Notable and Obvious Ketene Substituent-Dependent Effect of Temperature on the Stereoselectivity in the Staudinger Reaction

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Supplemental Materials

Content S1

Experimental Details

General. *S*-Phenyl 2-diazoethanethioate **1**[1] and imines **2a-c**[2,3,4] were prepared according to published procedures. Toluene, xylene, and 1,3,5-mesitylene were refluxed with sodium and freshly distilled prior to use. All reactions were performed under a nitrogen atmosphere. The reaction temperature was controlled carefully with a fine temperature controller in a big water-bath with a large amount of water, covered with paraffin oil, and a thick asbestos coating outside the bath within less than ± 0.5 ^{o}C, in the temperature region of 40 – 90 ^{o}C, in a big oil-bath with a large amount of oil and a thick asbestos coating outside the bath within less than ± 2~3 ^{o}C in the temperature region of 100 – 150 ^{o}C. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ with TMS as an internal standard. All known products **3**, **4**, **5**, **6**, **7**, **8**, **9**, **10**, **11**, **12**, **13**, **14**, **15**, **16**, **19**, **20**, **23**, and **24** show the identical analytic data to reported data in the literatures.[3,4,5,6,7]

Determination of the cis/trans Ratios of the Crude β-Lactam Products.

1. For the reaction of propionyl chloride (**1a**) with imine **2a**, the cis/trans ratios were obtained by the integrals of the corresponding C(4) protons of β-lactams **3** and **4** in ^{1}H NMR spectra (the proton of *cis*-isomer **3** appears at about 4.87 ppm, while the proton of *trans*-isomer **4** appears at 4.22 ppm) of the crude reaction mixture. (Propionyl chloride and propionic acid have peaks at 2.93 and 2.38 ppm, respectively.)

2. For the reaction of phenylacetyl chloride (**1b**) and imine **2a**, the cis/trans ratios were obtained by the integrals of the corresponding C(3) and/or C(4) protons of β-lactams **5** and **6** in ^{1}H NMR spectra (the protons of *cis*-isomer **5** appear at 5.17 and 4.88 ppm, while the protons of *trans*-isomer **6** appear at 4.61 and 4.07 ppm) of the crude reaction mixture after washing with saturated sodium bicarbanate to remove unreacted phenylacetyl chloride and phenylacetic acid. (Phenylacetyl chloride and phenylacetic acid have peaks at 4.08 and 3.64 ppm, respectively.)

3. For the reaction of phenoxyacetyl chloride (**1c**) and imine **2b**, the cis/trans ratios were obtained by the integrals of the C(3) proton of β-lactams **7** and the C(4) proton of β-lactam **8** in ^{1}H NMR spectra (the C(3) proton of *cis*-isomer **7** appears at 5.32 ppm, while the C(4) proton of *trans*-isomer **8** appears at 4.49 ppm, while the peaks of the C(4) proton of β-lactams **7** and the C(4) proton of β-lactam **8** appear near 4.89 ppm, unseparable) of the crude reaction mixture after washing with saturated sodium bicarbanate to remove unreacted phenoxyacetyl chloride and phenoxyacetic acid, which have peaks at 4.88 and 4.67 ppm, respectively, affecting the accurate determination.

[1] Danheiser, R. L.; Okamoto, I.; Lawlor, M. D.; Lee, T. W. *Org. Synth.* Vol. *80*, 160-171.
[2] Linder, M. R.; Frey, W. U.; Podlech, J. *J. Chem. Soc., Perkin Trans. 1* **2001**, 2566-2577.
[3] Jiao, L.; Liang, Y.; Xu, J. X. *J. Am. Chem. Soc.* **2006**, *128*, 6060-6069.
[4] Ohmori, H.; Maeda, H.; Kikuoka, M.; Maki, T.; Masui, M. *Tetrahedron* **1991**, *47*, 767-776.
[5] Ejaegher, Y.; Denolf, B.; Stevens, C. V.; De Kimpe, N. *Synthesis* **2005**, 193-198.
[6] Abd-Elzaher, M. M.; Fischer, H. *J. Organomet. Chem*. **1999**, *588*, 235-241.
[7] Wang, Y. K.; Liang, Y.; Jiao, L.; Du, D. M.; Xu, J. X. *J. Org. Chem*. **2006**, *71*, 6983-6990.

4. For the reaction of chloroacetyl chloride (**1d**) and imine **2a**, the cis/trans ratios were obtained by the integrals of the corresponding C(3) and C(4) protons of *β*-lactams **9** and **10** in ^{1}H NMR spectra (the protons of *cis*-isomer **9** appear at 5.07 and 5.10 ppm, while the protons of *trans*-isomer **10** appear at 4.45 and 4.63 ppm) of the crude reaction mixture. (Chloroacetyl chloride and chloroacetic acid have peaks at 4.52 and 4.15 ppm, respectively.)

5. For the reaction of phthalimidoacetyl chloride (**1e**) and imine **2b**, the cis/trans ratios were obtained by the integrals of the corresponding C(3) and C(4) protons of *β*-lactams **11** and **12** in ^{1}H NMR spectra (the protons of *cis*-isomer **11** appear at 5.03 and 5.36 ppm, while the protons of *trans*-isomer **12** appear at 4.92 and 5.09 ppm) of the crude reaction mixture after washing with saturated sodium bicarbanate to remove unreacted phthalimidoacetyl chloride and phthalimidoacetic acid. (Phthalimidoacetyl chloride and phthalimidoacetic acid have peaks at 4.84 and 4.35 ppm, respectively.)

6. For the reactions of phenylthioacetyl chloride (**1f**) and *S*-phenyl 2-diazoethanethioate (**1g**) with imine **2a**, the cis/trans ratios were obtained by the integrals of the corresponding C(3) and C(4) protons of *β*-lactams **13** and **14** in ^{1}H NMR spectra (the protons of *cis*-isomer **13** appear at 4.91 and 5.17 ppm, while the protons of *trans*-isomer **14** appear at 4.02 and 4.45 ppm) of the crude reaction mixture. (*S*-Phenyl 2-diazoethanethioate has a peak at 5.26 ppm. Phenylthioacetyl chloride and phenylthioacetic acid have peaks at 3.62 and 3.69 ppm, respectively.)

7. For the reaction of phenylthioacetyl chloride (**1f**) with imine **2b**, the cis/trans ratios were obtained by the integrals of the corresponding C(3) and C(4) protons of *β*-lactams **15** and **16** in ^{1}H NMR spectra (the protons of *cis*-isomer **15** appear at 4.95 and 5.71 ppm, while the protons of *trans*-isomer **16** appear at 4.28 and 4.02 ppm) of the crude reaction mixture. (Phenylthioacetyl chloride and phenylthioacetic acid have peaks at 3.62 and 3.69 ppm, respectively.)

8. For the reaction of 4-methoxyphenylacetyl chloride (**1h**) with imine **2b**, the cis/trans ratios were obtained by the integrals of the corresponding C(3) and C(4) protons of *β*-lactams **17** and **18** in ^{1}H NMR spectra (the protons of *cis*-isomer **17** appear at 4.95 and 4.67 ppm, while the protons of *trans*-isomer **18** appear at 4.39 and 4.01 ppm) of the crude reaction mixture after washing with saturated sodium bicarbanate to remove unreacted 4-methoxyphenylacetyl chloride and 4-methoxyphenylacetic acid. (4-Methoxyphenylacetyl chloride and 4-methoxyphenylacetic acid have peaks at 4.02 and 3.68 ppm, respectively, for CH_2 group, 3.83 and 3.80 ppm for MeO group.)

9. For the reaction of phenylacetyl chloride (**1b**) and imine **2b**, the cis/trans ratios were obtained by the integrals of the corresponding C(3) and/or C(4) protons of *β*-lactams **19** and **20** in ^{1}H NMR spectra (the protons of *cis*-isomer **19** appear at 5.00 and 4.74 ppm, while the protons of *trans*-isomer **20** appear at 4.45 and 4.07 ppm) of the crude reaction mixture after washing with saturated sodium bicarbanate to

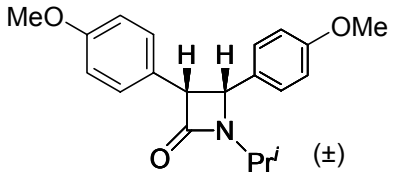
remove unreacted phenylacetyl chloride and phenylacetic acid. (Phenylacetyl chloride and phenylacetic acid have peaks at 4.08 and 3.64 ppm, respectively.)

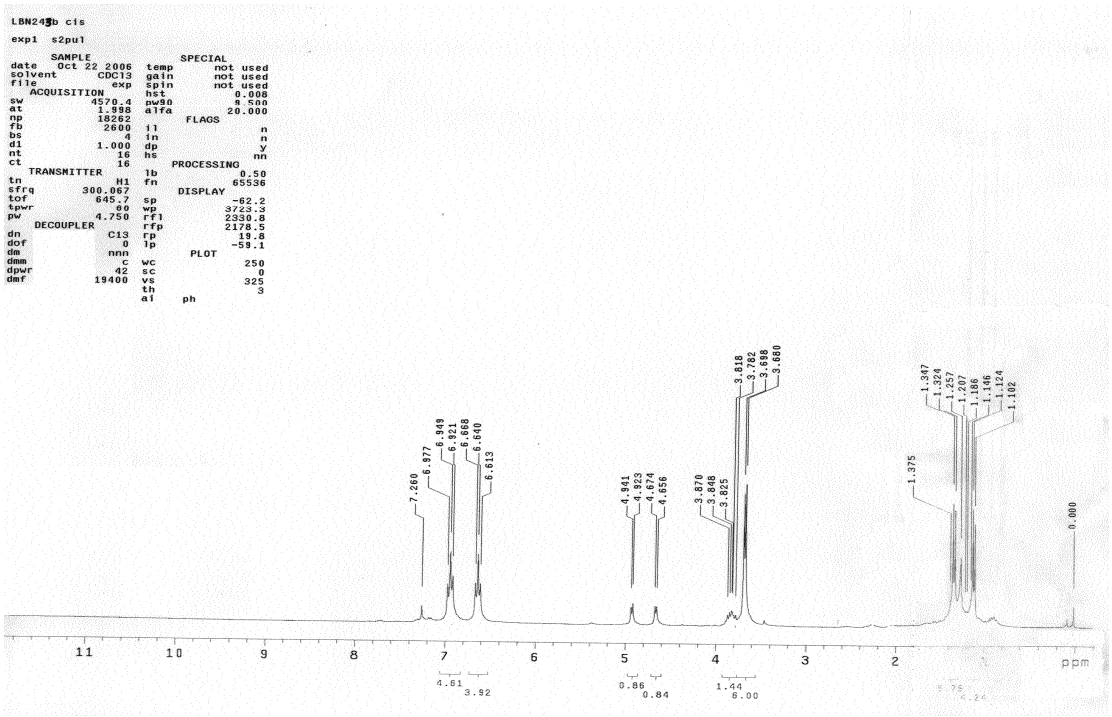
10. For the reaction of 4-nitrophenylacetyl chloride (**1i**) with imine **2b**, the cis/trans ratios were obtained by the integrals of the corresponding C(3) and C(4) protons of β-lactams **21** and **22** in ^{1}H NMR spectra (the protons of *cis*-isomer **21** appear at 5.05 and 4.78 ppm, while the protons of *trans*-isomer **22** appear at 4.47 and 4.17 ppm) of the crude reaction mixture. (4-nitrophenylacetyl chloride and 4-nitrophenylacetic acid have peaks at 4.30 and 3.75 ppm, respectively.)

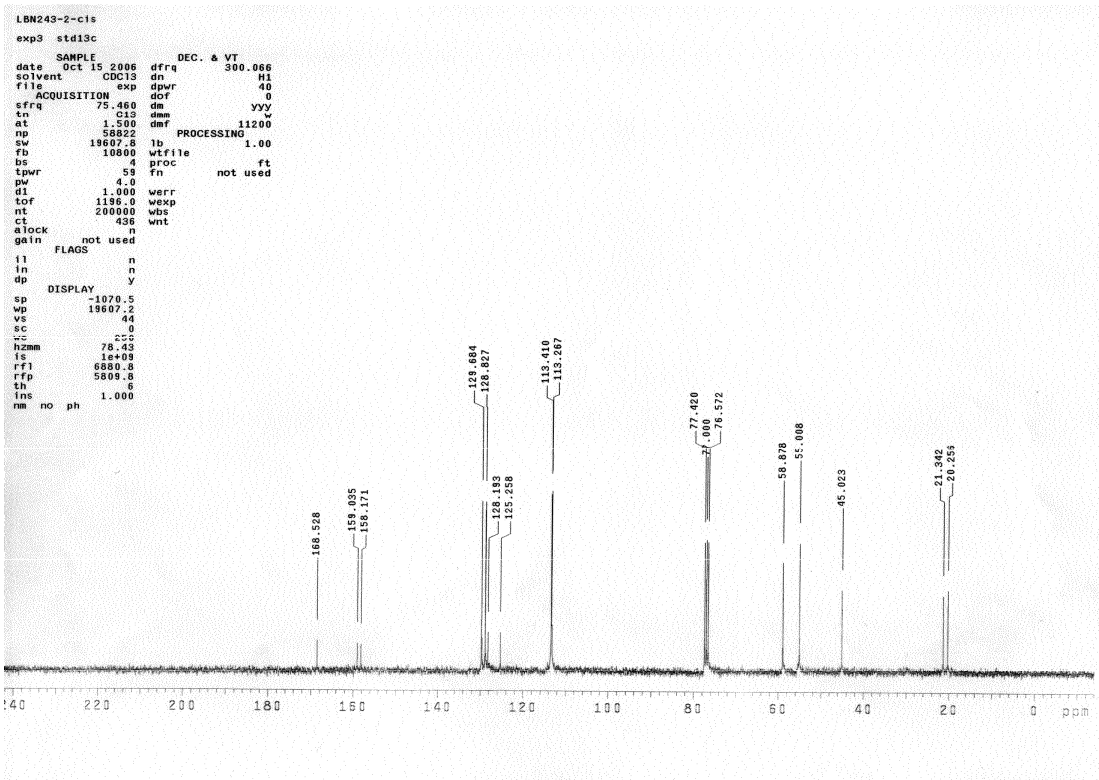
11. For the reaction of 4-nitrophenylacetyl chloride (**1i**) with imine **2a**, the cis/trans ratios were obtained by the integrals of the corresponding C(3) and C(4) protons of β-lactams **23** and **24** in ^{1}H NMR spectra (the protons of *cis*-isomer **23** appear at 5.24 and 4.95 ppm, while the protons of *trans*-isomer **24** appear at 4.65 and 4.20 ppm) of the crude reaction mixture after washing with saturated sodium bicarbanate to remove unreacted 4-nitrophenylacetyl chloride and 4-nitrophenylacetic acid. (4-nitrophenylacetyl chloride and 4-nitrophenylacetic acid have peaks at 4.30 and 3.75 ppm, respectively.)

Copies of ^{1}H and ^{13}C NMR Spectra of the Unknown Products

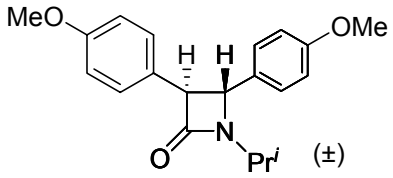
(±)−*cis*−1−Isopropyl−3−(4−methoxyphenyl)−4−(4-methoxyphenyl)azetidin−2−one (17)

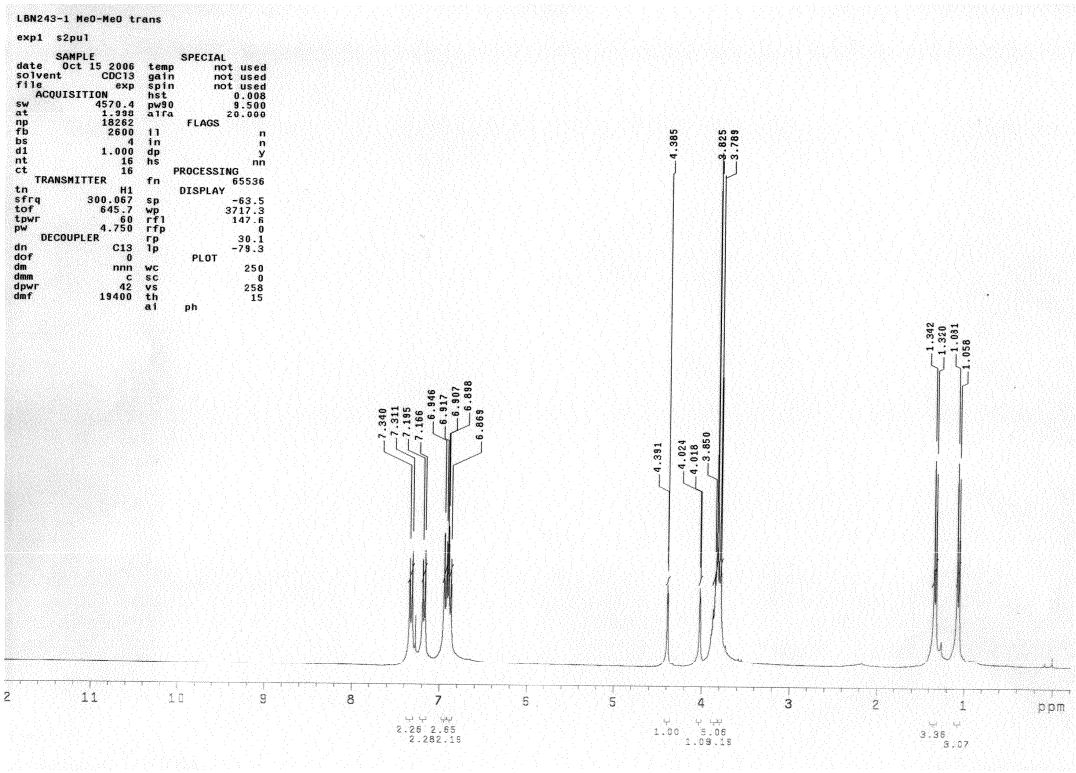


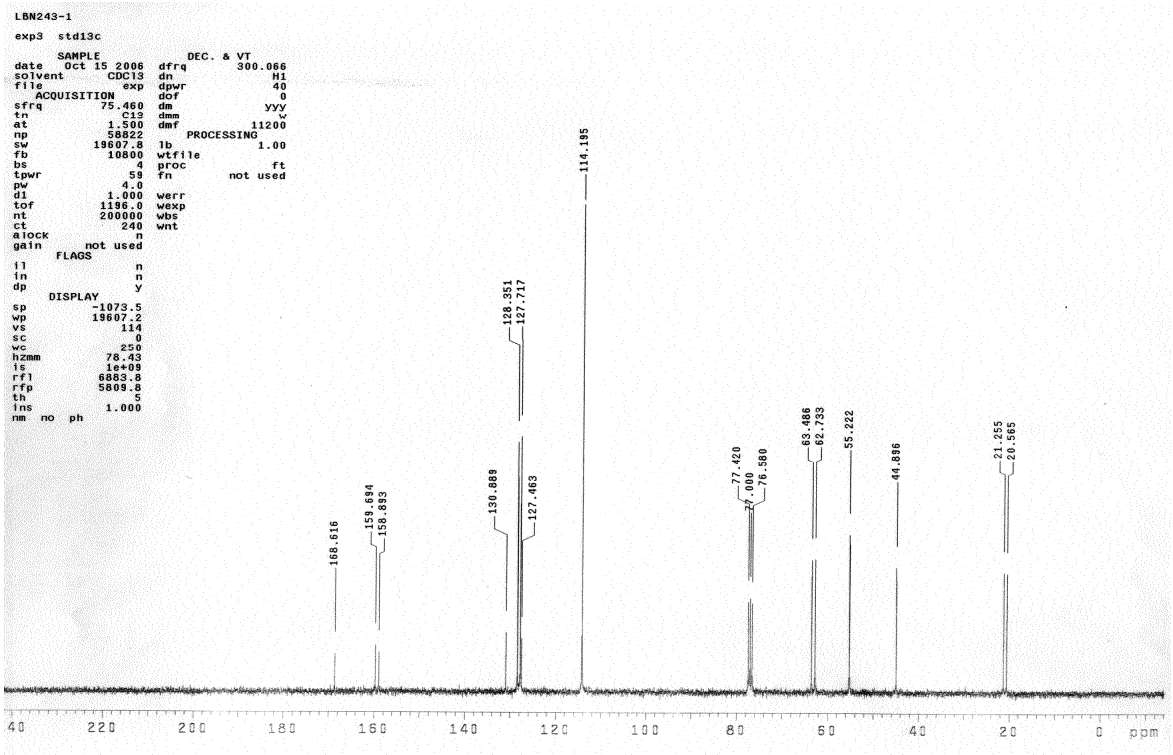




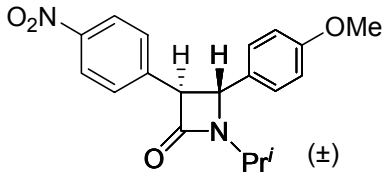
(±)−*trans*−1−Isopropyl−3−(4−methoxyphenyl)−4−(4-methoxyphenyl)azetidin−2−one (18)

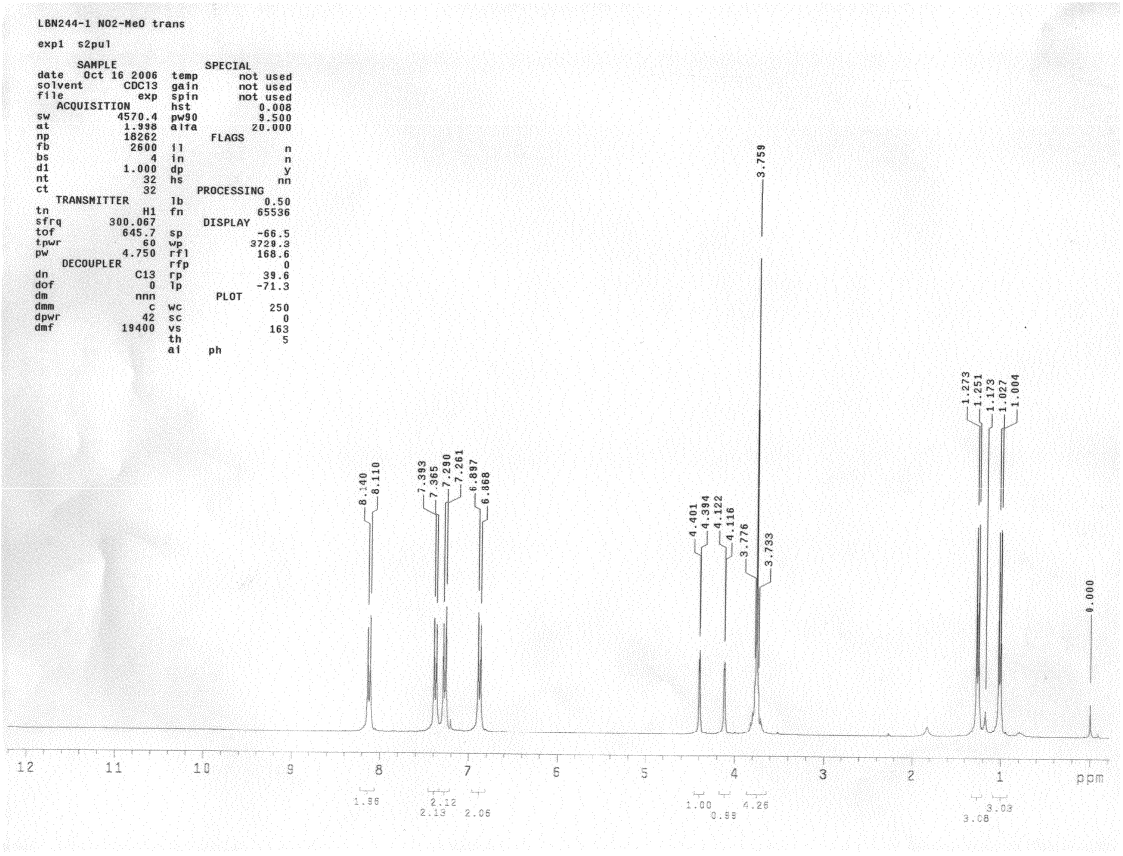


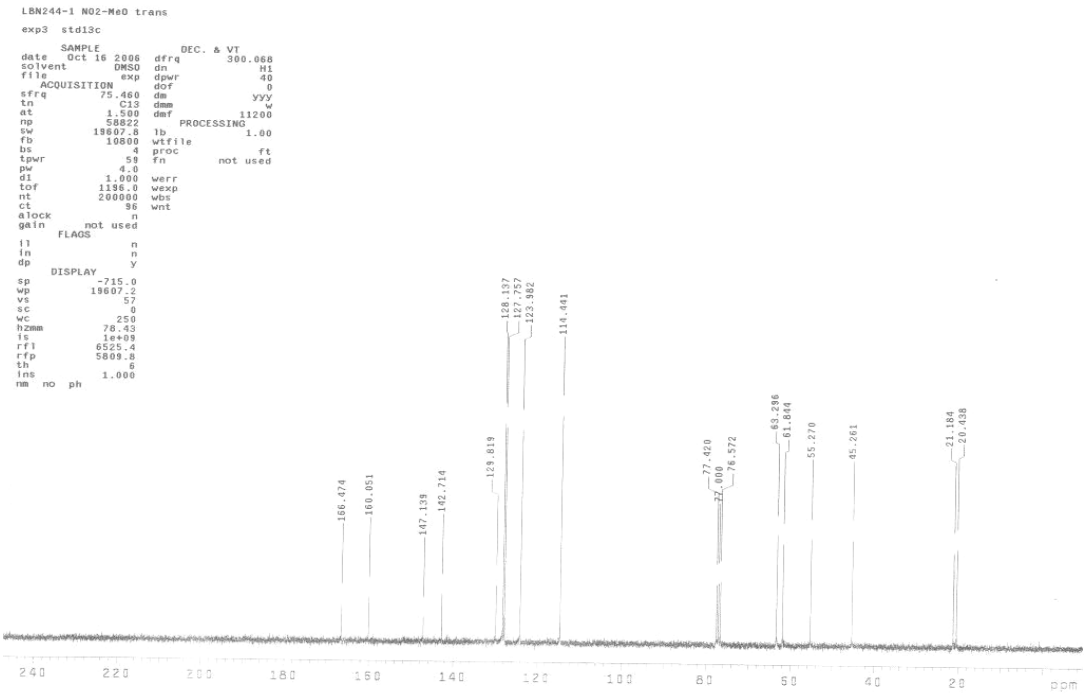




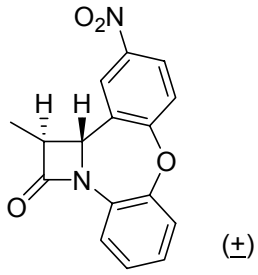
(±)−*trans*−1−Isopropyl−4−(4−methoxyphenyl)−3−(4−nitrophenyl)azetidin−2−one (22)



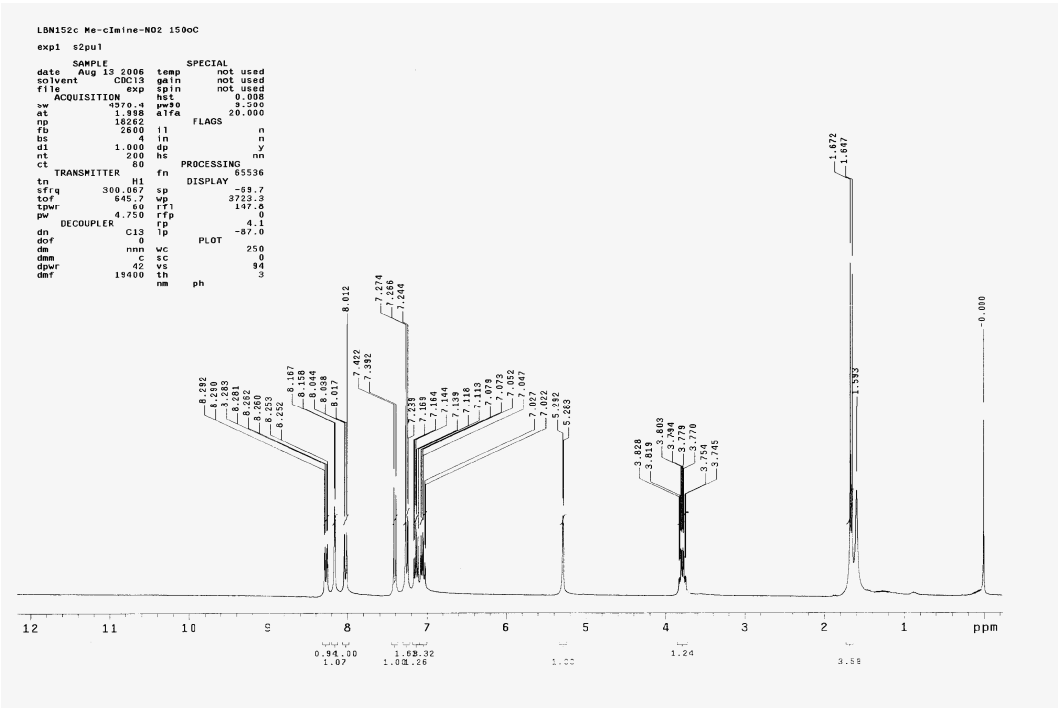


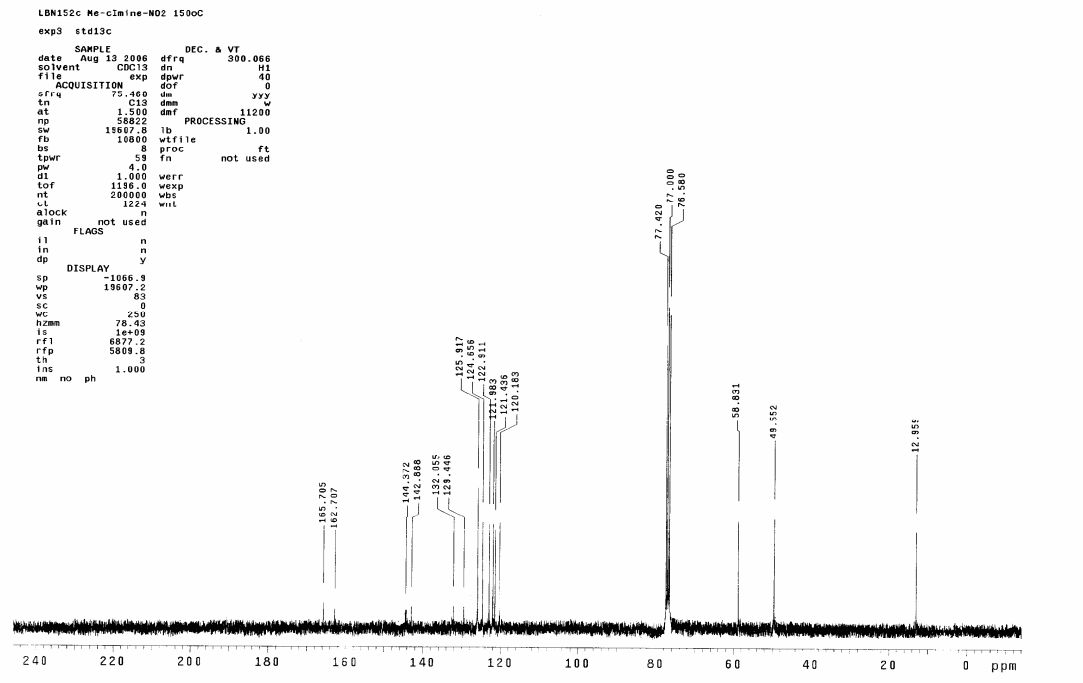


(±)−*trans*−2−Methyl−4−nitro−azeto[1,2−*d*]dibenzo[*b*,*f*]oxazepin−1−one (25a)

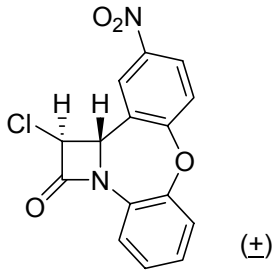


(±)





(±)−*trans*−2−Chloro−4−nitro−azeto[1,2−*d*]dibenzo[*b,f*]oxazepin−1−one (25b)



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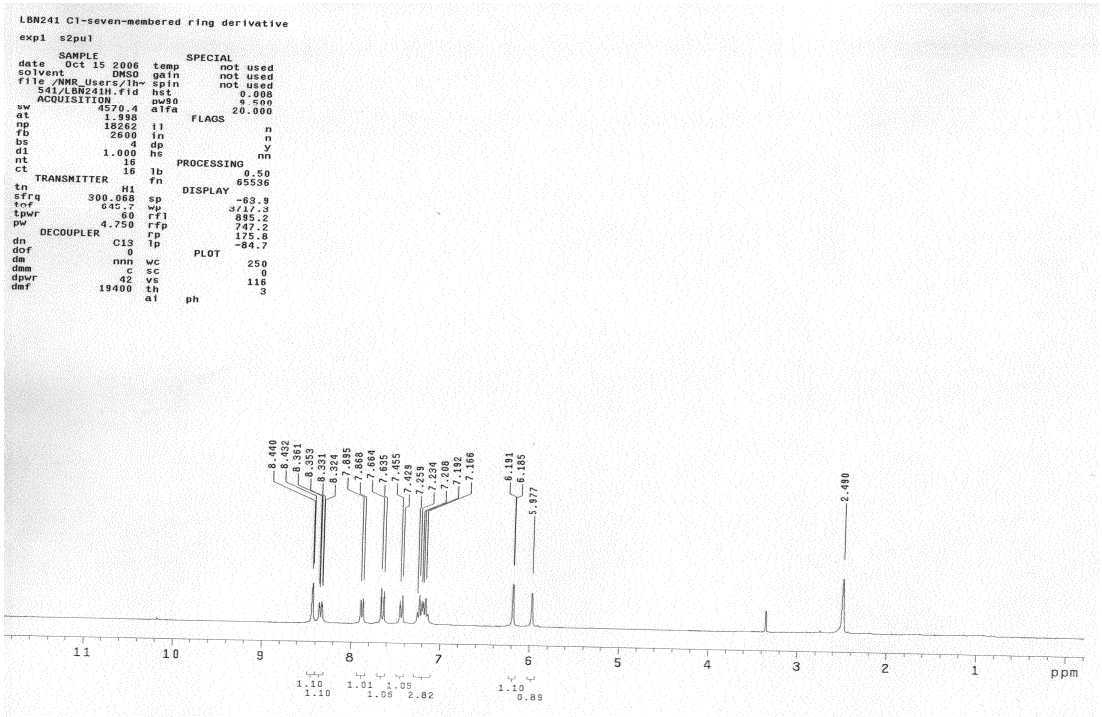
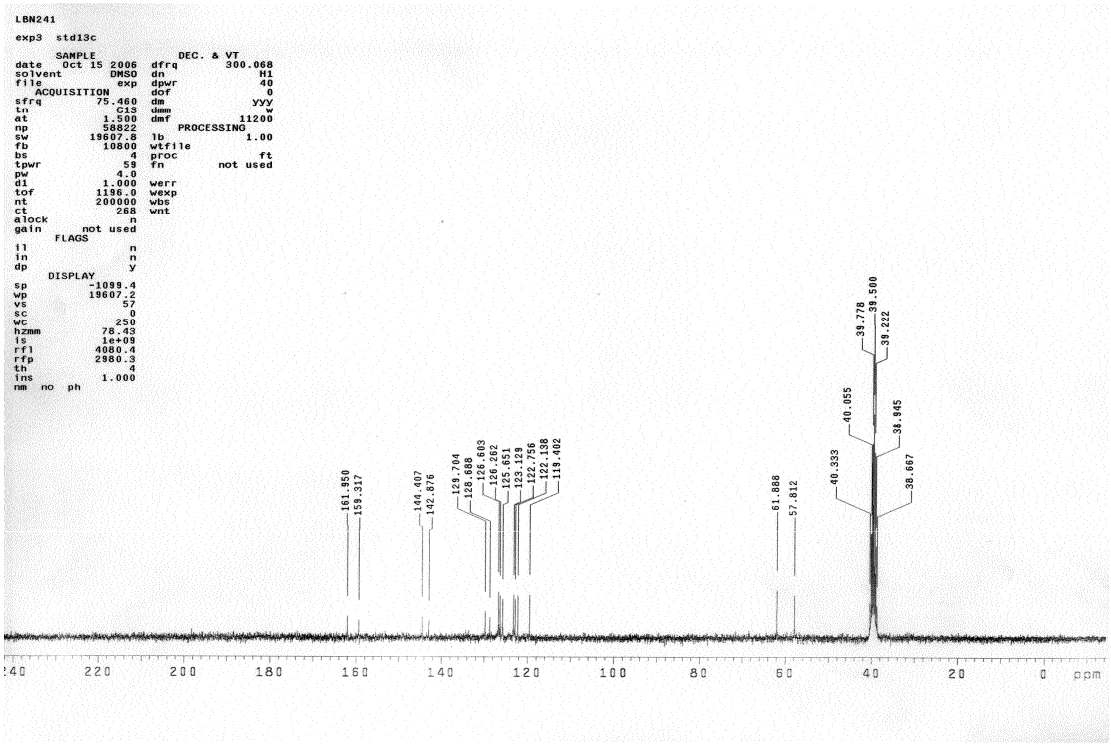
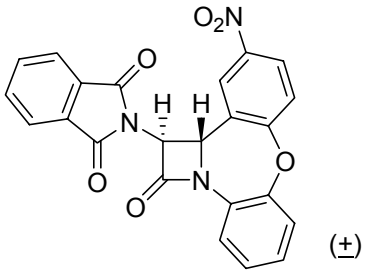
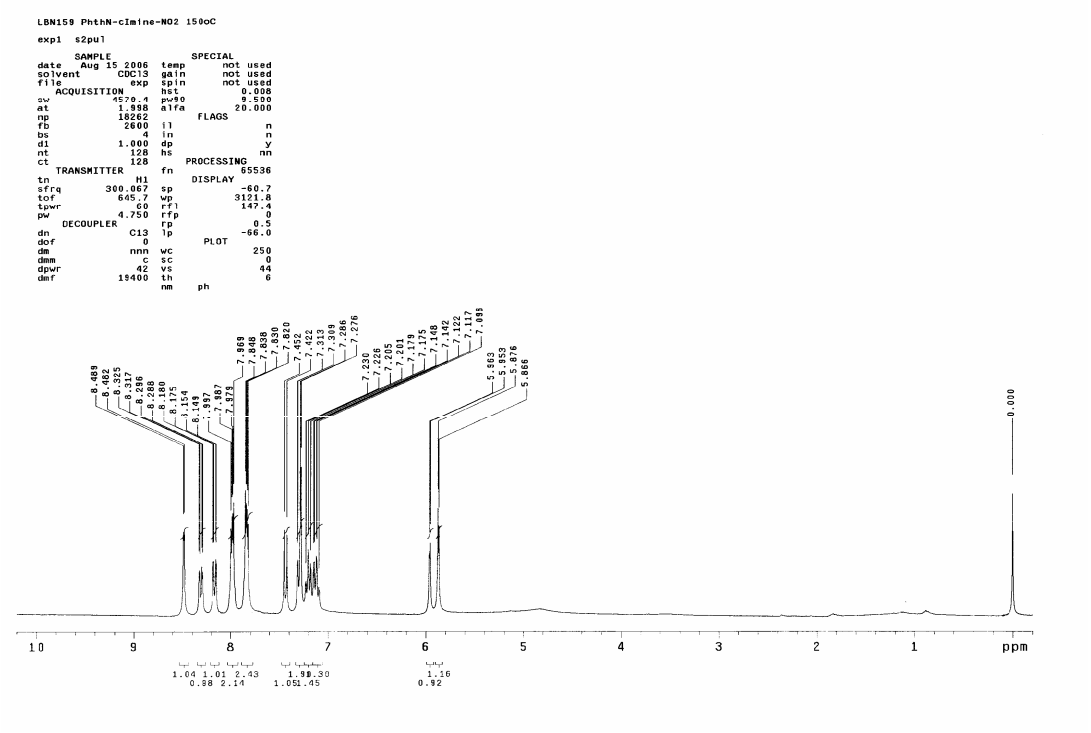


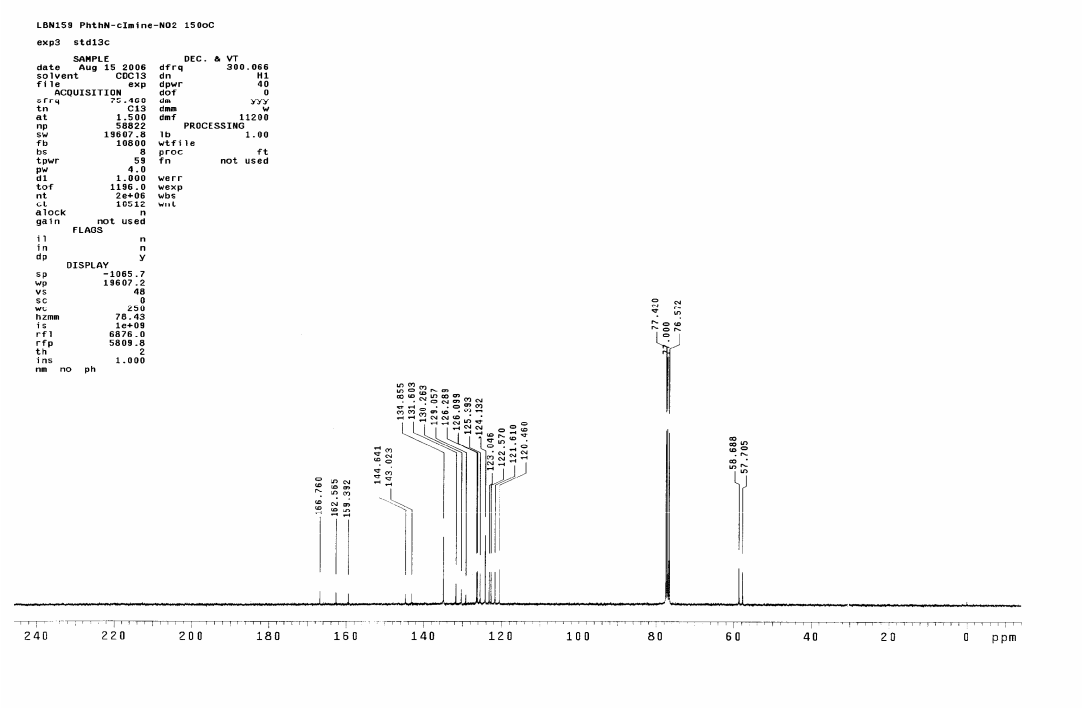


(±)−*trans*−4−Nitro−2−phthimido−azeto[1,2−*d*]dibenzo[*b,f*]oxazepin−1−one (25c)

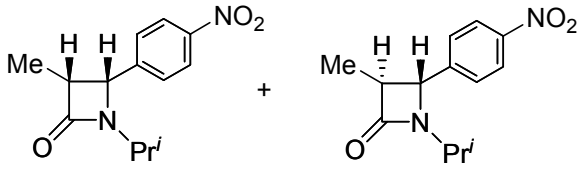


(±)





Copies of the Representative ^{1}H NMR Spectra for Determination of Cis/Trans Ratios



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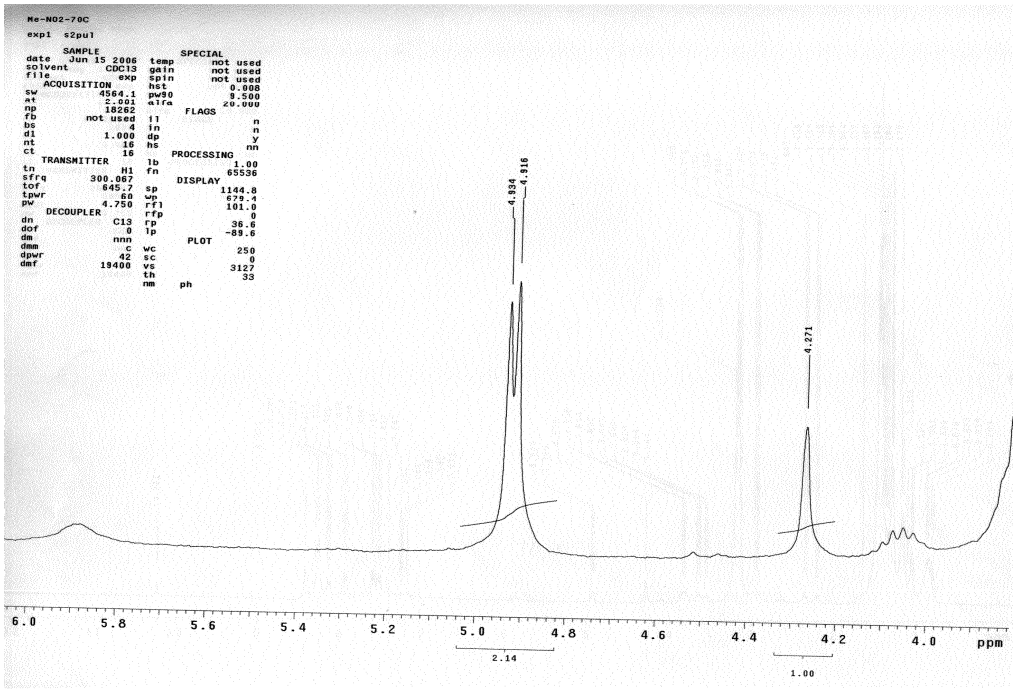
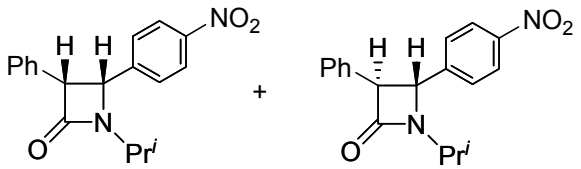
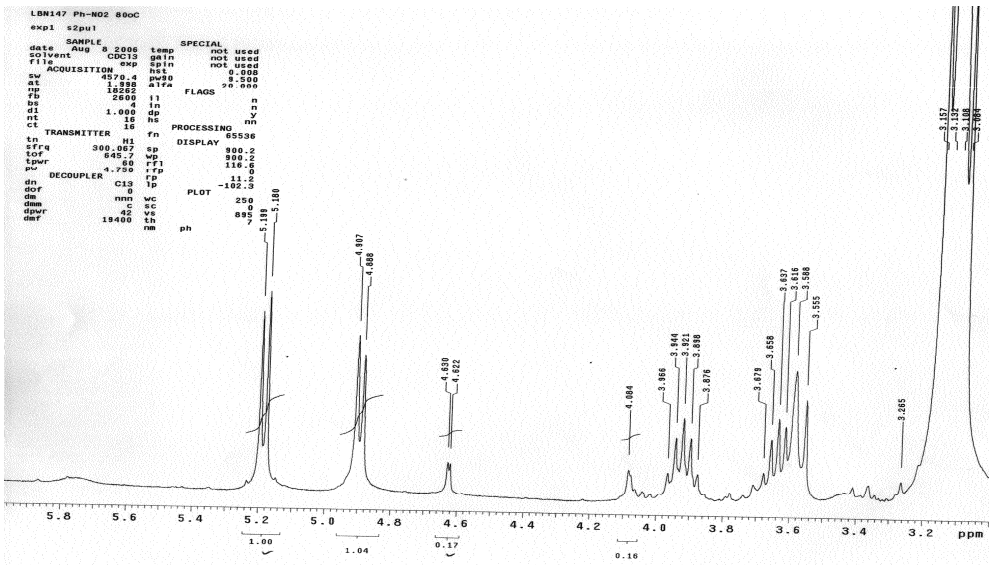
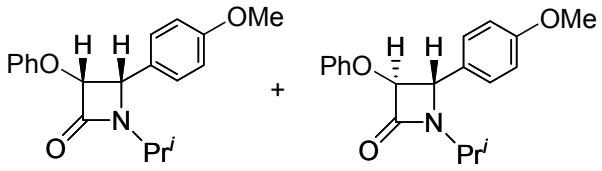




(±)–*cis* – **5** (±)–*trans* – **6**





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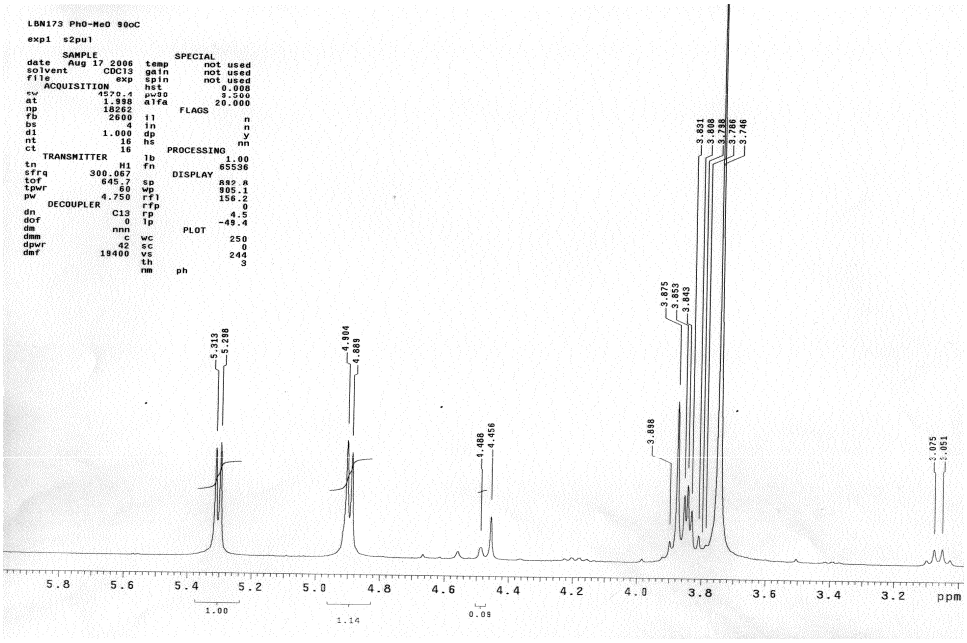

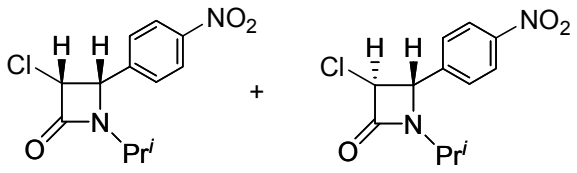

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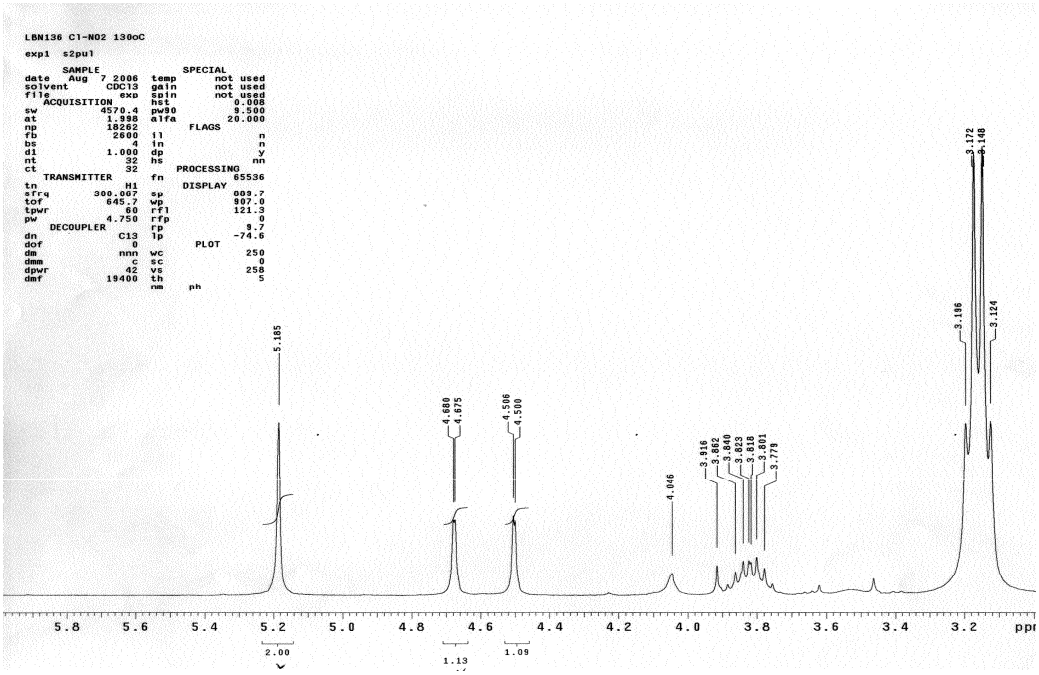

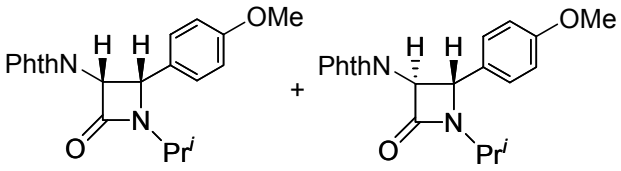

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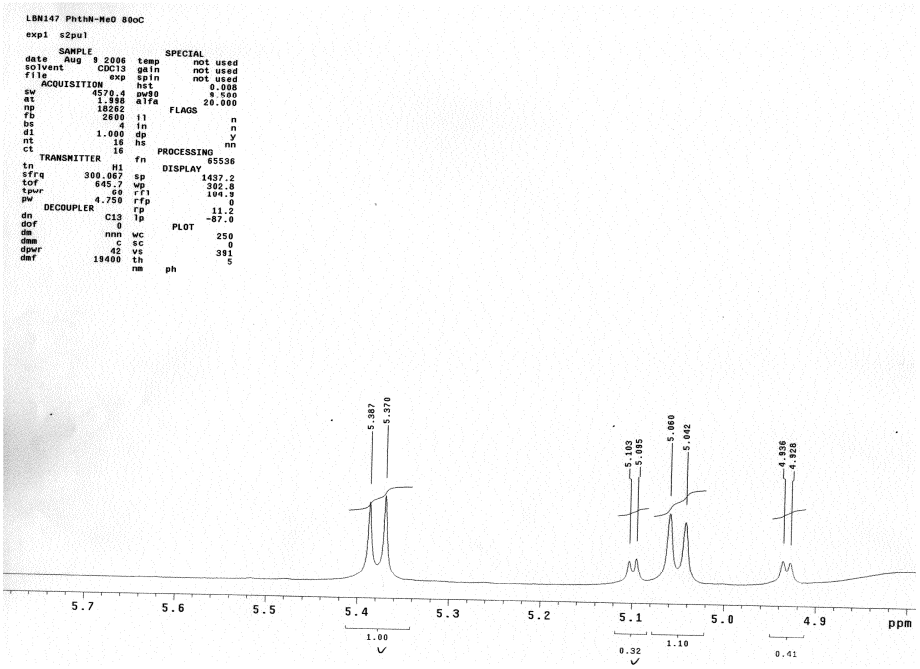

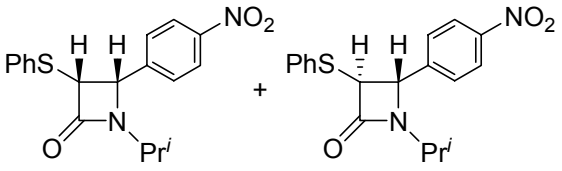

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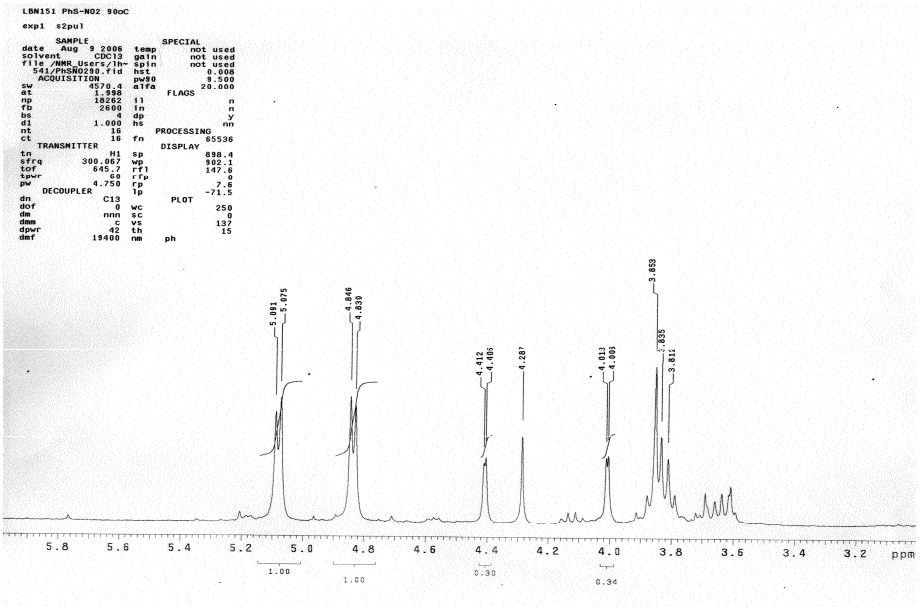

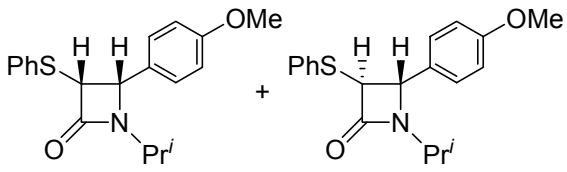

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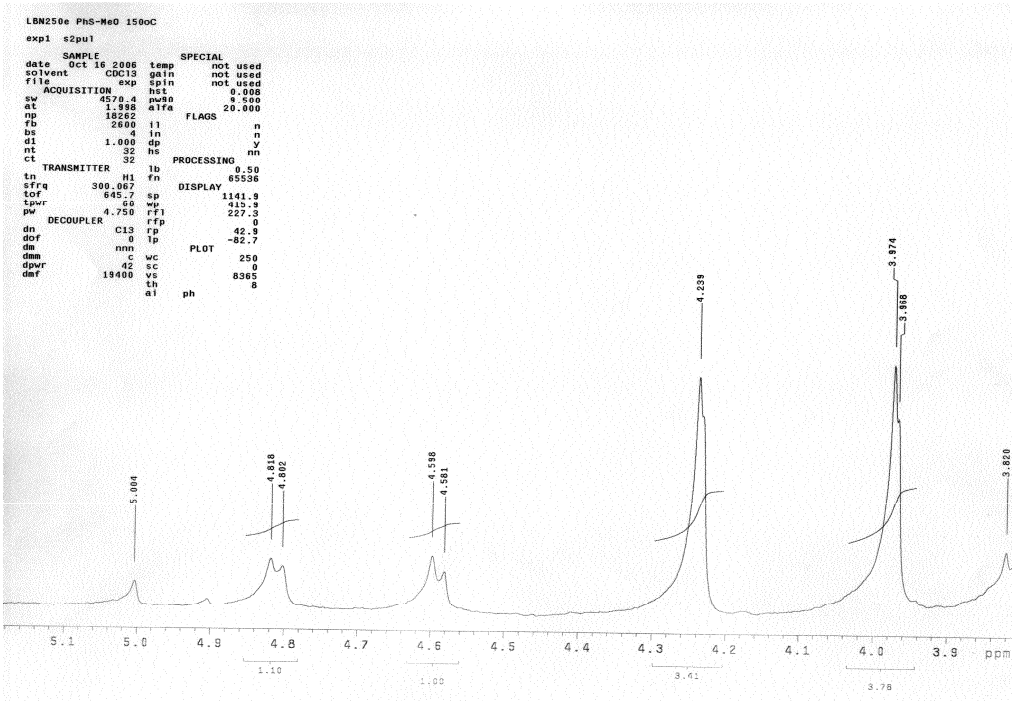
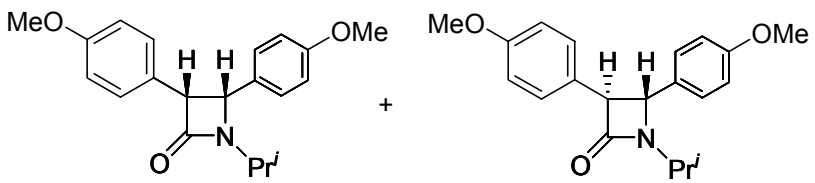
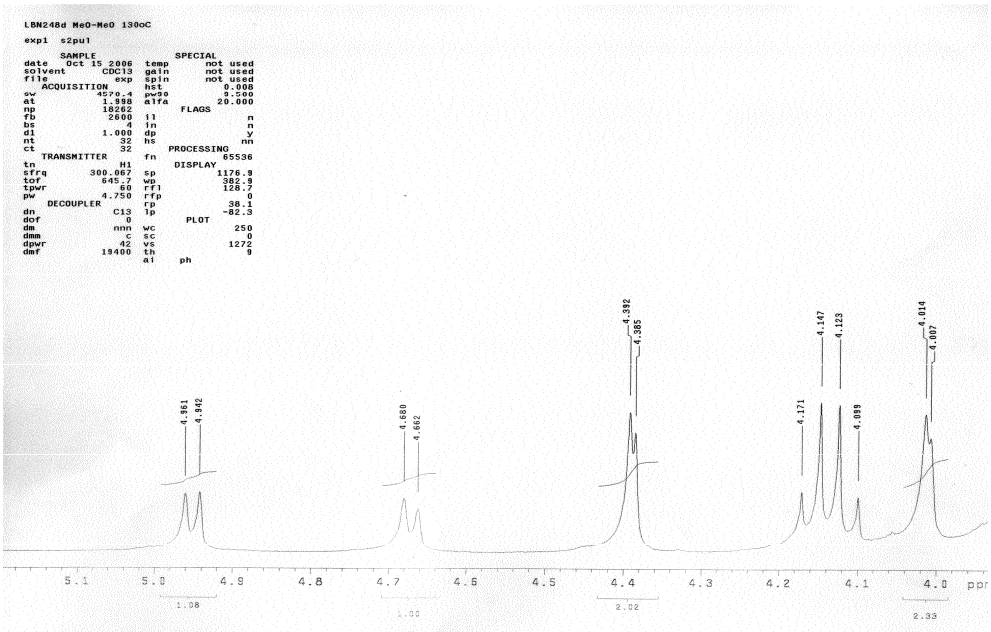
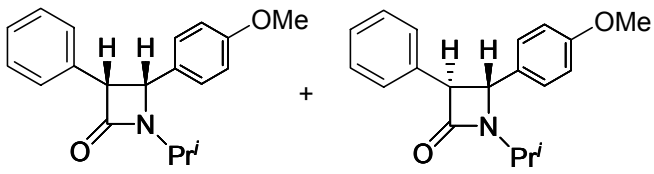




(±)–*cis* – **17** (±)–*trans* –**18**





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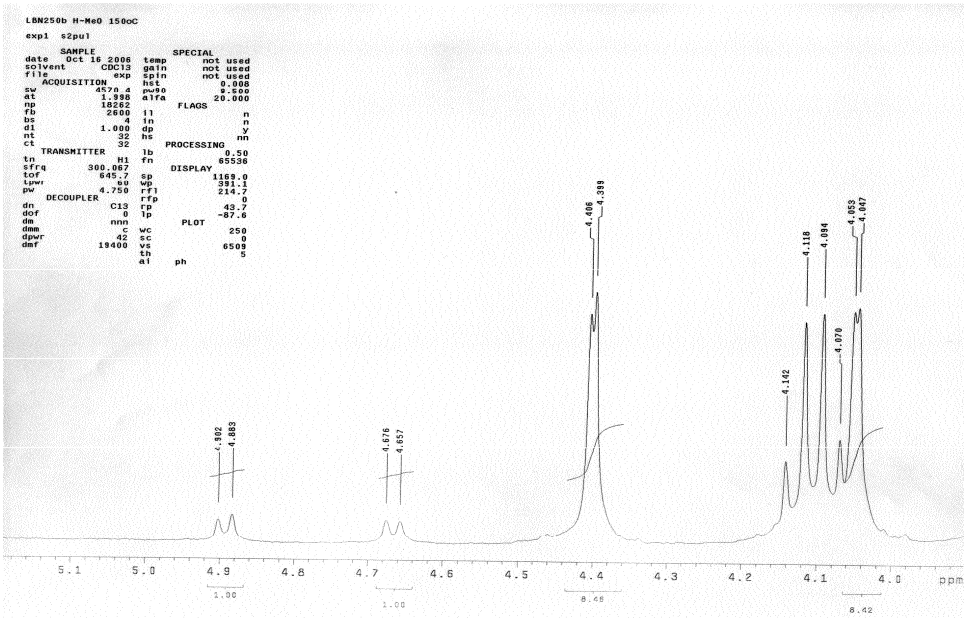
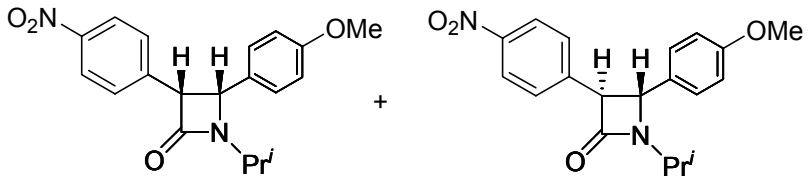
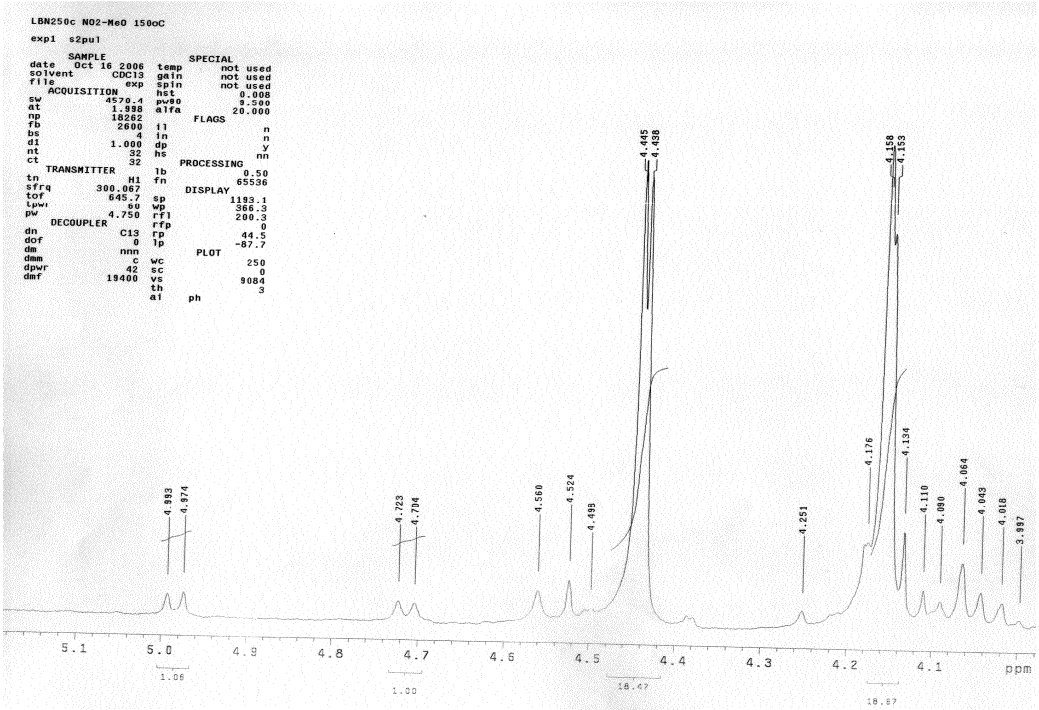
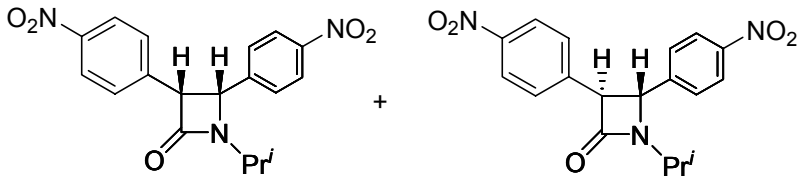




(±)–*cis* – **21** (±)–*trans* –**22**





(±)–*cis* – **23** (±)–*trans* –**24**