford 78 mg (67%) of **57** as a pale-yellow oil: IR (film) 3417, 1617, 1309, 1148 cm^{-1};^1HNMR (300 MHz) δ 7.86 (d, $J = 8.3$ Hz, 2 H), 7.55 (d, $J = 8.4$ Hz, 2 H), 4.83 (s, 2 H), 4.40−4.19 (m, 1 H), 3.26−3.06 (m, 1 H), 3.07−2.51 (m, 3 H), 2.19−1.24 (m, 11 H), 0.99 (t, $J = 7.3$, 3 H);^{13}C NMR (75 MHz,) δ 169.5, 146.2, 141.6, 127.0, 126.8, 109.9, 64.2, 64.1, 51.7, 29.1, 26.0, 25.8, 22.5, 19.6, 13.7; MS (*m*/*z*, %) 351 (M^+, 17), 350 (35), 155 (63), 42 (100); HRMS Calcd for $C_{18}H_{25}NO_4S$ (M^+): 351.1504; found: 351.1484.

7-*n*-Butyl-3-methyl-5-phenyl-6-(*p*-toluenesulfonyl)-2,3-dihydro-5H-pyrazolo[1,2-a]pyrazol-1-one (59a). Azomethine imine **23** (47 mg, 0.25 mmol) was added to a solution of acetylenic sulfone **28a** (59 mg, 0.25 mmol) in anisole (20 mL) and the reaction mixture was refluxed for 15 min. The solution was washed with water and brine, dried, filtered, evaporated under vacuum, and chromatographed (20−35% ethyl acetate−hexanes) to afford 34 mg (32%) of product **59a** as a pale-yellow oil: IR (film) 1721, 1324, 1151 cm^{-1}; ^1H NMR (300 MHz) δ 7.21−7.04 (m, 5 H), 6.99 (d, $J = 8.4$ Hz, 2 H), 6.92 (d, $J = 8.3$ Hz, 2 H), 5.09 (s, 1 H), 3.49 − 3.18 (m, 2 H), 3.13−2.95 (m, 1 H), 2.65 (dd, $J = 16.4$, 6.5 Hz, 1 H), 2.51 (dd, $J = 16.4$, 12.5 Hz, 1 H), 2.28 (s, 3 H), 1.80−1.68 (m, 1 H), 1.65−1.51 (m, 1 H), 1.50−1.38 (m, 2 H), 0.94 (t, $J = 7.4$ Hz, 3 H), 0.85 (d, $J = 6.1$ Hz, 3 H); ^{13}C NMR (75 MHz) δ 165.5, 147.2, 143.3, 138.84, 138.81, 129.1, 129.0, 128.0, 126.9, 118.6, 73.8, 62.7, 43.7, 30.8, 24.3, 22.7, 21.5, 17.4, 13.9; MS (*m*/*z*, %) 424 (M^+, 12), 347 (100), 218 (70); HRMS calcd for $C_{24}H_{28}N_2O_3S$ (M^+): 424.1821; found: 424.1816.

7-Butylidene-3-methyl-5-phenyl-6-(*p*-toluenesulfonyl)-tetrahydro-pyrazolo[1,2-a]pyrazol-1-one (59b). Product **59b** was prepared by the same procedure as **59a**, except that a longer reaction time of 2 h was employed. The crude product was chromatographed (5% methanol-chloroform) to afford 60 mg (57%) of product **59b** as a pale-yellow oil that crystallized from ethyl acetate−hexanes: mp 103−105 °C; IR (film) 1717, 1317, 1148 cm^{-1}; ^1H NMR (300 MHz) δ 7.77 (d, $J = 8.3$ Hz, 2 H), 7.51−7.29 (m, 7 H), 4.60 (d, $J = 3.3$ Hz, 1 H), 4.53 (t, $J = 7.4$ Hz, 1 H), 3.92 (d, $J = 3.0$ Hz, 1 H), 3.77−3.53 (m, 1 H), 2.70 (dd, $J = 15.9$, 7.6 Hz, 1 H), 2.57 (dd, $J = 15.9$, 11.3 Hz, 1 H), 2.46 (s, 3 H), 2.34−2.06 (m, 2 H), 1.49−1.21 (m, 2 H), 1.16 (d, $J = 6.3$ Hz, 3 H), 0.83 (t, $J = 7.3$ Hz, 3 H); ^{13}C NMR (75 MHz) δ 167.2, 145.4, 140.9, 132.5, 130.1, 129.6, 128.8, 128.0, 126.8, 124.6, 123.9, 77.4, 65.6, 61.2, 41.6, 31.7, 22.4, 21.7, 19.4, 13.7; MS (*m*/*z*, %) 424 (M^+, 23), 347 (100); HRMS calcd for $C_{24}H_{28}N_2O_3S$ (M^+): 424.1821; found: 424.1797.

3-(3,5-Diphenyl-1H-pyrazol-1-yl)butanoic acid (60). Product **60** was prepared by a similar procedure to that of **59a**, except that a longer reaction time of 4 h was employed. After chromatography (2−5% methanol-chloroform), **60** was obtained in 88% yield and was identical to the product obtained from **23** and **7b** (see Supporting Information).

3-(3-*n*-Butyl-5-phenyl-1H-pyrazol-1-yl)butanoic acid (61). Resin **7a** (0.50 g, 0.67 mmol/g) was stirred in anisole (30 mL) for 30 min. The azomethine imine **23** (126 mg, 0.67 mmol) was added and the reaction mixture was refluxed for 2 h. The resulting solid-supported cycloadduct was treated with LiOH in the usual manner. The resulting yellow oil was chromatographed (2% methanol-chloroform) to afford 35 mg (37%) of pyrazole **61** as a yellow oil that crystallized from ethyl acetate−hexanes: mp 98−99 °C; IR (film) 3500−2300, 1713, 765 cm^{-1}; ^1H NMR (400 MHz) δ 11.90 (s, 1 H), 7.50−7.34 (m, 5 H), 6.08 (s, 1 H), 4.71 (m, 1 H), 3.04 (dd, $J = 16.1$, 7.1 Hz, 1 H), 2.92 (dd, $J = 16.1$, 4.1 Hz, 1 H), 2.66 (t, $J = 7.6$ Hz, 2 H), 1.66 (m, 2 H), 1.49 (d, $J = 6.8$ Hz, 3 H,), 1.47−1.33 (m, 2 H), 0.95 (t, $J = 7.3$ Hz, 3 H); ^{13}C NMR (100 MHz) δ 173.5, 152.8, 144.3, 130.2, 128.9, 128.8, 128.7, 104.9, 50.1, 41.6, 31.4, 27.5, 22.4, 20.7, 13.8; MS (*m*/*z*, %) 286 (M^+, 4), 244 (67), 158 (100); HRMS calcd for $C_{15}H_{17}N_2O_2$ ($M^+ - C_2H_5$): 257.1290; found: 257.1282. Anal. Calcd for $C_{17}H_{22}N_2O_2$: C, 71.30; H, 7.74; N, 9.78. Found: C, 71.12; H, 7.93; N, 9.82. The ORTEP diagram and X-ray crystallographic data for structure **61** are provided in the Supporting Information.

3-*n*-Butyl-1-methyl-4-(*p*-toluenesulfonyl)-2,5-dihydro-1H-pyrrole (62). Sarcosine (67 mg, 0.75 mmol) and paraformaldehyde (43.5 mg) were added to a solution of acetylenic sulfone **28a** (59 mg, 0.25 mmol) in toluene (20 mL) in a flask equipped with a Dean−Stark trap and the solution was refluxed for 24 h. It was then washed with water and brine, dried, filtered, and concentrated in vacuo. The crude product was chromatographed (25% ethyl acetate−hexanes) to afford 56 mg (76%) of dihydropyrrole **62** as a pale-yellow oil: IR (film) 1670, 1304, 1147 cm^{-1}; ^1H NMR (300 MHz) δ 7.73 (d, $J = 8.2$ Hz, 2 H), 7.29 (d, $J = 8.3$ Hz, 3 H), 3.57 (t, $J = 3.4$ Hz, 2 H), 3.53 (t, $J = 3.7$ Hz, 2 H), 2.60 (t, $J = 7.2$ Hz, 2 H), 2.39 (s, 3 H), 2.33 (s, 3 H), 1.41−1.27 (m, 4 H), 0.89 (t, $J = 7.0$ Hz, 3 H); ^{13}C NMR (75 MHz) δ 154.8, 144.2, 138.1, 132.2, 129.8, 127.3, 65.8, 61.8, 42.0, 30.0, 26.8, 22.7, 21.5, 13.8; MS (*m*/*z*, %) 293 (M^+, 10), 249 (15), 95 (100); HRMS calcd for $C_{16}H_{23}NO_2S$: (M^+): 293.1450; found: 293.1461.

7-*n*-Butyl-5-methyl-6-(*p*-toluenesulfonyl)-2,3-dihydro-1H-pyrrolizine (64). Acetylenic sulfone **28a** (59 mg, 0.25 mmol), proline (70 mg, 0.61 mmol), and acetic anhydride (325 mg, 3.2 mmol) were refluxed in DMF (10 mL) for 30 min. The solution was diluted with water and extracted with ethyl acetate. The organic phase was washed with saturated $NaHCO_3$ solution, water, and brine. The organic phase was dried, filtered, and concentrated. The crude product was chromatographed (35% ethyl acetate−hexanes) to afford 73 mg (88%) of product **64** as a pale-yellow oil: IR (film)

1300, 1130, 1086, 816 cm^{-1}; ^1H NMR (300 MHz) δ 7.72 (d, J = 8.2 Hz, 2 H), 7.22 (d, J = 8.1 Hz, 2 H), 3.76 (t, J = 7.1 Hz, 2 H), 2.70 (t, J = 7.3 Hz, 2 H), 2.54 (t, J = 7.6 Hz, 2 H), 2.48 (s, 3 H), 2.47−2.39 (m, 2 H), 2.38 (s, 3 H), 1.49−1.17 (m, 4 H), 0.85 (t, J = 7.2 Hz, 3 H); ^{13}C NMR (75 MHz) δ 142.37, 142.35, 132.8, 129.3, 128.2, 126.3, 118.9 114.5, 44.5, 32.7, 26.8, 25.0, 23.7, 22.7, 21.5, 14.0, 11.7; MS (CI, *m*/*z*, %) 332 (M^+ + 1) 100); HRMS calcd for $C_{19}H_{25}NO_2S$ (M^+): 331.1606; found: 331.1593.

1-*n*-Butyl-2-[(*p*-hydroxymethyl)benzenesulfonyl]-3-methyl-5,6,7,8-tetrahydroindolizine (66). Resin **7a** (0.50 g, 0.67 mmol/g) was stirred in 40 mL of DMF for 30 min. Pipecolinic acid (129 mg, 1.00 mmol) and acetic anhydride (520 mg, 5.10 mmol) were added and the reaction mixture was refluxed for 30 min. The resulting yellow resin was filtered and washed with dichloromethane and methanol. The solid-supported cycloadduct was cleaved in the usual manner with LiOH and the product was chromatographed (65% ethyl acetate−hexanes) to afford 94 mg (78%) of cycloadduct **66** as a pale-yellow oil that crystallized from ethyl acetate−hexanes: mp 124.5−125.5 °C; IR (KBr) 3478, 1396, 1274, 1152, 1130 cm^{-1}; ^1H NMR (300 MHz) δ 7.78 (d, J = 8.3 Hz, 2 H), 7.40 (d, J = 8.1 Hz, 2 H), 4.72 (d, J = 5.9 Hz, 2 H), 3.71 (t, J = 6.1 Hz, 2 H), 2.58 (t, J = 6.3 Hz, 2 H), 2.54−2.39 (m, 3 H), 2.45 (s, 3 H), 1.92 (m, 2 H), 1.77 (m, 2 H), 1.42− 1.16 (m, 4 H), 0.85 (t, J = 6.9 Hz, 3 H); ^{13}C NMR (75 MHz) δ 145.2, 144.1, 131.6, 126.7, 126.3, 126.1, 118.3, 116.0, 64.3, 43.2, 33.3, 24.0, 23.3, 22.9, 21.8, 20.4, 13.9, 10.5; MS (*m*/*z*, %) 361 (M^+, 100), 318 (90); HRMS calcd for $C_{20}H_{27}NO_3S$ (M^+): 361.1712; found: 361.1678. Anal. Calcd for $C_{20}H_{27}NO_3S$: C, 66.45; H, 7.53; N, 3.87. Found: C, 66.37; H, 7.43; N, 3.79. The ORTEP diagram and X-ray crystallographic data for structure **66** are provided in the Supporting Information.

The above cycloaddition was repeated and cleavage of the resin was effected by reduction with sodium-amalgam[29] as follows. The resin (0.55 g) was stirred 30 min in 34 mL of DMF before the addition of 222 mg (1.56 mmol) of Na_2HPO_4, 7.4 g of 5% sodium amalgam (15 mmol) and 4.2 mL of methanol at room temperature. The reaction mixture was stirred vigorously overnight and filtered through a pad of celite. The filtrate was diluted with water and extracted with ethyl acetate. The organic solution was washed with water and brine, dried, and evaporated. The resulting residue was purified by chromatography (35% ethyl acetate−hexanes) to afford **65** in 67% yield.

Alternatively, reduction with samarium diiodide[30] was carried out as follows. The polymer (0.55 g) was stirred for 30 min in dry THF at room temperature. The solution was cooled to −78 °C and 228 mg of HMPA was added under argon, followed by 15 mL of 0.1 M samarium diiodide in dichloromethane via syringe. The reaction mixture was stirred at room temperature overnight. It was then filtered through a pad of celite, the filtrate was evaporated, and the resulting residue was chromatographed (35% ethyl acetate−hexanes) to produce the same compound **65** in 53% yield.

2-*n*-Butyl-3-(*p*-toluenesulfonyl)-5,6-dihydro-4H-pyrrolo[1,2-b]pyrazole (68). A mixture of acetylenic sulfone **28a** (59 mg, 0.25 mmol) and sydnone **27**[40] (47 mg, 0.38 mmol) was refluxed 30 min in anisole (5 mL). The solution was washed with water and brine, dried, filtered, and concentrated under vacuum. The crude product was chromatographed (25% ethyl acetate−hexanes) to afford 72 mg (90%) of product **68** as a pale yellow oil that crystallized from ethyl acetate−hexanes: mp 103−105 °C; IR (film) 1596, 1317, 1135 cm^{-1}; ^1H NMR (300 MHz) δ 7.76 (d, J = 8.3 Hz, 2 H), 7.27 (d, J = 8.3 Hz, 2 H), 4.07 (t, J = 7.7 Hz, 2 H,), 3.08 (t, J = 7.4 Hz, 2 H), 2.70 (t, J = 7.7 Hz, 2 H), 2.65−2.49 (m, 2 H), 2.39 (s, 3 H), 1.67−1.42 (m, 2 H), 1.40−1.19 (m, 2 H), 0.86 (t, J = 7.3 Hz, 3 H); ^{13}C NMR (75 MHz) δ 156.9, 149.8, 143.7, 140.8, 129.8, 126.8, 114.1, 48.5, 31.0, 27.3, 25.5, 24.3, 22.7, 21.6, 13.9; MS (*m*/*z*, %) 318 (M^+, 7), 276 (100), 211 (88); HRMS calcd for $C_{17}H_{22}N_2O_2S$ (M^+): 318.1402; found: 318.1384.

2-*n*-Butyl-3-[(*p*-hydroxymethyl)benzenesulfonyl]-5,6-dihydro-4H-pyrrolo[1,2-b]pyrazole (70). Similarly, resin **7a** (0.50 g, 0.67 mmol/g) was stirred in anisole (30 mL) for 30 min. Sydnone **27** (63 mg, 0.50 mmol was added and the reaction mixture was refluxed for 2 h. The resulting solid-supported cycloadduct was cleaved with LiOH in the usual manner. The resulting yellow oil was chromatograped (50% ethyl acetate−hexanes) to afford 92 mg (82%) of product **70** as a yellow oil that crystallized from ethyl acetate−hexanes: mp 106−107.5 °C; IR (KBr) 3339, 1596, 1322, 1130, 1052 cm^{-1}; ^1H NMR (300 MHz) δ 7.84 (d, J = 8.3 Hz, 2 H), 7.48 (d, J = 8.3 Hz, 2 H), 4.76 (d, J = 5.1 Hz, 2 H), 4.09 (t, J = 7.2 Hz, 2 H), 3.10 (t, J = 7.5 Hz, 2 H), 2.70 (t, J = 8.2 Hz, 2 H), 2.65−2.55 (m, 2 H), 2.32 (t, J = 5.2 Hz, 1 H), 1.77−1.44 (m, 2 H), 1.42−1.15 (m, 2 H), 0.88 (t, J = 7.3 Hz, 3 H); ^{13}C NMR (75 MHz) δ 157.1, 150.0, 146.4, 142.5, 127.1, 127.0, 113.8, 64.3, 48.5, 31.0, 27.3, 25.5, 24.4, 22.7, 14.0; MS (*m*/*z*, %) 334 (M^+, 20), 305 (90), 292 (100); HRMS calcd for $C_{17}H_{22}N_2O_3S$ (M^+): 334.1351; found: 334.1324. Anal. Calcd for $C_{17}H_{22}N_2O_3S$: C, 61.05; H, 6.63; N, 8.38. Found: C, 61.03; H, 6.80; N, 8.26. The ORTEP diagram and X-ray crystallographic data for structure **70** are provided in the Supporting Information.

The reduction of the cycloadduct obtained from sydnone **27** and the solid-supported acetylenic sulfone **7a** with samarium diiodide was carried out as in the case of the cycloadduct formed between dipole **26b** and **7a** (*vide supra*) to afford **68** in 77% yield.

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Supporting Information Available: Procedures for the preparation of **13, 14**, **33**, **34**, **40a**,**b**, **46**, **49**, **51**, **53**, **55**, **58**, **60**, **63**, **65**, **67**, **69**, and **71**; ^1H and ^{13}C NMR spectra of new compounds; ORTEP diagrams and cif files for the X-ray structures of compounds **32**, **35**, **48**, **51**, **54**, **61**, **66**, and **70**. This material is available free of charge via the Internet at http://pubs.acs.org.

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