

Mechanism Study of Copper-mediated One-pot Reductive Amination of Aryl Halides Using Trimethylsilyl Azide

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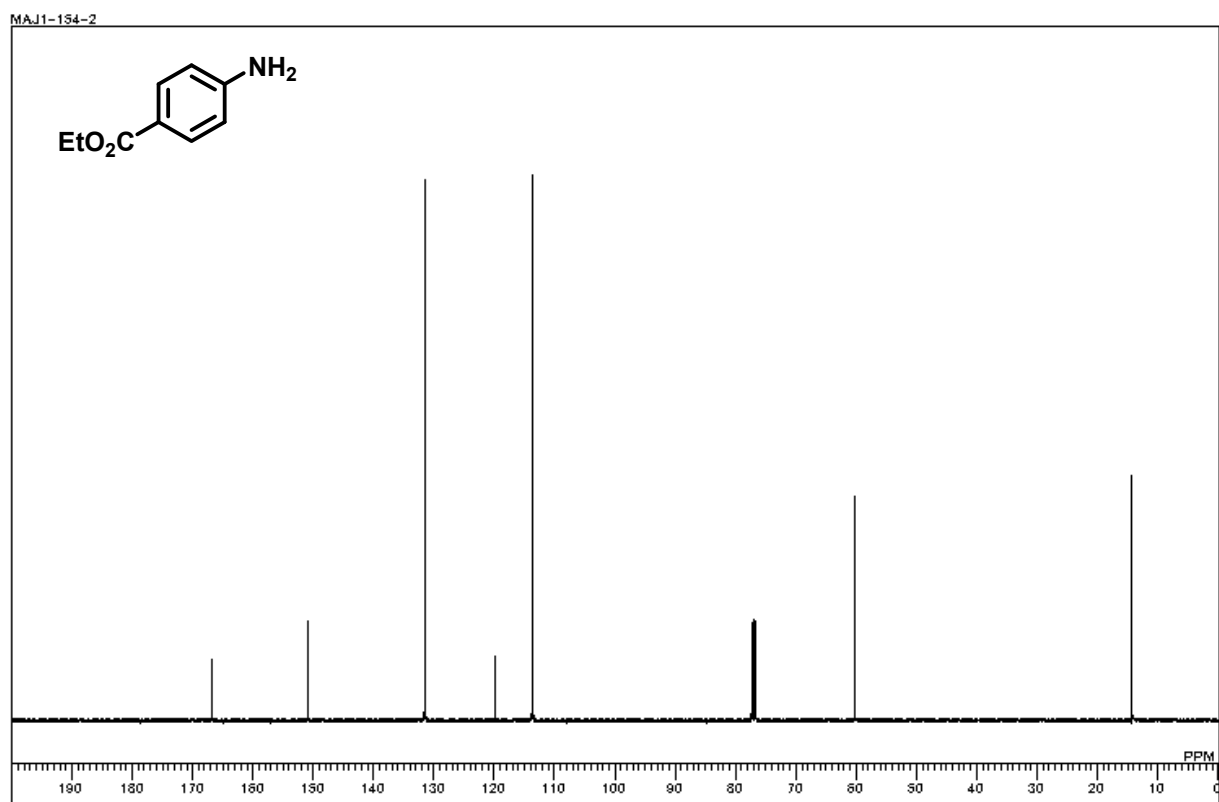
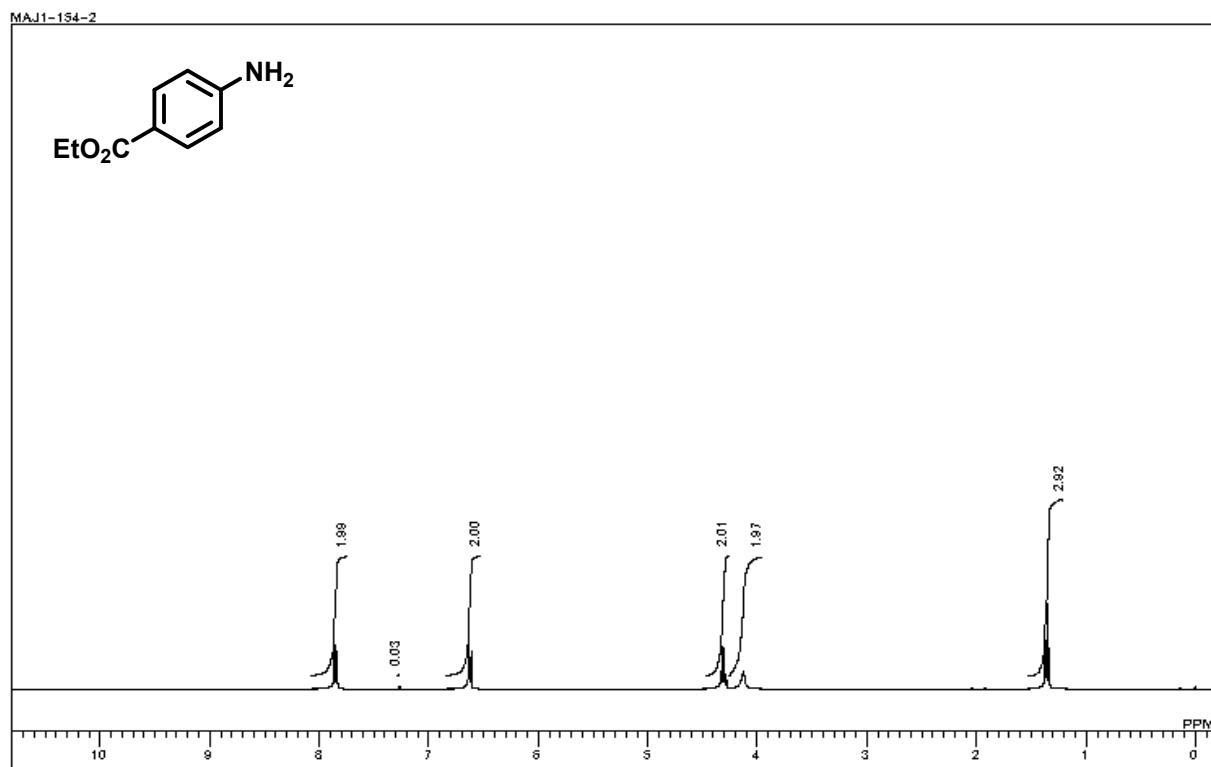
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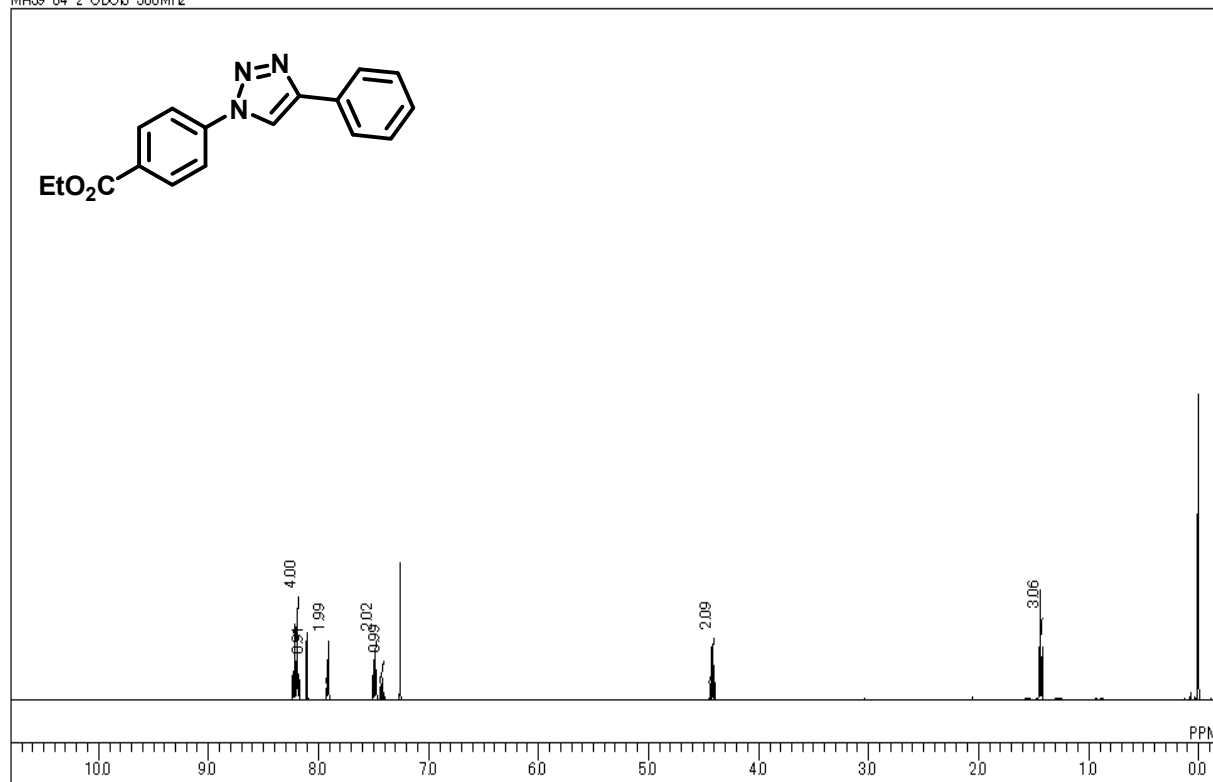
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1. ^1H and ^{13}C NMR spectra of ethyl 4-aminobenzoate (2).

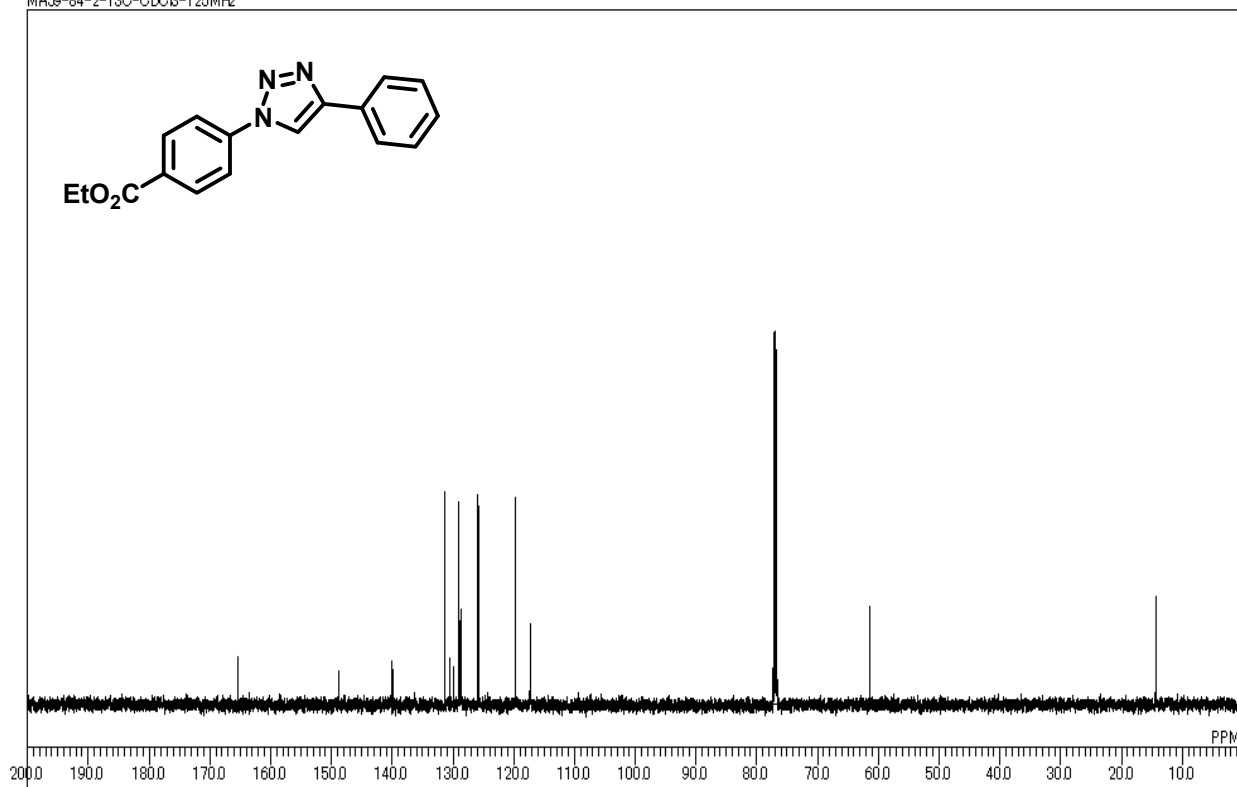


2. ^1H and ^{13}C NMR spectra of 4-(4-phenyl-1*H*-1,2,3-triazol-yl)benzoate (5).

MAJ9-84-2-CDCl₃-500MHz

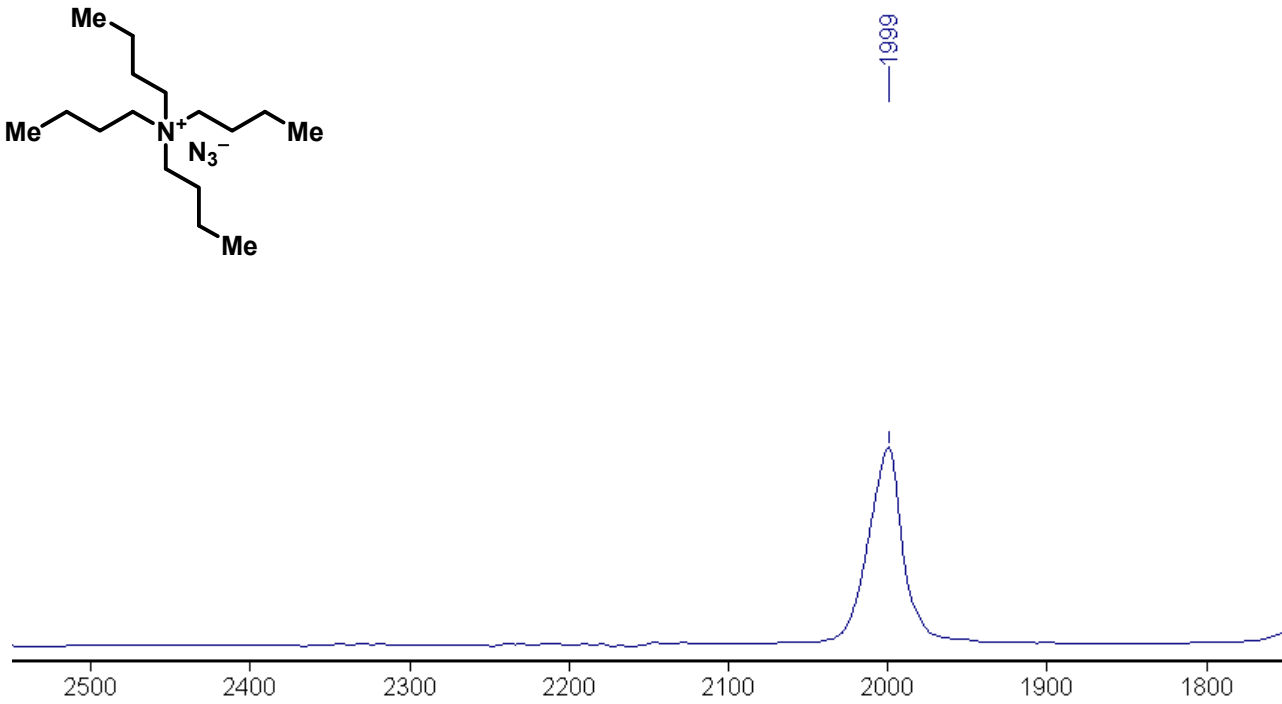
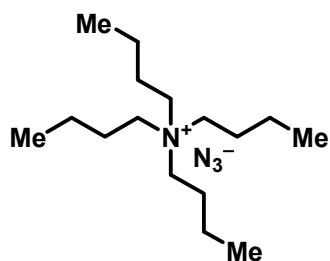


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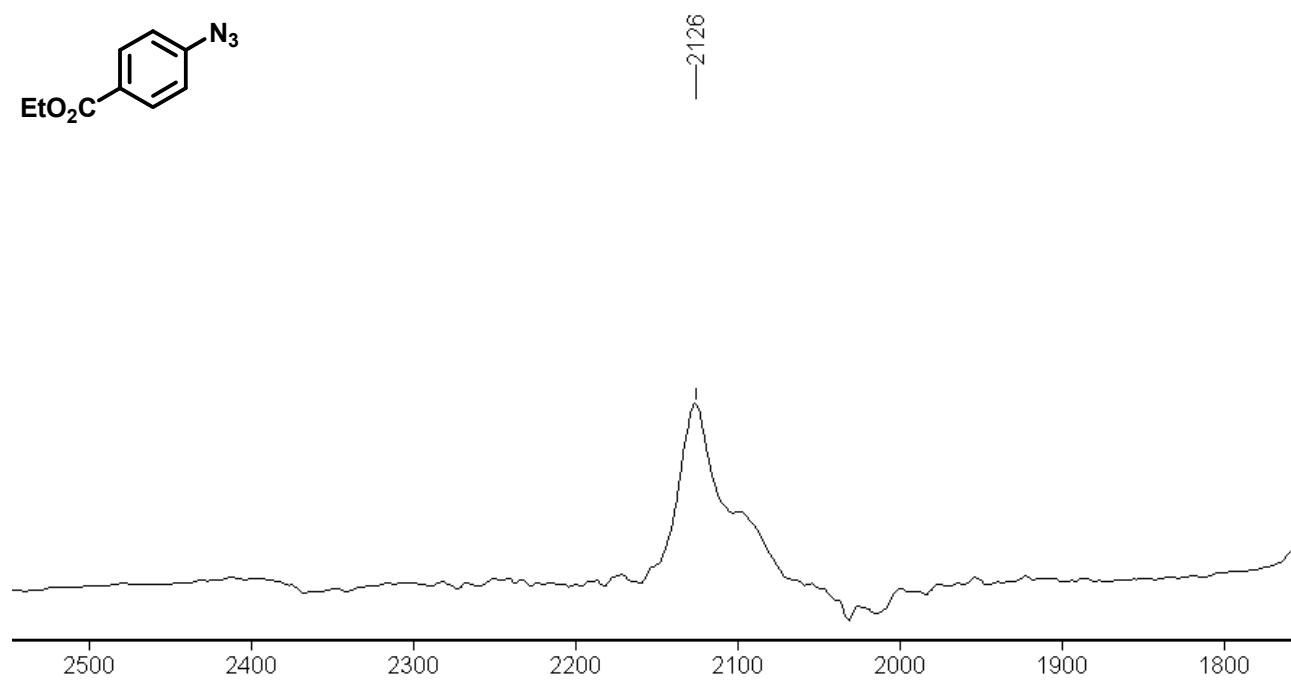
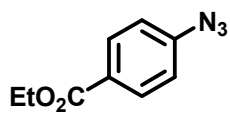


3. IR spectra

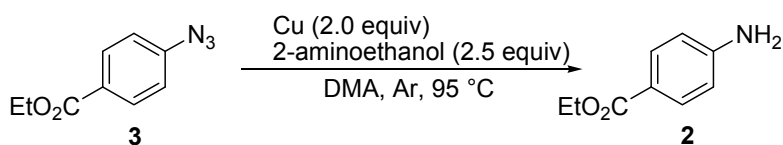
(1) Tetrabutylammonium azide in DMA



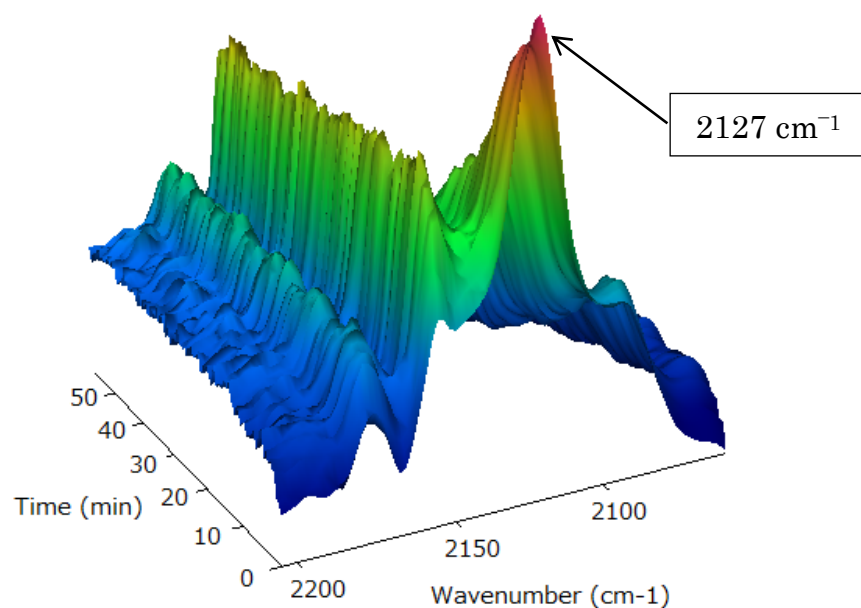
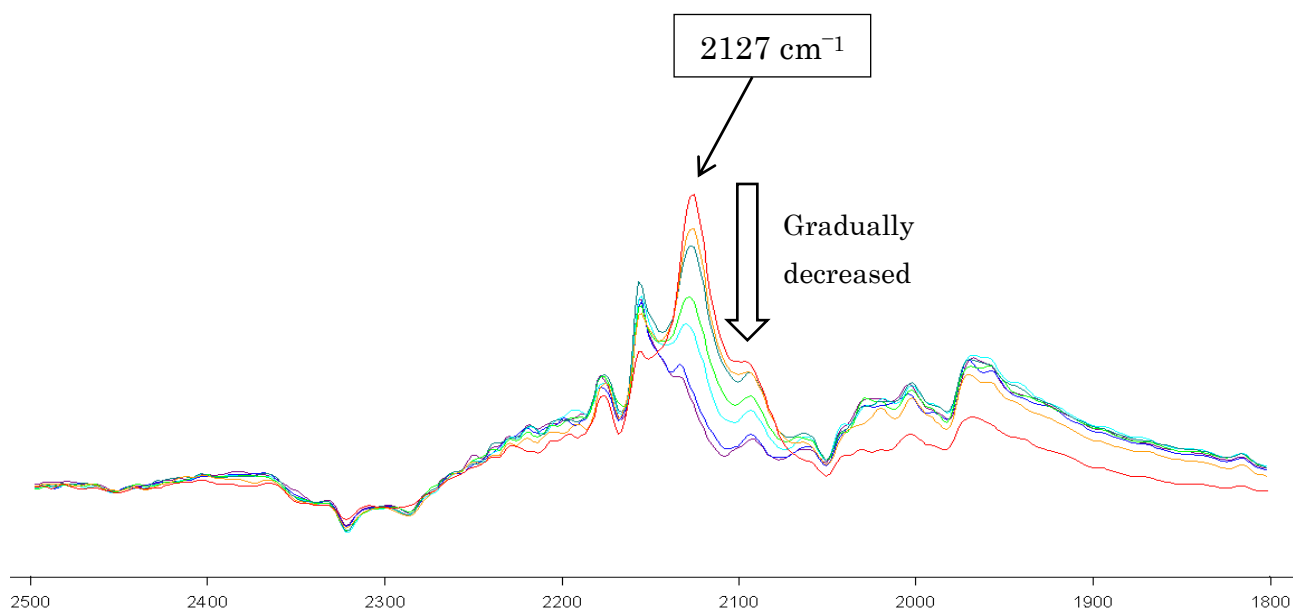
(2) Ethyl 4-azidobenzoate (3) in DMA



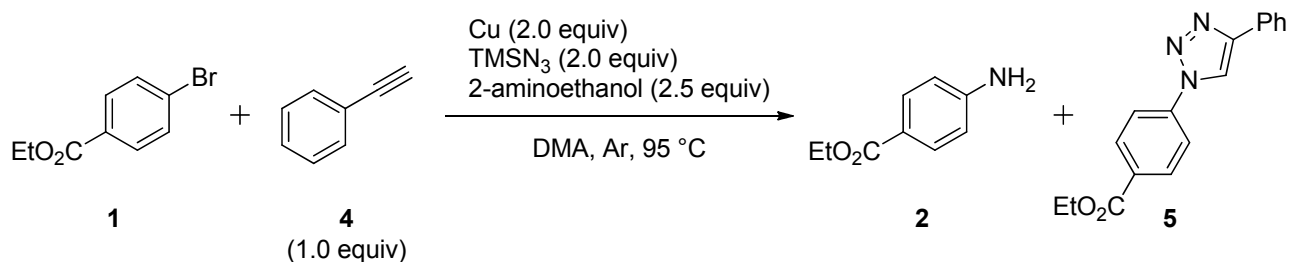
4. Time-course study using reaction monitoring FT-IR for the reaction of ethyl 4-azidobenzoate (3) with copper powder, and 2-aminoethanol in DMA at 95 °C for 1 h



A mixture of ethyl 4-azidobenzoate (**3**) (161 mg, 839 μmol), copper powder (107 mg, 1.68 mmol), and 2-aminoethanol (126 μL , 2.10 mmol) in DMA (1.7 mL) in a 10-mL two-neck flask was stirred under an Ar atmosphere (balloon) at 95 °C, and the IR peak of the mixture was monitored vs. time.

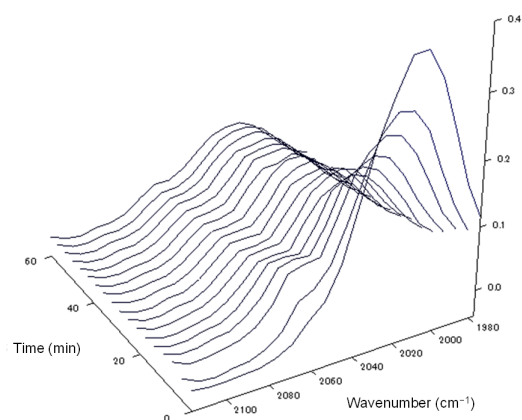
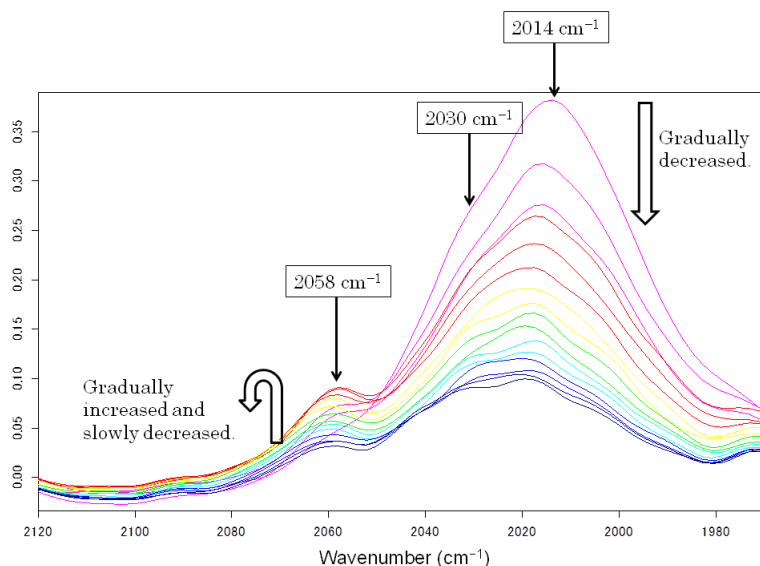


5. Time-course study using reaction monitoring FT-IR for the reaction of ethyl 4-bromobenzoate (1) with copper powder, and 2-aminoethanol in DMA in the presence of ethynylbenzene (4) at 95 °C

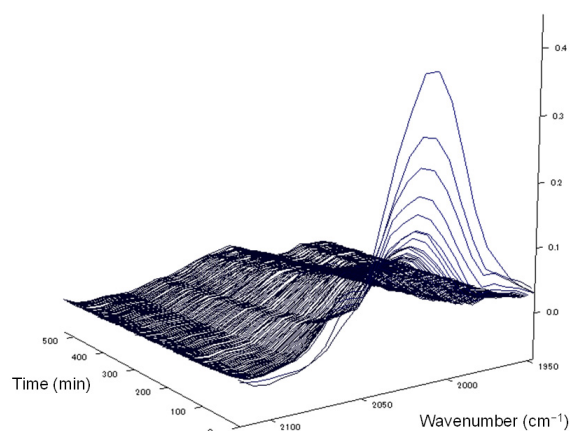
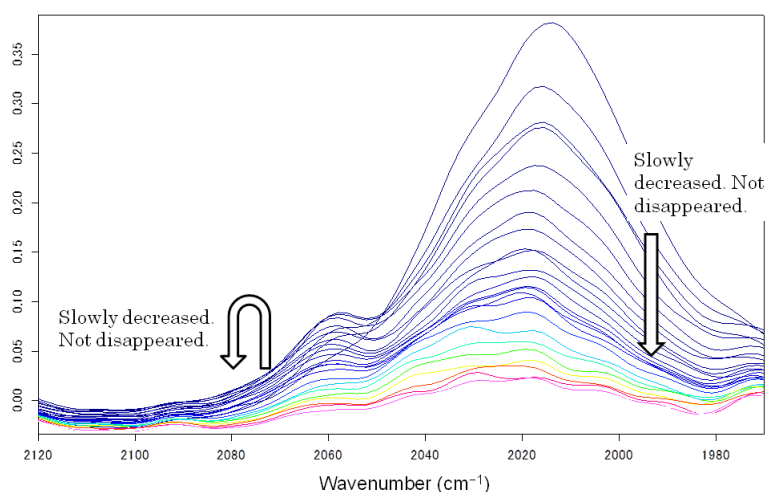


A mixture of ethyl 4-bromobenzoate (1) (229 mg, 1.00 mmol), ethynylbenzene (4) (102 mg, 1.00 mmol), copper powder (127 mg, 2.00 mmol), 2-aminoethanol (151 μ L, 2.50 mmol), and TMSN₃ (266 μ L, 2.00 mmol) in DMA (2 mL) in a 20-mL two-neck flask was stirred under an Ar atmosphere (balloon) at 95 °C, and the IR peak of the mixture was monitored vs. time.

(1) 0–1 h. (pink \rightarrow red \rightarrow yellow \rightarrow green \rightarrow sky blue \rightarrow blue \rightarrow grey)



(2) 0–9 h.

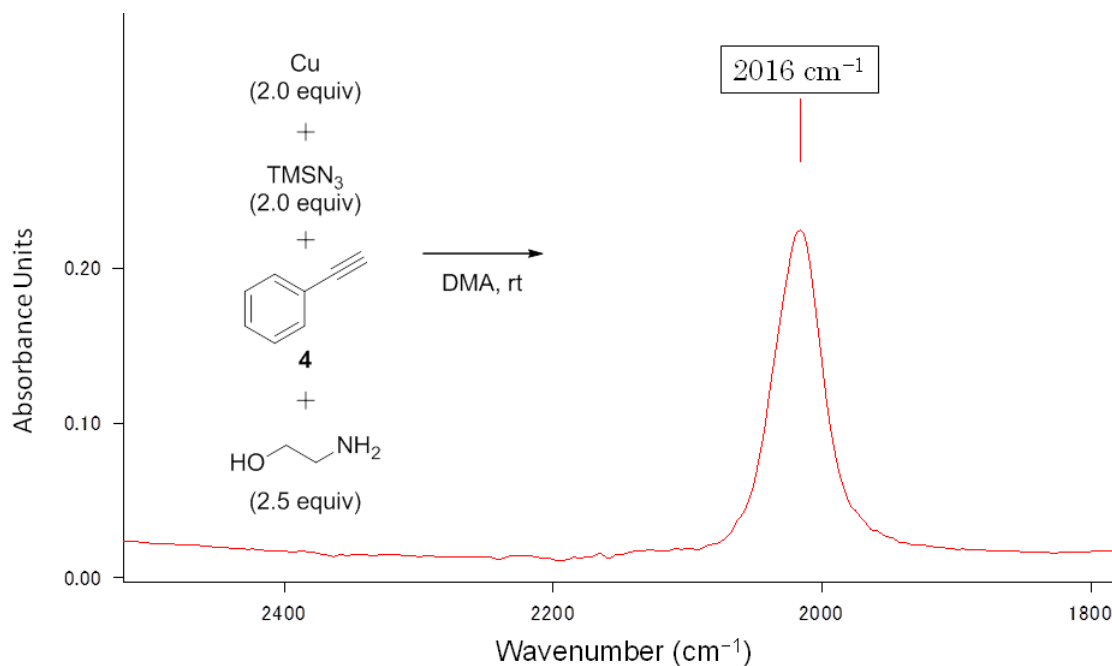


The copper-mediated amination of ethyl 4-bromobenzoate (**1**) with TMSN_3 and 2-aminoethanol in DMA in the presence of ethynylbenzene (**4**) was monitored by the reaction-monitoring FT-IR spectrometer. The peaks at 2014 and 2030 (shoulder) cm^{-1} were initially observed, and the peak strength gradually and slowly decreased over more than 9 hours. The new peak at 2058 cm^{-1} , which is considered to be for CuN_3 , appeared just after heating, and the peak also decreased over hours. These phenomena suggest that the reaction is likely to proceed in a different manner from the case without **4**; the 2030 cm^{-1} peak was not observed, the peak at 2012 cm^{-1} disappeared within 1 h, and newly observed peak at 2058 cm^{-1} was not declined after 1 h, in the absence of **4**. The difference might come from the possible involvement of copper species with acetylene, e.g., formation of copper acetylide.

Furthermore, the generation of aryl azide, ethyl 4-azidobenzoate (**3**), as the intermediate, was not confirmed by this experiment. It was also difficult to observe the formation of triazole (**5**) because of its overlapped IR peaks with those of other materials, such as starting materials and DMA.

(3) The influence of ethynylbenzene (**4**) on IR spectrum of a mixture of copper, TMSN_3 , and 2-aminoethanol in the absence of ethyl 4-bromobenzoate (**1**)

Ethynylbenzene (**4**) (102 mg, 1.00 mmol), copper powder (127 mg, 2.00 mmol), 2-aminoethanol (151 μL , 2.50 mmol), and TMSN_3 (266 μL , 2.00 mmol) in DMA (2 mL) was mixed and stirred at rt, and the IR absorbance of the mixture was measured.



A slight change was observed in the IR spectrum by the addition of ethynylbenzene (**4**) in the mixture of copper, and TMSN_3 in DMA, since the IR absorbance was detected at 2012–2013 cm^{-1} regardless of the existence of ethyl 4-bromobenzoate (**1**) in the absence of **4** (Figures 1–3).