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Formation of six- versus five-membered cyclic sulfones by C–H insertion

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ABSTRACT

Selectivity of six- versus five- membered ring formation in C–H insertion on alkylsulfonyl diazoacetates is sensitive to the substrate structure and catalyst used.

Rhodium-catalyzed insertion of carbenoids into C–H bonds has developed into a useful and powerful synthetic method.[1] A number of total syntheses have been performed taking advantage of this methodology.[2]

A unique feature of this reaction, which is also its key advantage, is that no functionality needs to be present at the reactive center (C–H bond). In addition, formation of a carbon–carbon bond occurs—pivotal transformation in organic synthesis. However, with the advantage also comes a challenge—numerous potential reactive sites are commonly present in organic compounds. Consequently, selectivity becomes the central issue in this reaction.

Greater susceptibility of certain C–H bonds for insertion (such as ethereal or allylic) makes it possible to perform a selective intermolecular reaction on some classes of substrates.[3] More generally, intramolecular reaction is used to control the selectivity, relying on conformational restrictions, or, particularly, on the usual overwhelming preference for formation of five-membered rings.[4]

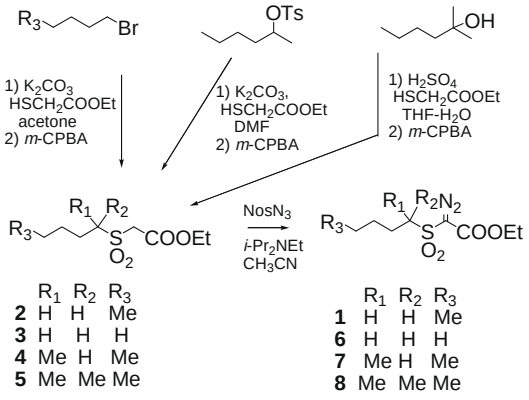
We previously reported that carbene C–H insertion on diazosulfone and diazosulfonate substrates, in contrast, leads to preferential formation of six-membered rings when the sulfonyl group is incorporated into the forming ring.[5] The subsequent report by the Du Bois group[6] demonstrated that in case of diazosulfonates this preference persists on a variety of substrates, even when formation of a strained system is required. This unusual preference has been explained by different bond lengths and bond angle around SO_2 fragment that favor the six-membered ring geometry, as in case of the nitrene insertion on similar substrates.[7]

In our follow-up studies of this reaction, we have uncovered the tenuous nature of this preference on diazosulfone substrates. Herein, we report the result of these studies.

In our initial report,[6] we identified sulfone **1.1a** as the major product of cyclization of diazosulfone **1**. A more detailed analysis of the reaction mixture revealed the presence of small amounts of the cis-isomer, **1.1b**, as well as five-membered isomers, **1.2a,b**. The difficult separation was further complicated by concurrent equilibration of **1.2b** to **1.2a** during chromatography. Fortunately, it was found that equilibration of the mixture of **1.2a** and **1.2b** with DBU in CH_2Cl_2 at rt provided virtually exclusively **1.2a**. Prior equilibration simplified the separation. Curiously, under these equilibration conditions the six-membered isomers **1.1a** and **1.1b** form a mixture with a close to 1:1 ratio.

We continued by testing other catalysts for this transformation (Table 1). Doyle's $Rh_2(cap)_4$ (rhodium caprolactam), which was known to amplify C–H insertion selectivity,[4b] and Du Bois tethered $Rh_2(esp)_2$[8] catalysts proved effective for this transformation, showing results similar to rhodium (II) acetate. $Rh_2(cap)_4$ catalyst was unreactive at rt or at reflux in dichloromethane, necessitating the switch to the higher boiling solvent dichloroethane. Unexpectedly, $Rh_2(pfb)_4$ (rhodium(II) perfluorobutyrate) catalyst leads to reversal of the usual selectivity, giving primarily the five-membered products.

We then explored the effect of substitution adjacent to the reactive sites (Table 2). Preparation of the necessary substrates is shown in Scheme 1 (the characterization data for the substrates and intermediates are provided[10]). Substrates **1**, **6,** and **7** were pre-



	R_1	R_2	R_3
2	H	H	Me
3	H	H	H
4	Me	H	Me
5	Me	Me	Me

	R_1	R_2	R_3
1	H	H	Me
6	H	H	H
7	Me	H	Me
8	Me	Me	Me

Scheme 1. Preparation of substrates.

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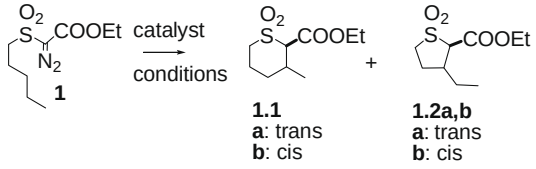
Table 1
Effect of catalyst on five- versus six-membered ring selectivity



Catalyst, conditions[a]	Yield of **1.1**[b] (%)	Yield of **1.2**[b] (%)
$Rh_2(OAc)_4$, rt, CH_2Cl_2	65	9
$Rh_2(esp)_2$, rt, CH_2Cl_2	70	9
$Rh_2(cap)_4$, 80 °C, $(CH_2Cl)_2$	60	8
$Rh_2(pfb)_4$, rt, CH_2Cl_2	27	49

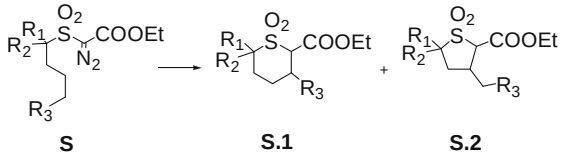
[a] All reactions were carried out by slow addition of the solution of diazocompound to 1 mol % of the catalyst.[9]
[b] Isolated yields, combined for both diastereomers.

pared by our previously reported procedure,[5] with a minor modification in case of **7** (switch of the solvent to DMF). Preparation of substrate **8** was achieved by acid-catalyzed S_N1 substitution to make the sulfide, which was further processed as usual.

Decrease in substitution at the insertion site (substrate **6**, Table 2) predictably disfavored the insertion, leading to preferential formation of the five-membered products, with only small amounts of the six-membered sulfone. Notably, use of $Rh_2(pfb)_4$ made the preference for the five-membered ring complete, also greatly improving the yields of the product.

Less expectedly, substitution next to sulfone center would also increase the fraction of the five-membered products. Monomethyl substitution (substrate **7**, Table 2) leads to formation of close to equivalent amounts of five and six-membered products. Use of $Rh_2(pfb)_4$ amplified this bias to make five-membered sulfone prevalent. Notably, selectivity in formation of the center at β-position was observed for this substrate. The stereochemistry of the principal products is shown in Figures 1 and 2. Formation of small amounts (5–10% combined) of several products possibly containing the opposite configuration at β-position was observed. We were unable to sufficiently purify them for definitive identification. The dimethyl-substituted diazosulfone, **8**, was stable to rhodium catalysts at rt or reflux in methylene chloride, requiring reflux in dichloroethane to react. The reaction resulted in greatly prevalent

Table 2
Effects of structure on selectivity



S R_1 R_2 R_3	Method[a]	Yield of **S.1**[b] (%)	Yield of **S.2**[b] (%)
1 H, H, Me	A	65	9
6 H, H, H	A	2	25
6 H, H, H	B	4	45
6 H, H, H	C	Not detected	80
7 Me, H, Me	A	40	24
7 Me, H, Me	B	26	34
7 Me, H, Me	C	8	60
8 Me, Me, Me	D	5	75
8 Me, Me, Me	E	Not detected	64

[a] Methods: A—$Rh_2(OAc)_4$, CH_2Cl_2, rt; B—$Rh_2(esp)_2$, CH_2Cl_2, rt; C—$Rh_2(pfb)_2$, CH_2Cl_2, rt; D—$Rh_2(OAc)_2$, $(CH_2Cl)_2$, reflux; E—$Rh_2(pfb)_2$, $(CH_2Cl)_2$, reflux.[9]
[b] Isolated yields, combined for both diastereomers.

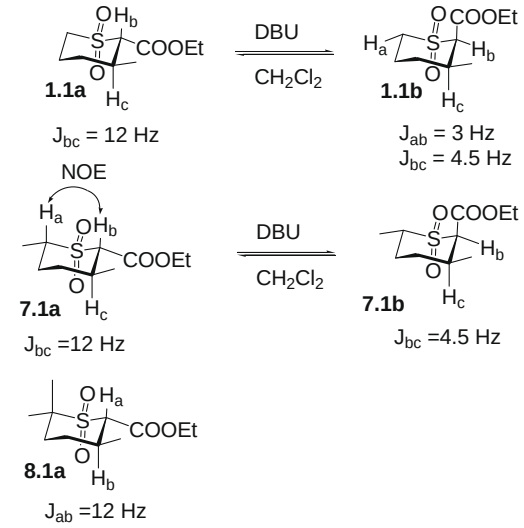


Figure 1. Stereochemical assignments of the six-membered products.

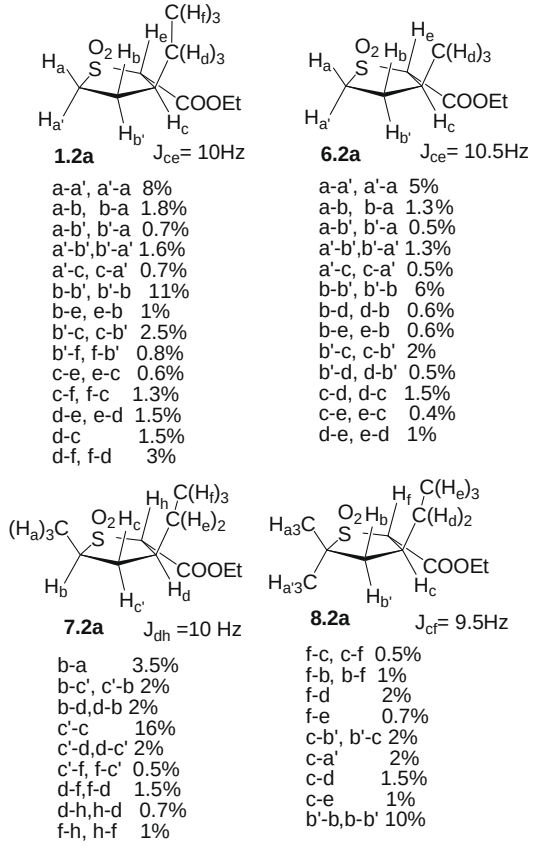


Figure 2. Stereochemical assignments of the five-membered products.

formation of the five-membered product even with $Rh_2(OAc)_4$ catalyst. Use of $Rh_2(pfb)_4$ leads to complete selectivity toward the five-membered product at the expense of the decreased yield. The tendency can be explained by the decrease in the angle of C–C–SO_2 fragment due to steric compression, favoring the five-membered ring geometry.

The structural and stereochemical assignments of the products have been performed on the basis of their interconversion, ^1H, ^{13}C,

COSY, DEPT, and 1D NOE difference spectra (the characterization data for the cyclization products are provided[10]).

The relative configuration of stereocenters in **1.1b** was assigned on the basis of the coupling constants between H_b and H_c (Fig. 1). Smaller coupling constant and appearance of another coupling constant to H_a (confirmed by COSY) indicate the equatorial position of H_b. Similarly, diaxial arrangement of H_b and H_c is established in **7.1a**, while indicating the cis-arrangement in **7.1b**. Bidirectional NOE correlation between H_a and H_b established the configuration of the β-center. While formation of the cis-isomer of **8.1a** appeared to occur in the reaction of **8** (by presence of characteristic peaks in the crude spectra), it appeared to recede after equilibration, and only **8.1a** was isolated. It has been verified that **8.1a** does not change upon treatment with DBU, unlike **1.1a** and **7.1a**, which produces mixtures of cis- and trans-isomers. This could be explained by unfavorable diaxial interaction with the methyl group that would be present in the cis-isomer of **8.1a**, but not in **1.1b** and **7.1b**.

All five-membered products were isolated as single isomers after equilibration.

They all show similar patterns of chemical shifts and NOE correlations between protons. They have been assigned trans-configuration on the basis of NOE data and coupling constants. Observed NOEs and their relative intensities are consistent with the proposed structures, while several disagreements can be found with the cis-isomers. Additionally, the large coupling constant (10 Hz) between H_c and H_e in **1.2a** (H_c and H_e in **6.2a**, H_d and H_h in **7.2a**, H_c and H_f in **8.2a**) indicates a dihedral angle that is close to either 0° or 180°. Weak NOE correlations between these hydrogens suggest against the small dihedral angle that would force these hydrogens to a proximity. For **7.2a**, relative configuration of the C5 center was unambiguously confirmed by a bidirectional NOE between H_b and H_d.

In summary, C–H insertion on the alkylsulfonyl diazoacetate substrates has demonstrated a sensitive nature of the earlier discovered preference for formation of six-membered rings. Substitution next to sulfone was found to tilt it toward the formation of five-membered sulfones. Unexpectedly, same influence is also exerted by $Rh_2(pfb)_4$ catalyst. This permits a degree of control over the reaction outcome to form either thiofuran or thiopyran 1,1-dioxides, both of which are useful intermediates in synthesis.

Further studies of this reaction will be reported in due course.

Acknowledgments

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2009.02.044.

References and notes

1. A recent review: Davies, H. M. L.; Manning, J. R. *Nature* **2008**, *451*, 417.
2. (a) Wee, A. G. H. *Curr. Org. Syn.* **2006**, 499; (b) Taber, D. F.; Stiriba, S.-E. *Organic Synthesis Highlights IV* **2000**, 130.
3. For instance, for allylic substrates: Davies, H. M. L.; Nikolai, J. *Org. Biomol. Chem.* **2005**, *3*, 4176.
4. (a) Taber, D. F.; Malcolm, S. C. *J. Org. Chem.* **1998**, *63*, 3717; (b) Doyle, M. P.; Dyatkin, A. B.; Roos, G. H. P.; Canas, F.; Pierson, D. A.; Van Basten, A.; Mueller, P.; Polleux, P. *J. Am. Chem. Soc.* **1994**, *116*, 4507; (c) Doyle, M. P.; Westrum, L. J.; Wolthuis, W. N. E.; See, M. M.; Boone, W. P.; Bagheri, V.; Pearson, M. M. *J. Am. Chem. Soc.* **1993**, *115*, 958; (d) Taber, D. F.; Petty, E. H. *J. Org. Chem.* **1982**, *47*, 4808.
5. John, J. P.; Novikov, A. V. *Org. Lett.* **2007**, *9*, 61.
6. Wolckenhauer, S. A.; Devlin, A. S.; Du Bois, J. *Org. Lett.* **2007**, *9*, 4363.
7. Espino, C. G.; Wehn, P. M.; Chow, J.; Du Bois, J. *J. Am. Chem. Soc.* **2001**, *123*, 6935.
8. Espino, C. G.; Fiori, K. W.; Kim, M.; Du Bois, J. *J. Am. Chem. Soc.* **2004**, *126*, 15378.
9. *General procedure for C–H insertion*: To the suspension of the catalyst (1 mol %) in CH_2Cl_2 (or $ClCH_2CH_2Cl$, 4 ml/mmol), a solution of the corresponding diazo compound (1 equiv, 0.1–1 mmol) in CH_2Cl_2 (or $ClCH_2CH_2Cl$, 2 ml/mmol) was added at rt (or reflux) over a period of 1 h using a syringe pump. Upon completion of the addition, the reaction mixture was stirred at rt for additional 8 h. The volatiles were removed under reduced pressure. The crude reaction mixture was separated on silica column (ethyl acetate–hexanes, 0–40%). Typically, it was possible to divide the mixture into three parts—the unpolar decomposition products, mixture or various cyclization products, and the more polar six-membered trans-isomer. In some cases, isolation of the cis six-membered product was also possible. The incompletely separated mixture of the cyclization products was dissolved in CH_2Cl_2 and treated with 1 eqiv of DBU for 24 h. HCl (1 M) was added, and the reaction mixture was stirred for 15 more minutes. The layers were separated, aqueous layer was washed with CH_2Cl_2, and the combined organic layers were dried and concentrated. The chromatography on silica column (ethyl acetate–hexanes, 0–40%) at this point permitted to isolate the trans five-membered product, cis six-membered product, and additional amount of the trans six-membered product, formed by equilibration from the cis-isomer.
10. *Physical data for compounds*: Compounds **1**, **1.1a**, and **3** have been previously reported. ^1H and ^{13}C for **3** are provided as they do not appear to have been reported.
Ethyl 2-(butylsulfonyl)acetate (**3**): colorless oil, ^1H NMR (500 MHz, $CDCl_3$): δ 4.26 (q, *J* = 7 Hz, 2H), 3.94 (s, 2H), 3.22–3.26 (m, 2H), 1.81–1.88 (m, 2H), 1.49 (q, *J* = 7.5 Hz, 2H), 1.31 (t, *J* = 7 Hz, 3H), 0.97 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR ($CDCl_3$, 125 Mhz): δ 163.3, 62.8, 57.5, 53.5, 24.0, 21.8, 14.1, 13.6.
Ethyl 2-(hexan-2-ylsulfonyl)acetate (**4**): pale yellow oil, ^1H NMR (500 MHz, $CDCl_3$): δ 4.27 (q, *J* = 7 Hz, 2H), 3.99 (d, *J* = 14.5 Hz, 1H), 3.94 (d, *J* = 14.5 Hz, 1H), 3.35–3.43 (m, 1H), 1.99–2.07 (m, 1H), 1.52–1.66 (m, 2H), 1.47 (d, *J* = 6.5 Hz, 3H), 1.30–1.45 (m, 6H), 1.42 (t, *J* = 6.5 Hz), 1.33 (t, *J* = 7 Hz), 0.94 (t, *J* = 7 Hz, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 163.3, 62.8, 58.2, 55.2, 28.8, 28.3, 22.6, 14.2, 14.0, 12.9. HRMS (ESI) calcd for $C_{10}H_{24}NO_4S$ [M+NH$_4$] 254.1420, found 254.1404.
Ethyl 2-(2-methylhexan-2-ylsulfonyl)acetate (**5**): pale yellow oil, ^1H NMR (500 MHz, $CDCl_3$): δ 4.28 (q, *J* = 7 Hz, 2H), 3.94 (s, 2H), 1.76–1.81 (m, 2H), 1.30–1.46 (m, 13H), 1.40 (s), 1.33 (t, *J* = 7 Hz), 0.93 (t, *J* = 7 Hz, 3H). ^{13}C NMR ($CDCl_3$, 125 Mhz): δ 162.9, 65.3, 62.8, 53.3, 35.0, 26.1, 23.3, 20.7, 14.2, 14.1. HRMS (ESI) calcd for $C_{11}H_{26}NO_4S$ [M+NH$_4$] 254.1577, found 254.1609.
Note: The signal for the diazo carbon was not observed in ^{13}C for any of the diazocompounds, possibly due to quadrupole broadening. IR spectra showing the diazo stretch (~2130 cm^{-1}) are provided for diazo compounds.
Ethyl 2-(butylsulfonyl)diazoacetate (**6**): yellow oil, ^1H NMR (500 MHz, $CDCl_3$): δ 4.33 (q, *J* = 7 Hz, 2H), 3.35–3.43 (m, 2H), 1.77–1.86 (m, 2H), 1.48 (q, *J* = 7.5 Hz, 2H), 1.33 (t, *J* = 7 Hz, 3H), 0.96 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 160.3, 62.7, 56.6, 24.8, 21.5, 14.5, 13.7. IR (neat, cm^{-1}): 2129, 1714, 1467.
Ethyl 2-(hexan-2-ylsulfonyl)diazoacetate (**7**): yellow oil, ^1H NMR (500 MHz, $CDCl_3$): δ 4.33 (q, *J* = 7 Hz, 2H), 3.44–3.51 (m, 1H), 1.98–2.06 (m, 1H), 1.56–1.65 (m, 1H), 1.44–1.52 (m, 1H), 1.42 (d, *J* = 7 Hz, 3H), 1.31–1.40 (m, 6H), 1.34 (t, *J* = 7 Hz), 0.94 (t, *J* = 7 Hz, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz)): δ 160.4, 62.7, 61.7, 28.8, 28.7, 22.6, 14.5, 14.0, 13.2. IR (neat, cm^{-1}): 2127, 1714, 1463.
Ethyl 2-(2-methylhexan-2-ylsulfonyl)diazoacetate (**8**): yellow oil, ^1H NMR (500 MHz, $CDCl_3$): δ 4.32 (q, *J* = 7 Hz, 2H), 1.77–1.81 (m, 2H), 1.31–1.46 (m, 13H), 1.41 (s), 1.32 (t, *J* = 7 Hz), 0.94 (t, *J* = 7 Hz, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 160.4, 69.0, 62.6, 34.9, 26.2, 23.4, 20.9, 14.5, 14.1. IR (neat, cm^{-1}): 2125, 1727, 1465.
cis-Ethyl tetrahydro-3-methyl-2H-thiopyran-1,1-dioxide-2-carboxylate (**1.1b**): white flaky solid, mp 36–37 °C, ^1H NMR (500 MHz, $CDCl_3$): δ 4.27 (qd, *J* = 7, 1 Hz, 2H), 3.77 (dd, *J* = 4.5, 3 Hz, 1H), 3.56 (td, *J* = 13, 5 Hz, 1H), 2.93 (dq, *J* = 14, 3 Hz, 1H), 2.50–2.59 (m, 1H), 2.04–2.16 (m, 2H), 1.84 (qd, *J* = 13, 5 Hz, 1H), 1.55–1.65 (m, 1H; overlapped with water peak), 1.33 (t, *J* = 7 Hz, 3H), 1.06 (d, *J* = 7 Hz, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 166.3 (C), 70.1 (CH), 62.4 (CH_2), 48.0 (CH_2), 34.4 (CH), 26.7 (CH_2), 23.3 (CH_2), 19.8 (CH_3), 14.3 (CH_3). HRMS (ESI) calcd for $C_9H_{20}NO_4S$ [M+NH$_4$] 238.1107, found 238.1095.
trans-Ethyl tetrahydro-3-ethylthiophene-1,1-dioxide-2-carboxylate (**1.2a**): pale yellow oil, ^1H NMR (500 MHz, $CDCl_3$): δ 4.25–4.48 (m, 2H), 3.58 (d, *J* = 10 Hz, 1H), 3.28 (ddd, *J* = 13, 7, 2 Hz, 1H), 3.10 (td, *J* = 13, 7 Hz, 1H), 2.68–2.77 (m, 1H), 2.35–2.42 (m, 1H), 1.76–1.86 (m, 1H), 1.60–1.69 (m, 1H), 1.49–1.56 (m, 1H), 1.34 (t, *J* = 7 Hz, 3H), 0.97 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 165.8 (C), 70.9 (CH), 62.9 (CH_2), 52.9 (CH_2), 41.7 (CH), 27.4 (CH_2), 26.3 (CH_2), 14.3 (CH_3), 11.5 (CH_3). HRMS (ESI) calcd for $C_9H_{17}O_4S$ [M+H] 221.0842, found 221.0854, $C_9H_{20}NO_4S$ [M+NH$_4$] 238.1107, found 238.1121.
Ethyl tetrahydro-2H-thiopyran-1,1-dioxide-2-carboxylate (**6.1**): pale yellow oil, ^1H NMR (500 MHz, $CDCl_3$): δ 4.24–4.34 (m, 2H), 3.85 (ddd, *J* = 6.5, 4.5, 2 Hz, 1H), 3.45 (ddd, *J* = 14, 9, 4.5 Hz, 1H), 2.95–3.02 (m, 1H), 2.26–2.39 (m, 2H), 2.07–2.17 (m, 2H), 1.89–1.98 (m, 1H), 1.57–1.65 (m, 1H), 1.33 (t, *J* = 7 Hz, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 166.1 (C), 65.2 (CH), 62.6 (CH_2), 51.1 (CH_2), 28.1 (CH_2), 24.3 (CH_2), 20.1 (CH_2), 14.2 (CH_3). HRMS (ESI) calcd for $C_8H_{18}NO_4S$ [M+NH$_4$] 224.0951, found 224.0951.
trans-Ethyl tetrahydro-3-methylthiophene-1,1-dioxide-2-carboxylate (**6.2a**): white flaky solid, mp 42–44 °C, ^1H NMR (500 MHz, $CDCl_3$): δ 4.25–4.39 (m, 2H), 3.52 (d, *J* = 10.5 Hz, 1H), 3.31 (ddd, *J* = 13, 7, 1.5 Hz, 1H), 3.13 (td, *J* = 13, 7 Hz, 1H), 2.76–2.87 (m, 1H), 2.30–2.36 (m, 1H), 1.82 (qd, *J* = 13, 7 Hz, 1H), 1.34 (t, *J* = 7 Hz,

3H), 1.22 (d, J = 6.5 Hz, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 165.1 (C), 72.3 (CH), 62.9 (CH_2), 53.4 (CH_2), 35.2 (CH), 28.7 (CH_2), 19.2 (CH_3), 14.3 (CH_3). HRMS (ESI) calcd for $C_8H_{15}NO_4S$ [M+H] 207.0686, found 207.0695; $C_8H_{14}NO_4NaS$ [M+Na] 229.0505, found 207.0515.

(2R,3R,6R)-Ethyl tetrahydro-3,6-dimethyl-2H-thiopyran-1,1-dioxide-2-carboxylate (**7.1a**): white solid, mp 102–103 °C, ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.33 (qd, J = 7, 4 Hz, 2H), 3.51 (d, J = 12 Hz, 1H), 2.87–2.96 (m, 1H), 2.52–2.60 (m, 1H), 1.88–1.99 (m, 3H), 1.38 (d, J = 6.5 Hz, 3H), 1.27–1.36 (m, 4H), 1.34 (t, J = 7 Hz), 1.03 (d, J = 6.5 Hz, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 163.8 (C), 73.0 (CH), 62.6 (CH_2), 57.6 (CH), 34.8 (CH), 33.1 (CH_2), 31.4 (CH_2), 19.9 (CH_3), 14.4 (CH_3), 10.9 (CH_3). HRMS (ESI) calcd for $C_{10}H_{22}NO_4S$ [M+NH_4] 252.1264, found 252.1255.

(2S,3R,6R)-Ethyl tetrahydro-3,6-dimethyl-2H-thiopyran-1,1-dioxide-2-carboxylate (**7.1b**): white solid, mp 77–78 °C, ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.27 (q, J = 7 Hz, 2H), 3.83 (d, J = 4.5 Hz, 1H), 3.60–3.68 (m, 1H), 2.51–2.59 (m, 1H), 1.81–2.02 (m, 3H), 1.55–1.61 (m, 1H; overlapped with water peak), 1.35 (d, J = 7 Hz, 3H), 1.33 (t, J = 7 Hz, 3H), 1.06 (d, J = 7 Hz, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 166.4 (C),70.0 (CH), 62.3 (CH_2), 52.7 (CH), 34.7 (CH), 31.6 (CH_2), 27.7 (CH_2), 19.7 (CH_3), 14.3 (CH_3), 10.7 (CH_3). HRMS (ESI) calcd for C10H19NO4S [M+H] 235.0999, found 235.1014.

(2S,3S,5R)-Ethyl tetrahydro-3-ethyl-5-methylthiophene-1,1-dioxide-2-carboxylate (**7.2a**): pale yellow oil, ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.25–4.37 (m, 2H), 3.57 (d, J = 10 Hz, 1H), 3.14–3.24 (m, 1H), 2.60–2.70 (m, 1H), 2.37 (dt, J = 13, 6.5 Hz, 1H), 1.55–1.64 (m, 1H; overlapped with water peak), 1.42–1.52 (m, 2H), 1.39 (d, J = 6.5 Hz, 3H), 1.34 (t, J = 7 Hz, 3H), 0.94 (t, J = 7 Hz, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 166.1 (C), 70.7 (CH), 62.9 (CH_2), 58.6 (CH), 39.2 (CH), 34.5 (CH_2), 27.6 (CH_2), 14.3 (CH_3), 11.4 (CH_3), 11.1 (CH_3). HRMS (ESI) calcd for $C_{10}H_{22}NO_4S$ [M+NH_4] 252.1264, found 252.1250.

trans-Ethyl tetrahydro-3,6,6-trimethyl-2H-thiopyran-1,1-dioxide-2-carboxylate (**8.1a**): pale yellow oil, ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.30–4.37 (m, 2H), 3.73 (d, J = 12 Hz, 1H), 2.52–2.61 (m, 1H), 2.16–2.23 (m, 1H), 1.71–1.77 (m, 2H), 1.44–1.51 (m, 4H), 1.47 (s), 1.40 (s, 3H), 1.34 (t, J = 7 Hz, 3H), 1.03 (d, J = 6.5 Hz, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 164.1 (C), 67.8 (CH), 62.6(CH_2), 59.0 (C), 36.5 (CH_2), 34.8 (CH), 28.7 (CH_2), 21.5 (CH_3), 21.1 (CH_3), 20.0 (CH_3), 14.4 (CH_3). HRMS (ESI) calcd for $C_{11}H_{24}NO_4S$ [M+NH_4] 266.1421, found 266.1411.

trans-Ethyl tetrahydro-3-ethyl-5,5-dimethylthiophene-1,1-dioxide-2-carboxylate (**8.2a**): pale yellow oil, ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.26–4.37 (m, 2H), 3.61 (d, J = 9.5 Hz, 1H), 2.73–2.82 (m, 1H), 2.10 (dd, J = 13, 6.5 Hz, 1H), 1.73 (t, J = 13 Hz, 1H), 1.48–1.55 (m, 2H; overlapped with water peak), 1.42 (s, 3H), 1.44 (s, 3H), 1.34 (t, J = 7 Hz, 3H), 0.92 (t, J = 7.5 Hz, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 166.4 (C), 71.3 (CH_3), 62.8 (CH_2), 62.3(C), 41.5 (CH_2), 37.2 (CH), 28.1 (CH_2), 22.1 (CH_3), 21.5 (CH_3), 14.3 (CH_3), 11.6 (CH_3). HRMS (ESI) calcd for $C_{11}H_{21}NO_4S$ [M+H] 249.1155, found 249.1176; $C_{11}H_{24}NO_4S$ [M+NH_4] 266.1421, found 266.1441.