Supporting Information

New chemical agents against orthopoxvirus infections based on adamantane-monoterpene conjugates

Evgeny V. Suslov,*[a] Evgeny S. Mozhaytsev,[a] Dina V. Korchagina,[a] Nikolay I. Bormotov,[b] Olga I. Yarovaya,[a,c] Konstantin P. Volcho,[a,c] Olga A. Serova,[b] Alexander P. Agafonov,[b] Rinat A. Maksyutov,[b] Larisa N. Shishkina,[b] Nariman F. Salakhutdinov[a,c]

a. Novosibirsk Institute of Organic Chemistry, Siberian Branch of the Russian Academy of Sciences, Lavrentjev Avenue 9, 630090 Novosibirsk, Russia.

b. Department of prevention and treatment of especially dangerous infections, State Research Center of Virology and Biotechnology VECTOR, Koltsovo, Novosibirsk Region, 630559, Russian Federation

c. Novosibirsk State University, Pirogova St. 2, 630090 Novosibirsk, Russia

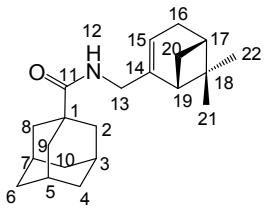
1. Experimental Section

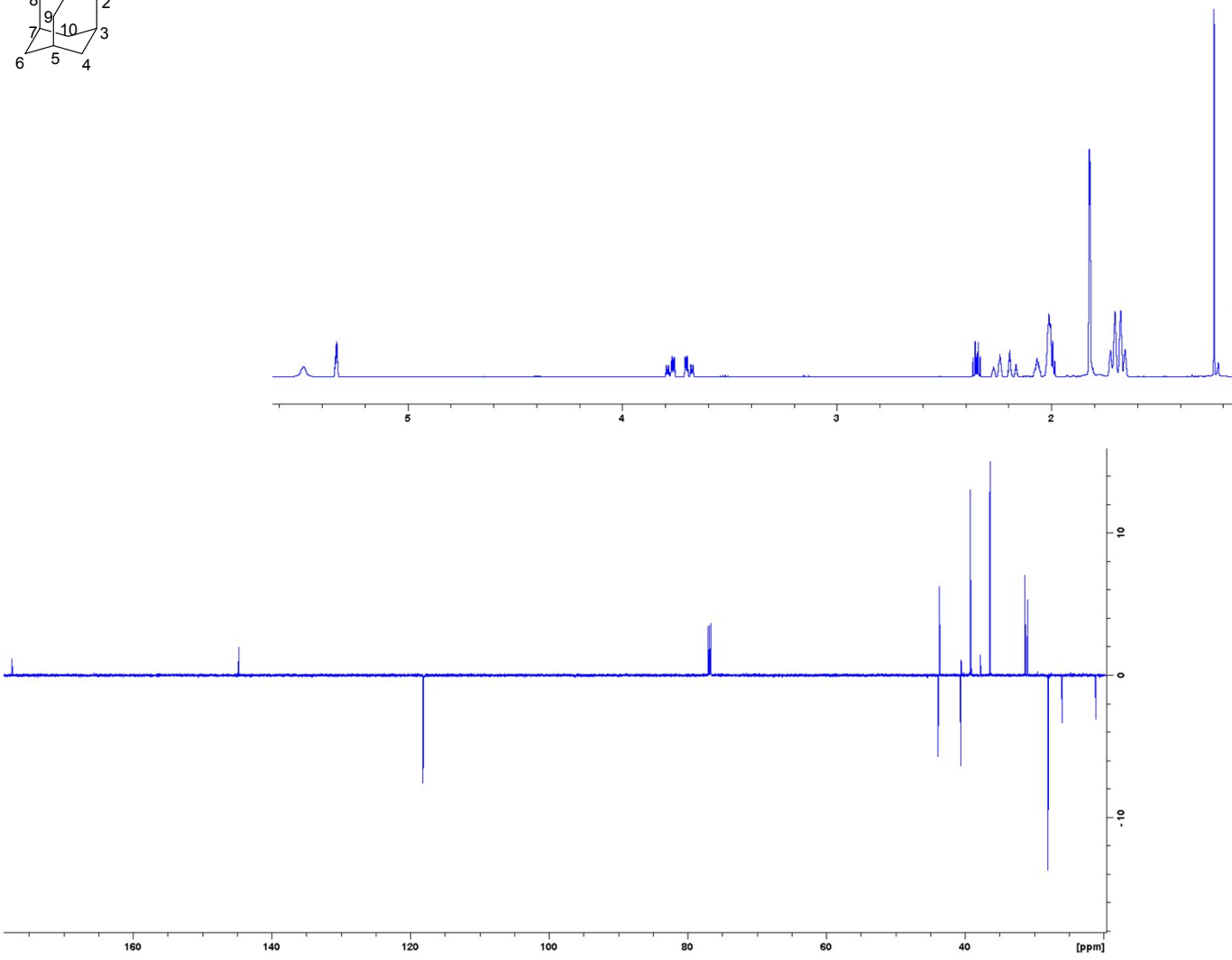
1.1. Chemistry

All chemicals were purchased from commercial vendors and used without further purification, unless indicated otherwise. Column chromatography was performed with silica gel (60–230 μ, Macherey-Nagel), solution containing from 0% to 5% ethylacetate in hexane. Optical rotations $[\alpha]_D^{T^\circ C}$ were measured on a PolAAr 3005 polarimeter, optical rotation values are given in 10^{-1} deg cm^2 g^{-1}. ^{1}H- and ^{13}C-NMR spectra were registered on a Bruker DRX-500 spectrometer (500.13 MHz (^{1}H) and 125.76 MHz (^{13}C) in $CDCl_3$) and on Bruker Avance – III 600 (600.30 MHz (^{1}H) and 150.95 MHz (^{13}C) in $CDCl_3$). Chemical shifts obtained are given in ppm, relative to residual chloroform (δ_H 7.24, δ_C 76.90 ppm), and J are given in Hz. The compound structures were determined by analyzing their ^{1}H-NMR spectra; ^{1}H, ^{1}H double resonance spectra and 2D correlation spectra ^{1}H-^{1}H (COSY, NOESY); J-modulated ^{13}C-NMR spectra (JMOD) and ^{13}C,^{1}H-type 2D heteronuclear correlation with one-bond and long-range spin–spin coupling constants (COSY and HSQC, J(C,H) = 135 Hz and 145 Hz respectively, COLOC and HMBC, ^{2,3}J(C,H) = 10 Hz and 7 Hz respectively). Numeration of atoms in the compounds (see Supplementary Materials) is given for assigning the signals in the NMR spectra and does not coincide with the nomenclature of the compounds. The elemental composition of compounds was determined from high-resolution mass spectra (HR-MS) recorded on a DFS Thermo Scientific spectrometer in full scan mode (0–500 m/z, 70 eV electron impact ionization, direct sample injection). The conversion of reagents, the content of the compounds in fractions during chromatography and the purity of the target compounds was determined using gas chromatography methods: 7820A gas chromatograph (Agilent Tech., USA), flame-ionization detector, HP-5 capillary column (0.25 mm×3m×0.25μm), helium carrier gas (flow rate 2 mL/min, flow division 99:1), temperature range from 120 °C to 280 °C, heating 20 °C/min. The purity of the target compounds for biological testing was confirmed to be more than 95%.

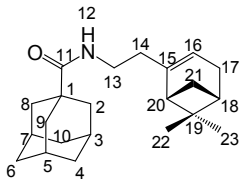
2. Copies of the NMR Spectra for compounds 40-42, 44, 46-49, 53, 54, 56, 61a, 61b, 63a, 63b.

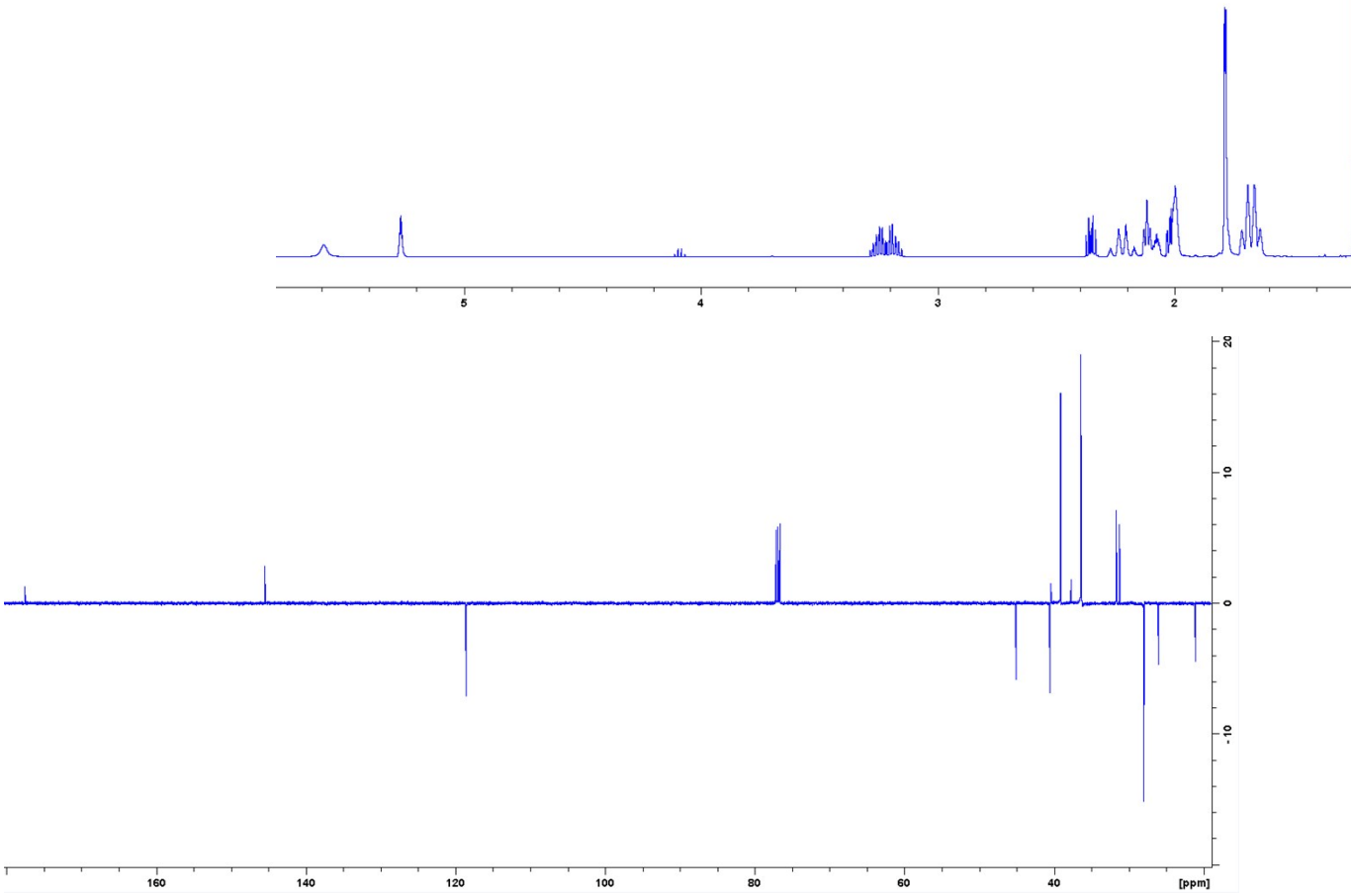
2.1. N-(((1*R*,5*S*)-6.6-dimethylbicyclo[3.1.1]hept-2-en-2-yl)methyl)adamantane-1-carboxamide 40



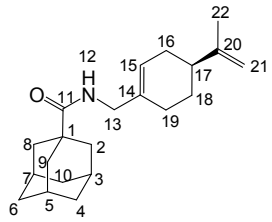


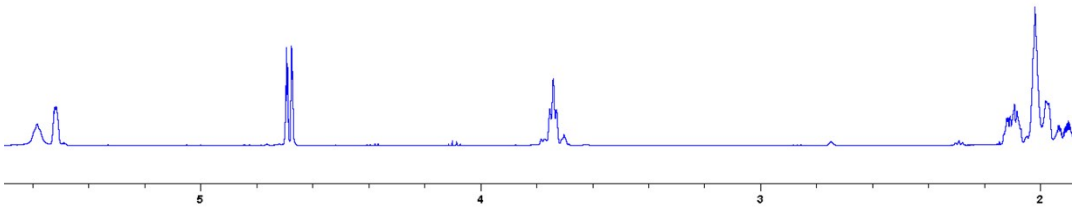
2.2. N-(2-((1*R*,5*S*)-6.6-dimethylbicyclo[3.1.1]hept-2-en-2-yl)ethyl)adamantane-1-carboxamide 41

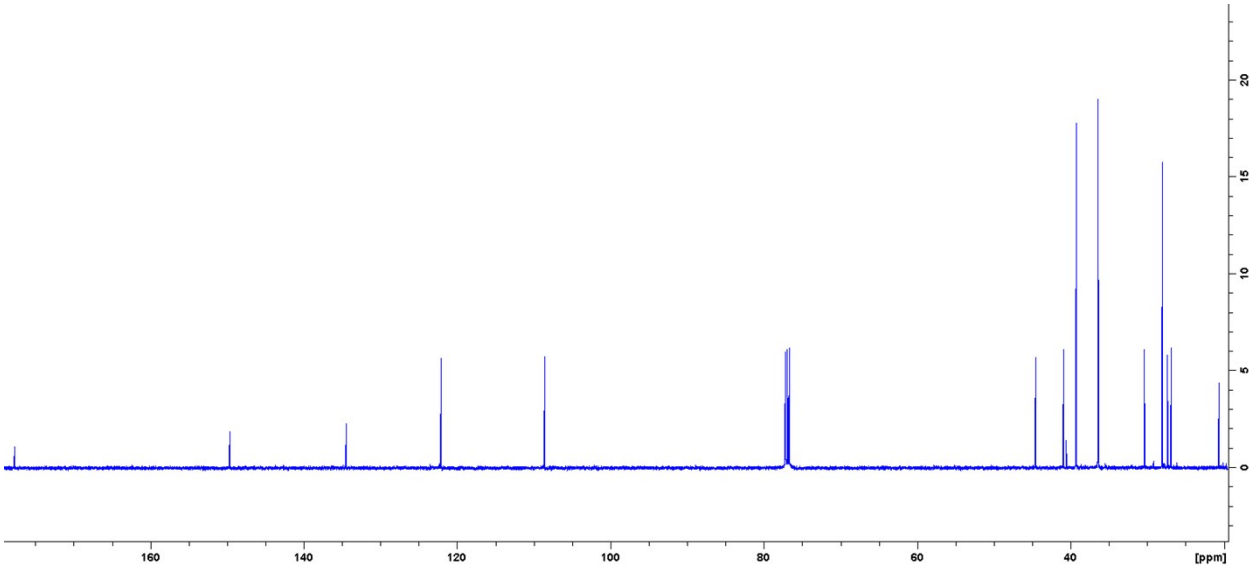




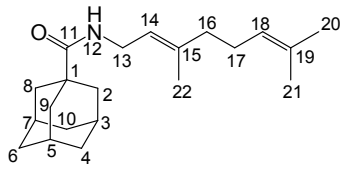
2.3. N-(((*S*)-4-(prop-1-en-2-yl)cyclohex-1-en-1-yl)methyl)adamantane-1-carboxamide 42

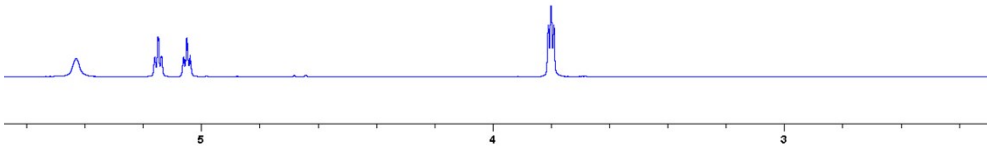


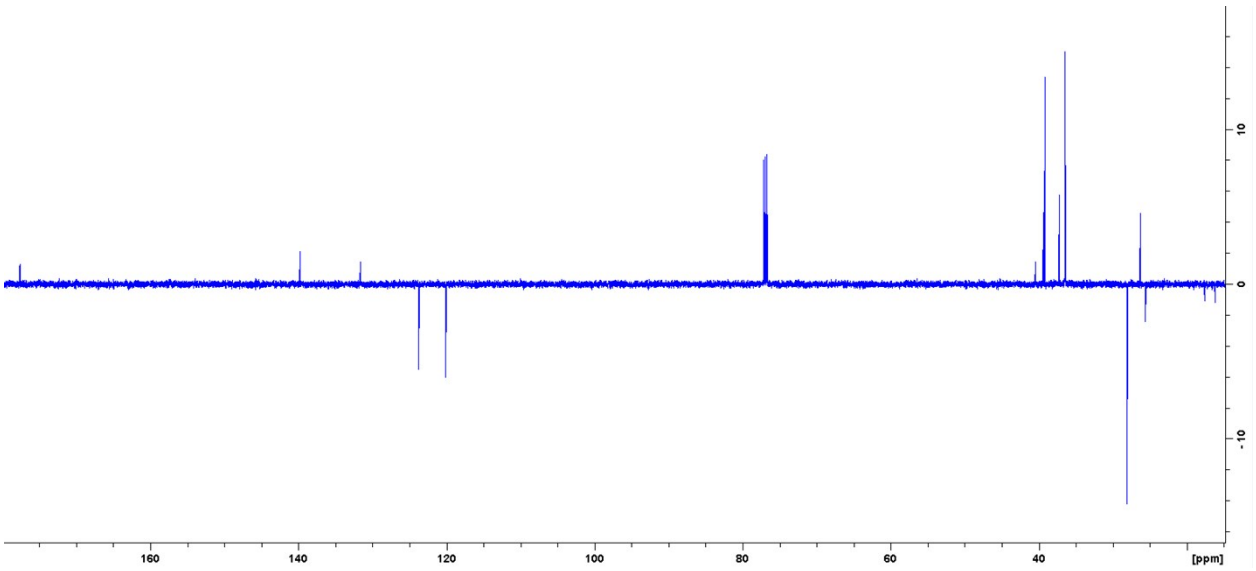




2.4. N-((*E*)-3.7-dimethylocta-2.6-dien-1-yl)adamantane-1-carboxamide 44







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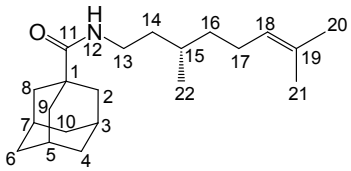
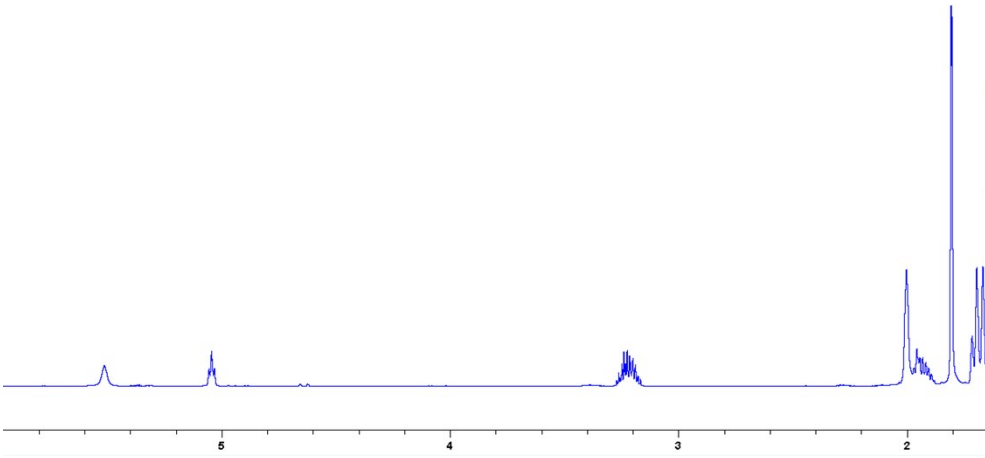
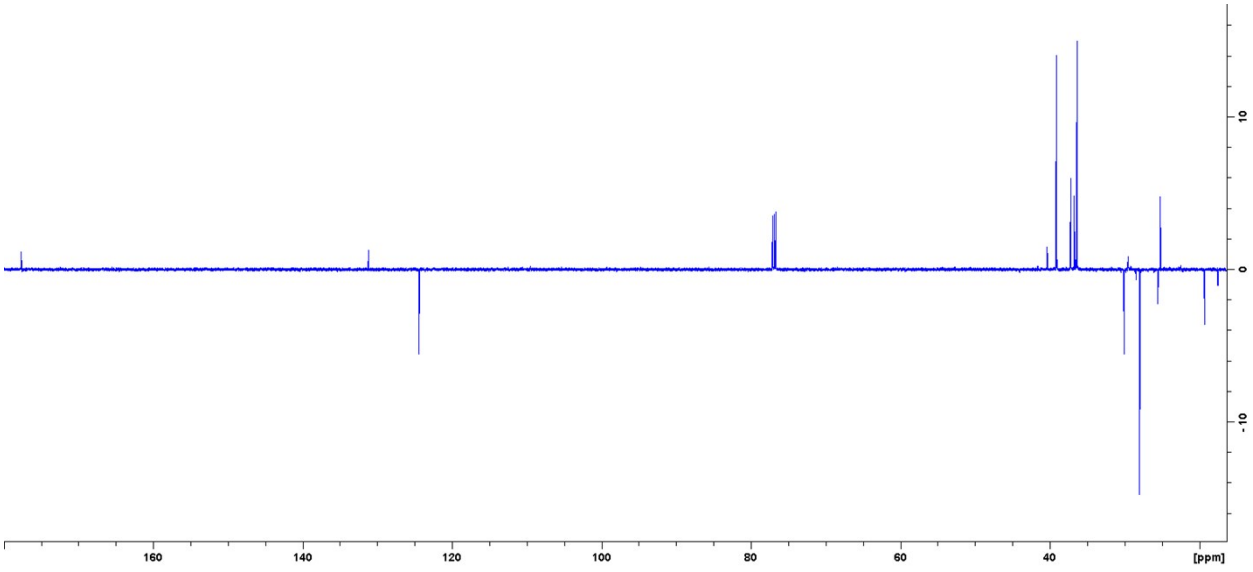
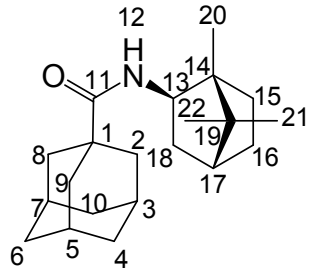
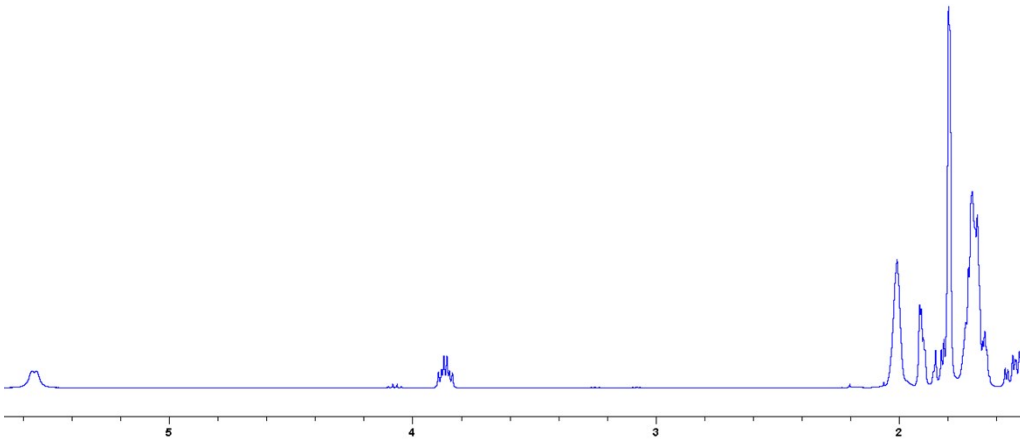


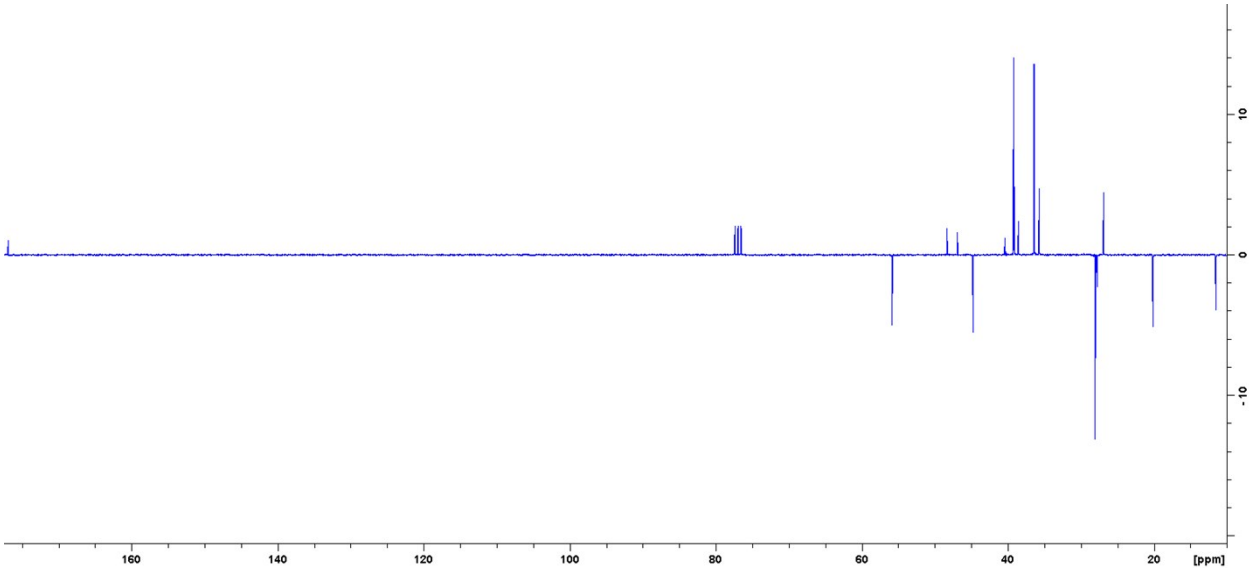




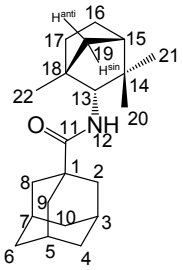
2.6. N-((1*R*,2*R*,4*R*)-1.7.7-trimethylbicyclo[2.2.1]heptan-2-yl)adamantane-1-carboxamide 47

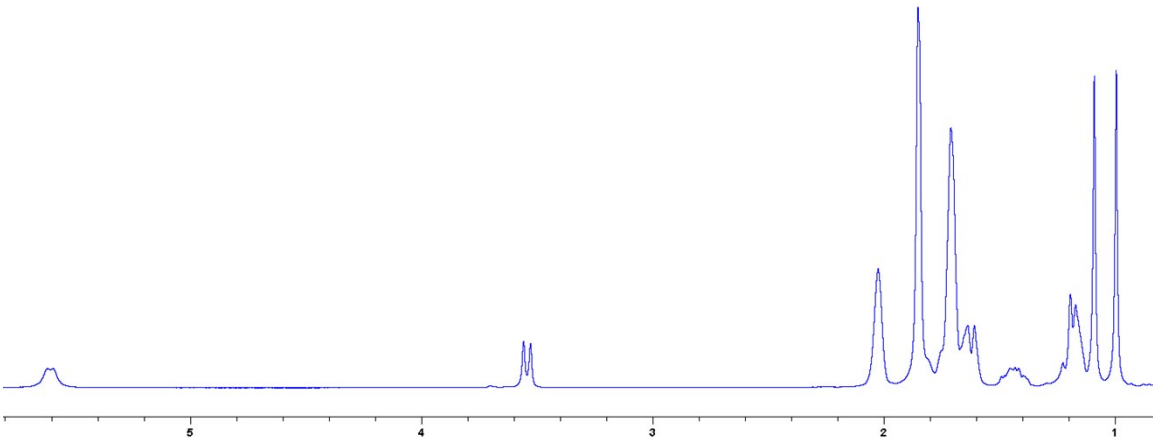


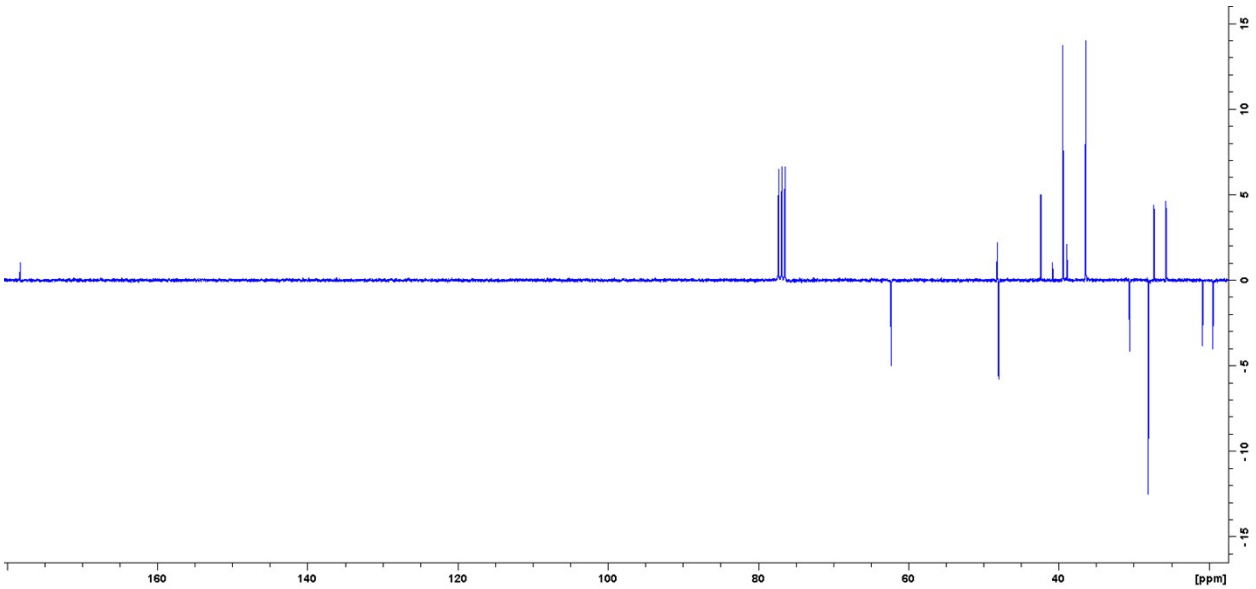




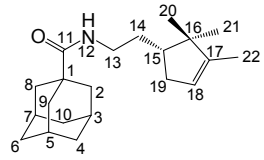
2.7. N-((1*R*,2*R*,4*S*)-1.3.3-trimethylbicyclo[2.2.1]heptan-2-yl)adamantane-1-carboxamide 48

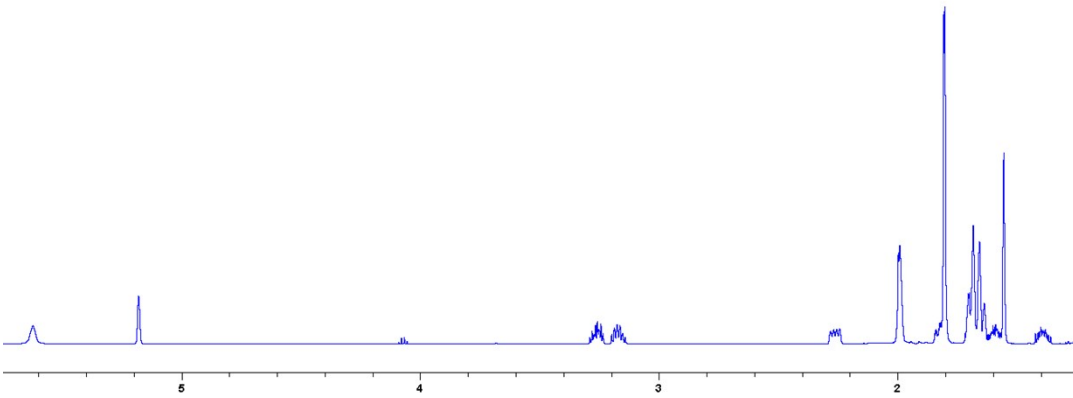


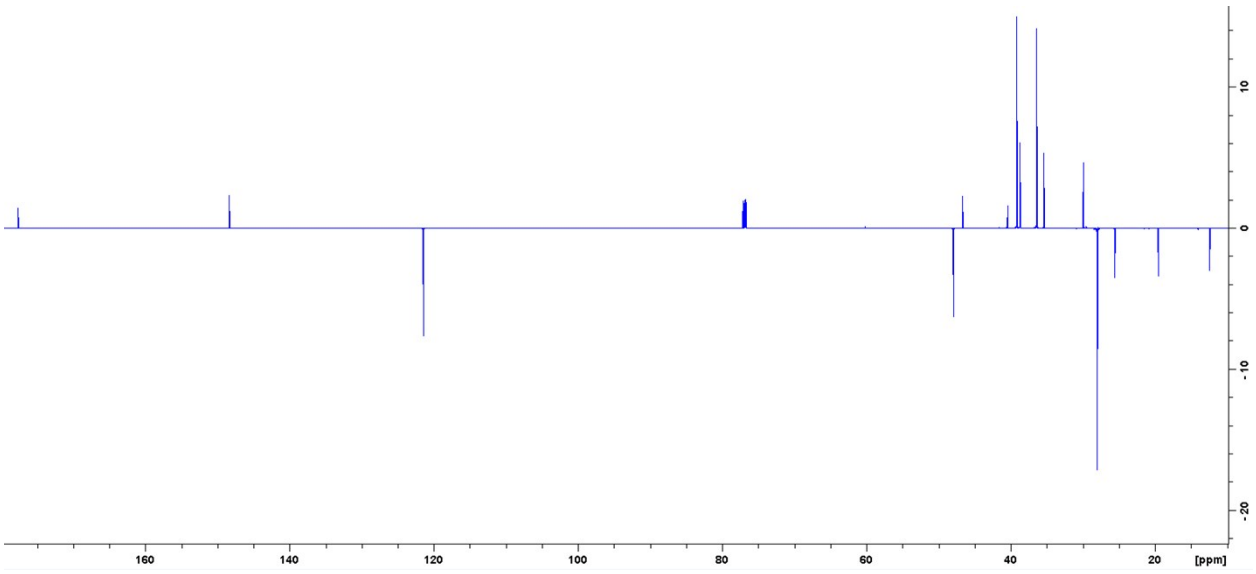




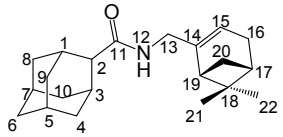
2.8. N-(2-((*R*)-2.2.3-trimethylcyclopent-3-en-1-yl)ethyl)adamantane-1-carboxamide 49

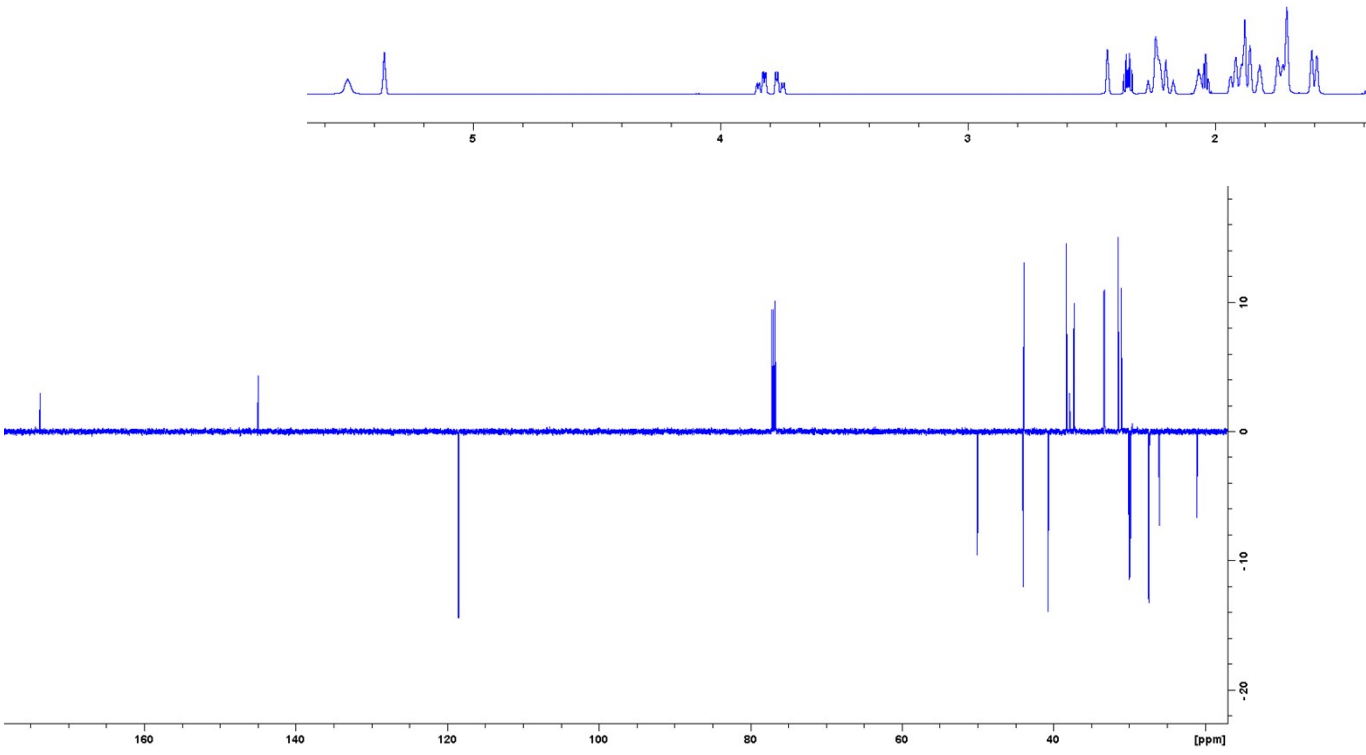




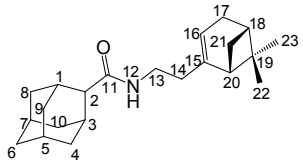


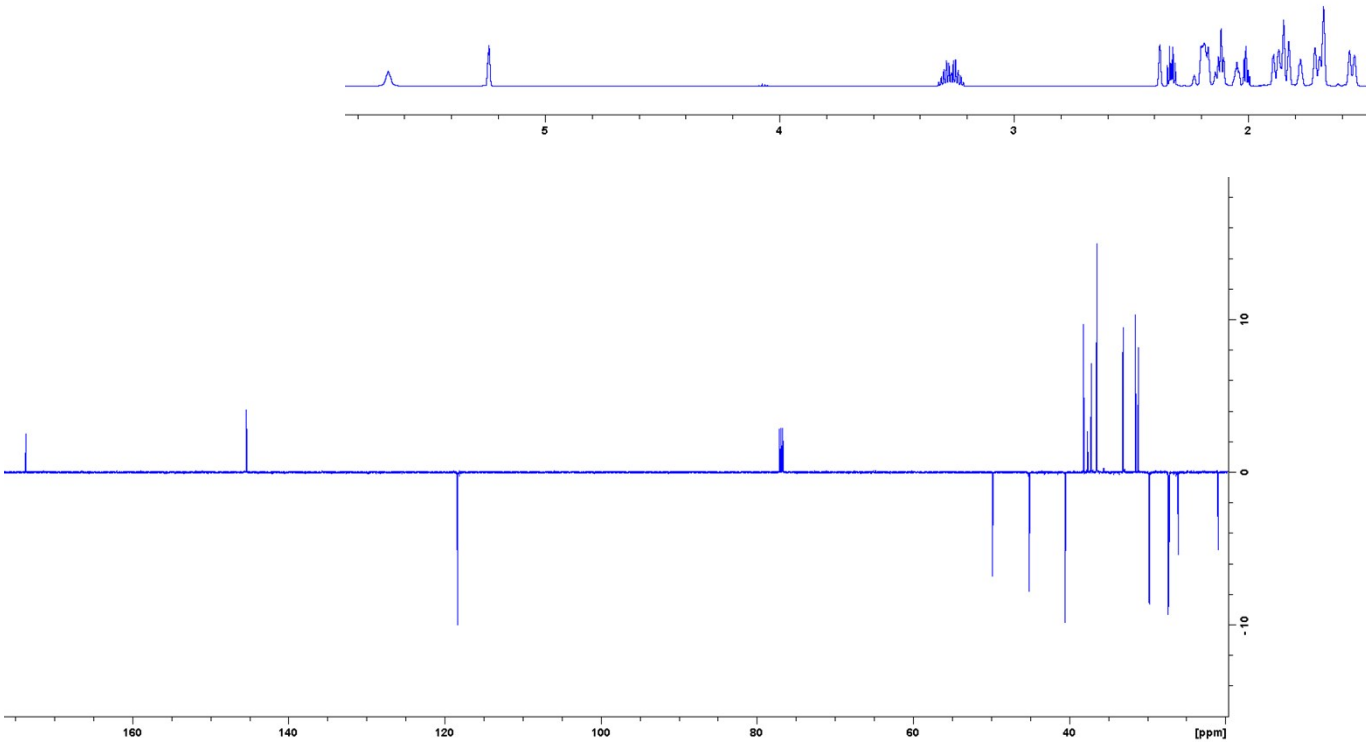
2.9. N-(((1*R*,5*S*)-6.6-dimethylbicyclo[3.1.1]hept-2-en-2-yl)methyl)adamantane-2-carboxamide 53



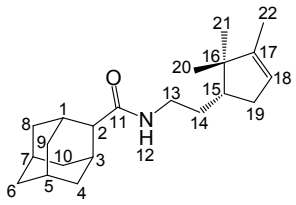


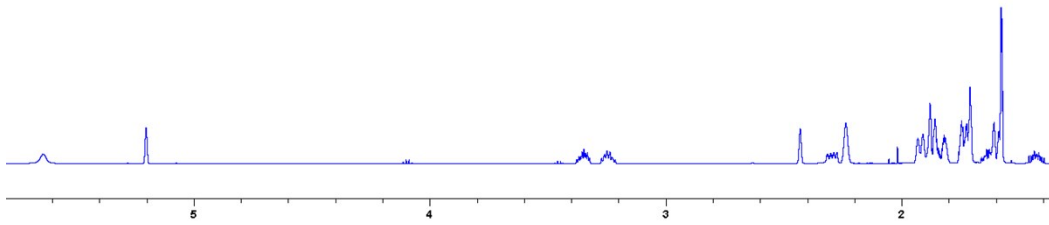
2.10. N-(2-((1*R*,5*S*)-6.6-dimethylbicyclo[3.1.1]hept-2-en-2-yl)ethyl)adamantane-2-carboxamide 54

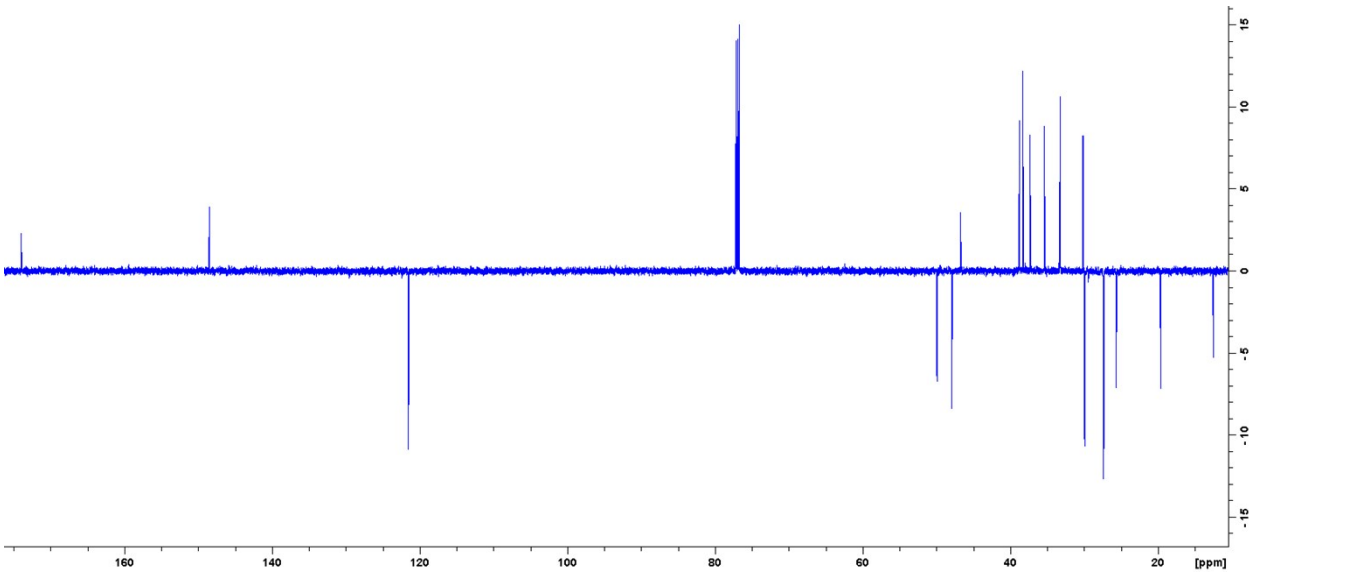




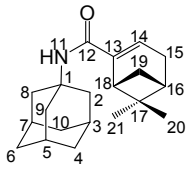
2.11. N-(2-((*R*)-2.2.3-trimethylcyclopent-3-en-1-yl)ethyl)adamantane-2-carboxamide 56

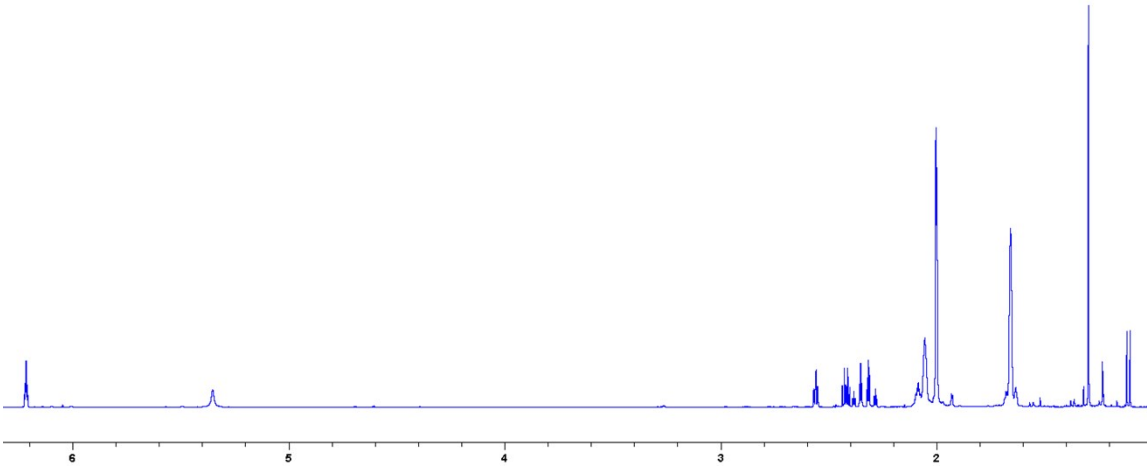


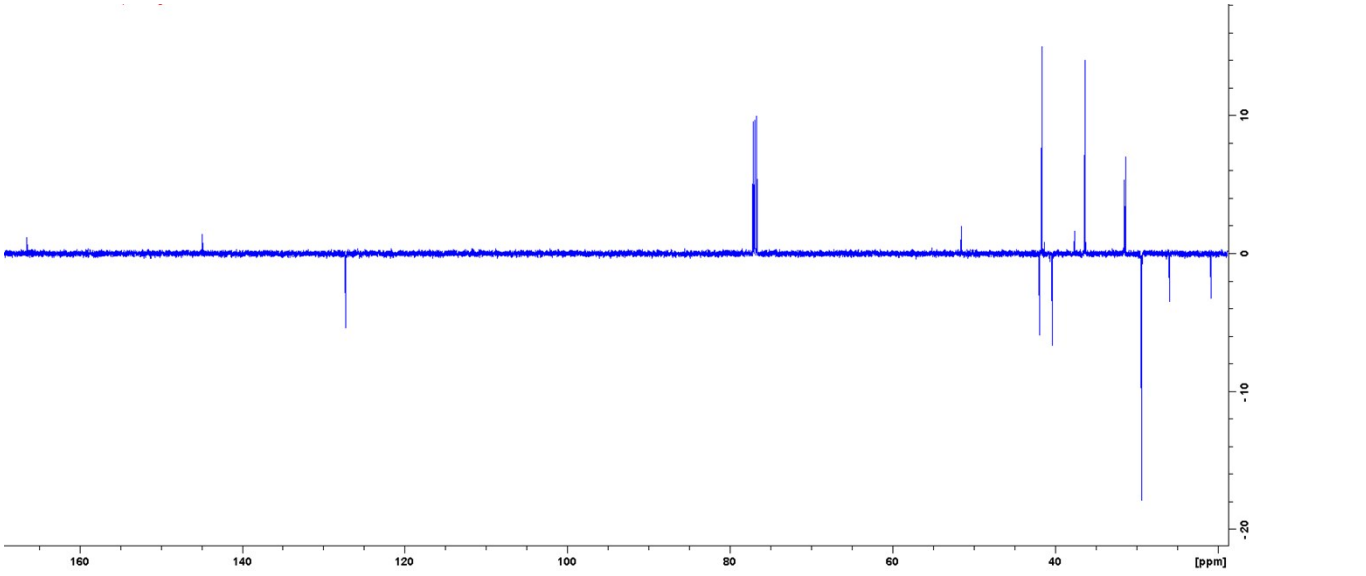




2.12. (1*R*,5*S*)-N-(adamantan-1-yl)-6.6-dimethylbicyclo[3.1.1]hept-2-ene-2-carboxamide 61a







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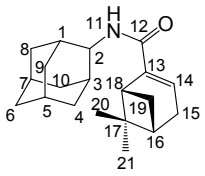
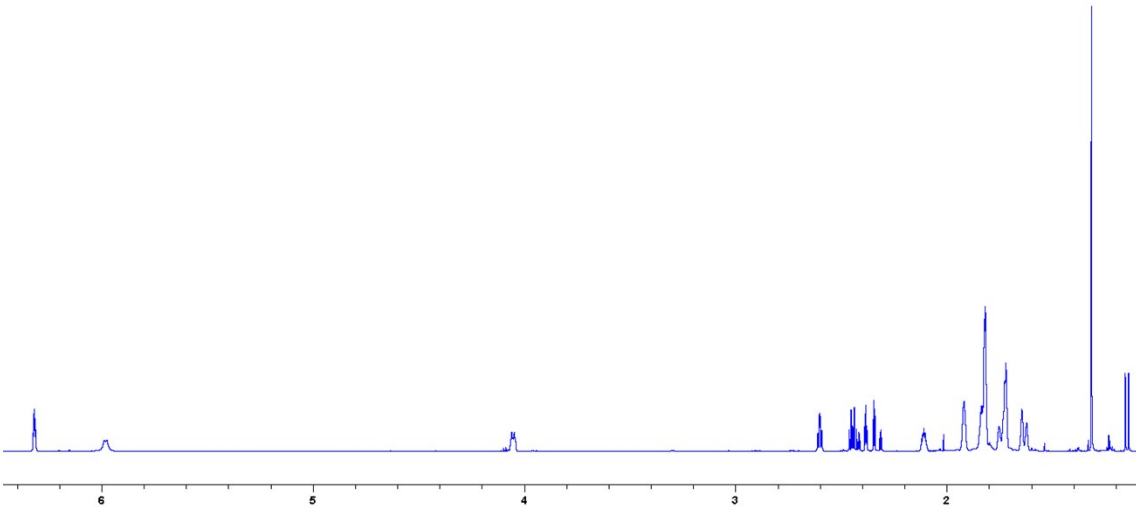
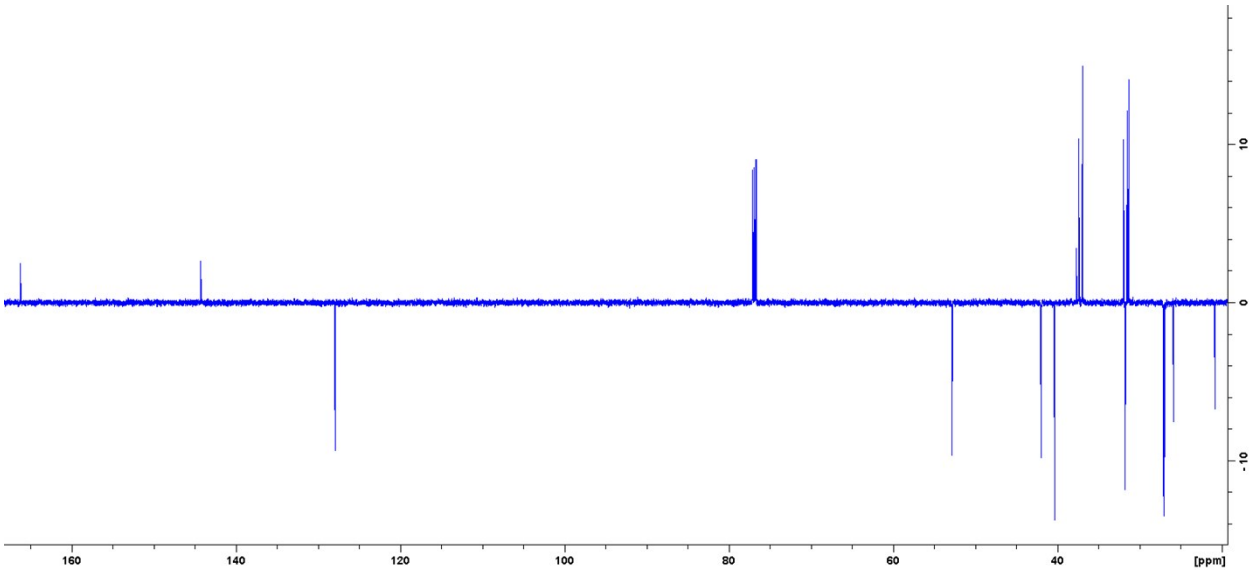
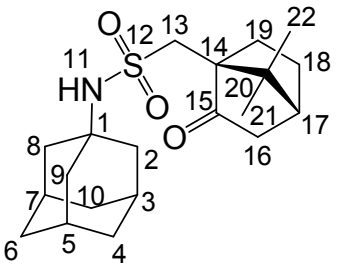
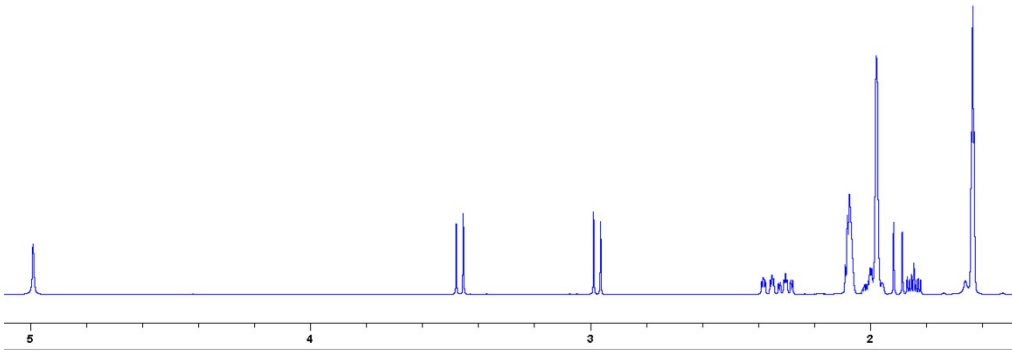


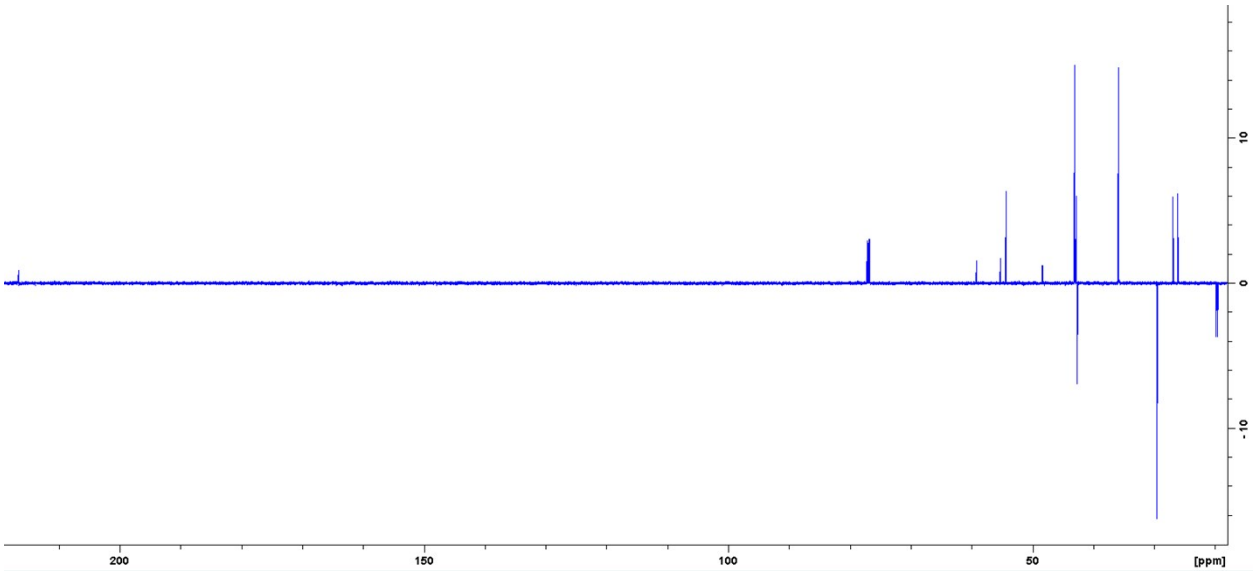




2.14. N-(adamantan-1-yl)-1-((1*S*,4*R*)-7.7-dimethyl-2-oxobicyclo[2.2.1]heptan-1-yl)methanesulfonamide 63a







2.15. N-(adamantan-2-yl)-1-((1*S*,4*R*)-7.7-dimethyl-2-oxobicyclo[2.2.1]heptan-1-yl)methanesulfonamide 63b