Tetrahedron Letters 49 (2008) 6797–6799

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

Nickel-catalyzed reactions of vinyl aziridines and aziridinylen-ynes

Gang Zuo, Kainan Zhang, Janis Louie *

University of Utah, Department of Chemistry, 315 South 1400 East, Salt Lake City, UT 84112, USA

ARTICLE INFO

Article history:
Received 27 August 2008
Accepted 10 September 2008
Available online 15 September 2008

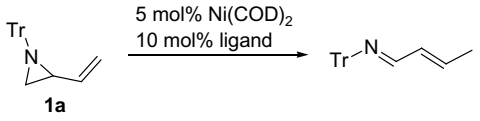
Keywords:
Nickel catalyst
N-Heterocyclic carbene
Vinyl aziridine
Aziridinylen-ynes
Imines
Heterocycles

ABSTRACT

Ni/NHC was found to catalyze the rearrangement of vinyl aziridines and aziridinylen-ynes under mild conditions.

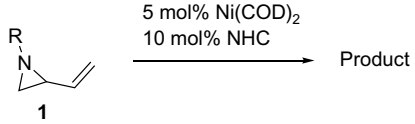
Published by Elsevier Ltd.

A primary interest of our group is the development of efficient cycloadditions that afford heterocycles and carbocycles. We have found that Ni/NHC complexes effectively catalyze the cycloaddition of diynes with CO_2,[1] isocyanates,[2] carbonyls,[3] and nitriles.[4] These reactions afford pyrones, pyridones, pyrimidinones, pyrans, and pyridines in high yields. In addition, the same Ni/NHC system also mediates the rearrangement of vinyl cyclopropanes[5] and cyclopropylen-ynes.[6] As part of our continuing effort in this field,[7] we present our investigations involving the Ni-catalyzed reactions of vinyl aziridines[8,9] and aziridinylen-ynes.



1a (1)

The Ni-catalyzed rearrangement of 1-trityl-2-vinylaziridine (**1a**)[10] was investigated, and a variety of tertiary phosphines and N-heterocyclic carbene ligands (NHCs)[11] were explored as potential ligands (Eq. 1, Table 1). In most cases, no reaction was observed (entries 2–7). However, when IPr was employed, vinylaziridine **1a** was smoothly converted to an α,β-unsaturated imine **2a**[12] (entry 1).[13] No rearrangement was observed in the absence of ligand (entry 8).



1 (2)

It is known that the type of protecting group can have a large influence on the product that is obtained.[8,14–16] As such, a variety of vinylaziridines containing different protecting groups were investigated using $Ni(COD)_2$/NHC as catalyst (Eq. 2, Table 2).[17] Most vinylaziridines underwent rearrangements at room temperature except 1-tosyl vinylaziridine (**1f**),[18] which destroyed the catalyst (entry 7). The Ni/NHC-catalyzed rearrangements of vinylaziridines were highly substrate-dependent. 1-Benzoyl vinylaziridine (**1b**),[19] 1-Boc vinylaziridine (**1c**),[20] and 1-methoxycarbonyl vinylaziridine (**1d**)[21] were isomerized to the corresponding 5-vinyl-2-oxazoline (entries 2–4).[22,23] Interestingly, the Ni/IPr-catalyzed rearrangement of 1-benzhydryl vinylaziridine (**1e**)[24] did not afford an α,β-unsaturated imine. Instead, a 1,3-butadienylamine (**2e**) was obtained (entry 5). However, when IPr was replaced with its saturated analog, SIPr, **1e** was converted to the expected α,β-unsaturated imine **2e′** (entry 6).

Table 1
Ni-catalyzed rearrangements of **1a**[a]

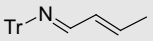
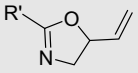
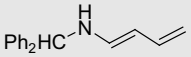
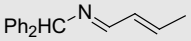
Entry	Ligand	% Conv. of **1a**[b]
1	IPr	100
2	SIPr	Trace
3	IMes	0
4	I*t*Bu	0
5	PPh_3	0
6	PCy_3	0
7	PBu_3	0
8	—	0

[a] Reaction conditions: 5 mol % $Ni(COD)_2$, 10 mol % ligand, toluene, 60 °C, overnight.
[b] Determined by GC using naphthalene as an internal standard.

* Corresponding author. Tel.: +1 801 581 7309; fax: +1 801 581 8433.
E-mail address: louie@chem.utah.edu (J. Louie).

0040-4039/$ - see front matter Published by Elsevier Ltd.
doi:10.1016/j.tetlet.2008.09.056

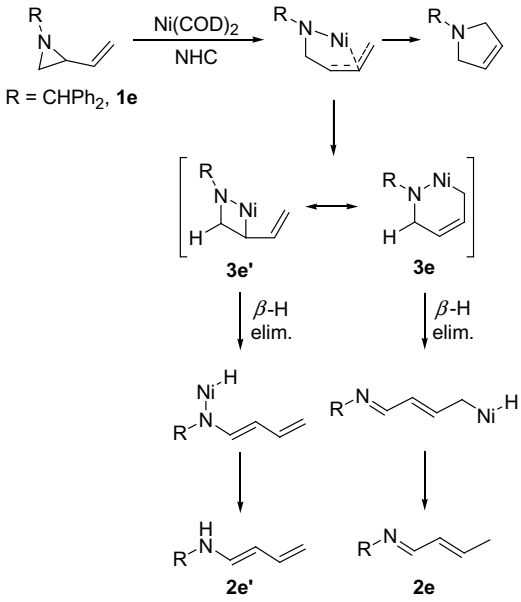
Table 2
Ni-catalyzed rearrangements of vinylaziridines[a]

Entry	R	NHC	Product[b]
1	Tr (**1a**)	IPr	 **2a**
2	Bz (**1b**)	IPr	 R' = Ph (**2b**)
3	Boc (**1c**)	IPr	R' = OBu^t (**2c**)
4	MeO_2C (**1d**)	IPr	R' = OMe (**2d**)
5	$CHPh_2$ (**1e**)	IPr	 **2e**
6	$CHPh_2$ (**1e**)	SIPr	 **2e'**
7	Ts (**1f**)	IPr	N.R.

[a] Reaction conditions: 5 mol % $Ni(COD)_2$, 10 mol % NHC, toluene, overnight.
[b] Determined by ^1H NMR.

The rearrangement of vinylaziridines to imines or 1,3-butadienylamines can be rationalized by the formation of a key π-allyl/Ni complex (Scheme 1). Due to the difficulty of reductive elimination of C(sp^3)–N bond,[25] this π-allyl/Ni complex undergoes β-hydride elimination followed by reductive elimination. 1,3-Butadienylamine or imine arises from metallazetidine intermediate (**3e′**) or metallapiperidine intermediate (**3e**), respectively.

In an effort to block competing β-hydride elimination pathways, the cycloaddition of a vinyl aziridine possessing a tethered alkyne was evaluated. 1-Trityl-2-(3-(2-butynyloxy)-1-propenyl)-aziridine (**4a**)[26] was subjected to the standard cycloaddition conditions in the presence of a variety of ligands (Table 3). No rearrangement was observed in the absence of ligand or when tertiary phosphines were used as ligands (entries 1–3). However, aziridinylen-yne **4a** did react when NHCs were employed (entries 4–7). Interestingly, the rearrangement of aziridinylen-yne **4a** afforded three different products whose ratios were dependent on which NHC ligand was employed. NHCs possessing an aromatic side chain (IPr, SIPr, and IMes) afforded two different azepines (**5a** and **6a**). IMes favored the formation of azepine **6a** (entry 4), whereas SIPr favored the formation of azepine **5a** (entry 6).[27] IPr showed no selectivity between these two azepines even at lower catalyst loading and less reaction time. In contrast, the Ni/I*t*Bu-catalyzed rearrangement of aziridinylen-yne **4a** gave a conjugated unsaturated imine (**7a**) selectively, which is consistent with the Ni/I*t*Bu-catalyzed rearrangement of cyclopropyen-yne.[6]



Scheme 1. Proposed mechanism of rearrangements of vinylaziridines.

Table 3
Ni-catalyzed rearrangements of **4a**[a]

Entry	L	time (h)	Ratio[b] **5a**:**6a**:**7a**	% Conversion of **4a**
1	None	12	—	0
2	PPh_3	12	—	0
3	PBu_3	12	—	0
4	IMes	6	1:2:trace	100
5	IPr	2	1:1:trace	100
6	SIPr	6	4:1:trace	100
7	I*t*Bu	2	Trace:trace:1	100

[a] Reaction conditions: 5 mol % $Ni(COD)_2$, 10 mol % ligand, C_6D_6, 60 °C.
[b] Determined by ^1H NMR.

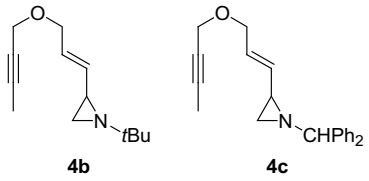
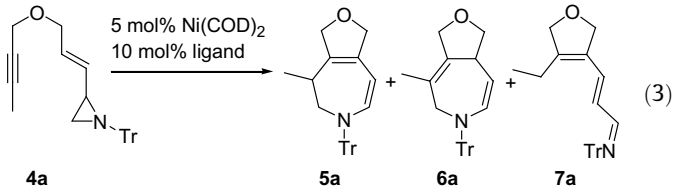


Figure 1. Aziridinylen-ynes.



(3)

Other aziridinylen-ynes possessing a bulky protecting group (i.e., *t*-butyl (**4b**)[28] and benzhydryl (**4c**),[29] Fig. 1) also underwent Ni-catalyzed rearrangement reactions. Conjugated imine products (**7b,c**) were again observed exclusively, when I*t*Bu was employed. Similarly, a mixture of bicyclic azepines (i.e., **5b,c** and **6b,c**) was observed, when *N*-aryl NHCs (i.e., IMes, IPr, SIPr) were employed. Interestingly, azepines **5** and **6** appear to arise from C–C cleavage, rather than C–N cleavage, of the aziridine ring. It is possible that the steric hindrance of N-protecting groups prevents the nitrogen atom from coordinating to nickel center and disfavors C–N bond cleavage.

In summary, the combination of $Ni(COD)_2$ and a bulky NHC ligand serves as a catalyst for the rearrangement of vinyl aziridines and aziridinylen-ynes. Vinyl aziridines were typically converted to straight chain products. Aziridinylen-ynes afforded a mixture of heterocyclic products. Mechanistic investigations are ongoing.

Acknowledgments

We gratefully acknowledge Merck, the Alfred P. Sloan Foundation, and the NIGMS for support of this research.

References and notes

1. (a) Louie, J.; Gibby, J. E.; Farnworth, M. V.; Tekavec, T. N. *J. Am. Chem. Soc.* **2002**, *124*, 15188; (b) Tekavec, T. N.; Arif, A. M.; Louie, J. *Tetrahedron* **2004**, *60*, 7431.
2. (a) Duong, H. A.; Cross, M. J.; Louie, J. *J. Am. Chem. Soc.* **2004**, *126*, 11438; (b) Duong, H. A.; Louie, J. *J. Organomet. Chem.* **2005**, *690*, 5098; (c) Duong, H. A.; Louie, J. *Tetrahedron* **2006**, *62*, 7547.

3. (a) Tekavec, T. N.; Louie, J. *Org. Lett.* **2005**, *7*, 4037; (b) Tekavec, T. N.; Louie, J. *J. Org. Chem.* **2008**, *73*, 2641.
4. (a) McCormick, M. M.; Duong, H. A.; Zuo, G.; Louie, J. *J. Am. Chem. Soc.* **2005**, *127*, 5030; (b) Tekavec, T. N.; Zuo, G.; Simon, K.; Louie, J. *J. Org. Chem.* **2006**, *71*, 5834.
5. Zuo, G.; Louie, J. *Angew. Chem., Int. Ed.* **2004**, *43*, 2777.
6. Zuo, G.; Louie, J. *J. Am. Chem. Soc.* **2005**, *127*, 5798.
7. Zhang, K.; Chopade, P. R.; Louie, J. *Tetrahedron Lett.* **2008**, *27*, 4306.
8. Thermal or nucleophile-promoted rearrangements of vinylaziridines generally lead to two different tautomers of pyrroline (a) Atkinson, R. S.; Rees, C. W. *Chem. Commun.* **1967**, 1232; (b) Gilchrist, T. L.; Rees, C. W.; Stanton, E. *J. Chem. Soc (C)* **1971**, 3036; (c) Hudlicky, T.; Frazier, J. O.; Seoane, G.; Tiedje, M.; Seoane, A.; Kwart, L. D.; Beal, C. *J. Am. Chem. Soc.* **1986**, *108*, 3755; (d) Hudlicky, T.; Seoane, G.; Lovelace, T. C. *J. Org. Chem.* **1988**, *53*, 2094; (e) Hudlicky, T.; Sinai-Zingde, G.; Seoane, G. *Synth. Commun.* **1987**, *17*, 1155; (f) Hirner, S.; Somfai, P. *Synlett* **2005**, 3099.
9. A rare $Pd(PPh_3)_4$-catalyzed rearrangement of vinyl aziridines has been reported: (a) Fugami, K.; Morizawa, Y.; Oshima, K.; Nozaki, H. *Tetrahedron Lett.* **1985**, *26*, 857; (b) Fugami, K.; Miura, K.; Morizawa, Y.; Oshima, K.; Utimoto, K.; Nozaki, H. *Tetrahedron.* **1989**, *45*, 3089.
10. Compound **1a**: ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.48 (d, 7.2 Hz, 6H), 7.20–7.30 (m, 9H), 5.83 (ddd, 7.8 Hz, 10.2 Hz, 17.4 Hz, 1H), 5.25 (d, 17.4 Hz, 1H), 5.16 (d, 10.2 Hz, 1H), 1.81 (d, 3.0 Hz, 1H), 1.69–1.73 (m, 1H), 1.35 (d, 6.0 Hz, 1H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$, ppm): δ 144.6, 139.4, 129.8, 127.6, 126.8, 116.5, 74.5, 35.0, 29.2.
11. IPr = 1,3-bis(2,6-diisopropylphenyl)-imidazol-2-ylidene; SIPr = 1,3-bis(2,5-diisopropylphenyl)-4,5-dihydroimidazolin-2-ylidene; IMes = 1,3-bis(2,4,6-trimethylphenyl)-imidazol-2-ylidene; I*t*Bu = 1,3-di-*tert*-butylimidazol-2-ylidene.
12. Compound **2a**: ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.61 (d, 1H), 7.49 (d, 6H), 7.09-7.20 (m, 9H), 6.60 (dd, 1H), 5.53 (dq, 1H), 1.45 (d, 3H).
13. 1,5-H shifts of vinyl aziridines to conjugated imines have been observed: (a) Borel, D.; Gelas-Mialhe, Y.; Vessière, R. *Can. J. Chem.* **1976**, *54*, 1590; (b) Hudlicky, T.; Frazier, J. O.; Kwart, L. D. *Tetrahedron Lett.* **1985**, *26*, 3523; (c) Pearson, W. H. *Tetrahedron Lett.* **1985**, *26*, 3527.
14. Hudlicky, T.; Reed, J. W. In *Comprehensive Organic Synthesis*; Trost, B., Fleming, I., Paquette, L. A., Eds.; Pergamon: Oxford, 1992; Vol. 5, p 899.
15. (a) Scheiner, P. *J. Org. Chem.* **1967**, *32*, 2628; (b) Pommelet, J. C.; Chuche, J. *Can. J. Chem.* **1976**, *54*, 1571; (c) Figeys, H. P.; Jammar, R. *Tetrahedron Lett.* **1980**, *21*, 2995; (d) Figeys, H. P.; Jammar, R. *Tetrahedron Lett.* **1981**, *22*, 637.
16. (a) Mente, P. G.; Heine, H. W.; Scharoubim, G. R. *J. Org. Chem.* **1968**, *33*, 4547; (b) Heine, H. W.; Mente, P. G. *J. Org. Chem.* **1971**, *36*, 3076.
17. *Compound* **2b**: ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 8.09 (d, 2H), 7.04–7.10 (m, 3H), 5.26 (ddd, 1H), 5.10 (dd, 1H), 4.90 (dd, 1H), 4.89 (dt, 1H), 3.83 (dd, 1H), 3.59 (dd, 1H). *Compound* **2c**: ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.60 (ddd, 1H), 5.03 (dd, 1H), 4.83 (dd, 1H), 4.50 (dt, 1H), 3.72 (dd, 1H), 3.40 (dd, 1H), 1.50 (s, 9H). *Compound* **2e**: ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.42–7.54 (m, 4H), 7.10–7.20 (m, 6H), 6.32 (dt, 1H), 6.08 (dd, 1H), 5.24 (dd, 1H), 5.18 (d, 1H), 4.92 (dd, 1H), 4.78 (dd, 1H), 3.25 (br, 1H) ppm. *Compound* **2e′**: ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.79 (d, 1H), 7.49 (d, 4H), 7.09–7.20 (m, 6H), 6.43 (dd, 1H), 5.76 (dq, 1H), 5.32 (s, 1H), 1.45 (d, 3H).
18. (a) Trost, B. M.; Fandrick, D. R. *J. Am. Chem. Soc.* **2003**, *125*, 11836; (b) Ali, S. I.; Nikalje, M. D.; Sudalai, A. *Org. Lett.* **1999**, *1*, 705.
19. Charrier, N.; Gravestock, D.; Zard, S. Z. *Angew. Chem., Int. Ed.* **2006**, *45*, 6520.
20. *Compound* **1c**: ^{1}H NMR (300 MHz, C_6D_6, ppm): δ 5.35 (ddd, 17.1 Hz, 9.9 Hz, 7.2 Hz, 1H), 5.20 (dd, 17.1 Hz, 1.8 Hz, 1H), 4.95 (dd, 9.9 Hz, 1.8 Hz, 1H), 2.62–2.68 (m, 1H), 2.10 (d, 6.3 Hz, 1H), 1.80 (d, 3.6 Hz, 1H), 1.35 (s, 9H); ^{13}C{^{1}H} NMR (75 MHz, C_6D_6, ppm): δ 161.8, 135.9, 117.8, 80.4, 39.2, 32.6, 27.9.
21. Aumann, R.; Froehlich, K.; Ring, H. *Angew. Chem.* **1974**, *86*, 309.
22. (a) Heine, H. W.; Proctor, Z. *J. Org. Chem.* **1958**, *23*, 1554; (b) Heine, H. W.; Fetter, M. E.; Nicholson, E. M. *J. Am. Chem. Soc.* **1959**, *81*, 2202; (c) Heine, H. W.; Kenyon, W. G.; Johnson, E. M. *J. Am. Chem. Soc.* **1961**, *83*, 2570; (d) Nishiguchi, T.; Tochio, H.; Nabeya, A.; Iwakura, Y. *J. Am. Chem. Soc.* **1969**, *91*, 5835; Nishiguchi, T.; Tochio, H.; Nabeya, A.; Iwakura, Y. *J. Am. Chem. Soc.* **1969**, *91*, 5841.
23. A similar reaction has been observed in the Ni-catalyzed rearrangement of acylvinylcyclopropanes to dihydrofurans: Bowman, R. K.; Johnson, J. S. *Org. Lett.* **2006**, *8*, 573.
24. *Compound* **1e**: ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.15–7.83 (m, 11H), 5.68 (m, 1H), 5.26 (dd, 17.1 Hz, 1.2 Hz, 1H), 5.11 (dd, 10.2 Hz, 1.2 Hz, 1H), 3.59 (s, 1H), 2.11 (m, 1H), 1.88 (d, 3.3 Hz, 1H), 1.73 (d, 6.6 Hz, 1H).
25. (a) Koo, K.; Hillhouse, G. L. *Organometallics* **1996**, *15*, 2669; (b) Lin, B. L.; Clough, C. R.; Hillhouse, G. L. *J. Am. Chem. Soc.* **2002**, *124*, 2890; (c) Macgregor, S. A.; Neave, G. W.; Smith, C. *Faraday Discuss.* **2003**, *124*, 111.
26. *1-Trityl-2-(3-(2-butynyloxy)-1-propenyl)-aziridine* **(4a)**: ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.28 (d, 7.2 Hz, 6H), 7.20–7.29 (m, 9H), 5.75–5.77 (m, 2H), 4.11–4.13 (m, 2H), 4.06–4.08 (m, 2H), 1.88 (t, 1.8 Hz, 3H), 1.80–1.81 (m, 1H), 1.75–1.78 (m, 1H), 1.24 (d, 6.3 Hz, 1H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$, ppm): δ 144.6, 135.6, 129.7, 128.0, 127.6, 126.9, 82.6, 74.5, 69.7, 58.4, 57.4, 33.9, 29.3, 3.8.
27. Azepine **5a** could be isolated in 66% yield. Unfortunately, azepine **6a** decomposed upon all purification attempts.
    General procedure: In a glove box, 2-(3-(2-butynyloxy)-1-propenyl)-1-triphenylmethyl-aziridine (**4a**, 50 mg, 0.13 mmol) was added to an oven dried scintillation vial equipped with a magnetic stir bar and was dissolved in toluene (0.5 mL). To the stirring solution, a solution of $Ni(COD)_2$ (2 mg, 0.007 mmol) and SIPr (5 mg, 0.013 mmol) was added. The reaction mixture was stirred at room temperature overnight (or until complete consumption of starting material was observed as judged by GC or TLC). The mixture was concentrated in vacuo and purified by silica gel column chromatography (10% Et_2O/pentanes) to afford 3-(1,3-butadienyl)-4-ethylidenetetrahydrofuran (**5a**, 33 mg, 66%) as a colorless oil. ^{1}H NMR (300 MHz, C_6D_6, ppm): δ 7.48 (d, 7.2 Hz, 6H), 6.97–7.14 (m, 9H), 6.47 (d, 9.3 Hz, 1H), 4.70–4.90 (m, 4H), 4.59 (d, 9.3 Hz, 1H), 3.34 (dd, 1.5 Hz, 12.9 Hz, 1H), 2.76–2.83 (m, 1H), 2.41 (dd, 7.8 Hz, 12.9 Hz, 1H), 0.60 (d, 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (75 MHz, C_6D_6, ppm): δ 144.8, 141.3, 133.6, 130.0, 129.0, 127.2, 94.9, 80.1, 79.4, 56.0, 36.0, 17.5.
28. *1-tert-Butyl-2-(3-(2-butynyloxy)-1-propenyl)-aziridine* **(4b)**: ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.81 (dt, 6.6 Hz, 15.6 Hz, 1H), 5.48 (dd, 7.8 Hz, 15.6 Hz, 1H), 4.05–4.07 (m, 2H), 3.99 (d, 6.6 Hz, 2H), 2.11–2.15 (m, 1H), 1.8 (t, 1.8 Hz, 3H), 1.69 (d, 6.6 Hz, 1H), 1.50 (d, 3.0 Hz, 1H), 0.97 (s, 9H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$, ppm): δ 136.2, 127.2, 82.6, 75.3, 69.9, 57.7, 53.3, 32.8, 28.4, 26.7, 3.8.
29. *1-Benzhydryl-2-(3-(2-butynyloxy)-1-propenyl)-aziridine* **(4c)**: ^{1}H NMR (300 MHz, C_6D_6, ppm): δ 7.43–7.56 (m, 4H), 7.04–7.16 (m, 6H), 5.75 (dt, 5.4 Hz, 15.3 Hz, 1H), 5.62 (dd, 7.2 Hz, 15.3 Hz, 1H), 4.02 (q, 2.1 Hz, 2H), 3.94 (d, 5.4 Hz, 2H), 3.33 (s, 1H), 1.80–1.84 (m, 1H), 1.62 (d, 3.3 Hz, 1H), 1.47 (t, 2.1 Hz, 3H), 1.33 (d, 6.6 Hz, 1H); ^{13}C{^{1}H} NMR (75 MHz, C_6D_6, ppm): δ 144.2, 144.0, 133.5, 127.2, 127.0, 82.0, 78.4, 76.1, 69.3, 57.5, 40.7, 35.8, 3.2.