Supplementary Materials

Microwave-assisted, one-pot synthesis of Doxycycline under heterogeneous catalysis in water

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NMR characterization

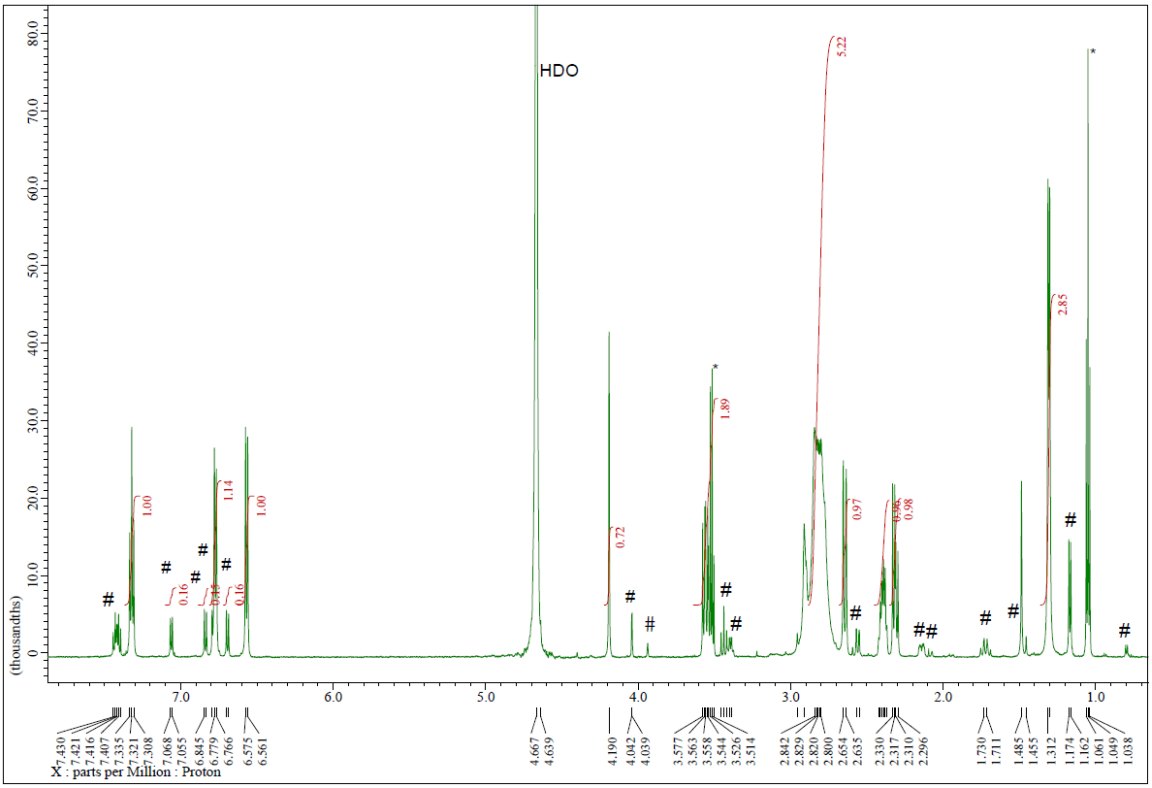

Figure S1. 1H-NMR spectrum of reaction products obtained in presence of β-cyclodextrin. Most abundant signals are attributed to α-doxycycline, signals labelled with * are those of methanol, whereas signals identified with # are relative to different isomers (β-doxycycline and, probably, 4-epidoxycycline). 600MHz, D_2O, RT.

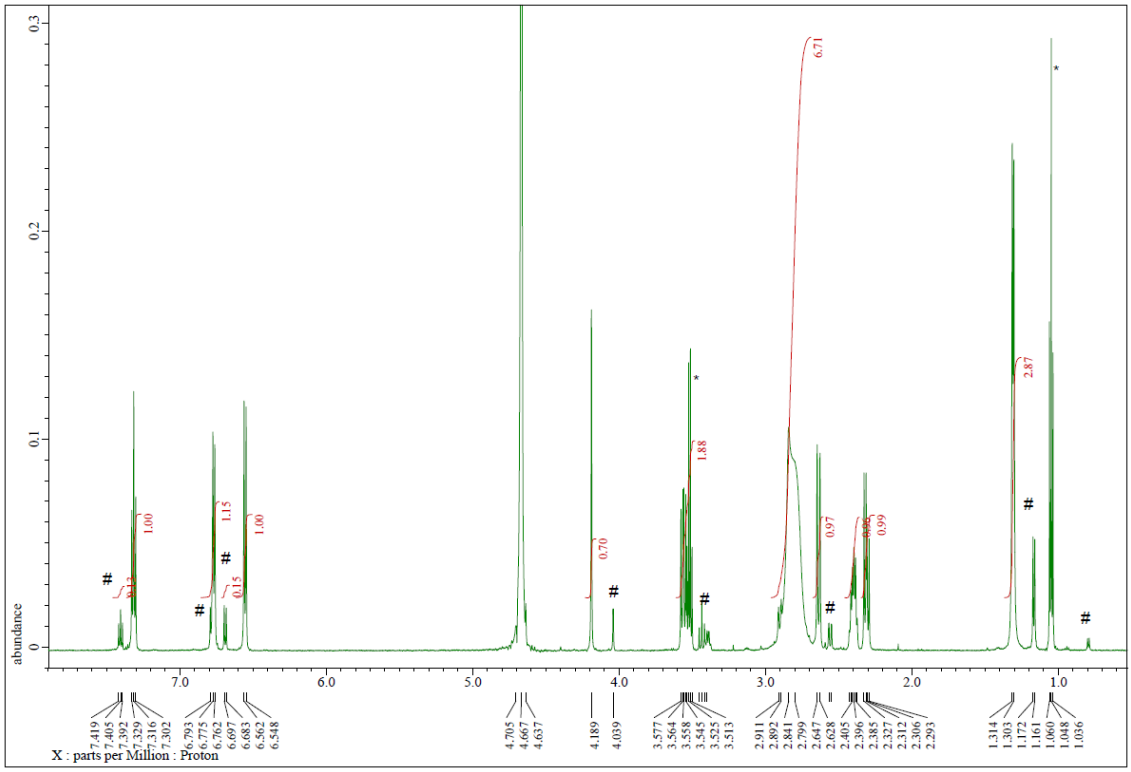

Figure S2. 1H-NMR spectrum of α-doxycycline reference compound (technical grade). signals labelled with * are those of methanol, whereas signals identified with # are relative to different isomer (β-doxycycline). 600MHz, D_2O, RT.

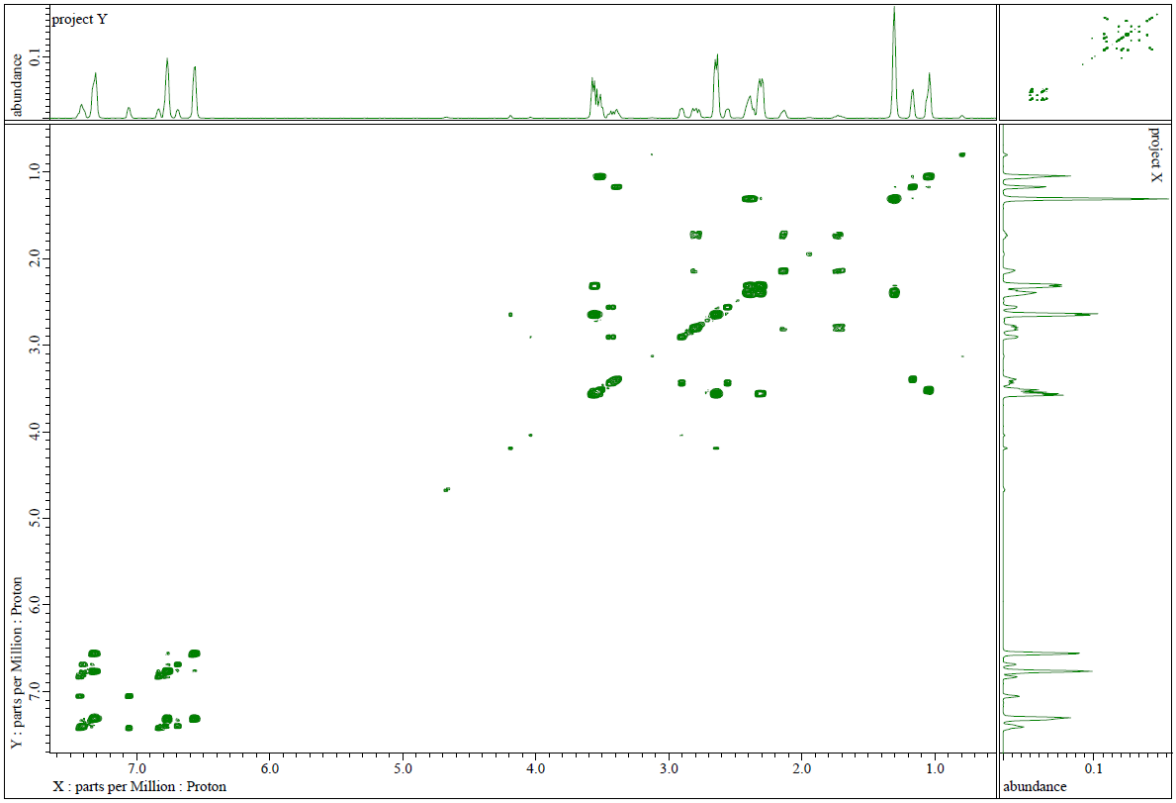

Figure S3. DQF-COSY spectrum of reaction products obtained in presence of β-cyclodextrin.

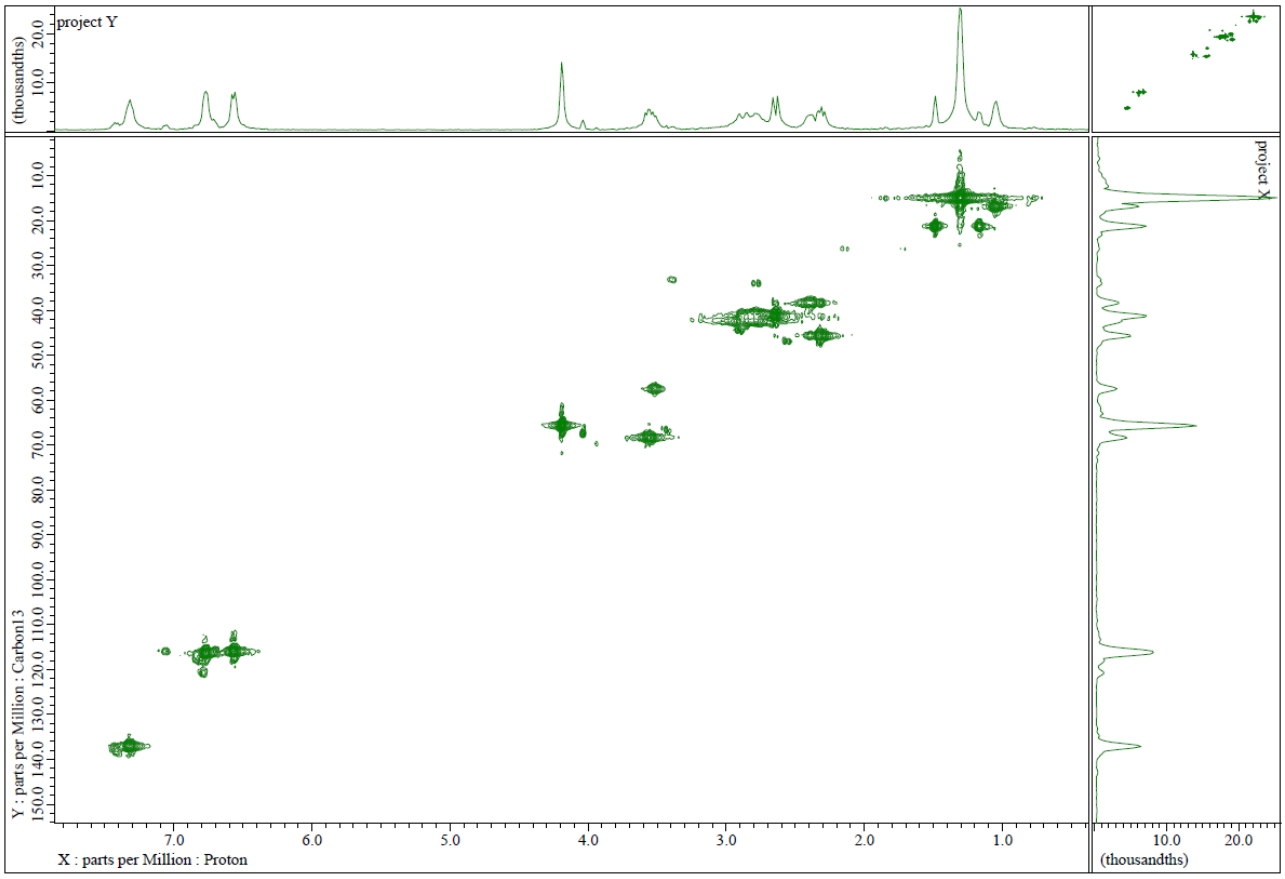

Figure S4. 1H-13C-HMQC spectrum of reaction products obtained in presence of β-cyclodextrin.

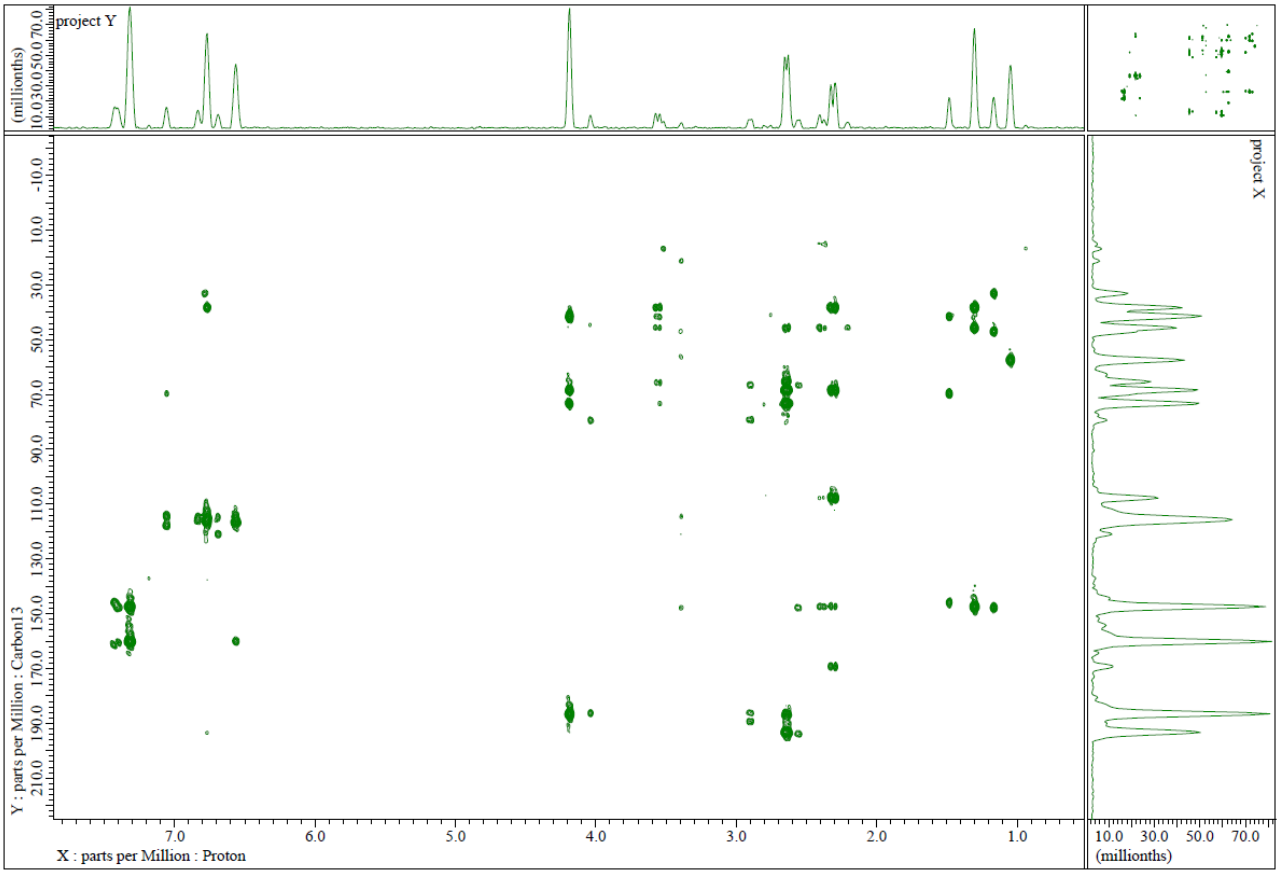

Figure S5. 1H-13C-HMBC spectrum of reaction products obtained in presence of β-cyclodextrin.

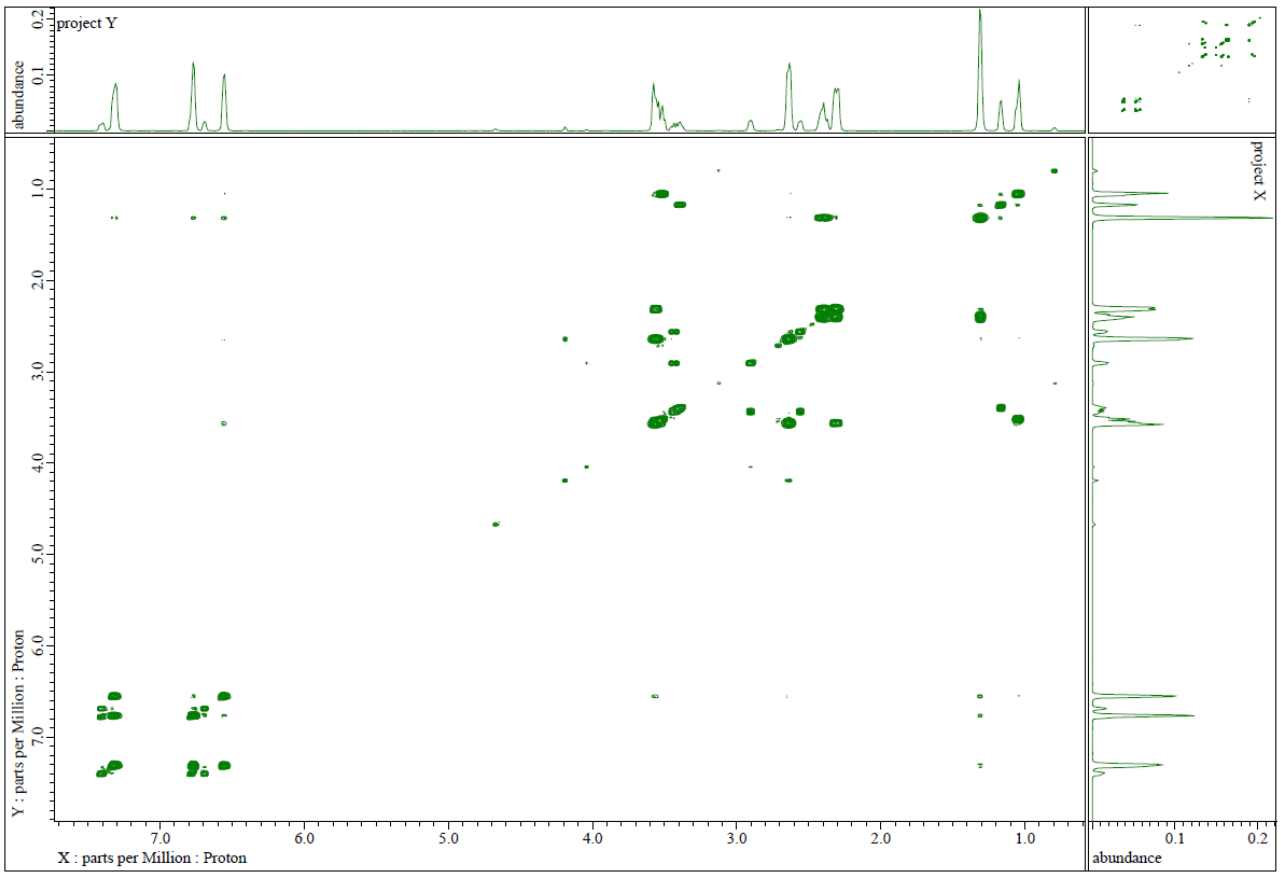

Figure S6. DQF-COSY spectrum of α-doxycycline reference compound.

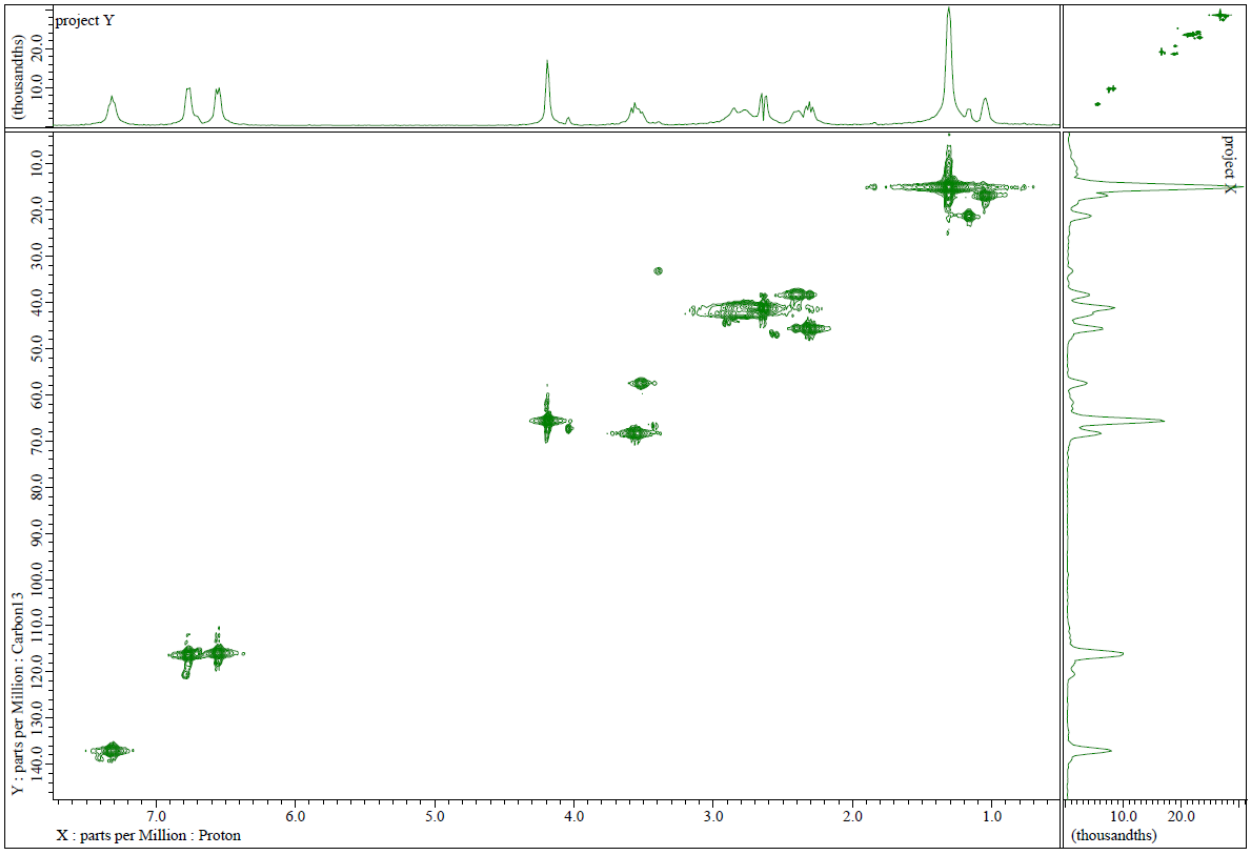

Figure S7. 1H-13C-HMQC spectrum of α-doxycycline reference compound.

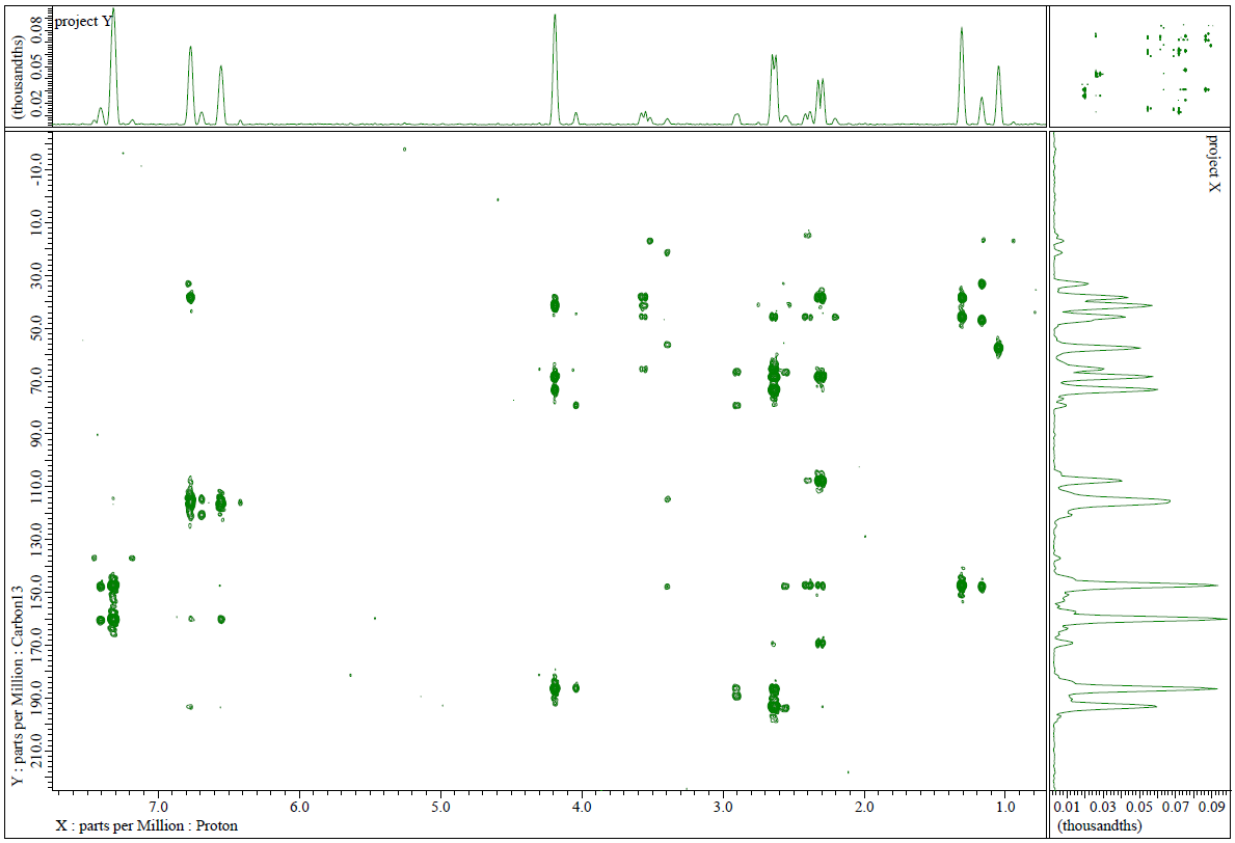

Figure S8. 1H-13C-HMBC spectrum of α-doxycycline reference compound.

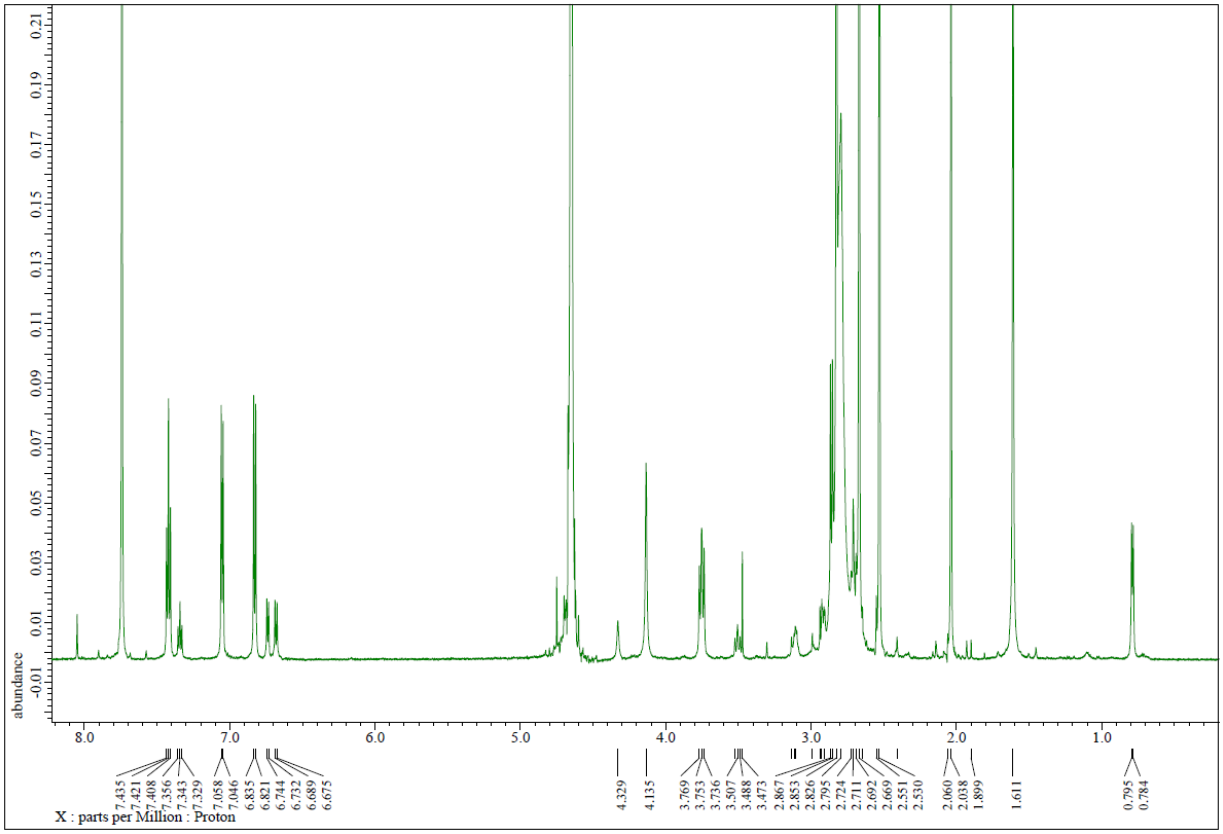

Figure S9. 1H-NMR spectrum of β-doxycycline (reaction products obtained without β-cyclodextrin).

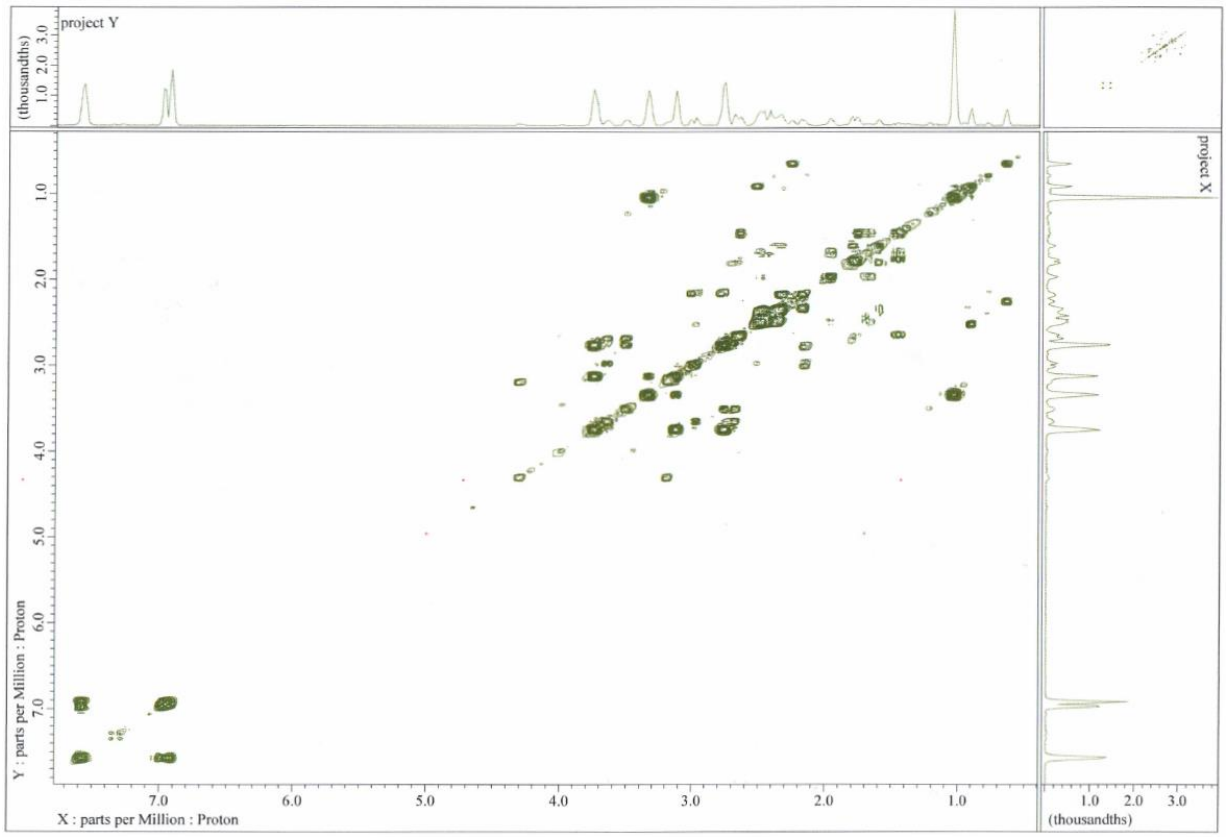

Figure S10. COSY spectrum of β-doxycycline (reaction products obtained without β-cyclodextrin).

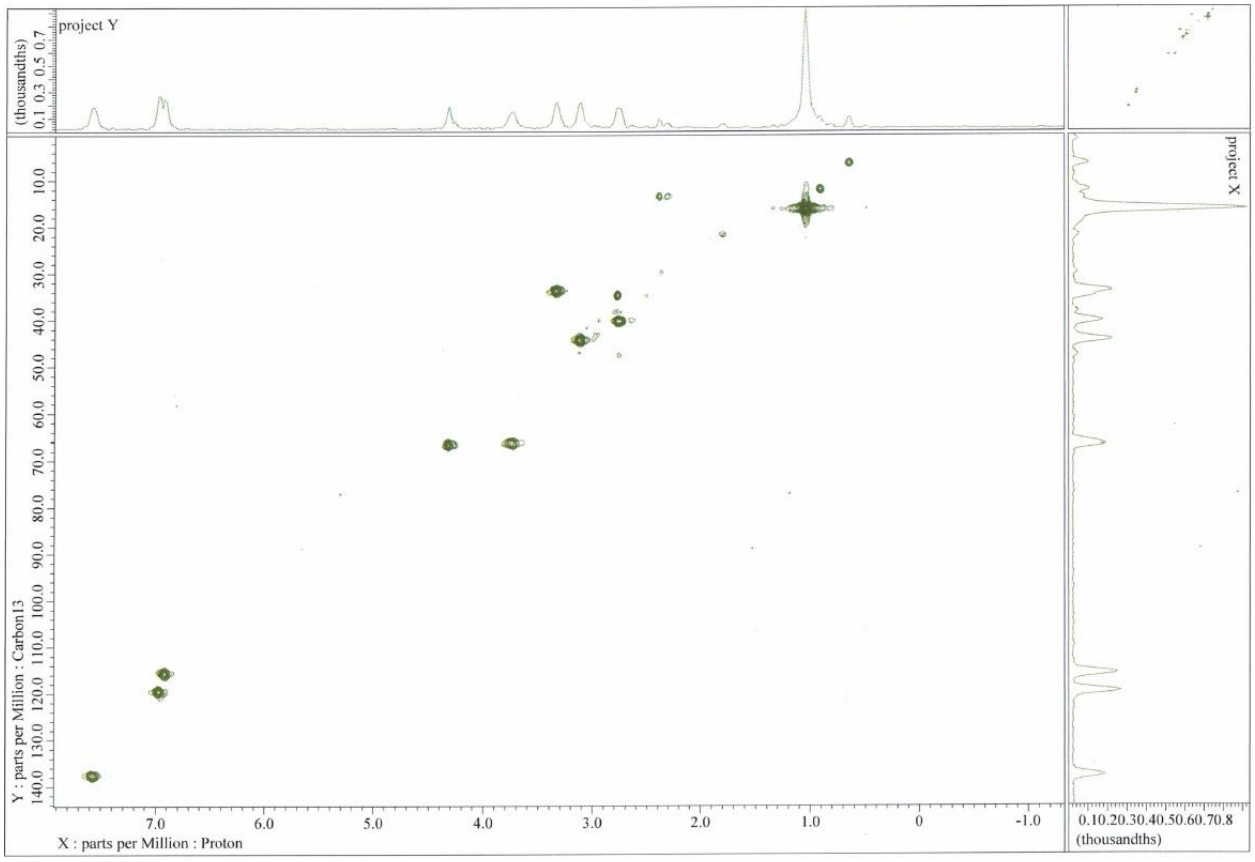

Figure S11. 1H-13C HMQC spectrum of β-doxycycline (reaction products obtained without β-cyclodextrin).

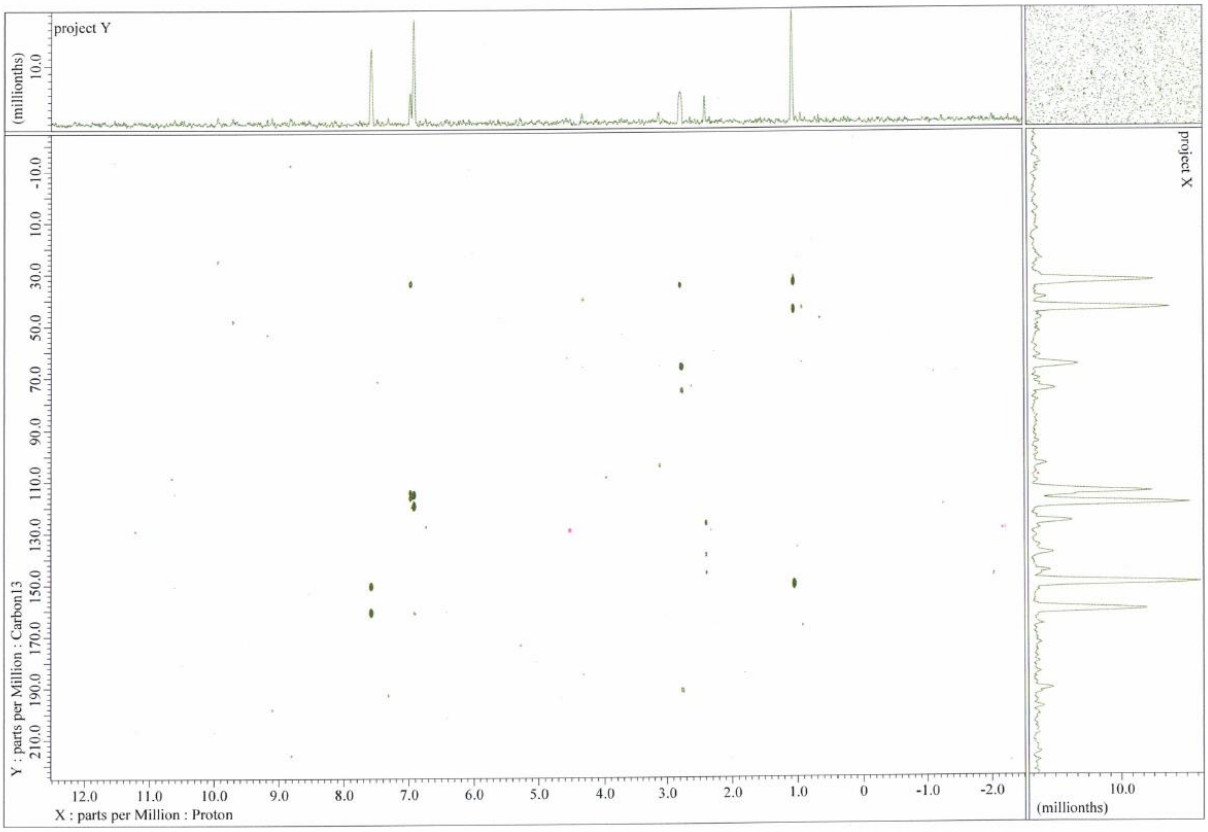

Figure S12. 1H-13C HMBC spectrum of β-doxycycline (reaction products obtained without β-cyclodextrin).

HPLC-MS analysis

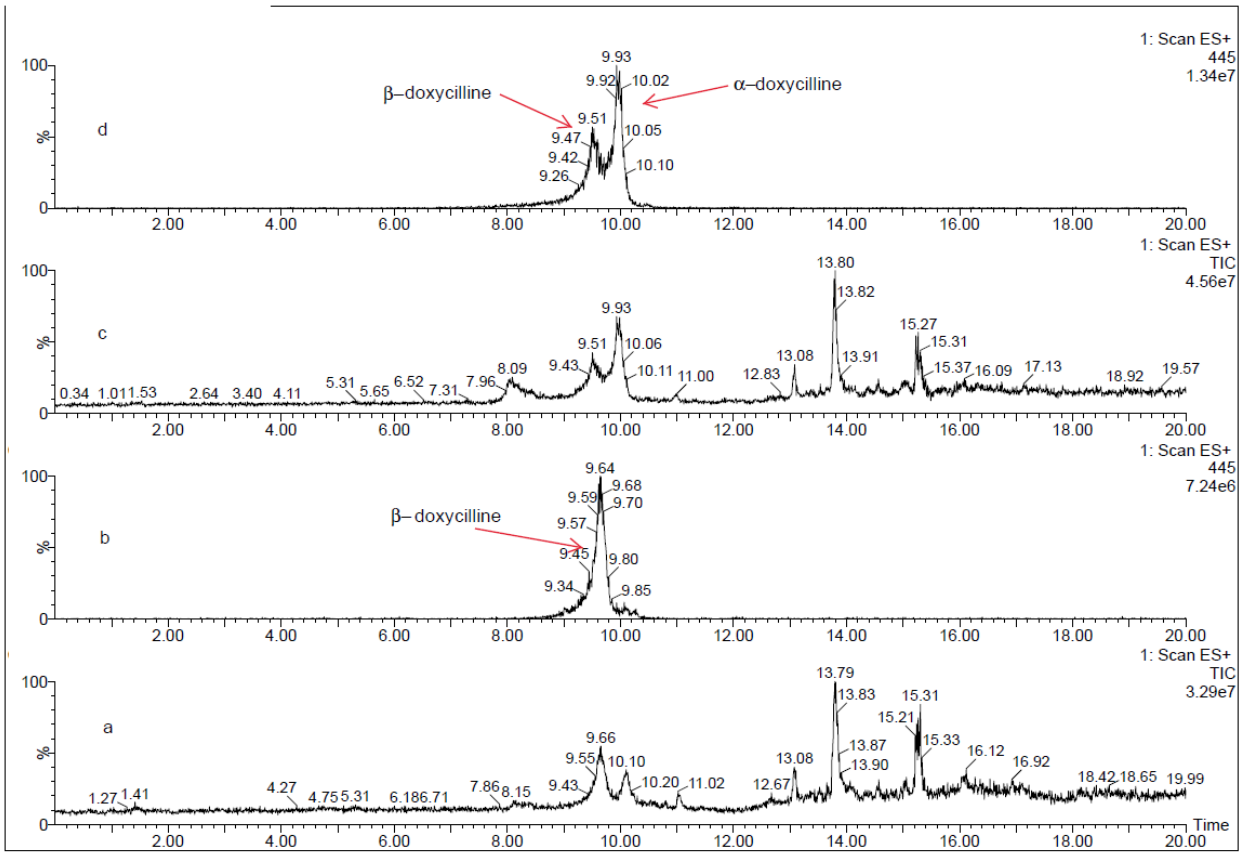

Figure S13. Example of HPLC-MS trace of a reaction product obtained without CD addition (trace "a" total ion current, trace "b" extraction of ion with m/z= 445), before and after (trace "c" total ion current, trace "d" extraction of ion with m/z= 445) the addition of *α*-doxycycline reference compound.

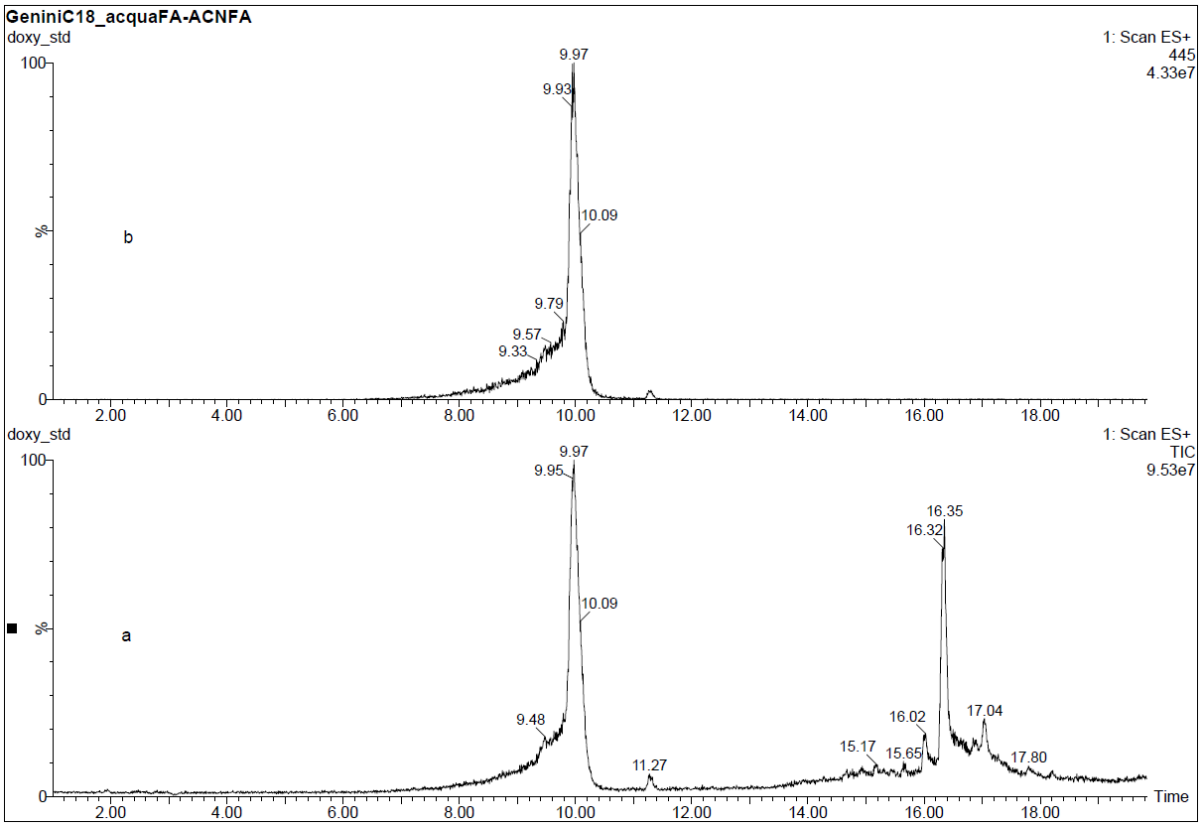

Figure S14. HPLC-MS trace of α-doxycycline reference material (trace "a" total ion current, trace "b" extraction of ion with m/z= 445).

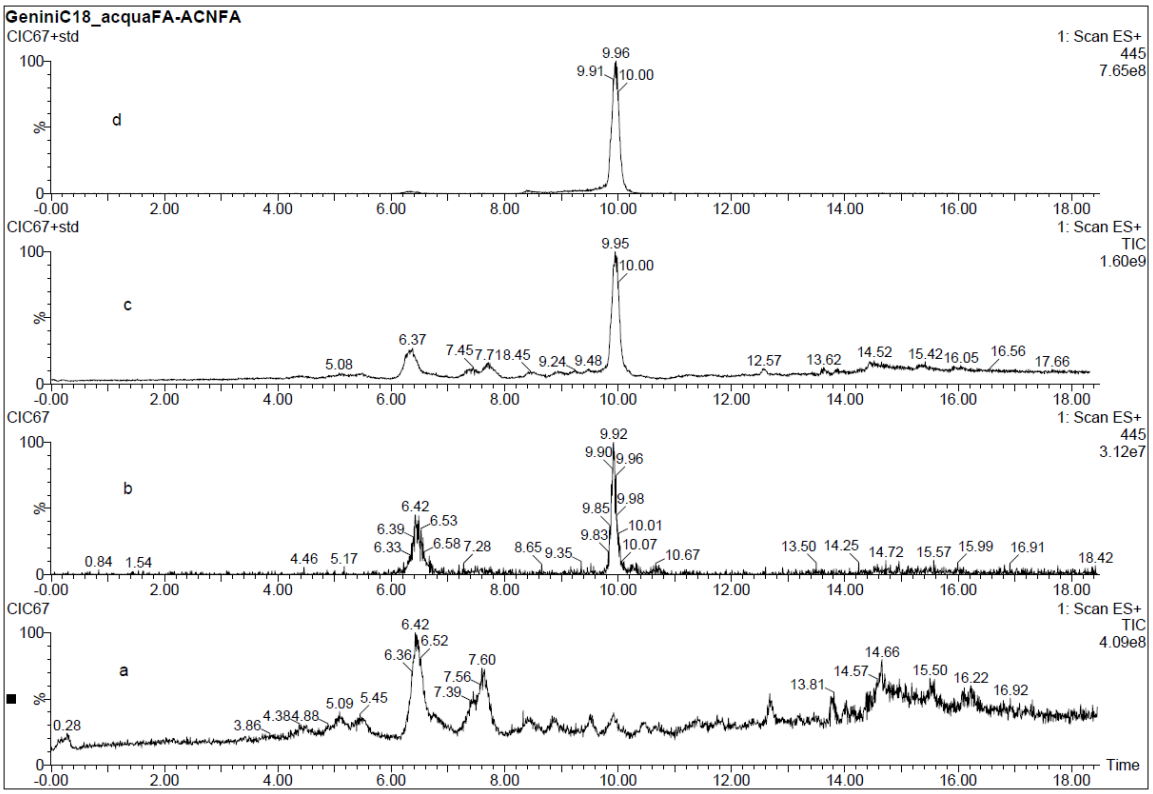

Figure S15. Example of HPLC-MS trace of reaction product obtained in presence o cyclodextrin (trace "a" total ion current, trace "b" extraction of ion with m/z= 445), before and after (trace "c" total ion current, trace "d" extraction of ion with m/z= 445) the addition of α-doxycycline reference compound.