SYNTHESIS AND REACTIONS OF *N*-SUBSTITUTED PYRAZOLO-3-SULFOLENES

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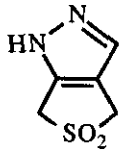
Abstract -*N*-Toluenesulfonyl- and *N*-(anilinocarbonyl)pyrazolo-3-sulfolenes have been prepared from the protected oxotetrahydrothiophenecarbaldehyde (**7**) *via* a sequence of hydrazone formation, ketal hydrolysis, cyclization, dehydration, and oxidation reactions. These *N*-substituents migrate between the two nitrogen atoms of the pyrazole ring at different stages. Extrusion of SO_2 from *N*-anilinocarbonylpyrazolo-3-sulfolenes was achieved at 180–200 °C and the transient intermediate, the pyrazolo-*o*-quniodimethane, could be trapped with dienophiles.

Recently, the study of heteroaromatic *o*-quinodimethanes (**1**) has drawn great interests in both synthetic and theoretical aspects.[1] Among the known approaches toward the generation of this class of unstable compounds, the use of heteroaromatic-fused 3-sulfolenes (**2**) as precursors for the corresponding heteroaromatic *o*-quinodimethanes (**1**) is most ideal for synthetic purposes.[2–9] 3-Sulfolenes are in general stable toward moderately acidic, basic, and thermal conditions. The extrusion of SO_2 from **2** can be accomplished at mild temperatures where the reactive intermediates (**1**) may be trapped as [4+2] cycloadducts in good yields. In addition, 3-sulfolenes can be functionalized by deprotonation/alkylation reaction sequence so that derivation of **1** and **2** is possible.[10]

1

2

We have reported the preparation of pyrazole-fused 3-sulfolene (**3**)and its *N*-phenyl derivative (**4**).[8] Compound (**3**) is not a good precursor for the *o*-quinodimethane (**5**) because the extrusion of SO_2 was low yield. Moreover, attempted substitution reactions of **3** with methyl or benzoyl groups produced unseparable mixtures of *N*-substituted products.[3] On the other hand, compound (**4**) was proved to be a valuable precursor for **6** and its derivatives.[8] A minor dissatisfaction of using **4** as the precursor for pyrazolo-*o*-quinodimethanes is the difficulty in replacing the *N*-phenyl group with a hydrogen atom or another substituent. Therefore, attempts were made to prepare pyrazolo-3-sulfolenes whose nitrogen is attached to a carbonyl or a sulfonyl group. These *N*-substituents are desirable because they not only may survive through certain functionality manipulation processes, but also could be removed under moderate conditions.



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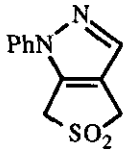

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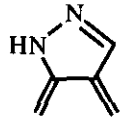

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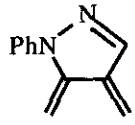

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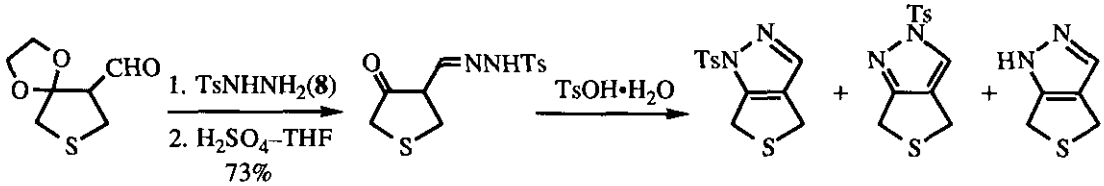
The synthesis of the *N*-tosylpyrazolo-3-sulfolene started with ketal aldehyde (**7**).[4] The reaction of **7** with tosylhydrazine (**8**) followed by acid-induced deprotection of the ketal group produced **9** in good yield. Treatment of the ketohydrazone (**9**)with TsOH caused pyrazole formation (Scheme 1).

Scheme 1



7 **9** **10** **11** **12**

However, mixtures of products were obtained from **9** and the ratio of the products was dependent on the reaction conditions (Table I). Product (**10**) was formed in a very small amount when the reaction was performed at a low temperature and for a short period of time (entries 1 and 2). Raising the reaction temperature or lengthening the reaction time enhanced the consumption of the starting material (**9**), but did not increase the yield of the desired product (**10**). On the contrary, compound (**10**) was not obtained in entries 4 and 5 where compounds (**11**) and (**12**) were the major products. Apparently, isomerization from **10** to **11** and

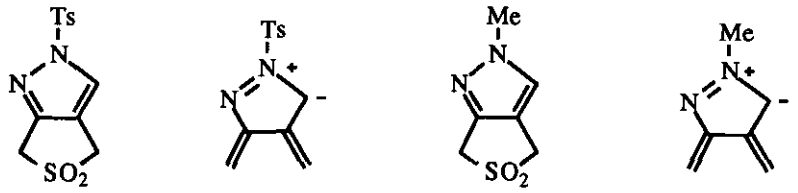
hydrolysis of **10** to **12** readily took place under the reaction conditions. In a separate experiment, compound (**10**) was completely isomerized to **11** upon heating at 110 °C for 30 min. Such an isomerization might involve an intramolecular [1,5] tosyl group shift process or an intermolecular tosyl group exchange process. It is clear that **11** is thermodynamically more stable than **10**.

Table I Formation of Pyrazole-fused 2,5-Dihydrothiophenes from Compound (**9**)

entry	reaction temp	reaction time	products and yields (%)			
			9 (recovered)	**10**	**11**	**12**
1	30 °C	12 h	80	6	2	1
2	50 °C	15 min	60	17	1	2
3	50 °C	3 h	32	12	39	5
4	50 °C	8 h	0	0	62	14
5	110°C	20 min	0	0	32	25

The assignment of the structures of **10** and **11** was based on their ^{1}H nmr spectral data. The chemical shifts of the protons of **11** at the α- and α'-positions of the sulfur atom are identical (δ 3.84, s), whereas those of compound (**10**) are well separated (δ 3.82 and 4.22). These data reflect that α- and α'-protons of **10** have a more different environment than in **11**. Such an assignment is analogous to what Storr *et al.*[3] made in determining the structures of *N*-benzoylpyrazolo-3-sulfolenes.

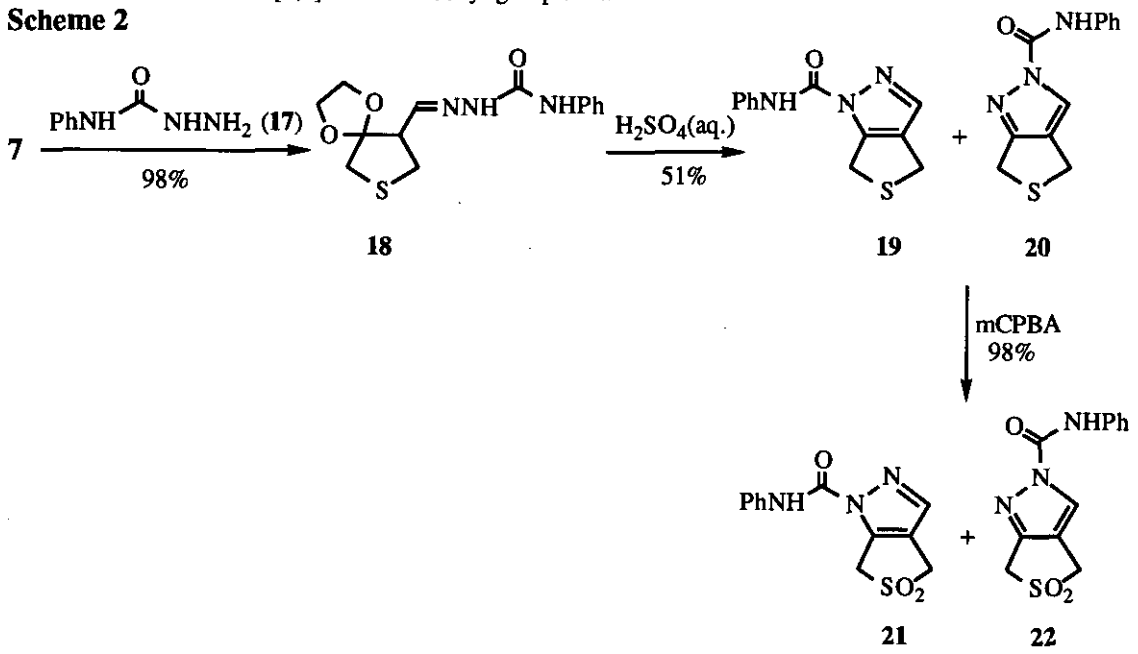
Oxidation of **11** with *m*-chloroperbenzoic acid (mCPBA) produced the fused 3-sulfolene (**13**) in 98% yield. Unfortunately, the attempts to extrude SO_2 from **13** to generate the *o*-quinodimethane (**14**) were unsuccessful. No reaction took place when **13** was heated at 230 °C for 1 h. This result is in sharp contrast to that observed when compound (**15**) was thermolyzed as reported by Storr *et al.*[3] Compound (**15**) was transformed to the corresponding *o*-quinodimethane (**16**) upon heating at 200 °C. The electron-withdrawing *N*-tosyl group may disfavor the formation of the azomethine imine moiety so that **14** was not obtained.



13 **14** **15** **16**

The reaction of **7** with phenylsemicarbazide (**17**) produced **18** in almost quantitative yield. Acid-induced hydrolysis of the ketal was accompanied with cyclization and dehydration to give an inseparable mixture of two isomers (**19**) and (**20**) in 9:1 ratio. The structures of **19** and **20** were assigned on the basis of their ^{1}H nmr spectral data, similar to the structural assignments for **10** and **11**. Oxidation of the mixture of **19** and **20** with mcpba yielded another inseparable mixture of pyrazole-fused 3-sulfolenes (**21**) and (**22**) in 3:1 ratio (Scheme 2). The high yield (94%) of the oxidation reaction and the change of the isomeric ratios (from 9:1 to 3:1) indicate that isomerization reactions occurred under the oxidation conditions. Again, the isomerization might involve an intramolecular [1,5] anilinocarbonyl group shift.

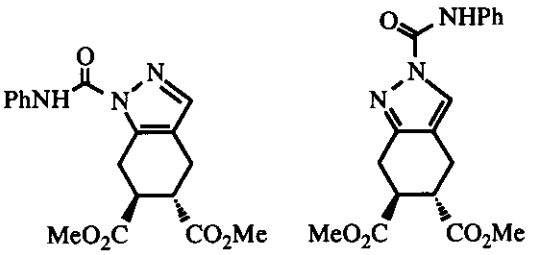
Scheme 2



18 **19** **20** **21** **22**

When the 3:1 mixture of **21** and **22** was heated in the presence of dimethyl fumarate at 180 °C, extrusion of SO_2 and the subsequent [4+2] cycloaddition reaction took place to produce the cycloadducts (**23**) and (**24**) as a mixture of two isomers in 5:2 ratio. The success of cycloaddition reaction indicates that the *o*-quinodimethane

(**25**) must be a transient intermediate in this reaction. Although **26** could also be an intermediate for the formation of cycloadducts, compound (**22**) was not expected to extrude SO_2 readily under the reaction conditions as in the case of compound (**13**). It is more likely that **22** was first isomerized to **21** to undergo the SO_2 extrusion and the Diels-Alder reactions *via* intermediate (**25**). The cycloadduct thus obtained was then transformed to a mixture of **23** and **24** *via* [1,5] anilinocarbonyl group shift under the reaction conditions.



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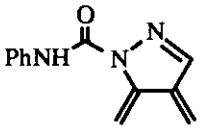

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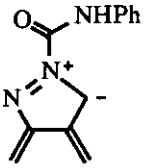

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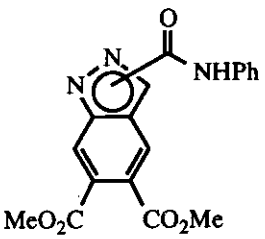

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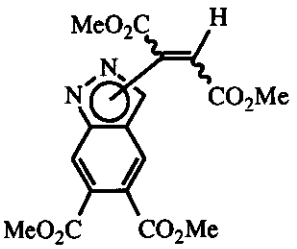

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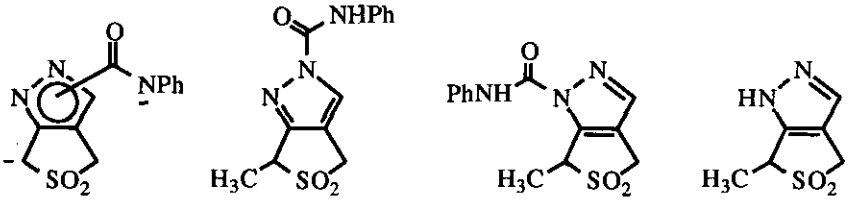
Treatment of the mixture of **21** and **22** with dimethyl acetylenedicarboxylate (DMAD) at 200 °C followed by DDQ oxidation gave a complex mixture from which compounds (**27**) and (**28**) could be isolated in 26% and 25% yields, respectively. By ^{13}C nmr analyses, compound (**27**) bwas identified as a single isomer whose regiochemistry was not determined. Compound (**28**) contained two regio- or stereoisomers (**28a**) and (**28b**) which could be separated but their detailed structures were not determined. These compounds must be produced from the hydrolysis of the *N*-anilinocarbonyl group, Michael addition to DMAD, and subsequent DDQ oxidation.

When the mixture of **21** and **22** was treated with 2 equiv. of lithium hexamethyldisilazide (LiHMDS) followed by excess of MeI, a methylated product (**30**) could be obtained.[10] Presumably the alkylation proceeded *via* the dianion **29**. Compound (**30**) was assigned to be a single isomer as analyzed by ^{13}C nmr.

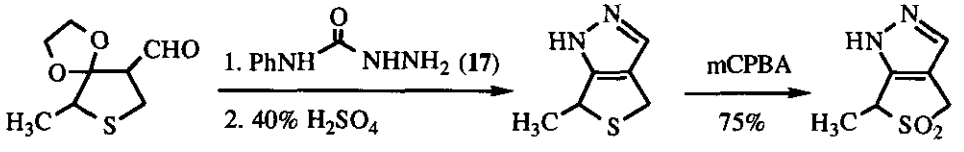
Deprotonation/alkylation reactions of heteroaromatic-fused 3-sulfolenes are generally highly regioselective.[4,5,7,9] Since [1,5] anilinocarbonyl group shift should be possible for compound (**30**), the absence of its isomer (**31**) reveals that **30** is thermodynamically more stable than **31**. This is conceivable because the severe steric repulsion between the anilinocarbonyl and methyl groups in **31** is absent in **30**. However, a phenyl group attached to the nitrogens of pyrazolo-3-sulfolene does not migrate under the deprotonation/methylation reaction conditions.[8]



29 **30** **31** **32**

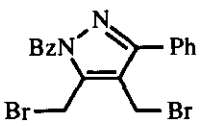
Treatment of **30** with hydrazine hydrate ($NH_2NH_2 \cdot H_2O$) gave the pyrazolo-3-sulfolene (**32**) (91%). To further confirm the structure of **32**, a totally different approach was used to prepare **32** from **33**[4] (Scheme 3). The methylated pyrazolo-3-sulfolene (**32**) obtained in Scheme 3 was found identical to that obtained from hydrazinolysis of compound (**31**). This result unambiguously proves the regioselectivity of the deprotonation/methylation reaction of **21** and **22**.

Scheme 3



33 **34** **32**

Substituted pyrazolo-*o*-quinodimethanes have been prepared by (i) NaI-induced 1,4-debromination of **35**,[11] (ii) flash vacuum pyrolysis of **36**,[3,12] and (iii) extrusion of SO_2 from pyrazole-fused 3-sulfolenes.[2,3,8] The results described herein represent a versatile variation of the third approach and it should find broad applications in synthesis.



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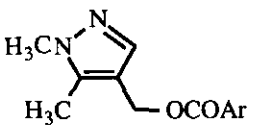

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EXPERIMENTAL SECTION

General methods ^{1}H Nmr spectra were determined on a Bruker ACF-200 NMR spectrometer as solutions in $CDCl_3$ or d_6-acetone. Ir spectra were determined on a Perkin-Elmer 290 IR spectrophotometer. Mass spectra were determined on a VG 70-250S mass spectrometer. Elemental Analyses were performed on a Perkin-Elmer 240C analyzer. All solvents were freshly distilled before use.

(2-Oxo-4-thiacyclopent-1-yl)carbaldehyde 4-Toluenesulfonylhydrazone (9). A solution of compound (**7**)[4] (254 mg, 1.46 mmol), TsOH (catalytic amount), and 4-toluenesulfonylhydrazine (**8**, 281 mg, 1.5 mmol) in 1,4-dioxane (5 ml) was stirred at room temperature for 4 h after which time the solvent was removed under reduced pressure. A solution of 20% H_2SO_4-THF (1:1, 10 ml) was added and the resulting mixture was stirred at room temperature for 10 h. Saturated brine (20 ml) was added and the aqueous solution was extracted with EtOAc (30 ml × 2). The combined organic layers were dried ($MgSO_4$) and concentrated under reduced pressure. Purification of the crude product by column chromatography (silica gel, EtOAc/hexane, 3:1) gave compound (**9**) (250 mg, 73%) as a white solid: mp 162 °C (decomp.); ^{1}H Nmr (acetone-d_6) δ 7.84 (d, J = 8.2 Hz, 2H), 7.35 (d, J = 8.2 Hz, 2H), 6.94 (d, J = 1.5 Hz, 1H), 6.21 (br s, 1H), 3.70 (d, J = 12.4 Hz, 1H), 3.59 (ddd, J = 8.7, 3.5, 1.5 Hz, 1H), 3.28 (d, J = 12.4 Hz, 1H), 3.24 (dd, J = 12.1, 8.7 Hz, 1H), 2.80 (dd, J = 12.1, 3.5 Hz, 1H), 2.40 (s, 3H); ir (KBr) 3461, 2926, 1588, 1328, 1151, 674 cm^{-1}; ms (*m/z*) 298 (M^+), 171, 156, 124, 91 (100); Anal. Calcd for $C_{12}H_{14}N_2O_3S_2$: C, 48.30; H, 4.73; N, 9.39. Found: C, 48.05; H, 4.32; N, 9.19.

1-Toluenesulfonyl-4,6-dihydrothieno[3,4-c]pyrazole (10). A solution of compound (**9**) (117 mg, 0.39 mmol), and TsOH (catalytic amount) in THF (10 ml) was heated at 50 °C for 3 h after which time the solvent was removed under reduced pressure. The crude product was purified by column chromatography (silica gel, EtOAc/hexane, 5:1) to give recovered starting material (**9**) (37.3 mg, 32%), compounds (**10**) (13.6 mg, 12%), (**11**) (43.0 mg, 39%), and (**12**) (2.5 mg, 5%). Compound (**10**) was colorless oil: ^{1}H Nmr ($CDCl_3$) δ 7.87 (d, J = 8.4 Hz, 2H), 7.40 (s, 1H), 7.35 (d, J = 8.4 Hz, 2H), 4.22 (t, J = 3.1 Hz, 2H), 3.82 (t, J = 3.1 Hz, 2H), 2.44 (s,

3H); ir (film) 2931, 1676, 1592, 1521, 1372, 1156, 755 cm^{-1}; ms (*m/z*) 280 (M^+), 216, 155, 125 (100); Hrms calcd for $C_{12}H_{12}N_2O_2S_2$: 280.0340; found: 280.0337.

2-Toluenesulfonyl-4,6-dihydrothieno[3,4-c]pyrazole (11). A solution of compound (**9**) (140 mg, 0.47 mmol), and TsOH (catalytic amount) in THF (10 ml) was heated at 50 °C for 8 h after which time the solvent was removed under reduced pressure. The crude product was purified by column chromatography (silica gel, EtOAc/hexane, 5:1) to give compound (**11**) (81.4 mg, 62%) along with compound (**12**) (8.6 mg, 14%). Compound (**11**) was a white solid: mp 148 °C (decomp.); ^1H Nmr (acetone-d_6) δ 8.00 (s, 1H), 7.88 (d, J = 8.4 Hz, 2H), 7.46 (d, J = 8.4 Hz, 2H), 3.84 (s, 4H), 2.42 (s, 3H); ir (KBr) 3113, 2926, 1575, 1355, 1280, 1158, 1076, 1043, 786, 662, 570 cm^{-1}; ms (*m/z*) 280 (M^+), 155, 125, 91 (100); Hrms calcd for $C_{12}H_{12}N_2O_2S_2$: 280.0340; found: 280.0337.

2-Toluenesulfonyl-4,6-dihydrothieno[3,4-c]pyrazole 5,5-Dioxide (13). A mixture of compound (**11**) (33 mg, 0.12 mmol) and mCPBA (55%, 80 mg, 0.26 mmol) in CH_2Cl_2 (5 ml) was stirred at room temperature for 20 min. CH_2Cl_2 (30 ml) was added and the organic layers were washed with saturated $Na_2S_2O_3$ (20 ml × 3) and saturated $NaHCO_3$ (20 ml × 3). The organic solution was dried ($MgSO_4$) and concentrated under reduced pressure to give essentially pure product (**13**) (36.1 mg, 98%) as a white solid: mp 170–171 °C; ^1H Nmr (acetone-d_6) δ 8.36 (s, 1H), 7.93 (d, J = 8,5 Hz, 2H), 7.49 (d, J = 8.5 Hz, 2H), 4.29 (s, 4H); ir (KBr) 3143, 1595, 1369, 1320, 1175, 1090, 672, 600 cm^{-1}; ms (*m/z*) 312 (M^+), 248, 169, 155, 91 (100); Anal. Calcd for $C_{12}H_{12}N_2O_4S_2$: C, 51.41; H, 4.31; N, 9.99. Found: C, 51.36; H, 4.32; N, 9.99.

(1,4-Dioxa-7-thiaspiro[4.4]non-9-yl)carbaldehyde 4-Phenylsemicarbazone (18). A solution of compound (**7**) (325 mg, 1.87 mmol), TsOH (catalytic amount), and 4-phenylsemicarbazide (**17**, 338 mg, 2.24 mmol) in THF (10 ml) was stirred at room temperature for 2 h after which time the solvent was removed under reduced pressure. The crude oil was purified by column chromatography (silical gel, EtOAc/hexane, 2:1) to give compound (**18**) (561 mg, 98%) as an inseparable mixture of stereoisomers in 2:1 ratio: mp 136–137 °C(decomp.) ; ^1H Nmr ($CDCl_3$) δ 9.42 (s, 0.67H), 9.33(br s, 0.33H), 8.19 (s, 0.67H), 8.01(s, 0.33H), 7.55–7.03 (m, 5.33H), 6.55 (d, J = 6.8 Hz, 0.67H), 4.10–3.92 (m, 4H), 3.64–3.52 (m, 0.67H), 3.16–2.86 (m, 4.33H); ir (KBr) 3359, 3189, 3090, 2973, 1667, 1516, 1290, 1090, 747 cm^{-1}; ms (*m/z*) 307 (M^+), 190, 176, 118, 99 (100), Anal. Calcd for $C_{14}H_{17}N_3O_3S$: C, 54.71; H, 5.57; N, 13.67. Found: C, 54.70; H, 5.52; N, 13.67.

*1-Anilinocarbonyl-4,6-dihydrothieno[3,4-c]pyrazole (**19**) and 2-Anilinocarbonyl-4,6-dihydrothieno[3,4-c]pyrazole (**20**).* A mixture of compound (**18**) (1.04 g, 3.4 mmol), 30% H_2SO_4 (5 ml), and THF (5 ml) was stirred at room temperature for 10 h after which time saturated brine (30 ml) was added and the resulting mixture was extracted with EtOAc (30 ml × 3). The combined organic layers were dried ($MgSO_4$) and concentrated under reduced pressure. The crude oil was purified by column chromatography (silica gel, EtOAc/hexane, 1:2) to give an inseparable mixture of compound (**19**) and (**20**) (420 mg, 51%) in 9:1 ratio as a white solid: mp 138 °C (decomp.); ^{1}H Nmr ($CDCl_3$) δ 8.94 (br s, 1.9H), 7.96(s, 0.1H) 7.60–7.52 (m, 2H), 7.39–7.32 (m, 3H), 7.19–7.11 (m, 1H), 4.30 (t, J = 3.2 Hz, 1.8H), 3.96 (br s, 0.2H), 3.91 (br s, 0.2H), 3.87(t, J=3.2H, 1.8H); ir (KBr) 3379, 2921, 1716, 1514 cm^{-1}; ms (*m/z*) 245 (M^+), 126 (100); Hrms calcd for $C_{12}H_{11}N_3OS$: 245.0623 ; found: 245.0601.

*1-Anilinocarbonyl-4,6-dihydrothieno[3,4-c]pyrazole 5,5-Dioxide (**21**) and 2-Anilinocarbonyl-4,6-dihydrothieno[3,4-c]pyrazole 5,5-Dioxide (**22**).* A mixture of compounds (**19**) and (**20**) (9:1, 239 mg, 0.97 mmol) and mCPBA (55%, 610 mg, 1.94 mmol) in CH_2Cl_2 (20 ml) was stirred at room temperature for 20 min. CH_2Cl_2 (50 ml) was added and the organic layers were washed with saturated $Na_2S_2O_3$ (50 ml × 3) and saturated $NaHCO_3$ (50 ml × 3). The organic solution was dried ($MgSO_4$) and concentrated under reduced pressure to give an inseparable mixture of compounds (**21**) and (**22**) (253 mg, 94%) in 3:1 ratio as a white solid: mp 184 °C (decomp.); ^{1}H Nmr ($CDCl_3$) δ 8.97 (br s, 1H), 8.31(s, 0.25H), 7.67 (s, 0.75H), 7.65–7.50 (m, 2H), 7.44–7.35, (m, 2H), 7.25–7.16 (m, 1H), 4.65 (s, 1.5H), 4.31 (s, 1H), 4.25(s, 1.5H); ir (KBr) 3354, 2987, 1732, 1524, 1301, 1109 cm^{-1}; ms (*m/z*) 277 (M^+), 190, 119 (100), 94; Hrms calcd for $C_{12}H_{11}N_3O_3S$: 277.0521; found: 277.0517.

*1-Anilinocarbonyl-5,6-di(methoxycarbonyl)-trans-4,5,6,7-tetrahydrobenzo[c]pyrazole (**23**) and 2-Anilinocarbonyl-5,6-di(methoxycarbonyl)-trans-4,5,6,7-tetrahydrobenzo[c]pyrazole (**24**).* A solution of the 3:1 mixture of **21** and **22** (66.1 mg, 0.24 mmol) and dimethyl fumarate (41 mg, 0.28 mmol) in $CHCl_3$ (2 ml) was heated in a sealed tube at 180 °C for 20 min after which time the solvent was removed under reduced pressure. The crude oil was purified by hplc (LiChrosorb column, EtOAc/hexane, 1:1) to give an inseparable mixture of compounds (**23**) and (**24**) (70 mg,82%) in 5:2 ratio as a white solid: mp 73–74 °C (decomp.); ^{1}H Nmr ($CDCl_3$) δ 9.12 (br s, 0.3H) δ 8.97 (br s, 0.7H), 8.03 (s, 0.7H), 7.62–7.11 (m, 5.3H), 3.76 (s, 1.8H), 3.74(s, 4.2H), 3.30–2.70 (m, 6H); ir (KBr) 3355, 2955, 1726, 1517, 1174, 748 cm^{-1}; ms (*m/z*) 357 (M^+), 306, 238, 178, 119 (100); Anal. Calcd for $C_{18}H_{19}N_3O$: C, 60.50; H, 5.36; N, 11.76. Found: C, 60.49; H, 5.48; N, 11.80.

*N-Anilinocarbonyl-5,6-di(methoxycarbonyl)benzo[c]pyrazole (**27**) and N-[1,2-di(methoxycarbonyl)vinyl]-5,6-di(methoxycarbonyl)benzo[c]pyrazoles (**28a,b**).* A solution of the 3:1 mixture of **21** and **22** (38.1 mg, 0.14mmol) and DMAD (0.025 ml, 0.20 mmol) in toluene (4 ml) was heated in a sealed tube at 200 °C for 30 min. 2,3-Dichloro-5,6-dicyano-*p*-quinone (DDQ, 71 mg, 0.31 mmol) was then added and the mixture was heated at 140 °C for another 1 h after which time the solvent was removed under reduced pressure. The crude oil was purified by hplc (LiChrosorb column, EtOAc/hexane, 1:1) to give compounds (**27**) (13 mg, 26%), (**28a**) (10 mg, 19%), and (**28b**) (3 mg, 6%). Compound (**27**) was a white solid: mp 156–158 °C; ^{1}H Nmr ($CDCl_3$) δ 9.06 (br s, 1H), 8.79 (s, 1H), 8.26 (s, 1H), 8.22 (s, 1H), 7.68–7.61 (m, 2H), 7.46–7.36 (m, 2H), 7.25–7.15 (m, 1H), 3.97 (s, 3H), 3.94 (s, 3H); ^{13}C Nmr ($CDCl_3$) δ 168.04, 167.11, 147.98, 139.49, 137.92, 136.60, 133.74, 129.27, 126.64, 126.27, 124.79, 123.50, 119.79, 115.67, 52.91, 52.78; ir (KBr) 3351, 2944, 1712, 1517, 1238, 1206, 765 cm^{-1}; ms (*m/z*) 353 (M^+), 177, 145 (100); Hrms calcd for $C_{18}H_{15}N_3O_5$: 353.1020; found: 353.1012. Compound (**28a**) was a white solid: mp 138–139 °C; ^{1}H Nmr ($CDCl_3$) δ 8.31 (s, 1H), 8.28 (s, 1H), 7.91 (s, 1H), 6.50 (s, 1H), 4.05 (s, 3H), 3.97 (s, 3H), 3.94 (s, 3H), 3.84 (s, 3H); ir (KBr) 3110, 2950, 1713, 1422, 1239, 1163, 775 cm^{-1}; ms (*m/z*) 376 (M^+), 345 (100); Hrms calcd for $C_{17}H_{16}N_2O_8$: 376.0906; found: 376.0897. Compound (**28b**) was a white solid: mp 122–123 °C; ^{1}H Nmr ($CDCl_3$) δ 8.30 (s, 1H), 8.16 (s, 1H), 8.04 (s, 1H), 6.95 (s, 1H). 4.07 (s, 3H), 3.94 (s, 3H), 3.91 (s, 3H), 3.85 (s, 3H); ir (KBr) 2978, 1707, 1158, 776 cm^{-1}; ms (*m/z*) 376 (M^+), 345, 177, 145 (100); Hrms calcd for $C_{17}H_{16}N_2O_8$: 376.0906; found: 376.0899.

*2-Anilinocarbonyl-6-methyl-4,6-dihydrothieno[3,4-c]pyrazole 5,5-Dioxide (**30**).* To a solution of the 3:1 mixture of **21** and **22** (52 mg, 0.19 mmol), hexamethylphosphoramide (HMPA, 0.15 ml), and MeI (0.1 ml, 1.6 mmol) in THF (3 ml) cooled at -105 °C was added dropwise a THF solution of LiHMDS [generated from n-BuLi (0.25 ml, 1.5 M, 0.375 mmol) and hexamethyldisilazane (0.12 ml), 0.37 mmol]. The mixture was stirred at -105 °C for 30 min after which time HOAc (0.1 ml) was added. The solvent was removed under reduced pressure and the crude oil was eluted through a silica gel column (EtOAc/hexane, 1:1) to remove HMPA. The mixture was then purified by hplc (LiChrosorb column, EtOAc/hexane, 1:1) to give compound (**30**) (11.6 mg, 22%) along with recovered starting material **21** and **22** (9.3 mg, 17%). Compound (**30**) was a white solid: mp 153 °C (decomp.); ^{1}H Nmr ($CDCl_3$) δ 8.96 (br s, 1H), 8.29 (t, J = 1.0 Hz, 1H), 7.65–7.57 (m, 2H), 7.46–7.37 (m, 2H), 7.26–7.17 (m, 1H), 4.28 (q, J = 7.1 Hz, 1H), 4.27 (d, J = 1.0 Hz, 2H), 1.73 (d, J = 7.1 Hz, 3H); ^{13}C Nmr ($CDCl_3$) δ 153.17, 146.12, 136.13, 129.32, 125.37, 125.17, 119.88, 112.85, 57.18, 51.65, 12.53; ir (KBr)

3371, 1735, 1535, 1306, 1109, 759 cm^{-1}; ms (*m/z*) 291 (M^+), 119 (100), 108; Hrms calcd for $C_{13}H_{13}N_3O_3S$: 291.0686; found: 291.0678.

6-Methyl-4,6-dihydrothieno[3,4-c]pyrazole 5,5-Dioxide (32).

Method A A solution of compound (**30**) (6.5 mg, 0.022 mmol) and 98% hydrazine hydrate (0.1 ml, 2.0 mmol) in THF (2 ml) was stirred at room temperature for 10 h after which time the solvent was removed under reduced pressure. The crude oil was purified by column chromatography (silica gel, EtOAc/hexane, 9:1) to give compound (**32**) (3.5 mg, 91%).

Method B A mixture of compound (**34**) (56 mg, 0.40 mmol) and mCPBA (55%, 300 mg, 0.90 mmol) in CH_2Cl_2 (4 ml) was stirred at room temperature for 20 min after which time the solvent was removed under reduced pressure. The crude oil was purified by thin layer chromatography (silica gel, EtOAc/hexane, 3:1) to give compound (**32**) (52.1 mg, 75%).

Compound (**32**) was a white solid: mp 100–102 °C; ^1H Nmr ($CDCl_3$) δ 7.54 (br s, 2H), 4.28 (q, J = 7.0 Hz, 1H), 4.24 (br s, 2H), 1.67 (d, J = 7.0 Hz, 3H); ir (KBr) 3294, 1296, 1124, 753 cm^{-1}; ms (*m/z*) 172 (M^+), 108 (100), 80; Hrms calcd for $C_6H_8N_2O_2S$: 172.0307; found: 172.0302.

6-Methyl-4,6-dihydrothieno[3,4-c]pyrazole (34). A solution of compound (**33**)[4] (580 mg, 3.07 mmol), TsOH (catalytic amount), and 4-phenylsemicarbazide (**17**, 510 mg, 3.38 mmol) in Et_2O (2 ml) was stirred at room temperature for 3 h. Aqueous H_2SO_4 (40% v/v, 2 ml) was then added and the stirring was continued for another 10 h. Saturated brine (10 ml) was added and the layers were separated. The aqueous layer was extracted with Et_2O (40 ml × 2) and the combined organic layers were dried ($MgSO_4$) and concentrated under reduced pressure. The crude product was purified by column chromatography to give **34** (230 mg, 53%) as a white solid: mp 110–111 °C; ^1H Nmr ($CDCl_3$) δ 7.22 (s, 1H), 7.24 (br s, 1H), 4.58 (qdd, J = 6.8, 2.7, 1.9 Hz, 1H), 3.97 (dd, J = 12.2, 2.7 Hz, 1H), 3.88 (dd, J = 12.2, 1.9 Hz, 1H), 1.64 (d, J = 6.8 Hz, 3H); ir (KBr) 3132, 2908, 1361, 1032, 952, 793 cm^{-1}; ms (*m/z*) 140 (M^+), 125 (100); Hrms calcd for $C_6H_8N_2S$: 140.0408; found: 140.0410.

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