Supporting Information

One-step synthesis of differently bis(functionalized) isoxazoles by cycloaddition of carbamoylnitrile oxide with β-keto esters

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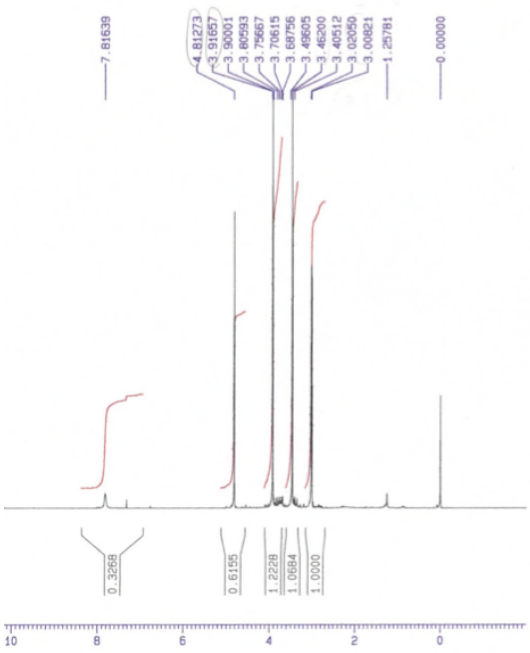
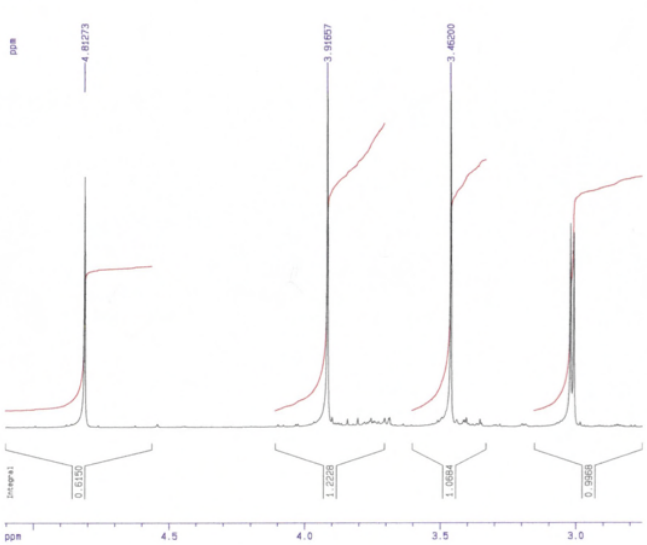
4-Methoxycarbonyl-5-methoxymethyl-3-(*N*-methylcarbamoyl)isoxazole (5f)

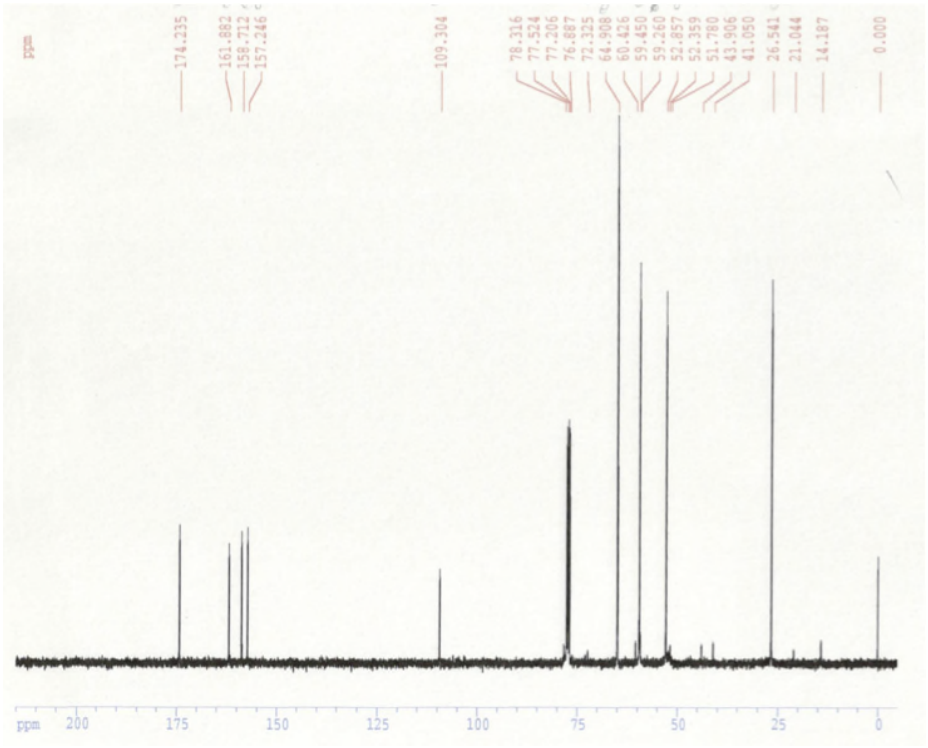
Colorless needles (from benzene/hexane = 1/1). Mp 40-44 °C. IR (KBr) 3267, 1723, 1671 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.02 (d, J = 4.9 Hz, 3H), 3.49 (s, 3H), 3.92 (s, 3H), 4.82 (s, 2H), 7.7-7.8 (br, 1H); ^{13}C NMR ($CDCl_3$) δ 26.5 (CH_3), 52.9 (CH_3), 59.5 (CH_3), 64.9 (CH_2), 109.3 (C), 157.3 (C), 158.7 (C), 161.9 (C), 174.2 (C); MS (FAB) m/z = 229 (M^++1, 100%). Anal. Calcd for $C_9H_{12}N_2O_5$: C, 47.37; H, 5.30; N, 12.28. Found: C, 47.01; H, 5.67; N, 12.42.

^1H NMR ($CDCl_3$)





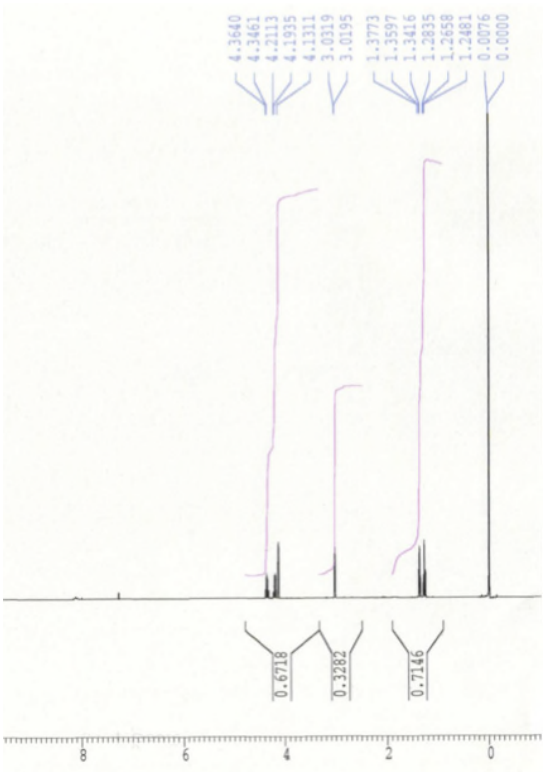
^{13}C NMR ($CDCl_3$)

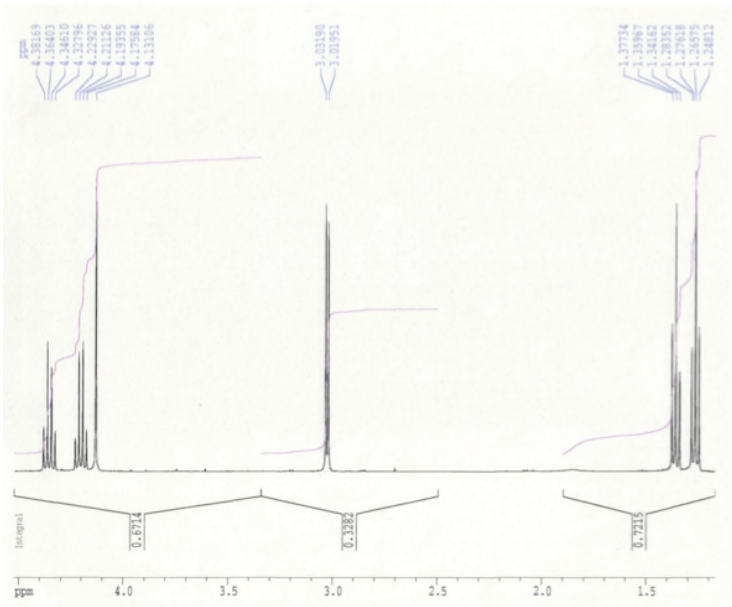


4-Ethoxycarbonyl-5-ethoxycarbonylmethyl-3-(*N*-methylcarbamoyl)isoxazole (5g)

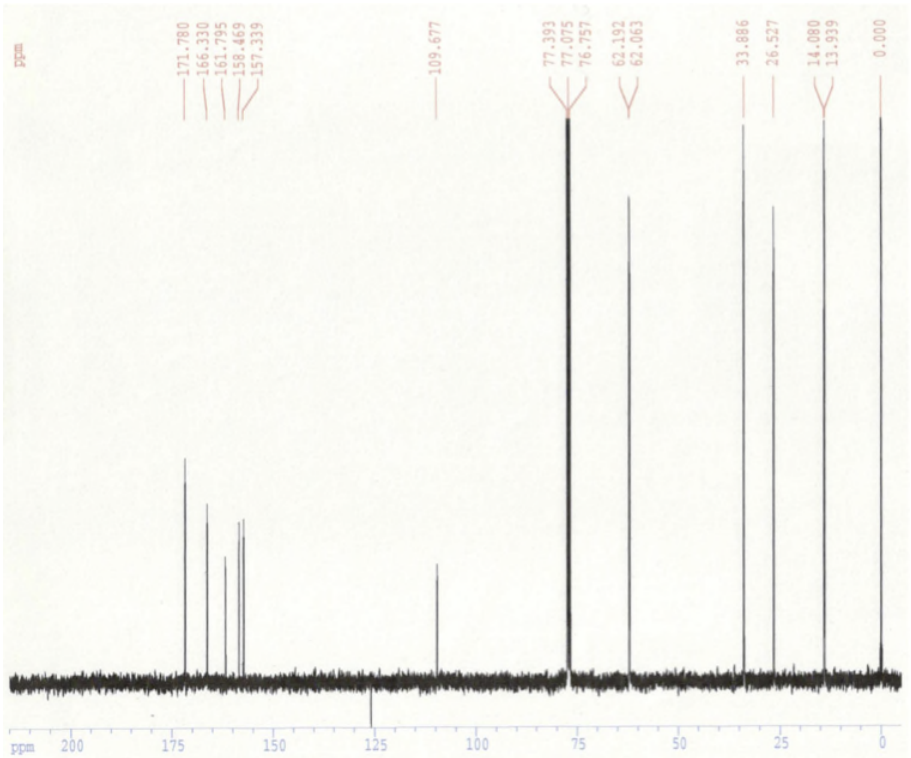
Brown oil. IR (KBr) 3303, 1739, 1674 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.26 (t, J = 7.1 Hz, 3H), 1.36 (t, J = 7.1 Hz, 3H), 3.02 (d, J = 5.0 Hz, 3H), 4.13 (s, 2H), 4.20 (q, J = 7.1 Hz, 2H), 4.35 (q, J = 7.1 Hz, 2H), 8.2-8.4 (br, 1H); ^{13}C NMR ($CDCl_3$) δ 13.9 (CH_3), 14.1 (CH_3), 26.5 (CH_3), 33.9 (CH_2), 62.1 (CH_2), 109.7 (C), 157.3 (C), 158.5 (C), 161.8 (C), 166.3 (C), 171.8 (C); MS (FAB) m/z = 285 (M^++1, 100%). Anal. Calcd for $C_{12}H_{16}N_2O_6$: C, 50.70; H, 5.67; N, 9.85. Found: C, 50.54; H, 5.85; N, 9.63.

^{1}H NMR ($CDCl_3$)





^{13}C NMR ($CDCl_3$)



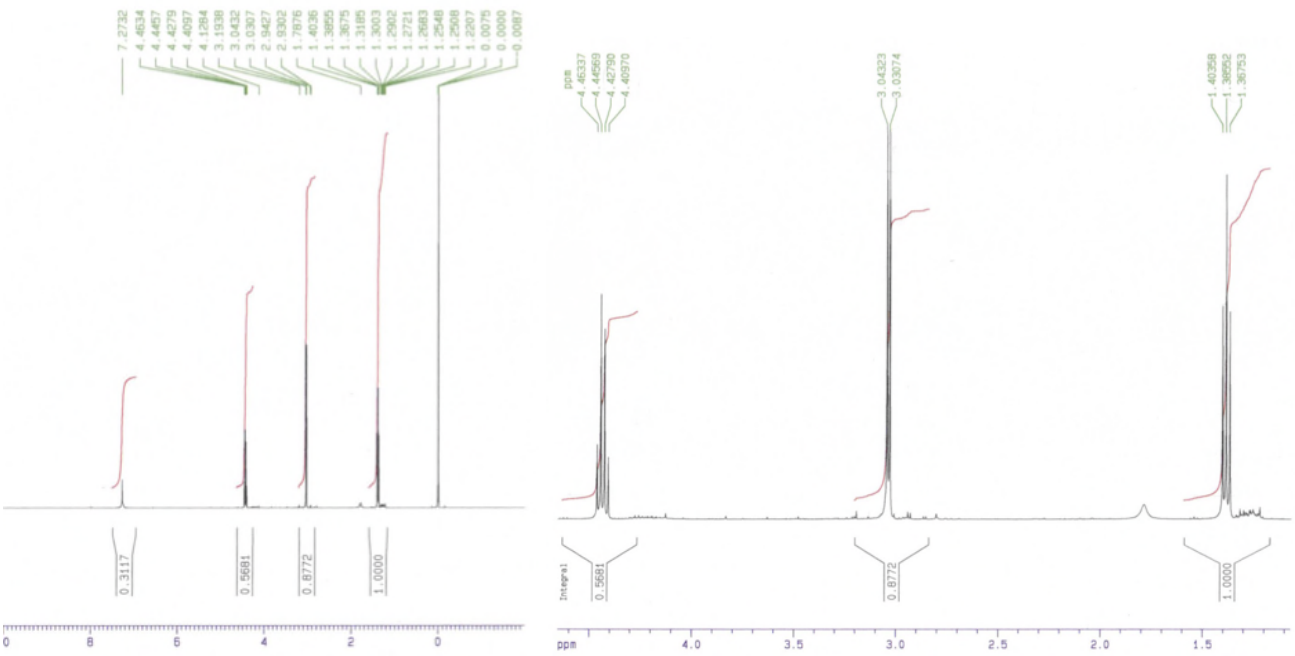
Cycloaddition using sodium enolate of ethyl trifluoroacetate 4h

To a solution of ethyl trifluoroacetoacetate **7h** (0.59 mL, 5 mmol) in ethanol (10 mL), sodium (115 mg, 5 mmol) was gradually added. After stirring at room temperature for 15 min, the mixture was dried up under reduced pressure, and then the residue was dissolved in THF (10 mL). To the solution, a solution of nitroisoxazolone **1** (144 mg, 1 mmol) in acetonitrile (10 mL) was added, and the resultant mixture was stirred at room temperature for 3 d. After addition of 1 M hydrochloric acid (10 mL, 10 mmol), solvents were removed under reduced pressure. The resultant aqueous solution was extracted with chloroform (50 mL × 5), and the organic layer was dried over magnesium sulfate, and concentrated. The residue was subjected to the column chromatography on silica gel to afford cycloadduct **5h** (125 mg, 0.51 mmol, 51%) eluted with ethyl acetate. Further purification was performed by recrystallization from a mixed solvent of hexane and benzene (1/1).

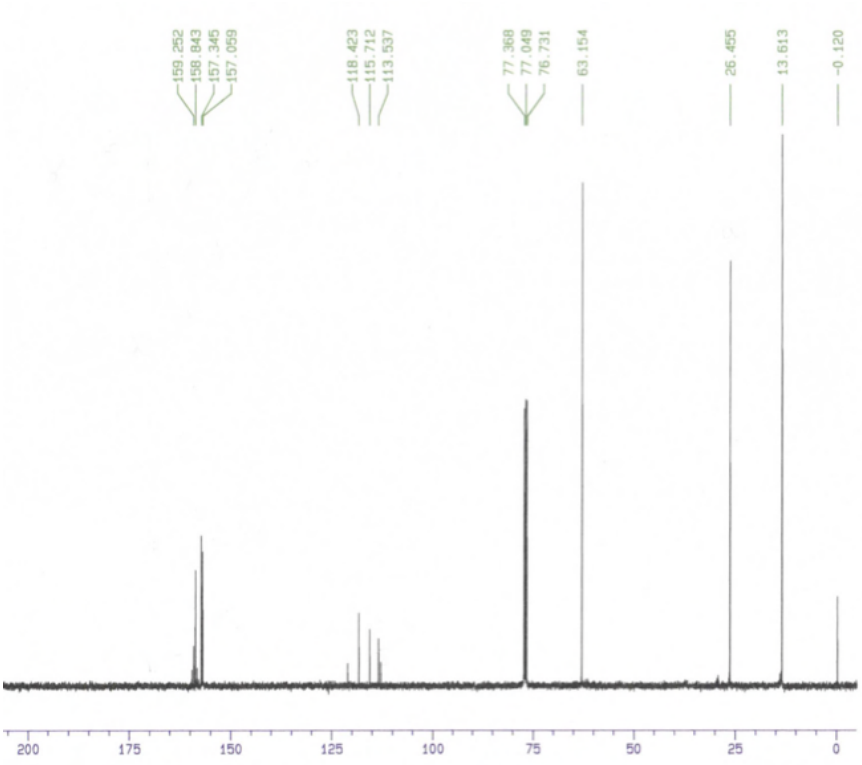
4-Ethoxycarbonyl-5-trifluoromethyl-3-(*N*-methylcarbamoyl)isoxazole (5h)

Colorless needles (from benzene/hexane = 5/4). Mp 81-83 °C. IR (KBr) 3291, 1745, 1656 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.39 (t, J = 7.1 Hz, 3H), 3.04 (d, J = 5.0 Hz, 3H), 4.44 (q, J = 7.1 Hz, 2H), 7.2-7.4 (br, 1H); ^{13}C NMR ($CDCl_3$) δ 13.6 (CH_3), 26.5 (CH_3), 63.2 (CH_2), 113.5 (C), 117.1 (q, J_{C-F} = 271 Hz, CF_3), 157.1 (C), 157.35 (C), 158.8 (C), 159.0 (q, J_{C-F} = 41 Hz, C-CF_3); MS (FAB) m/z = 213 (M^++1, 100%). Anal. Calcd for $C_9H_9N_2O_4F_3$: C, 40.61; H, 3.41; N, 10.52. Found: C, 40.80; H, 3.36; N, 10.63.

^{1}H NMR ($CDCl_3$)

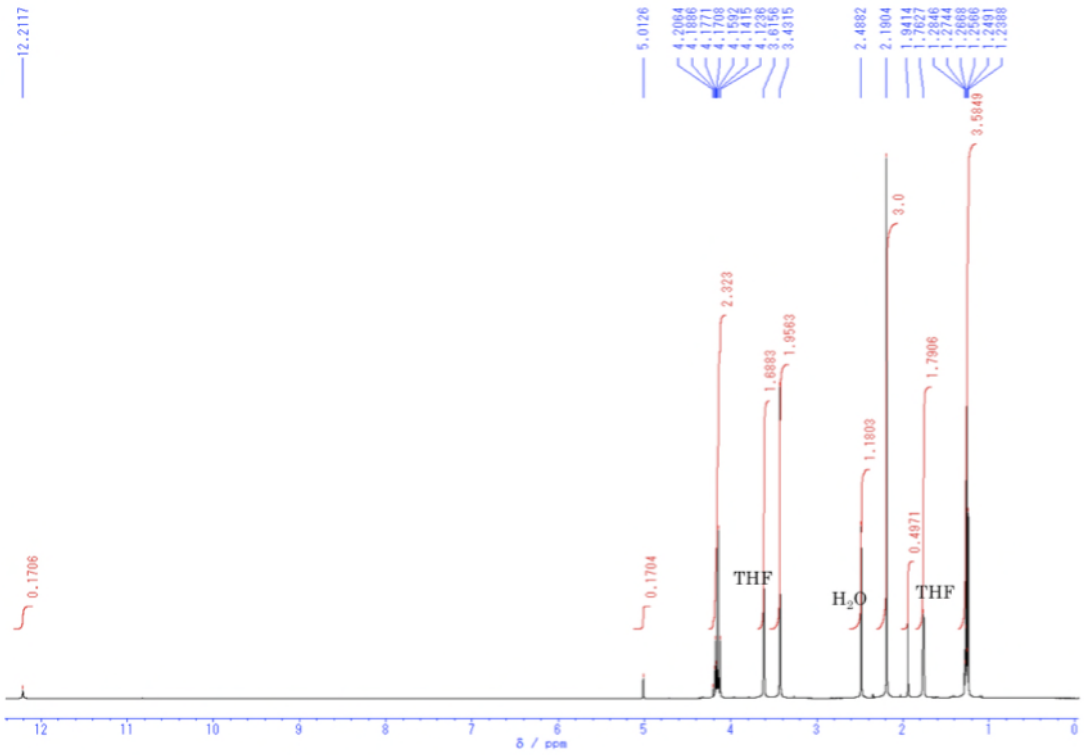


^{13}C NMR ($CDCl_3$)



Ethyl Acetoacetate (7a)

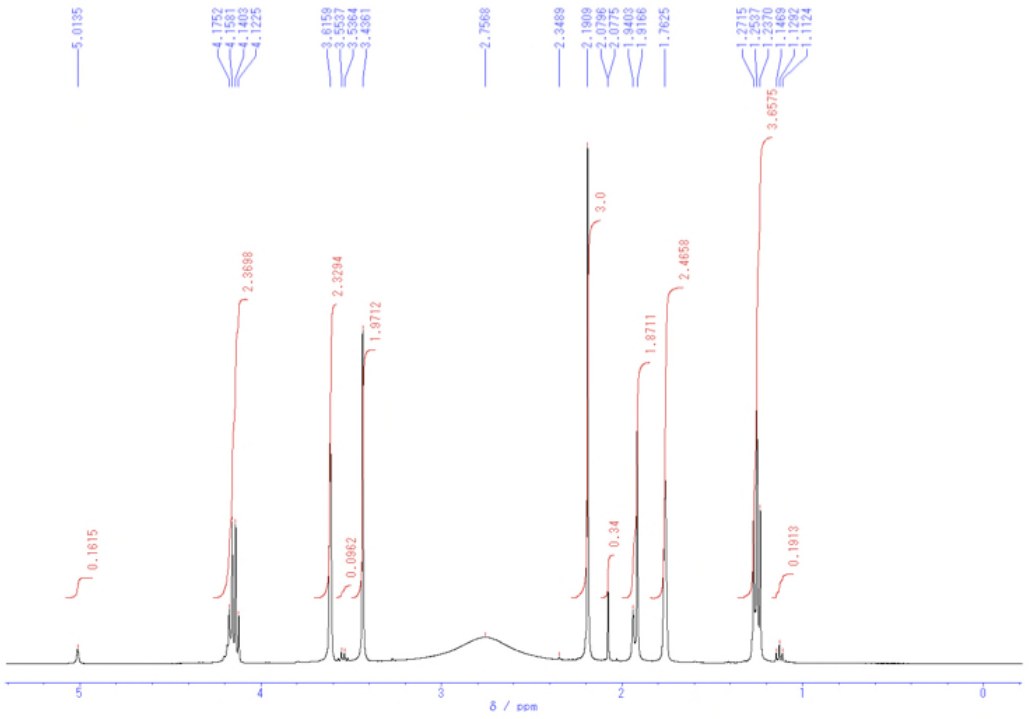
^{1}H NMR (THF-d_8) Keto form δ 1.25 (t, J = 7.1 Hz, 3H$_k$), 2.19 (s, 3H$_k$), 3.43 (s, 2H$_k$), 4.15 (q, J = 7.1 Hz, 2H$_k$); Enol form δ 1.27 (t, J = 7.1 Hz, 3H$_e$), 1.94 (s, 3H$_e$), 4.18 (q, J = 7.1 Hz, 2H$_e$), 5.01 (s, 1H$_e$), 12.21 (br s, 1H$_e$). H$_k$/H$_e$ = 85/15.



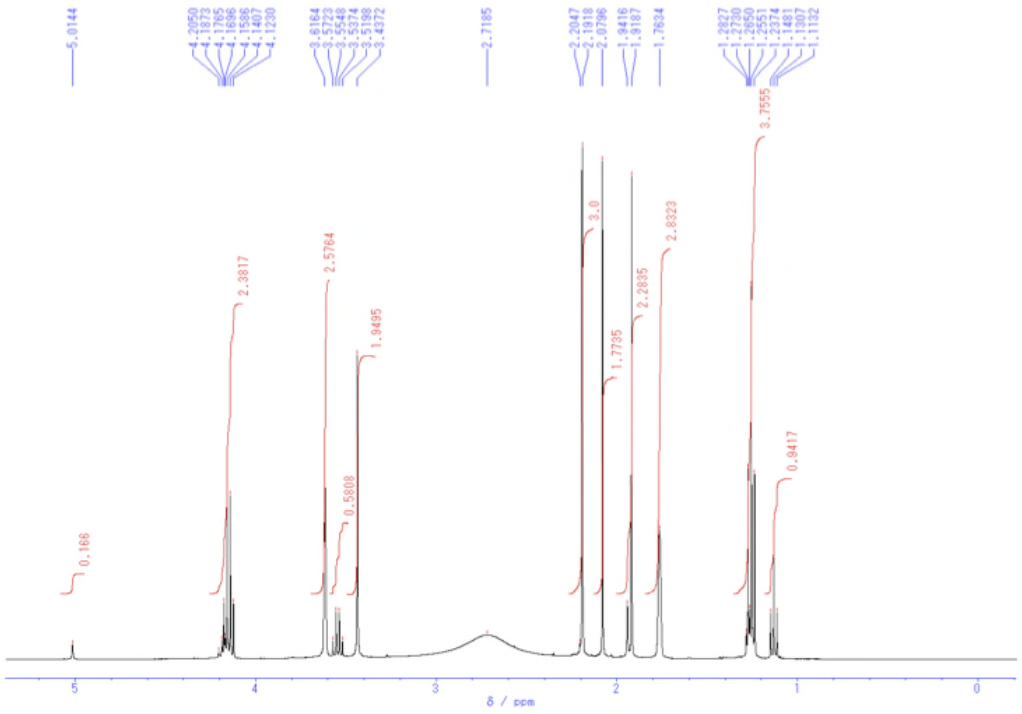
A mixture of ethyl acetoacetate (7a) and magnesium acetate

^{1}H NMR of magnesium enolate **9a** (THF-d_8) δ 1.13 (t, J = 7.0 Hz, 3H), 2.08 (s, 6H), 3.55 (q, J = 7.0 Hz, 2H). A signal of olefinic proton is overlapped with signals around 4.15 ppm, which is confirmed by comparison of integral values observed in several spectra with different heating time.

After heating at 70 °C for 1 d



After heating at 70 °C for 4 d



References

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