

Supplementary Materials for

Catalyst-Free Ullmann Coupling in Aqueous Microdroplets

Ming-Yang Jia^{†1}, Yue-Wen Zhou^{†1}, Jun-Lei Yang¹, Qinlei Liu^{*1} and Zhen-Feng Cai^{*1}

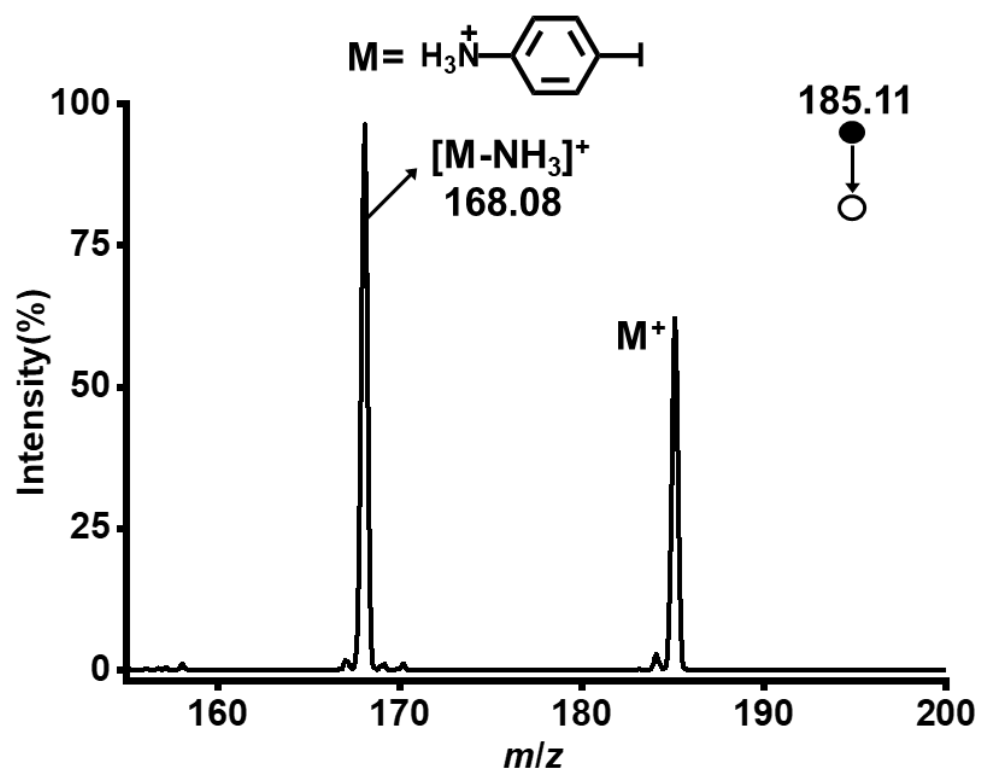
¹ Key Laboratory of Green Chemistry and Technology of Ministry of Education, College of Chemistry, Sichuan University 29 Wangjiang Road, Chengdu 610064 (P. R. China).

This PDF file includes:

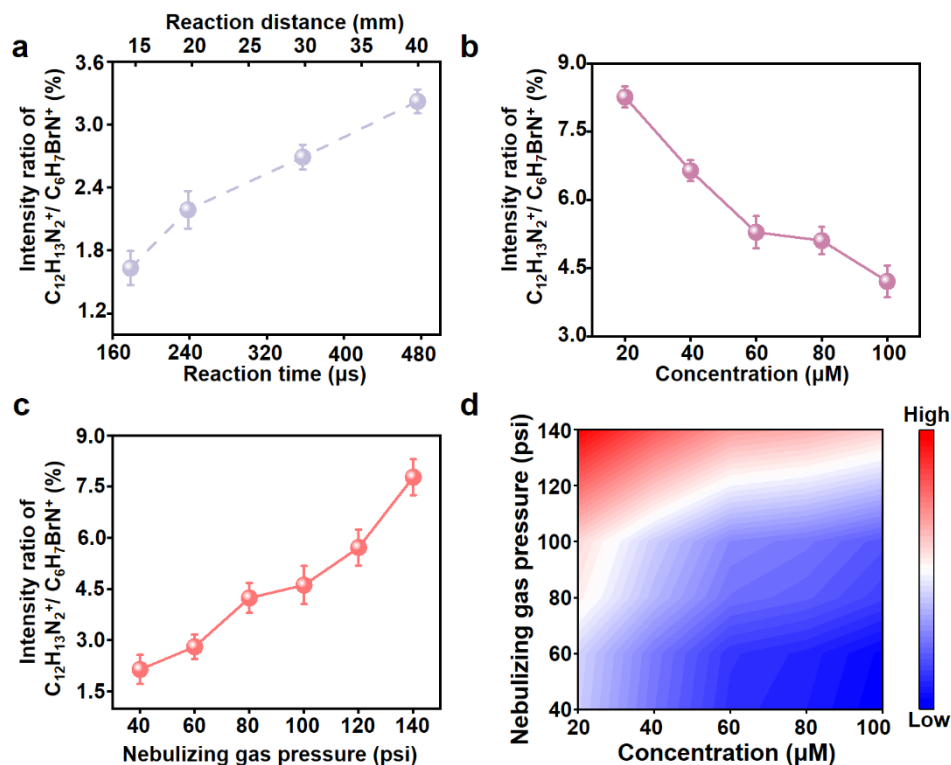
Supplementary Figs. 1 to 52

Tables S1-S4

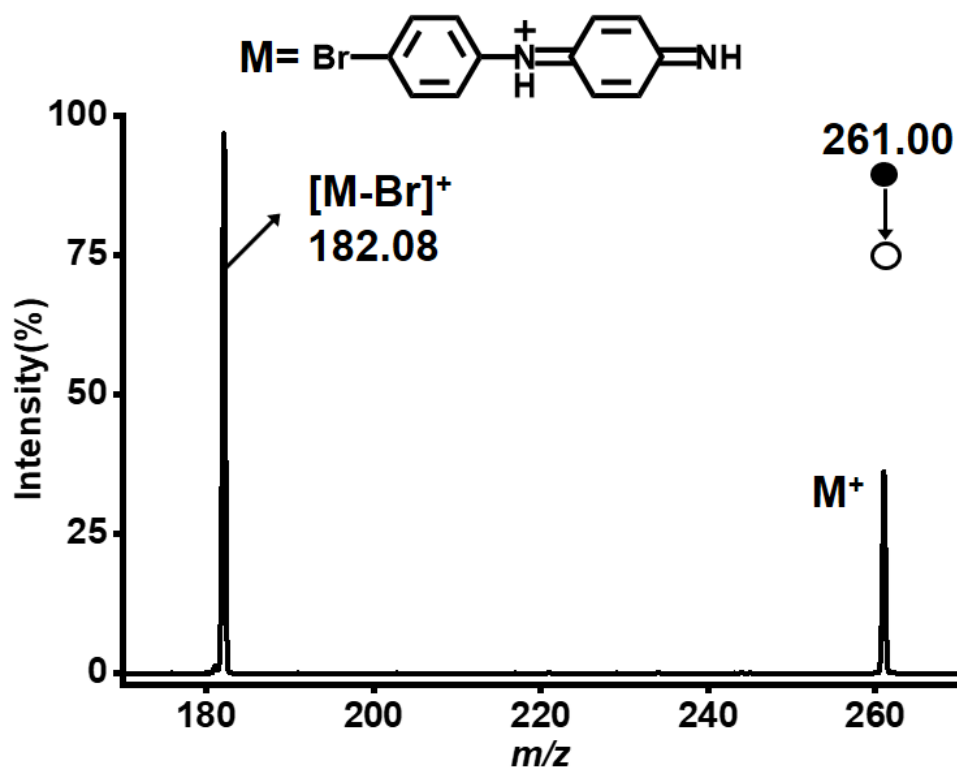
Appendix: Cartesian coordinates and energies of TS



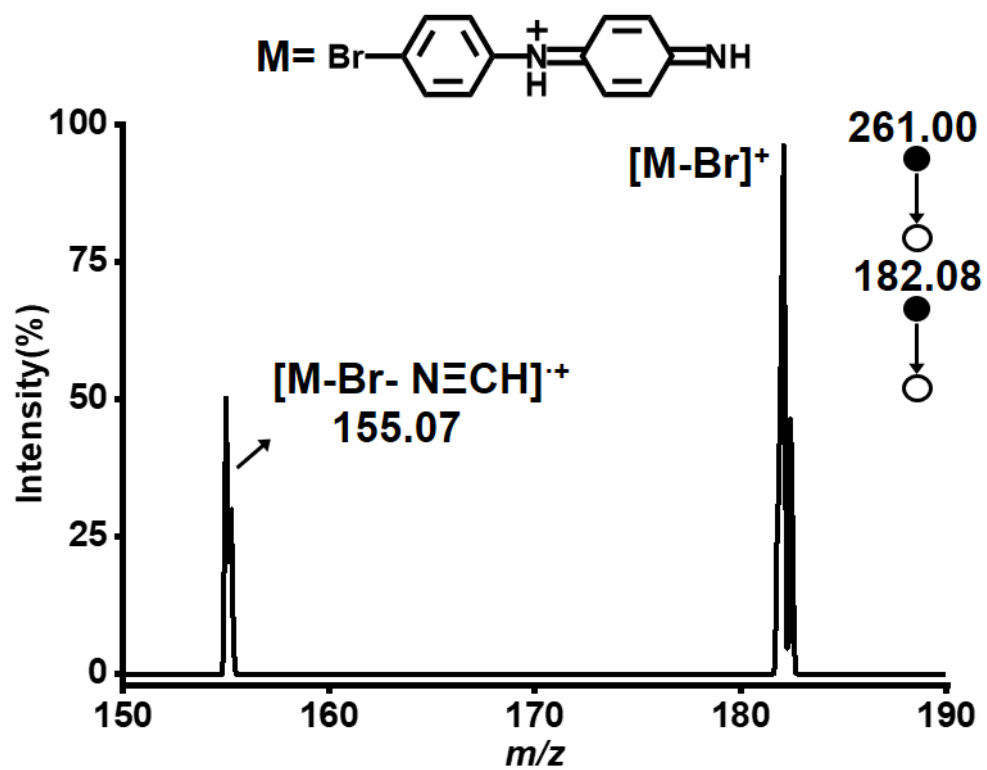
Supplementary Fig. 1. MS² spectrum of the peak at m/z 185.11 shown in Fig. 2c.



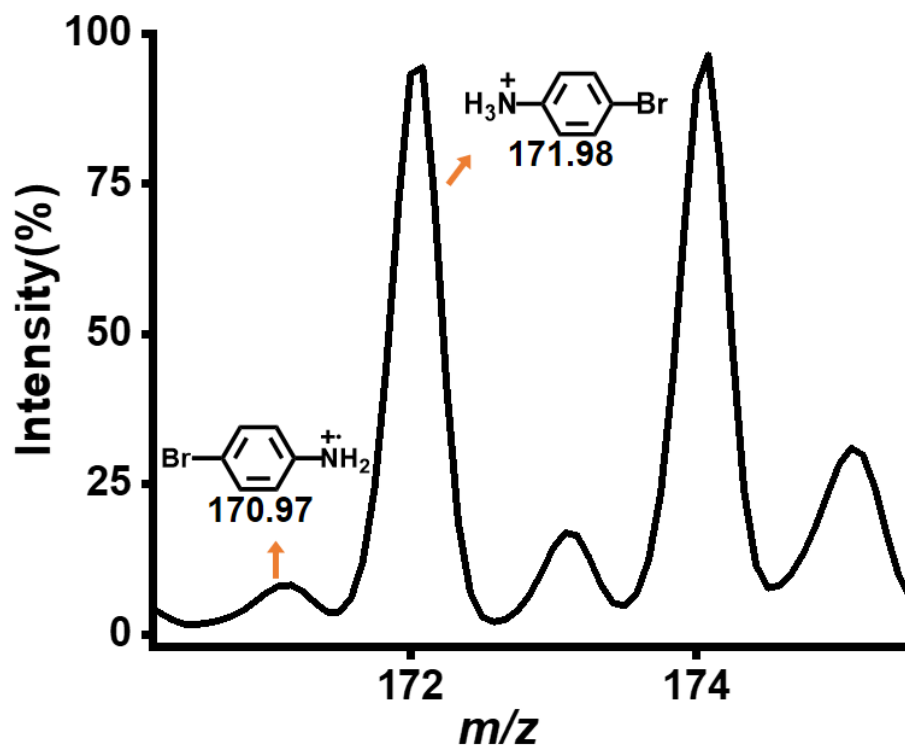
Supplementary Fig. 2. (a) Influence of the reaction time/ reaction distance on the intensity ratio of $C_{12}H_{13}N_2^+/C_6H_7BrN^+$ when reactant concentration is $100 \mu M$ and nebulizing gas pressure is 100 psi; (b) Influence of the solution concentration on the intensity ratio of $C_{12}H_{13}N_2^+/C_6H_7BrN^+$ when the reaction distance is 15 mm and the nebulizing gas pressure is 100 psi; (c) Influence of the nebulizing gas pressure on the intensity ratio of $C_{12}H_{13}N_2^+/C_6H_7BrN^+$ when the reaction distance is 15 mm and the reactant concentration is $100 \mu M$; (d) Heatmap of signal intensity of $C_{12}H_{13}N_2^+$ generated with varied solution concentration and nebulizing gas pressure, Each error bar represents the standard deviation of three experiments.



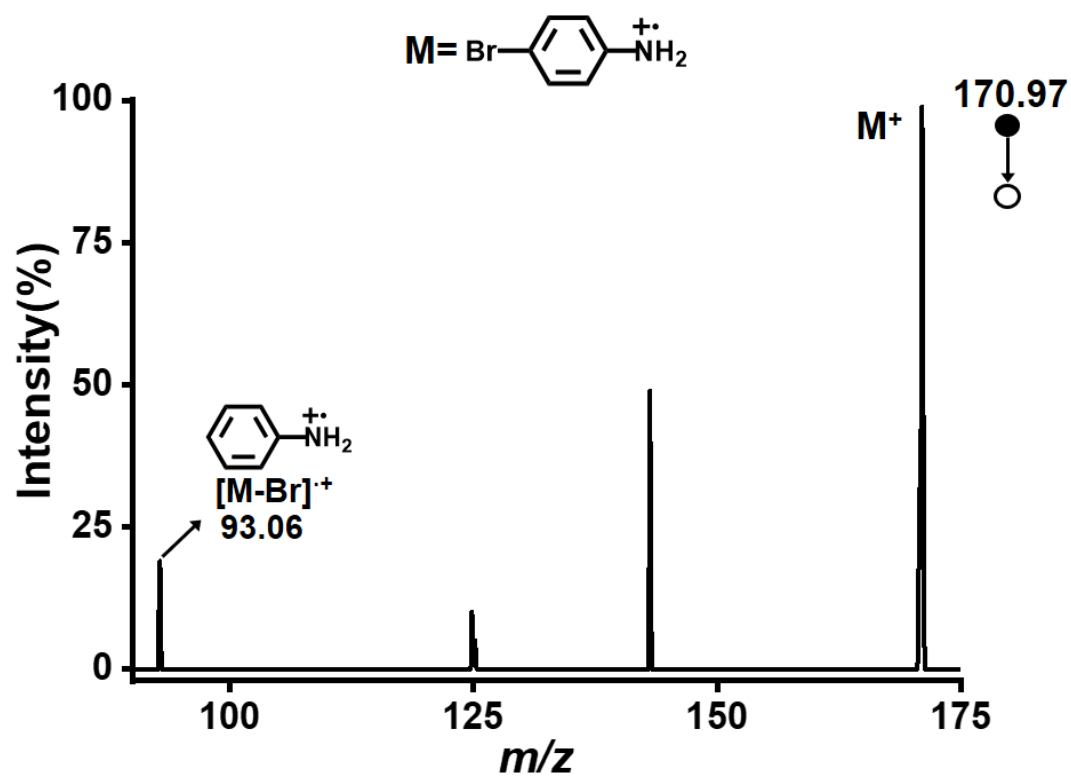
Supplementary Fig. 3. MS² spectrum of the peak at m/z 261.00 shown in Fig. 3a.



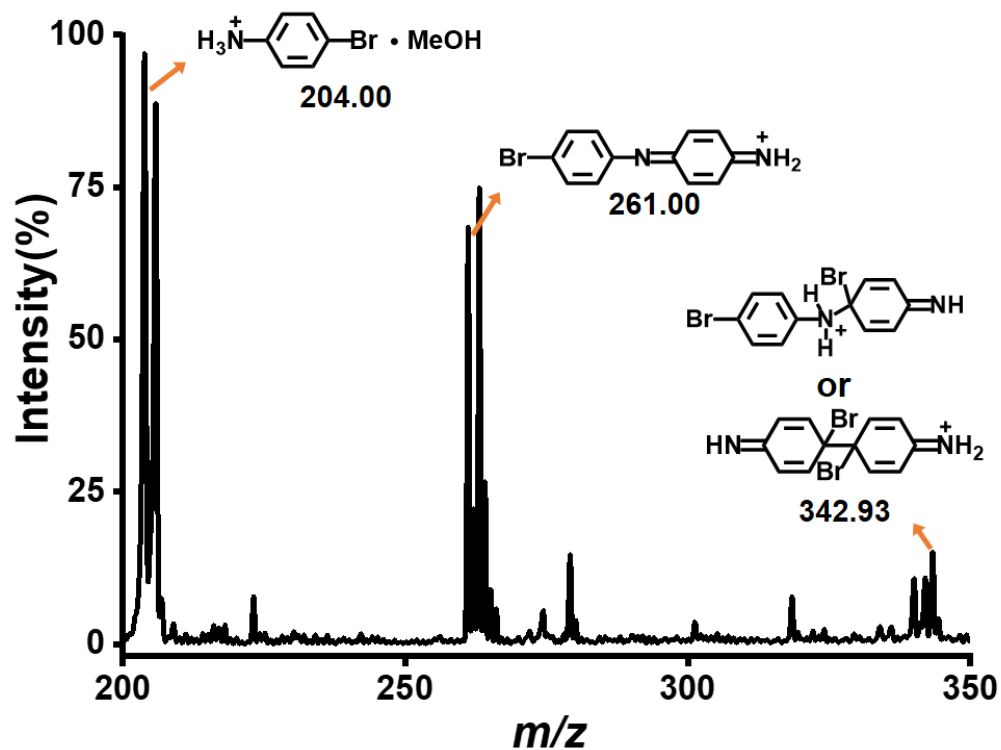
Supplementary Fig. 4. MS³ spectrum of the peak at m/z 261.00 shown in Fig. 3a.



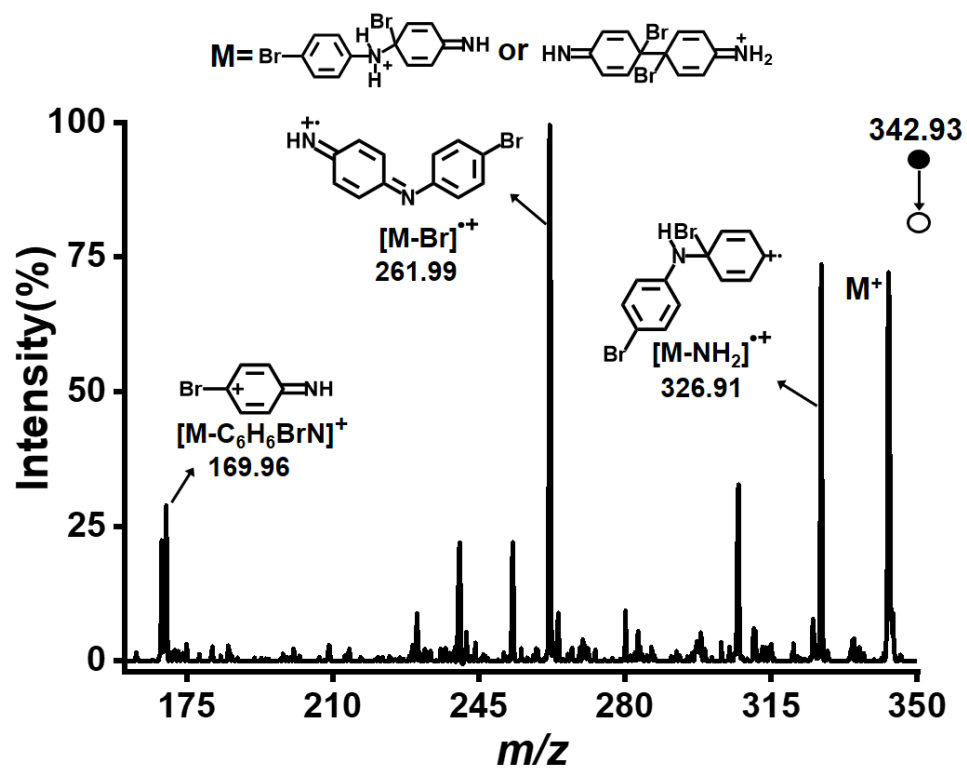
Supplementary Fig. 5. Mass spectrum showing intermediate I/VI detected in sprayed MeOH/H₂O microdroplets containing 4-bromoaniline.



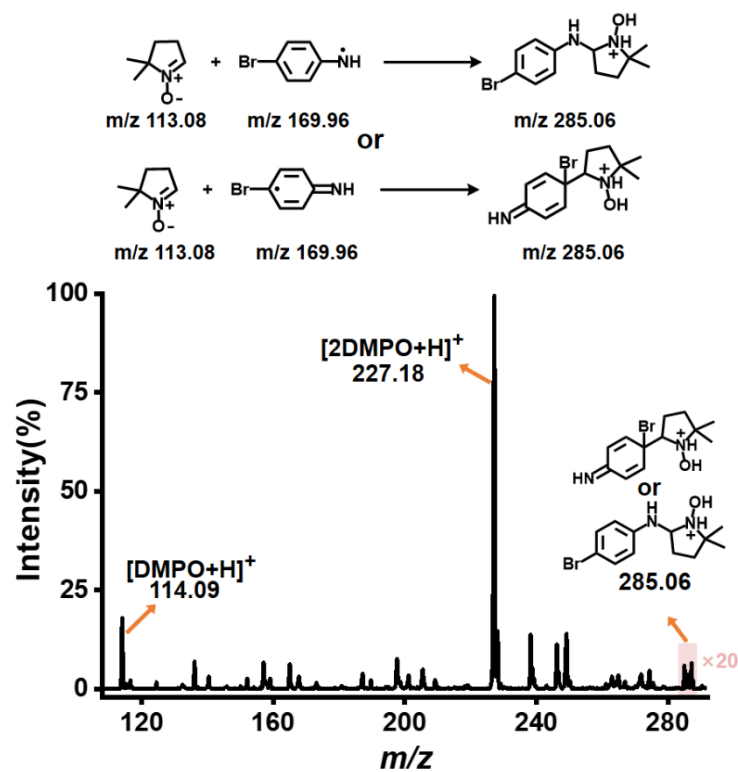
Supplementary Fig. 6. MS² spectrum of the peak at m/z 170.97 shown in Fig. S5.



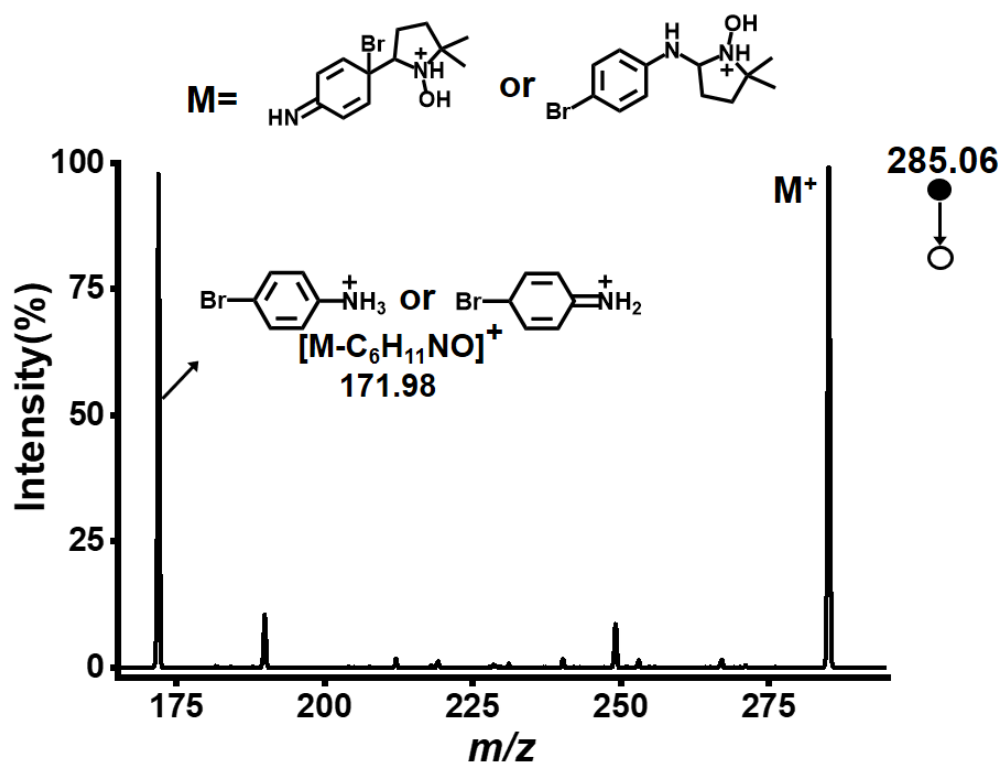
Supplementary Fig. 7. Mass spectrum showing intermediate **IV/IX** detected in sprayed MeOH/H₂O microdroplets containing 4-bromoaniline.



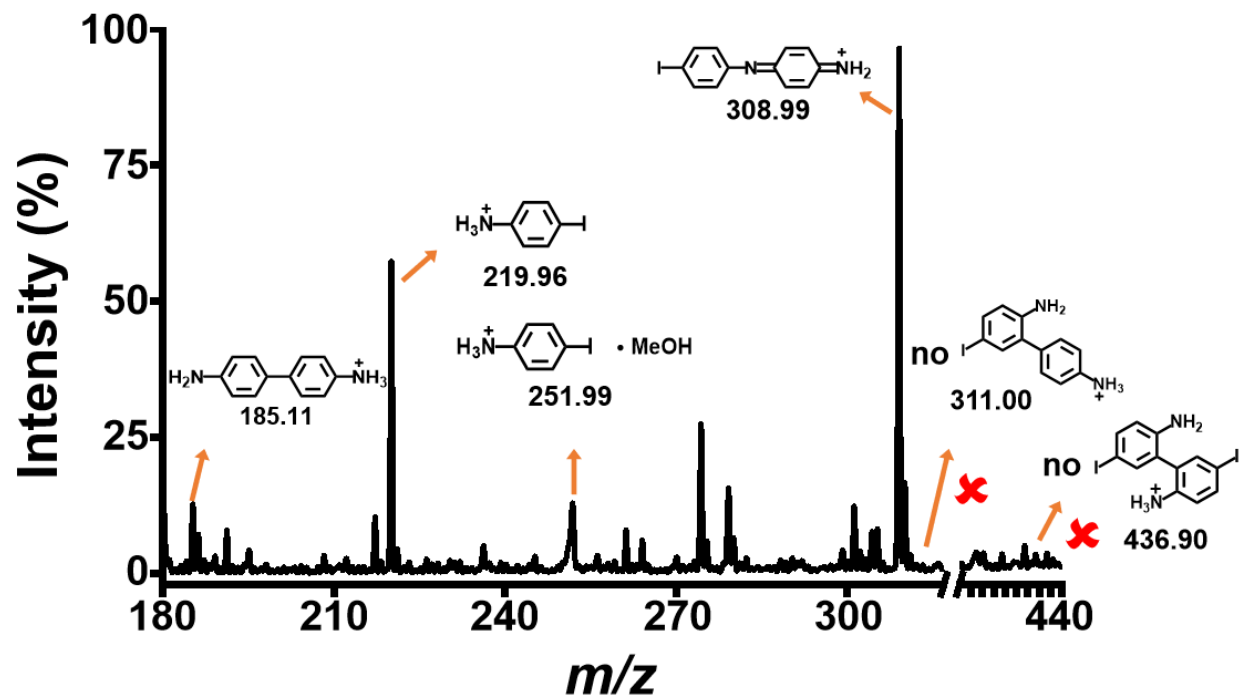
Supplementary Fig. 8. MS² spectrum of the peak at m/z 342.93 shown in Fig. S7.



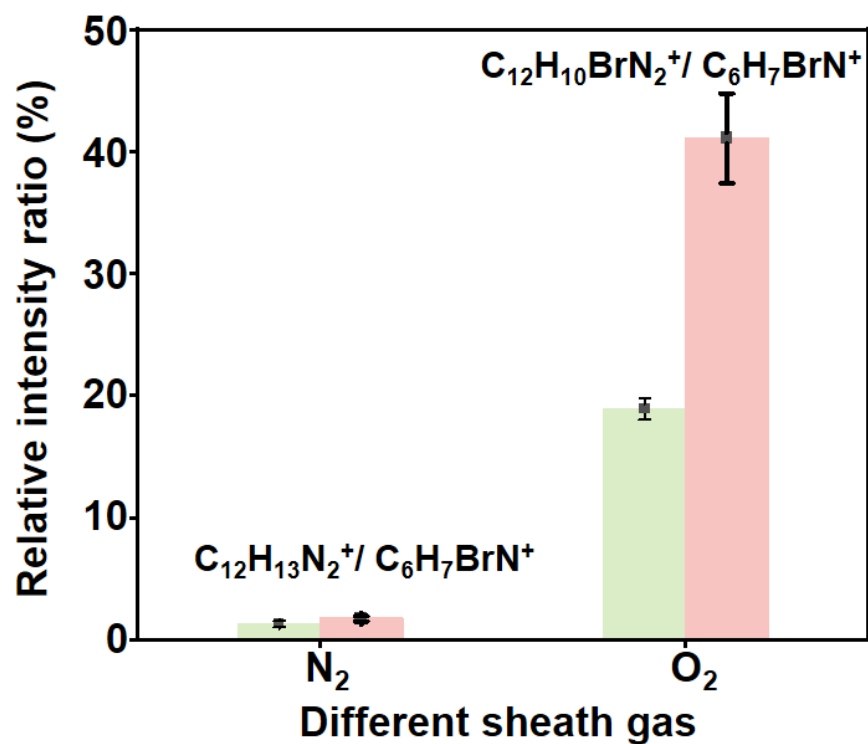
Supplementary Fig. 9. Mass spectrum showing intermediate **II/III/VII/VIII** detected in sprayed MeOH/H₂O microdroplets containing 4-bromoaniline with the addition of DMPO.



Supplementary Fig. 10. MS² spectrum of the peak at m/z 285.06 shown in Fig. S9.



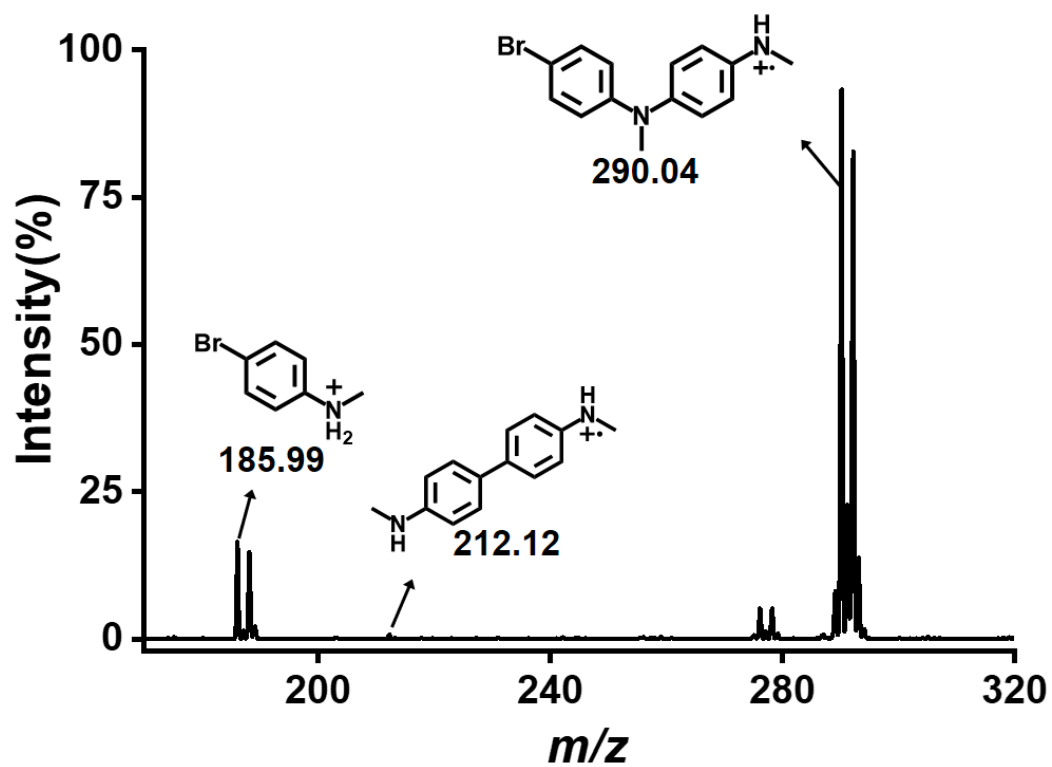
Supplementary Fig. 11. Mass spectrum of 4-iodoaniline-containing MeOH/H₂O microdroplets using N₂ as the nebulizing gas.



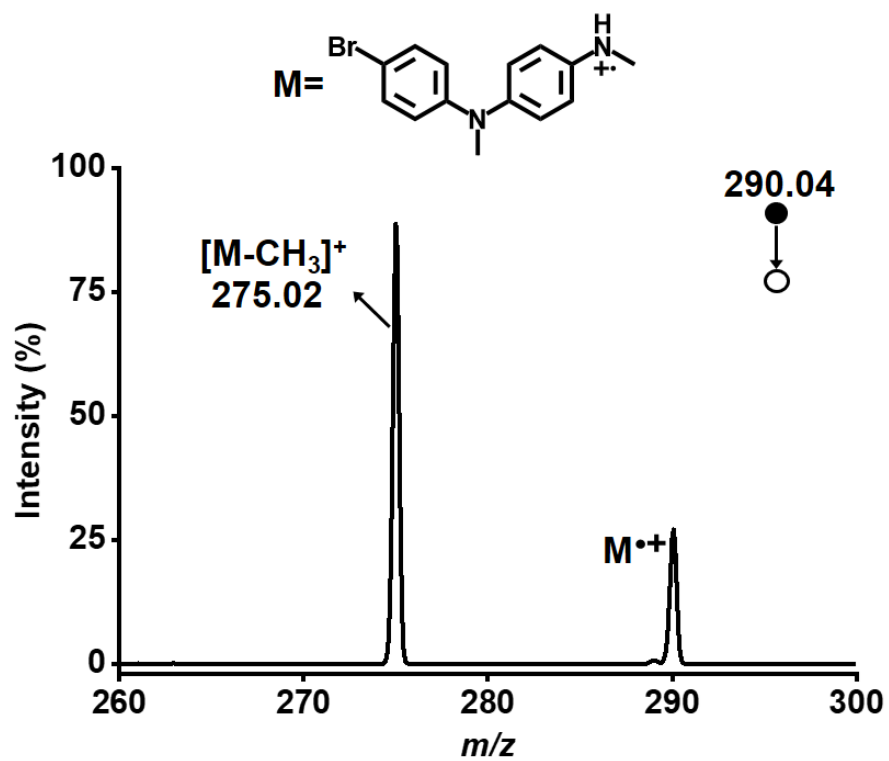
Supplementary Fig. 12. Effect of different sheath gases (N_2 and O_2) on the intensity ratios of $C_{12}H_{13}N_2^+/C_6H_7BrN^+$ and $C_{12}H_{10}BrN_2^+/C_6H_7BrN^+$, respectively. Each error bar represents the standard deviation from three independent experiments.

[illegible]

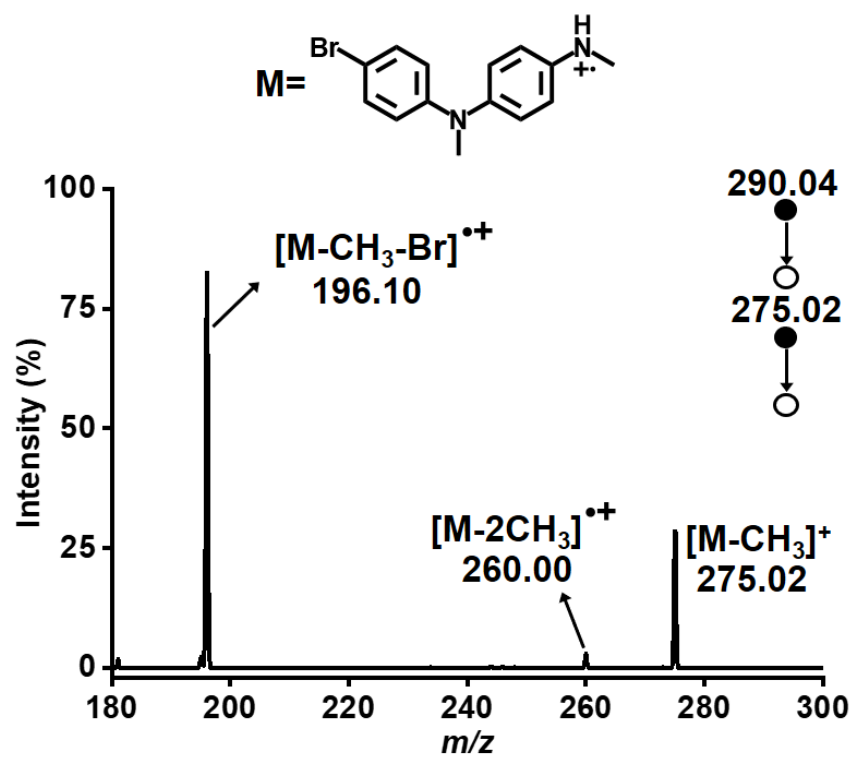
Supplementary Fig. 13. Transition states of Ullmann coupling reaction.



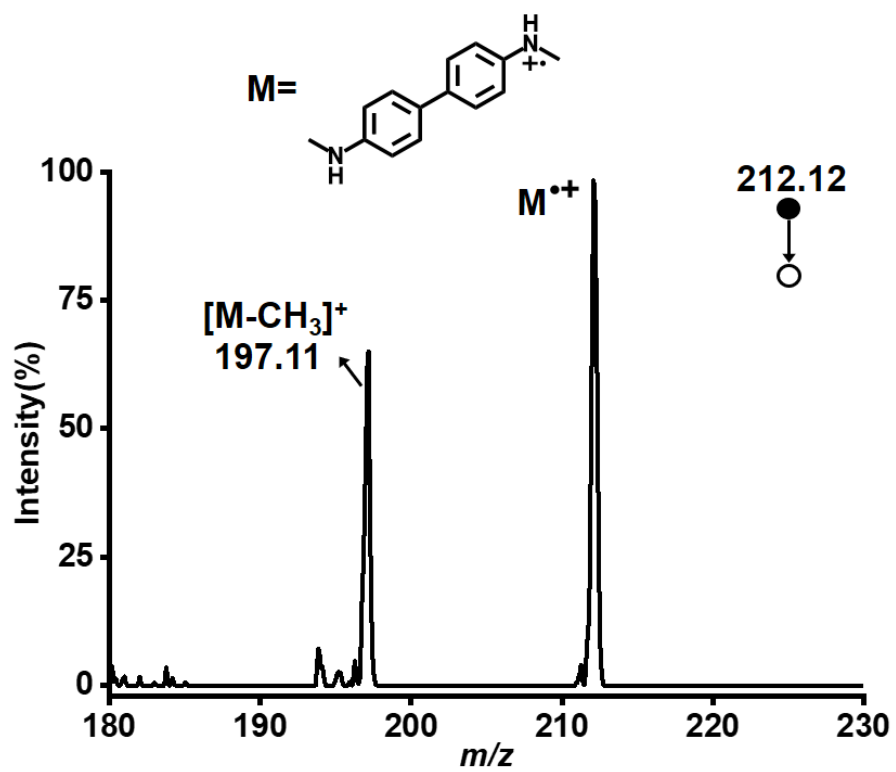
Supplementary Fig. 14. Mass spectrum of MeOH/H₂O microdroplets containing 4-bromo-N-methylaniline with N₂ as the nebulizing gas.



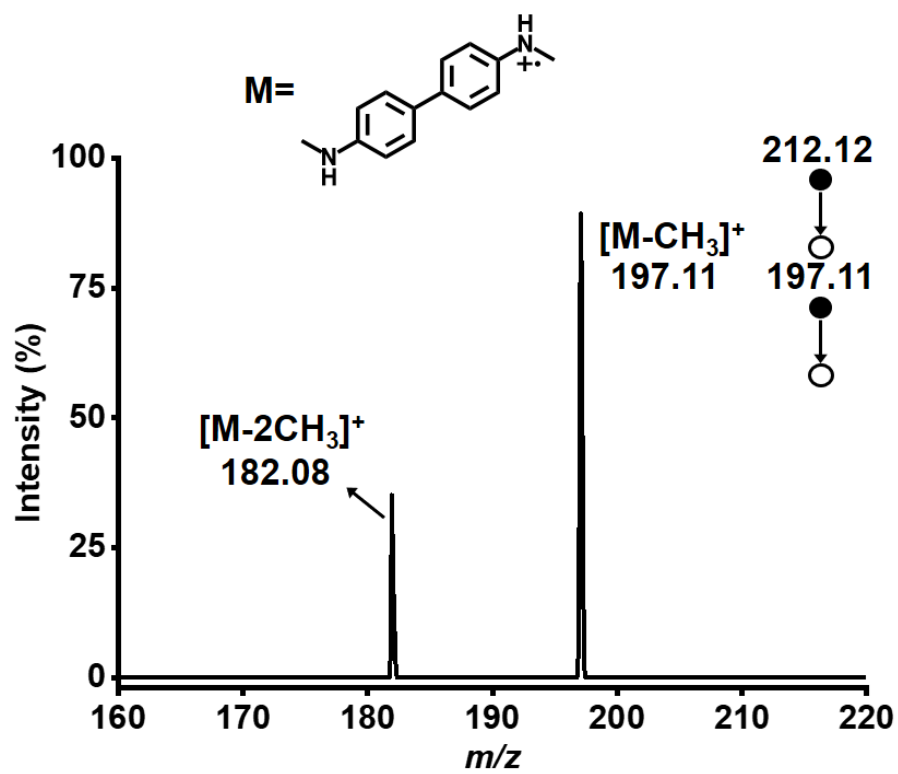
Supplementary Fig. 15. MS² spectrum of the peak at m/z 290.04 shown in Fig. S14.



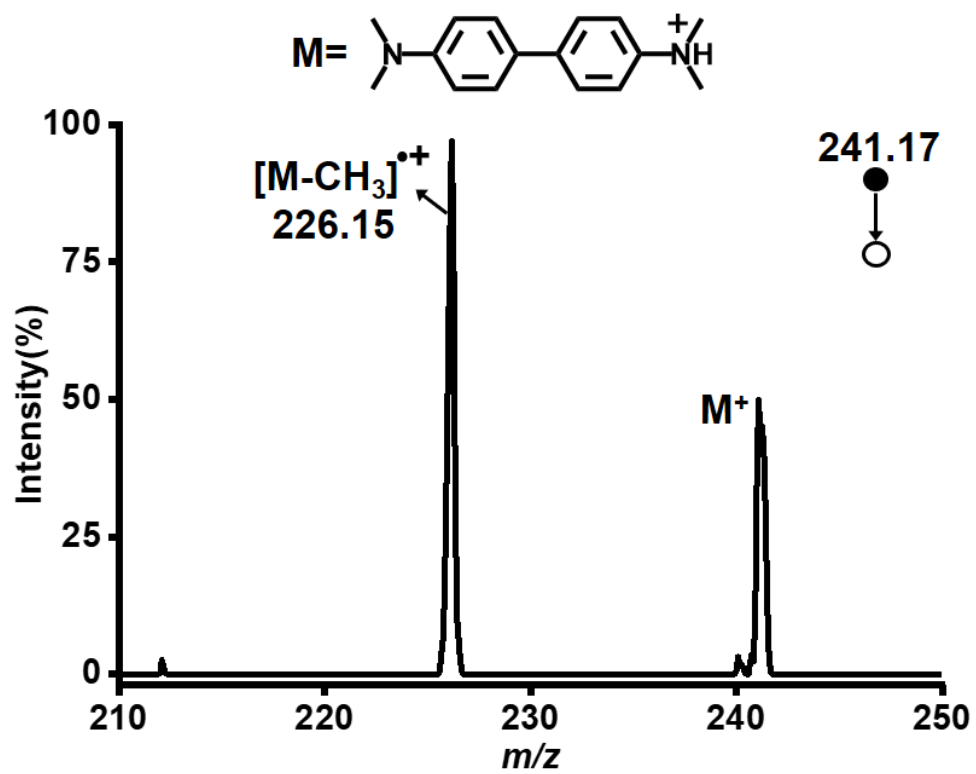
Supplementary Fig. 16. MS³ spectrum of the peak at m/z 290.04 shown in Fig. S14.



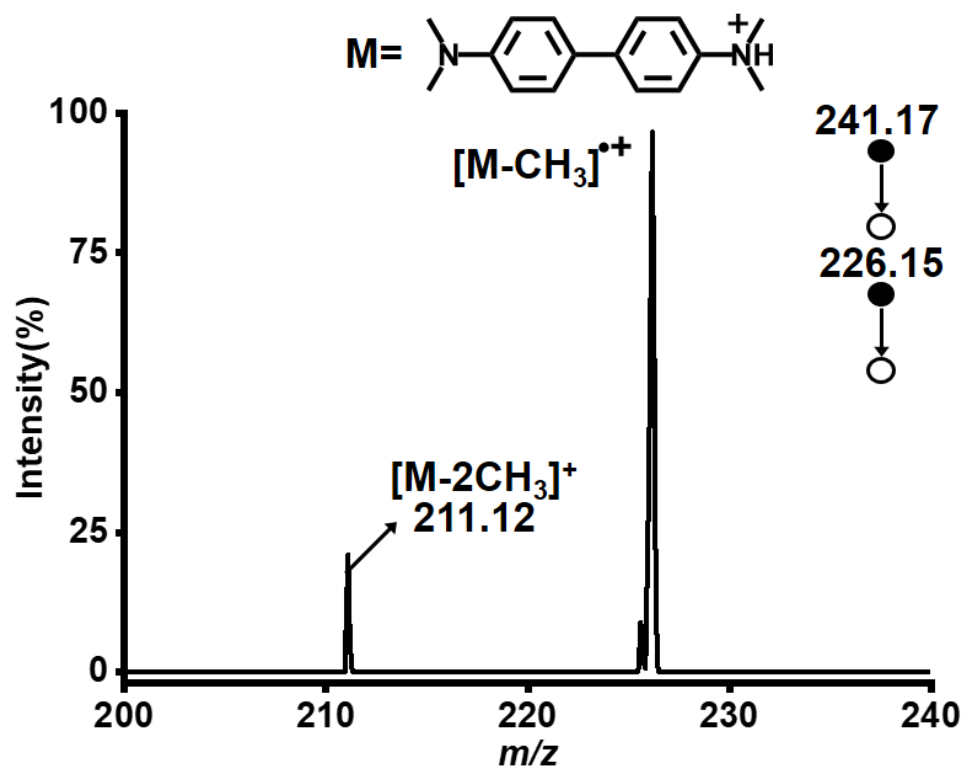
Supplementary Fig. 17. MS² spectrum of the peak at m/z 212.12 shown in Fig. S14.



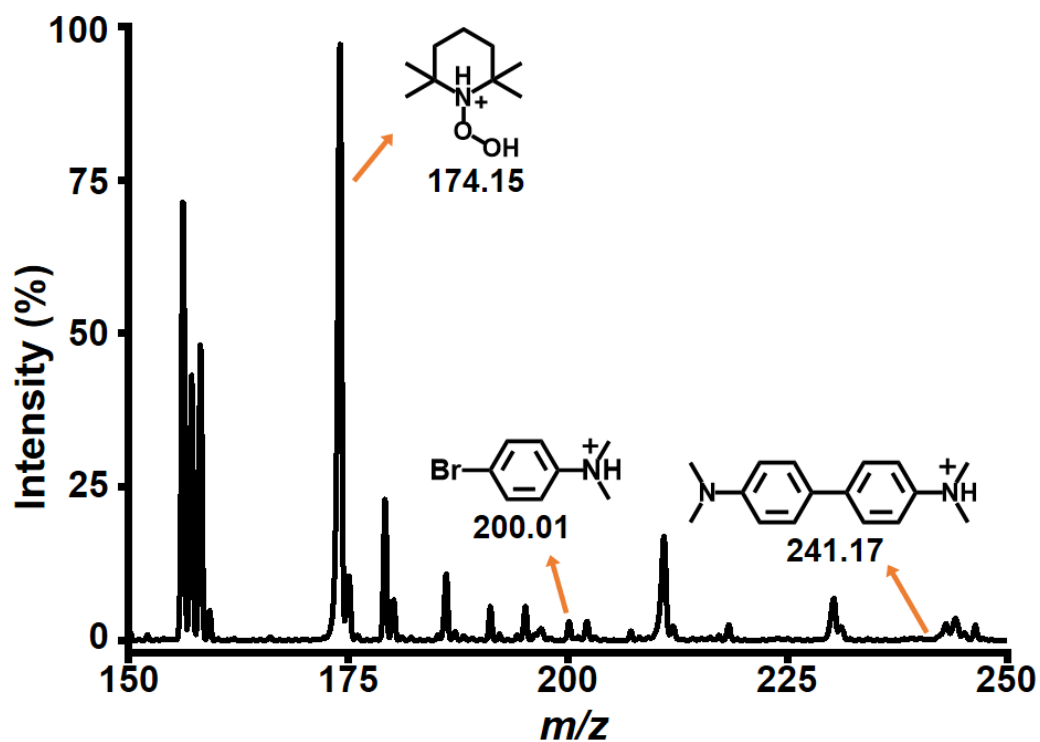
Supplementary Fig. 18. MS³ spectrum of the peak at *m/z* 212.12 shown in Fig. S14.



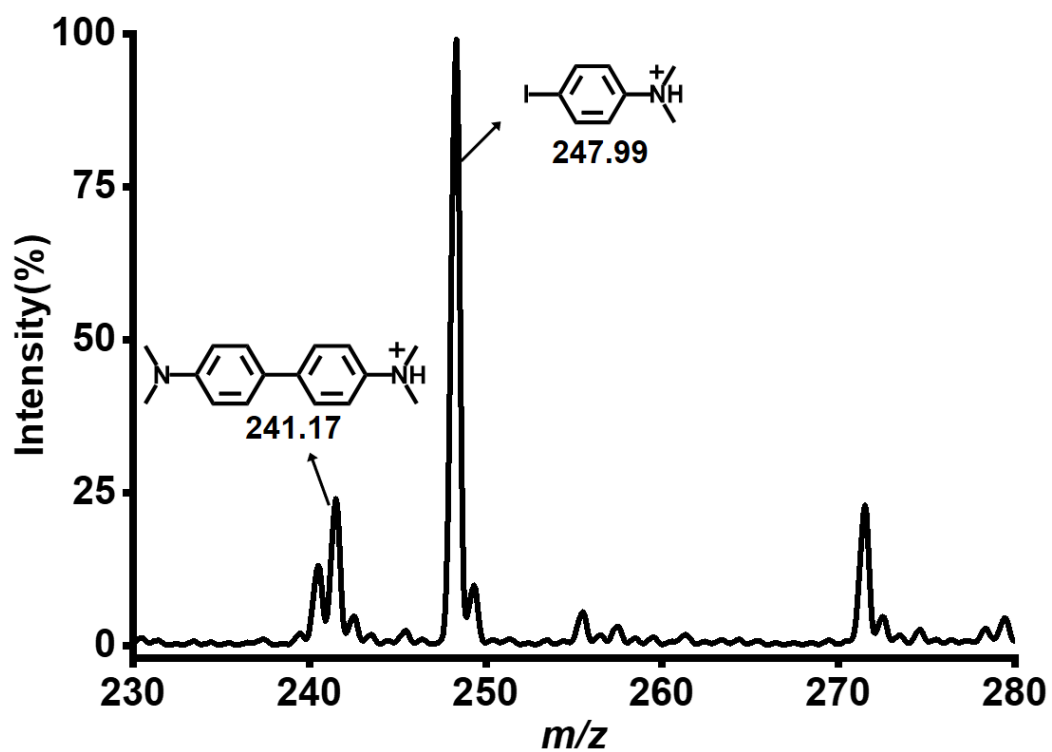
Supplementary Fig. 19. MS² spectrum of the peak at m/z 241.17 shown in Fig. 4a.



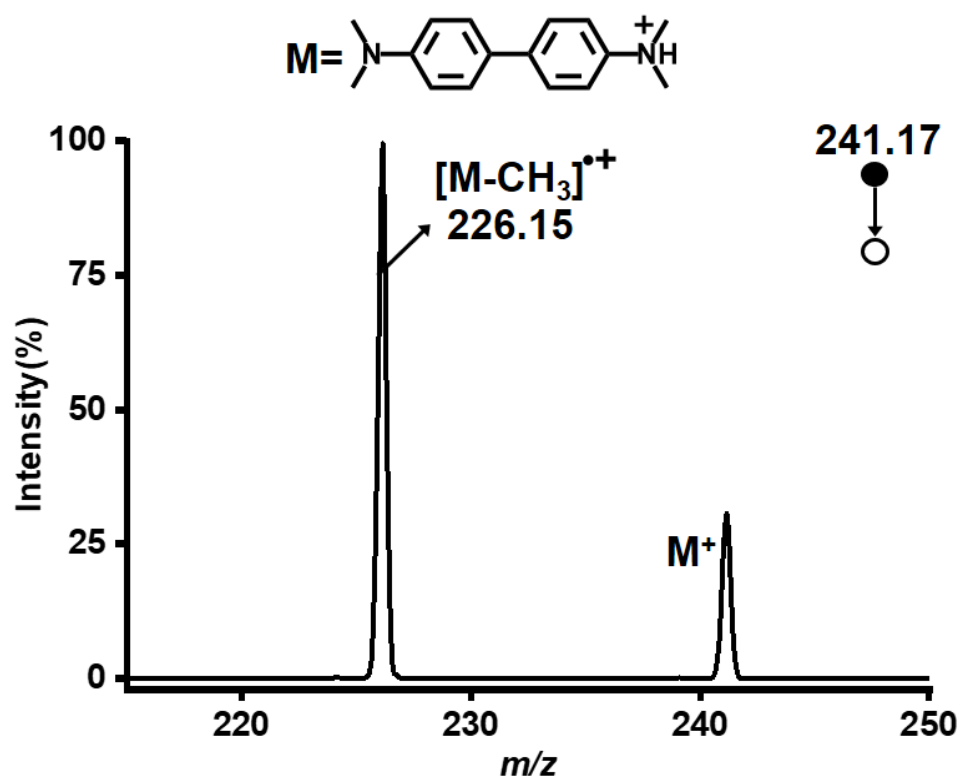
Supplementary Fig. 20. MS³ spectrum of the peak at m/z 241.17 shown in Fig. 4a.



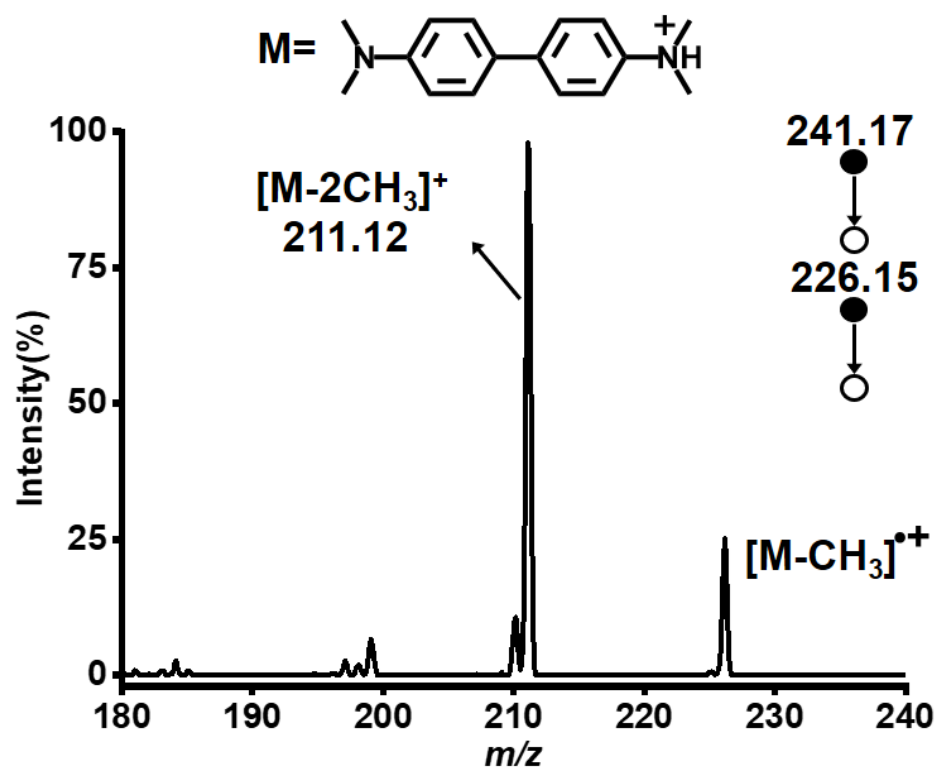
Supplementary Fig. 21. Mass spectrum of the MeOH/H₂O microdroplets containing 4-bromo-N,N-dimethylaniline with addition of radical scavenger TEMPO.



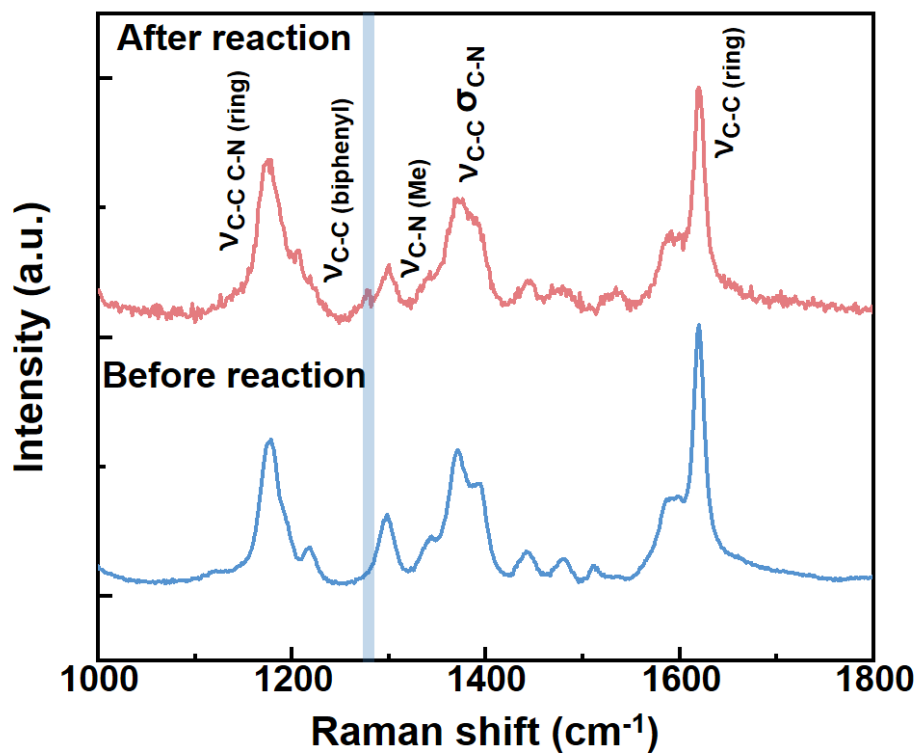
Supplementary Fig. 22. Mass spectrum of MeOH/H₂O microdroplets containing 4-iodo-N,N-dimethylaniline with N₂ as the nebulizing gas.



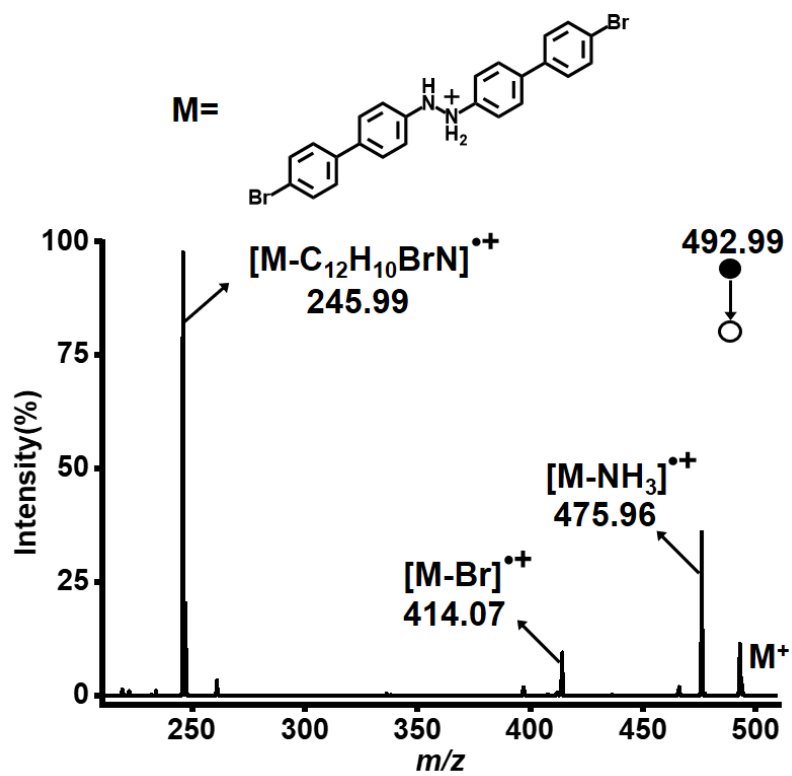
Supplementary Fig. 23. MS² spectrum of the peak at m/z 241.17 shown in Fig. S22.



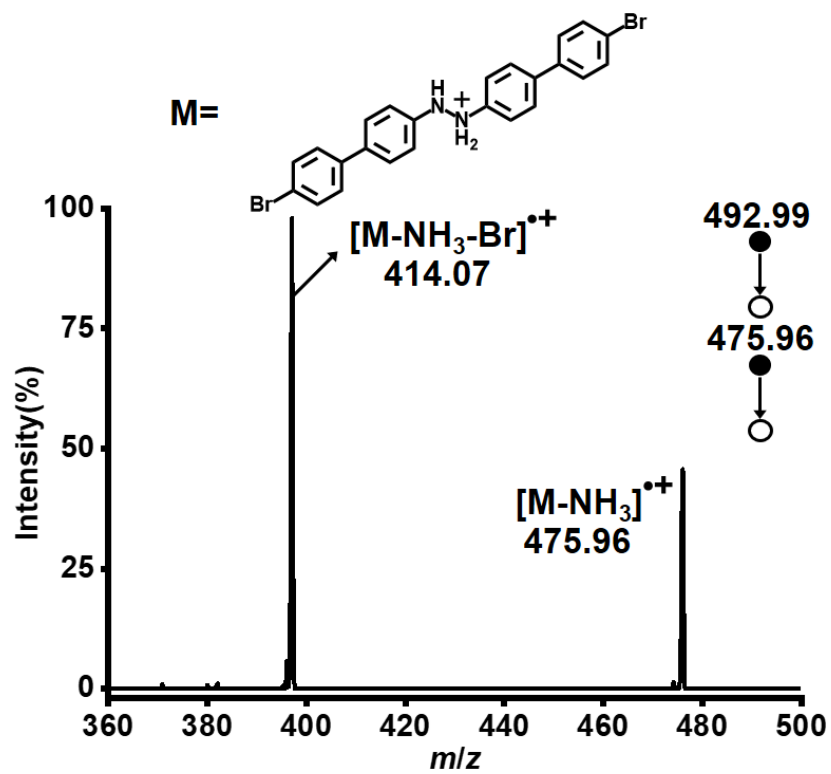
Supplementary Fig. 24. MS³ spectrum of the peak at m/z 241.17 shown in Fig. S22.



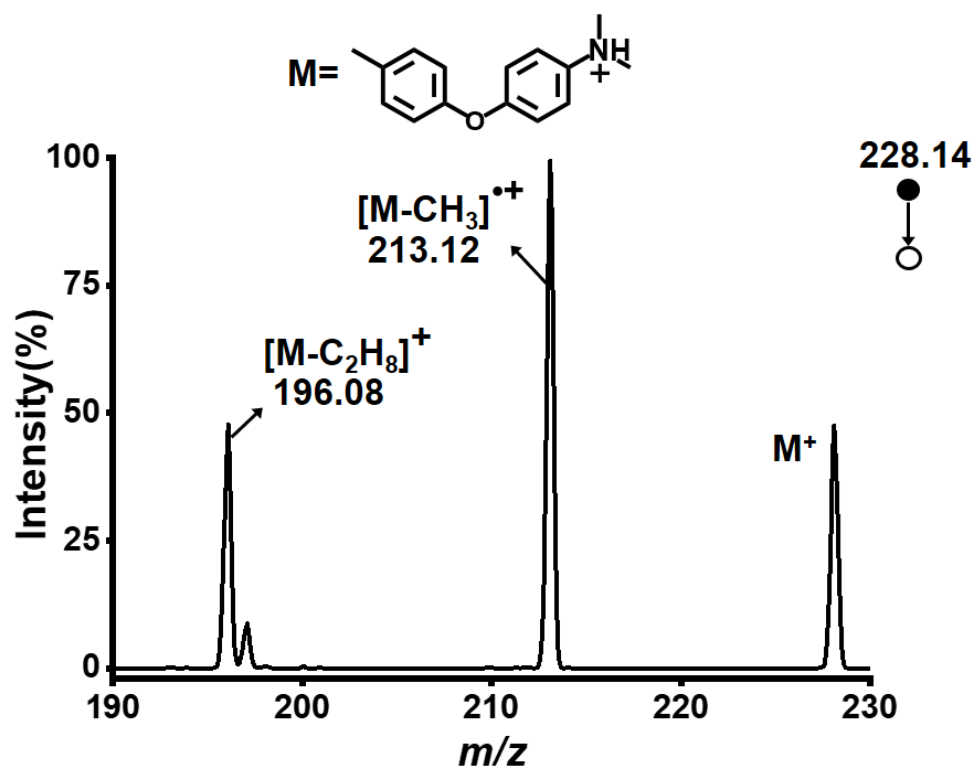
Supplementary Fig. 25. Averaged SERS spectra of 4-iodo-N,N-dimethylaniline modified AuNPs sample (blue trace), and MeOH/H₂O microdroplets containing 4-iodo-N,N-dimethylaniline sprayed onto the AuNPs sample (red trace).



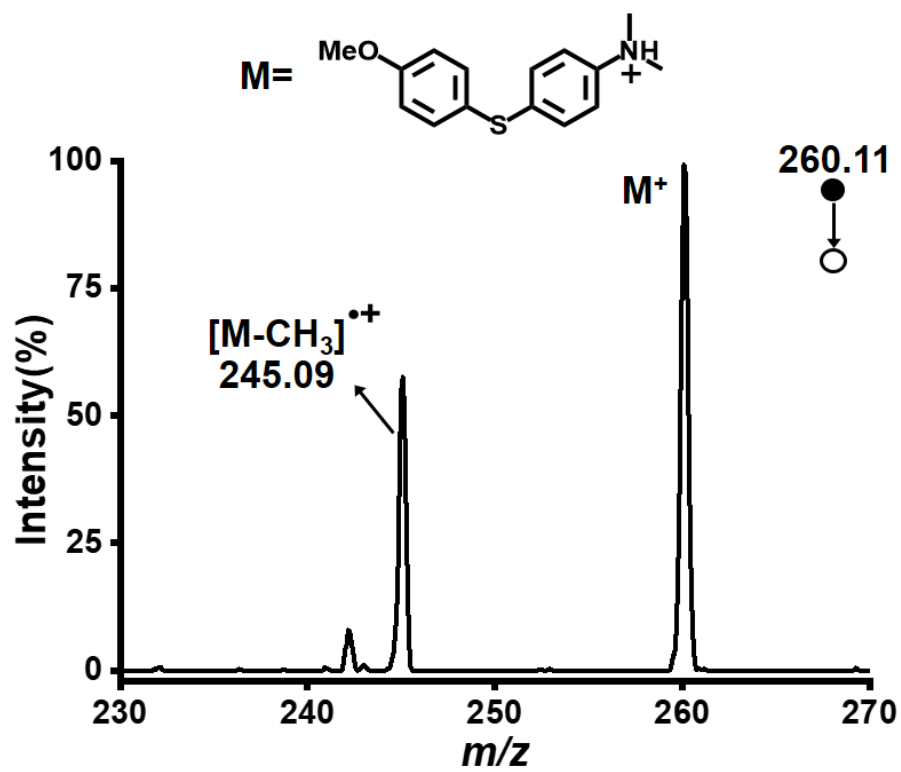
Supplementary Fig. 26. MS² spectrum of the peak at m/z 492.99 shown in Fig. 4d.



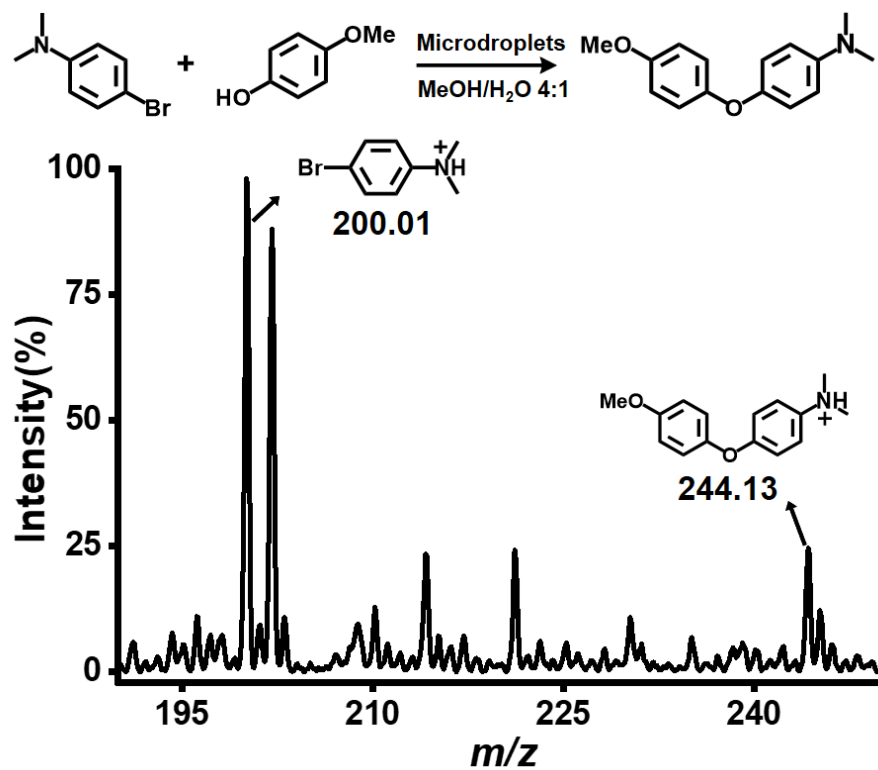
Supplementary Fig. 27. MS³ spectrum of the peak at m/z 492.99 shown in Fig. 4d.



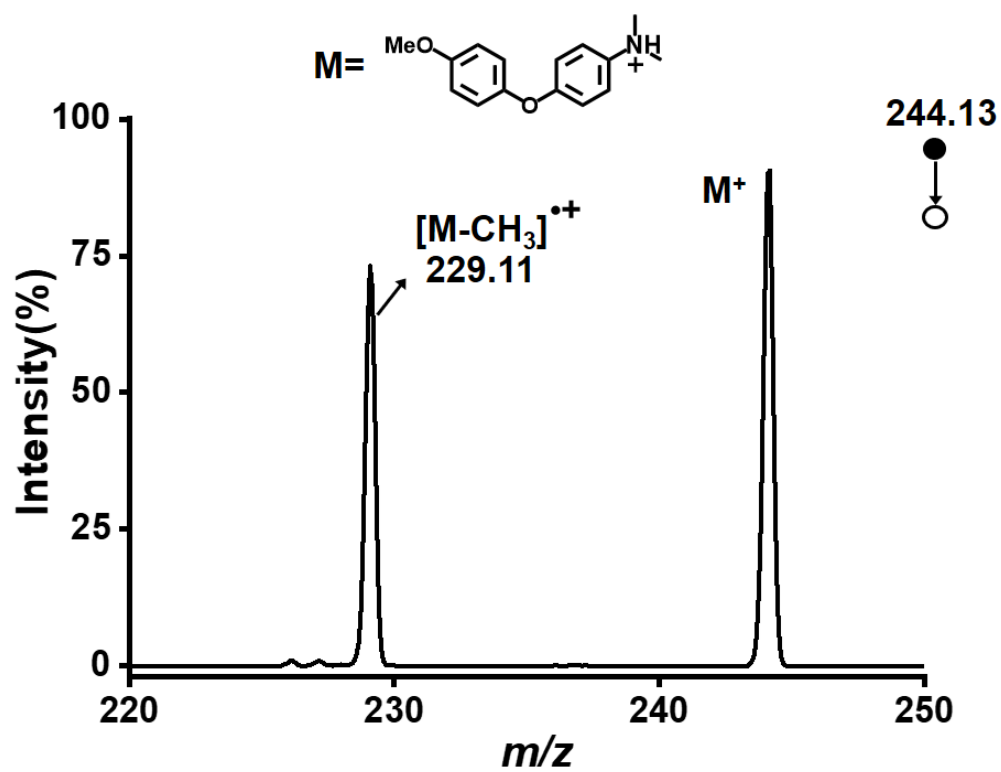
Supplementary Fig. 28. MS² spectrum of the peak at m/z 228.14 shown in Fig. 5b.



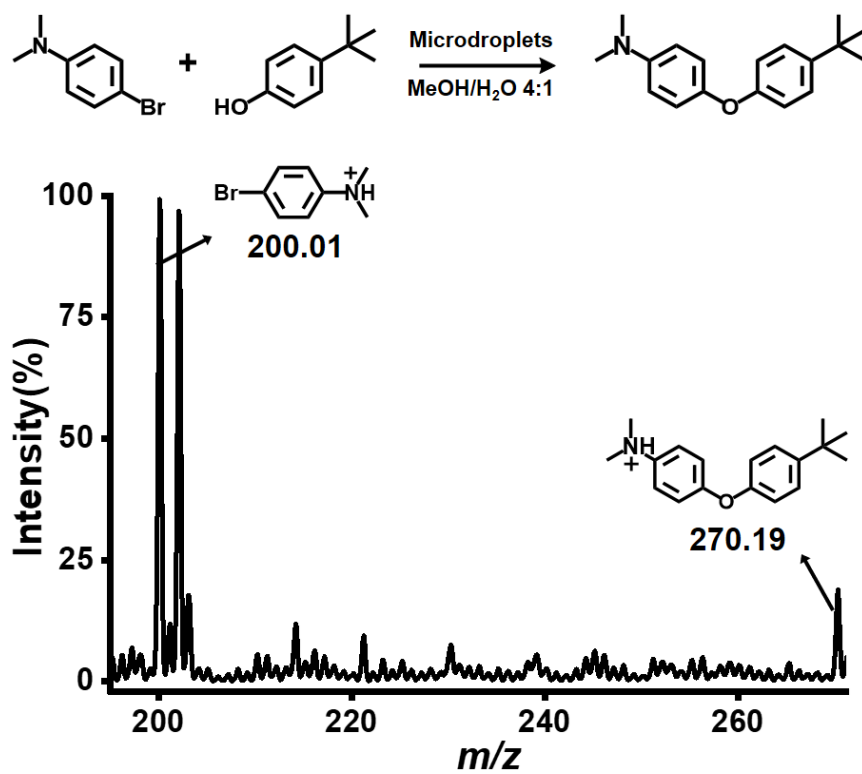
Supplementary Fig. 29. MS² spectrum of the peak at m/z 260.11 shown in Fig. 5d.



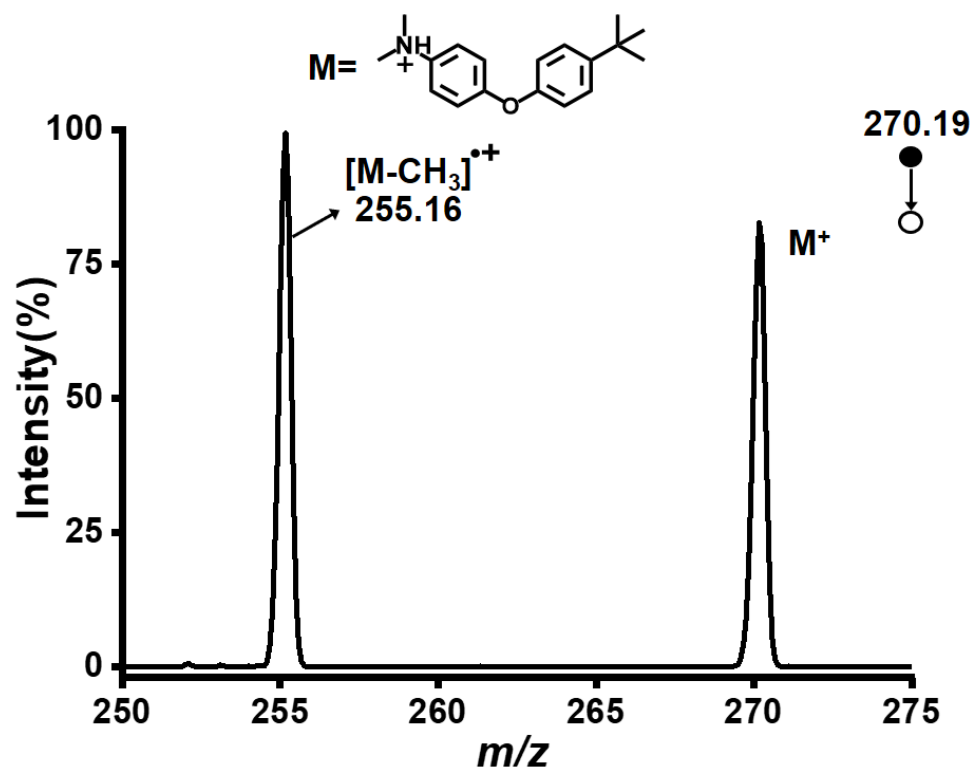
Supplementary Fig. 30. Mass spectrum of the MeOH/H₂O microdroplets containing both 4-bromo-N,N-dimethylaniline and 4-methoxyphenol.



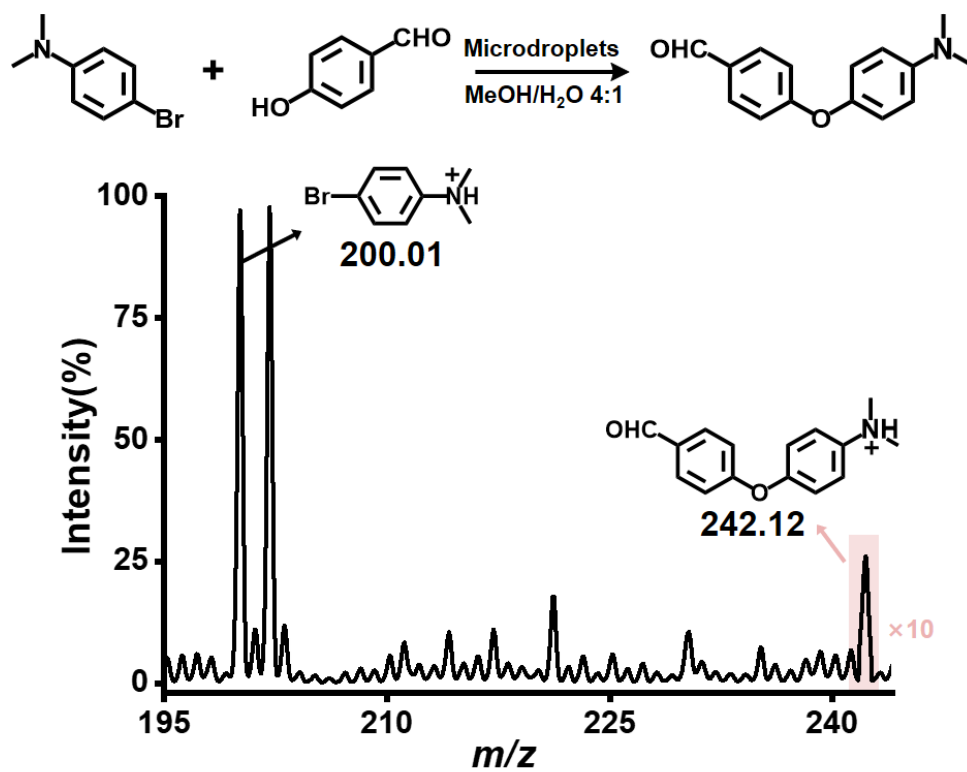
Supplementary Fig. 31. MS² spectrum of the peak at m/z 244.13 shown in Fig. S30.



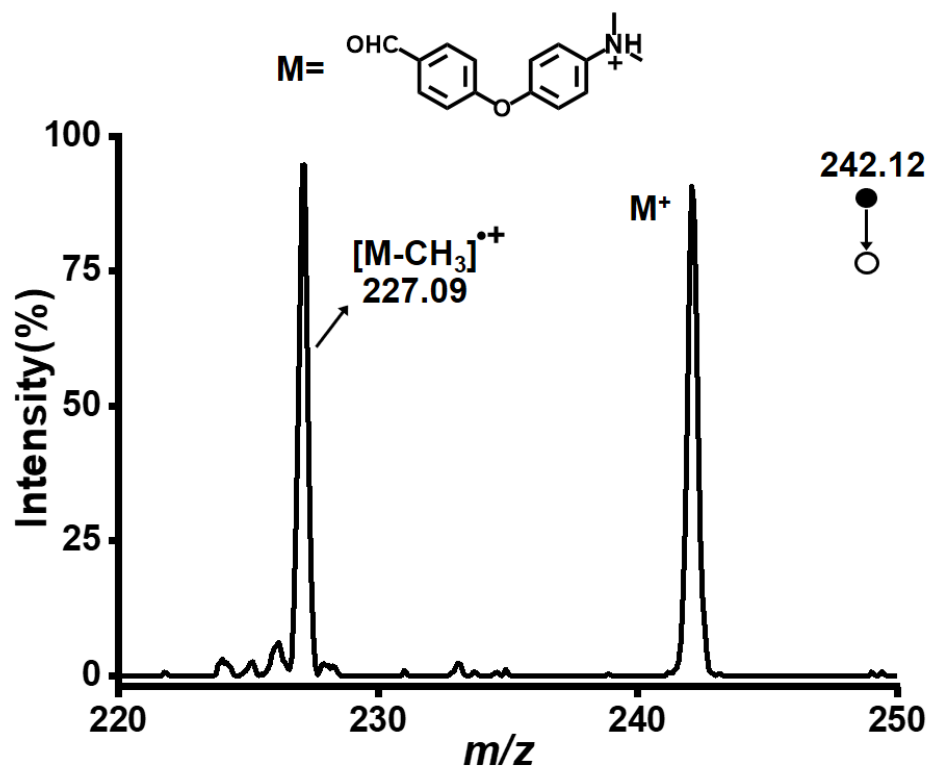
Supplementary Fig. 32. Mass spectrum of the MeOH/H₂O microdroplets containing both 4-bromo-N,N-dimethylaniline and 4-tert-butylphenol.



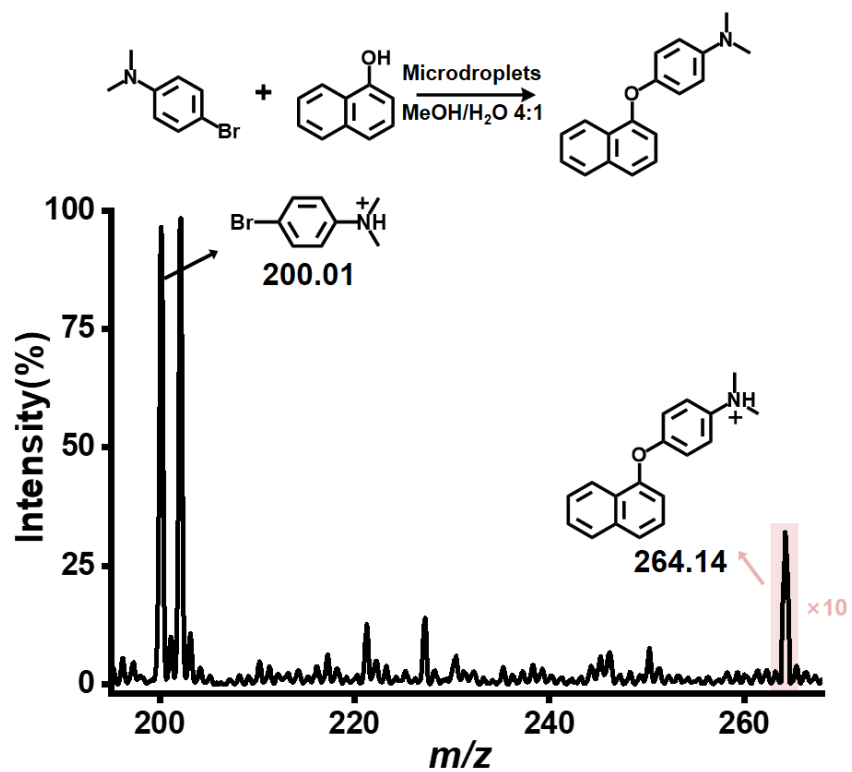
Supplementary Fig. 33. MS² spectrum of the peak at m/z 270.19 shown in Fig. S32.



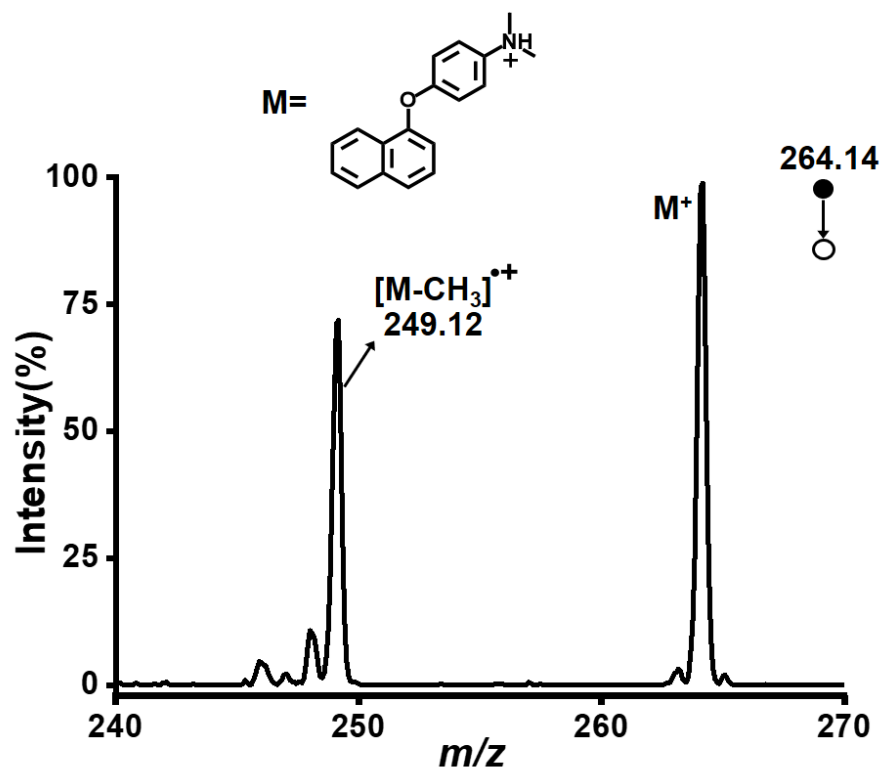
Supplementary Fig. 34. Mass spectrum of the MeOH/H₂O microdroplets containing both 4-bromo-N,N-dimethylaniline and 4-hydroxybenzaldehyde.



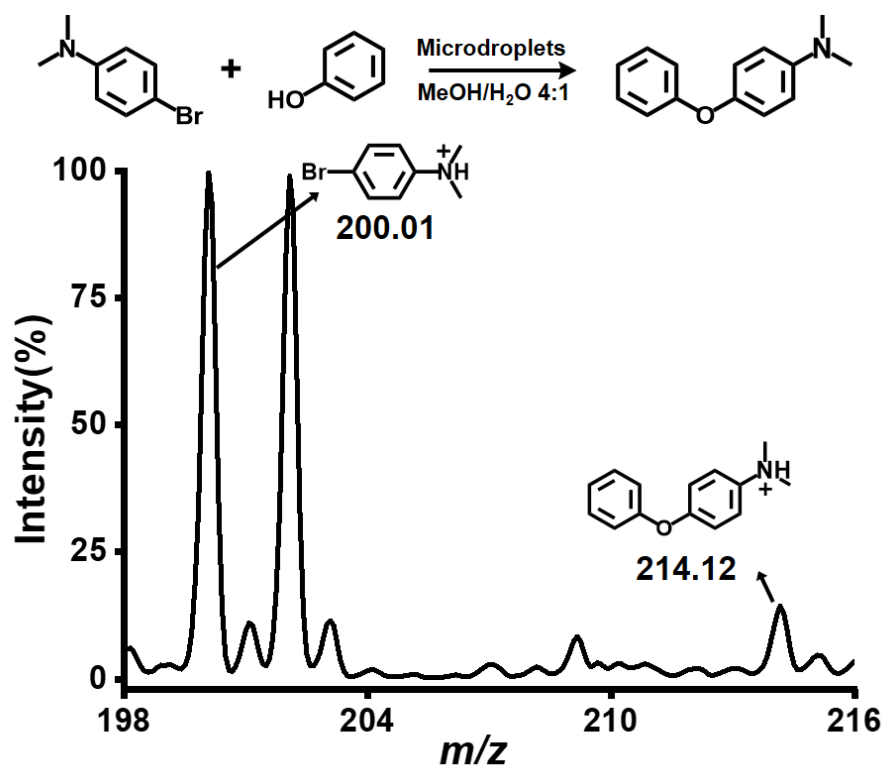
Supplementary Fig. 35. MS² spectrum of the peak at m/z 242.12 shown in Fig. S34.



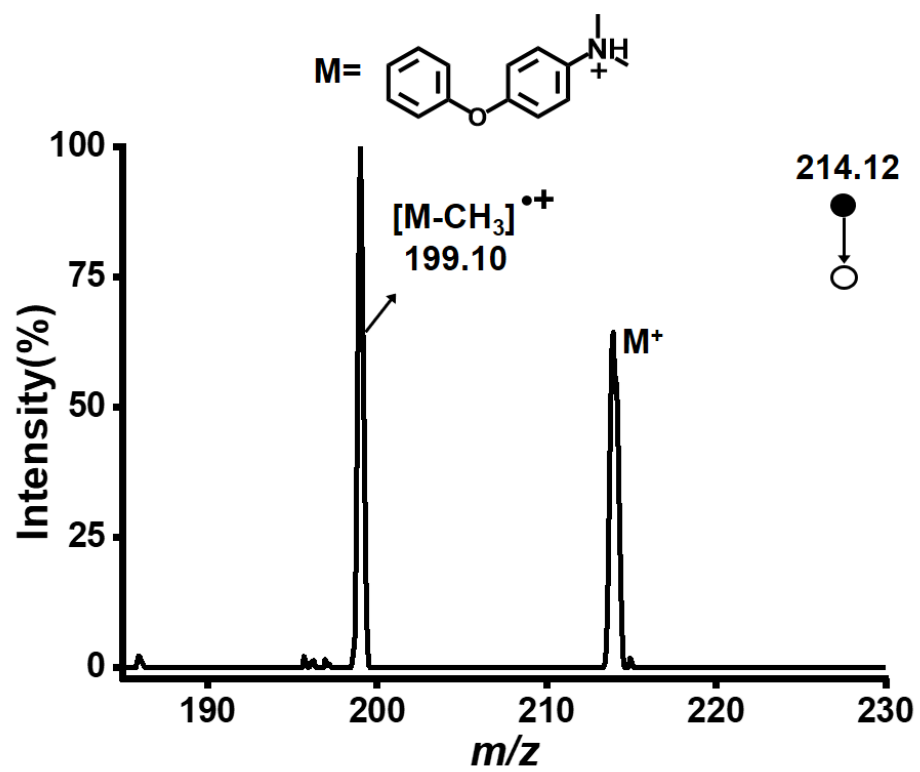
Supplementary Fig. 36. Mass spectrum of the MeOH/H₂O microdroplets containing both 4-bromo-N,N-dimethylaniline and naphthol.



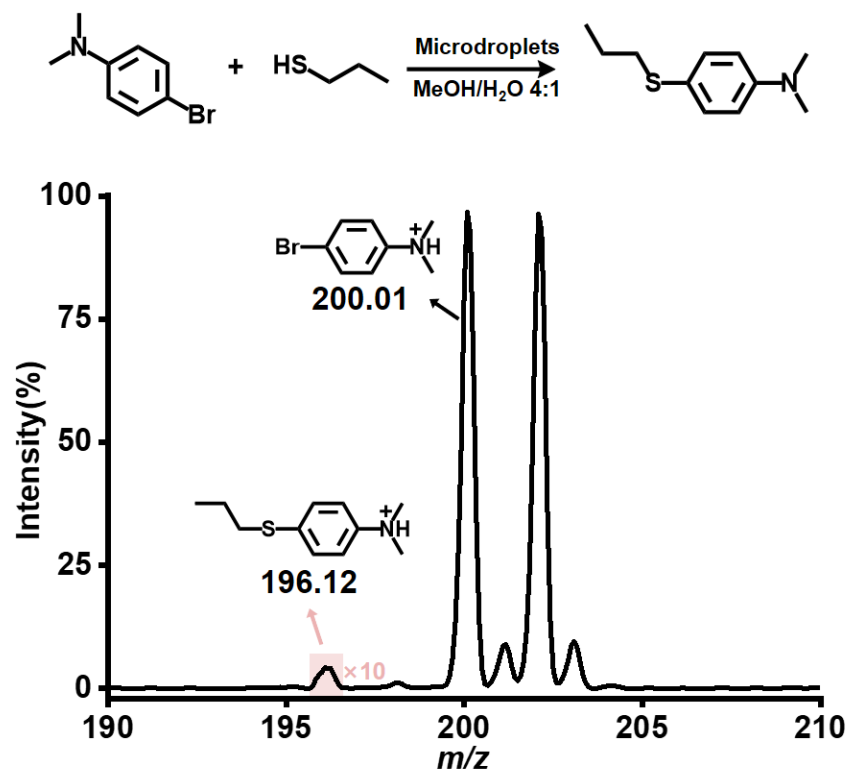
Supplementary Fig. 37. MS² spectrum of the peak at m/z 264.14 shown in Fig. S36.



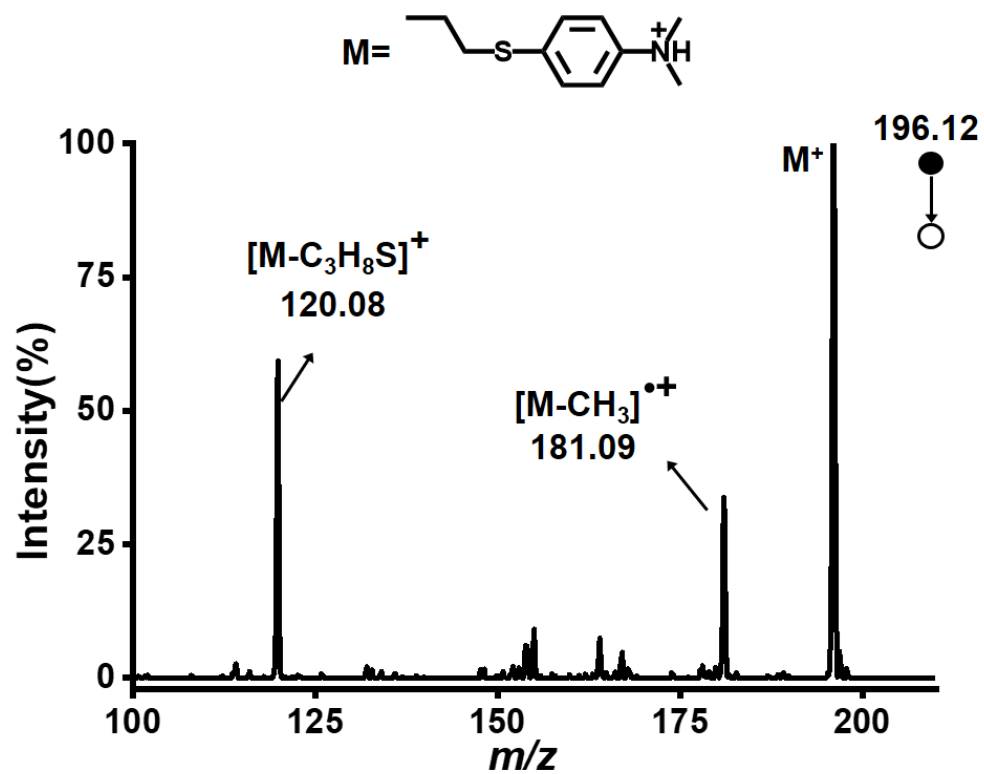
Supplementary Fig. 38. Mass spectrum of the MeOH/H₂O microdroplets containing both 4-bromo-N,N-dimethylaniline and phenol.



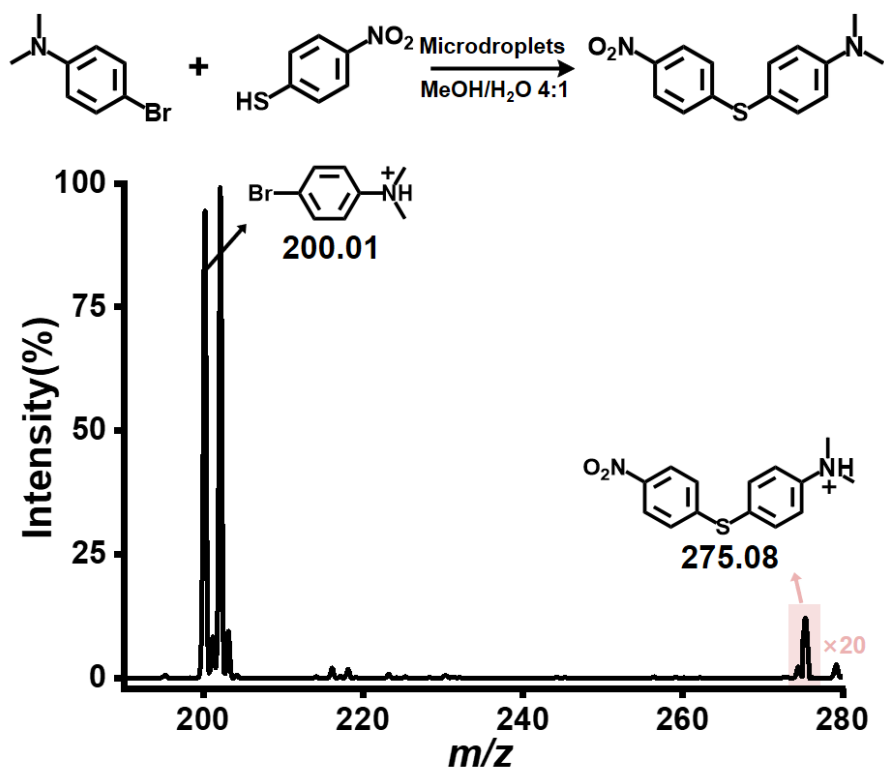
Supplementary Fig. 39. MS² spectrum of the peak at m/z 214.12 shown in Fig. S38.



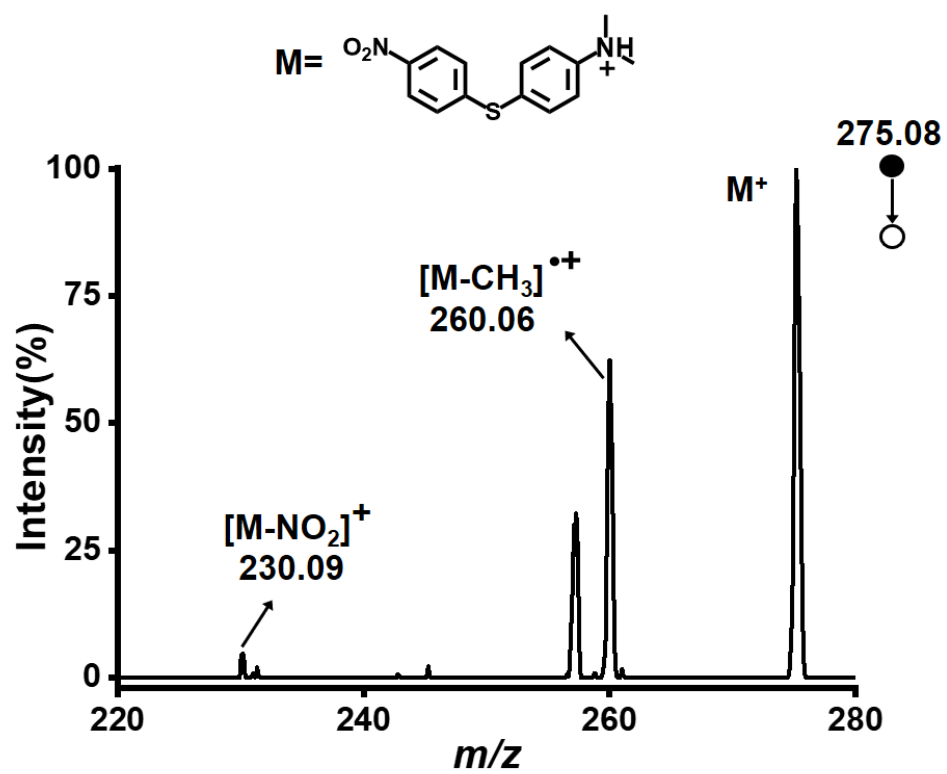
Supplementary Fig. 40. Mass spectrum of the MeOH/H₂O microdroplets containing both 4-bromo-N,N-dimethylaniline and 1-propanethiol.



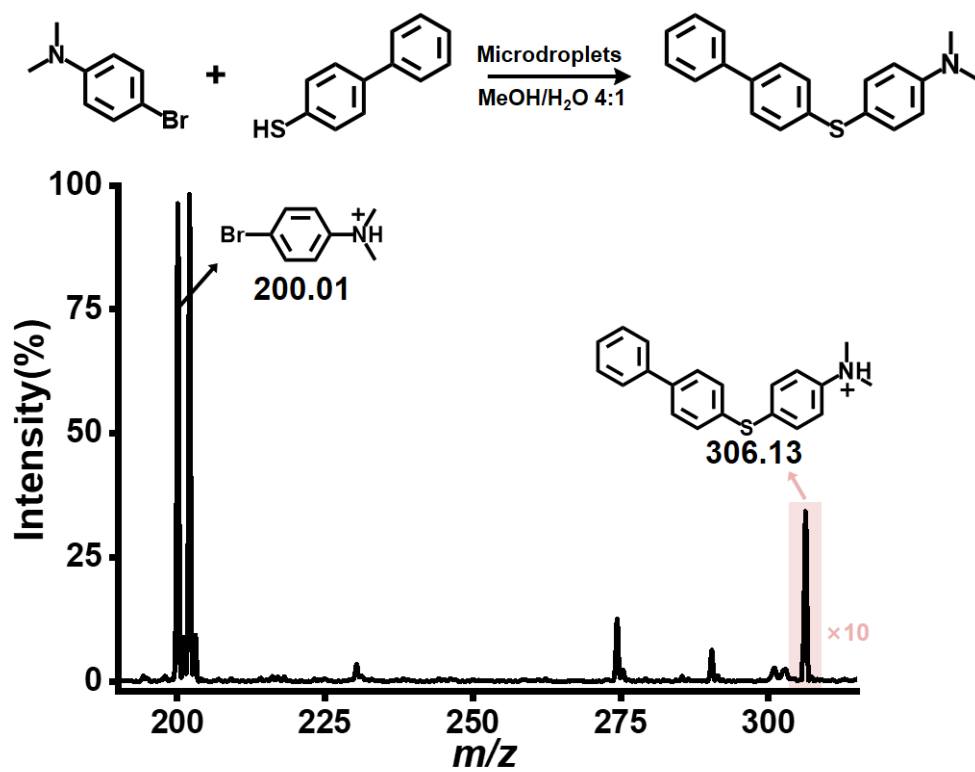
Supplementary Fig. 41. MS² spectrum of the peak at m/z 196.12 shown in Fig. S40.



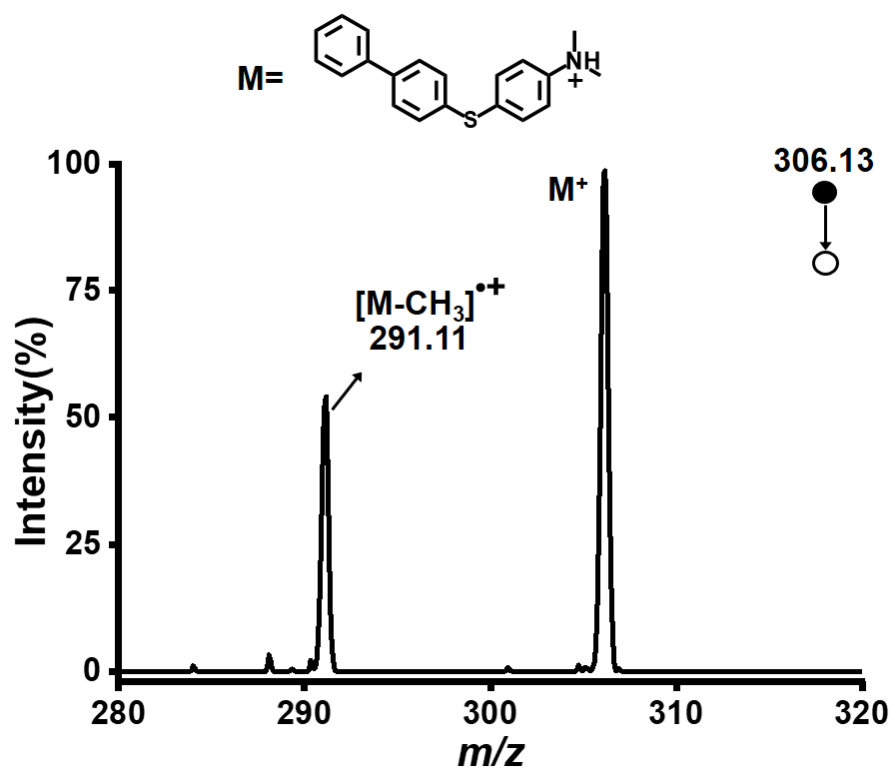
Supplementary Fig. 42. Mass spectrum of the MeOH/H₂O microdroplets containing both 4-bromo-N,N-dimethylaniline and 4-nitrothiophenol.



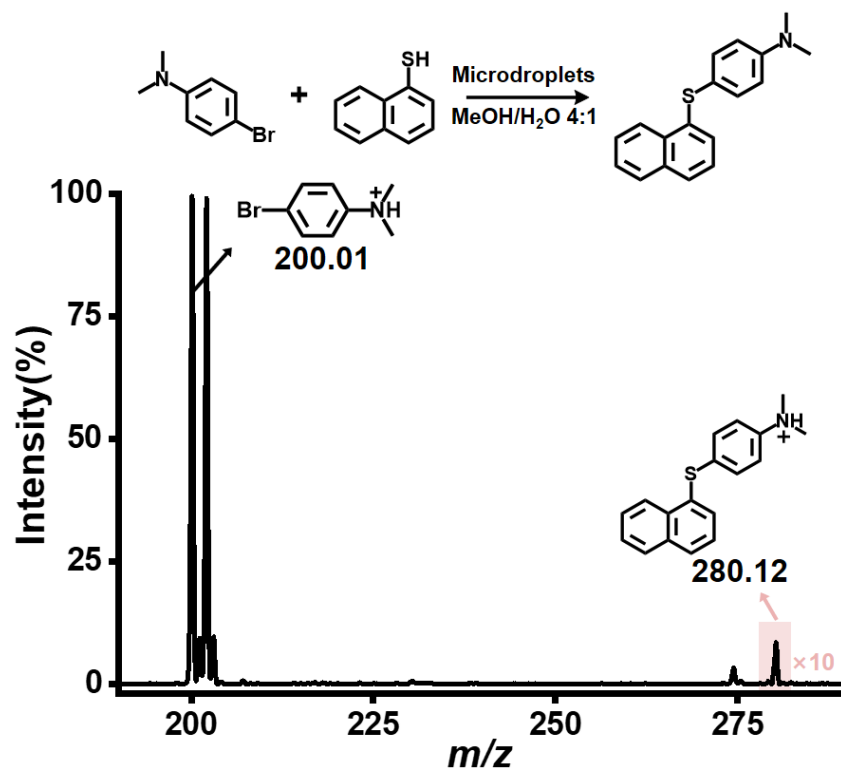
Supplementary Fig. 43. MS² spectrum of the peak at m/z 275.08 shown in Fig. S42.



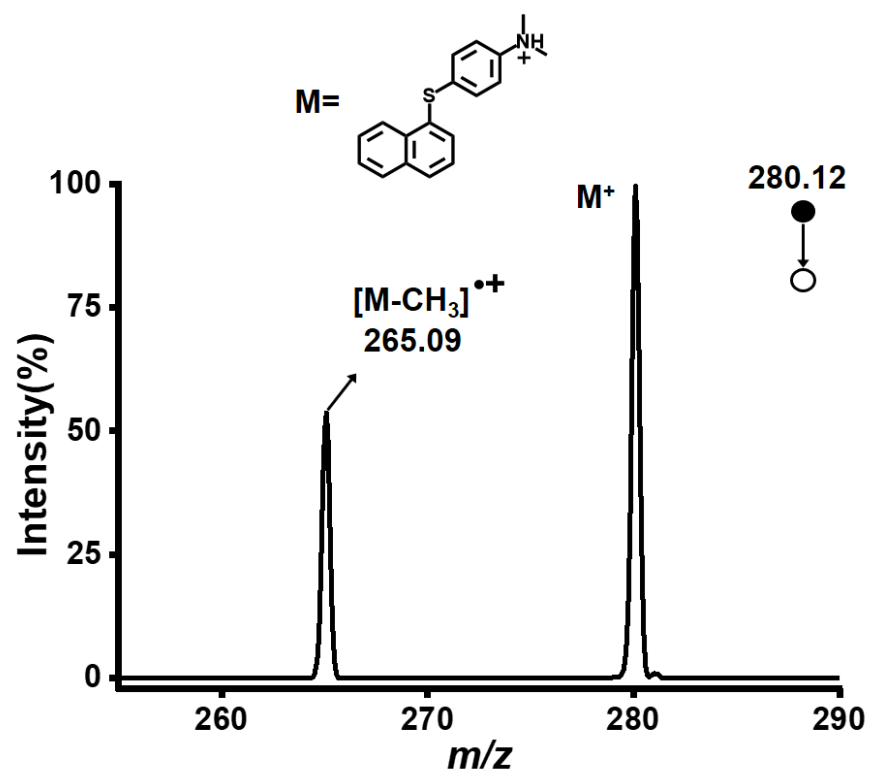
Supplementary Fig. 44. Mass spectrum of the MeOH/H₂O microdroplets containing both 4-bromo-N,N-dimethylaniline and 4-biphenylthiol.



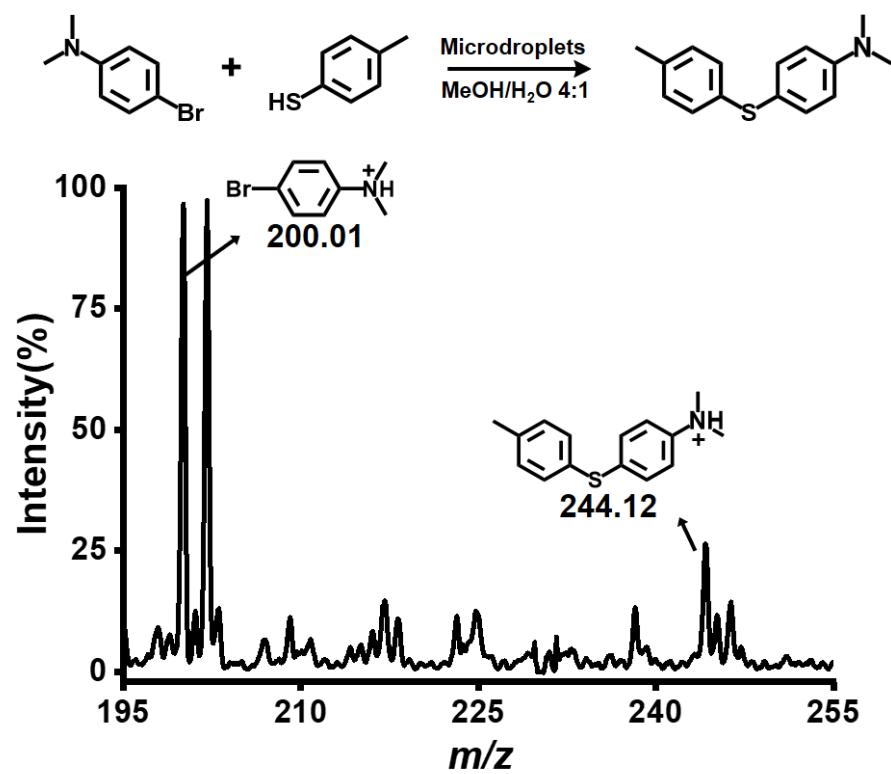
Supplementary Fig. 45. MS² spectrum of the peak at m/z 306.13 shown in Fig. S44.



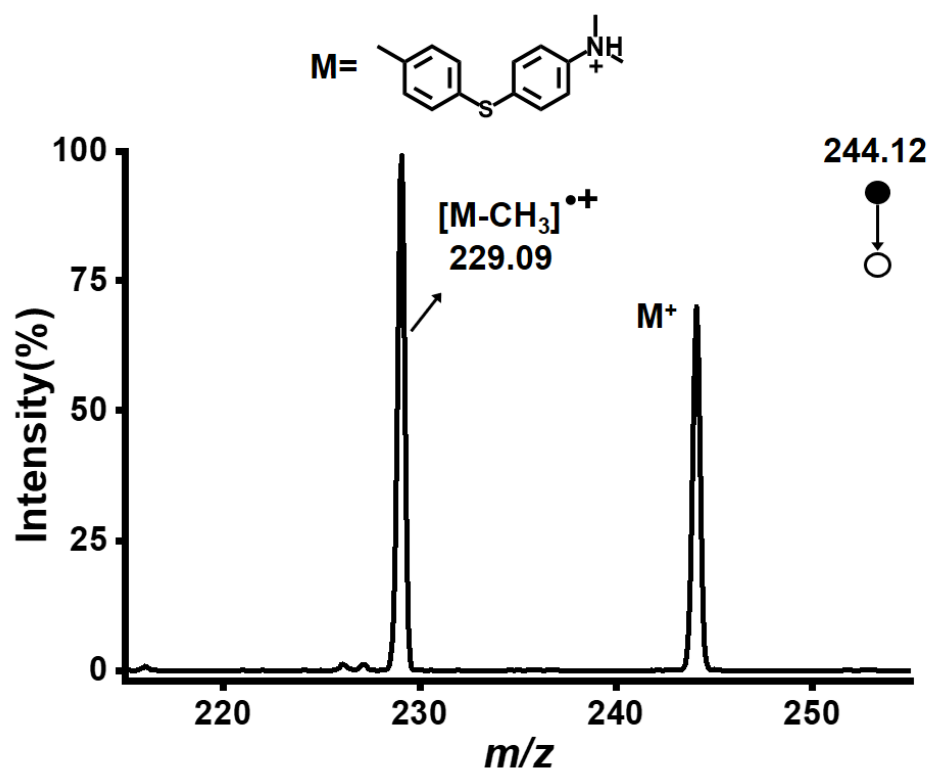
Supplementary Fig. 46. Mass spectrum of the MeOH/H₂O microdroplets containing both 4-bromo-N,N-dimethylaniline and 2-naphthalenethiol.



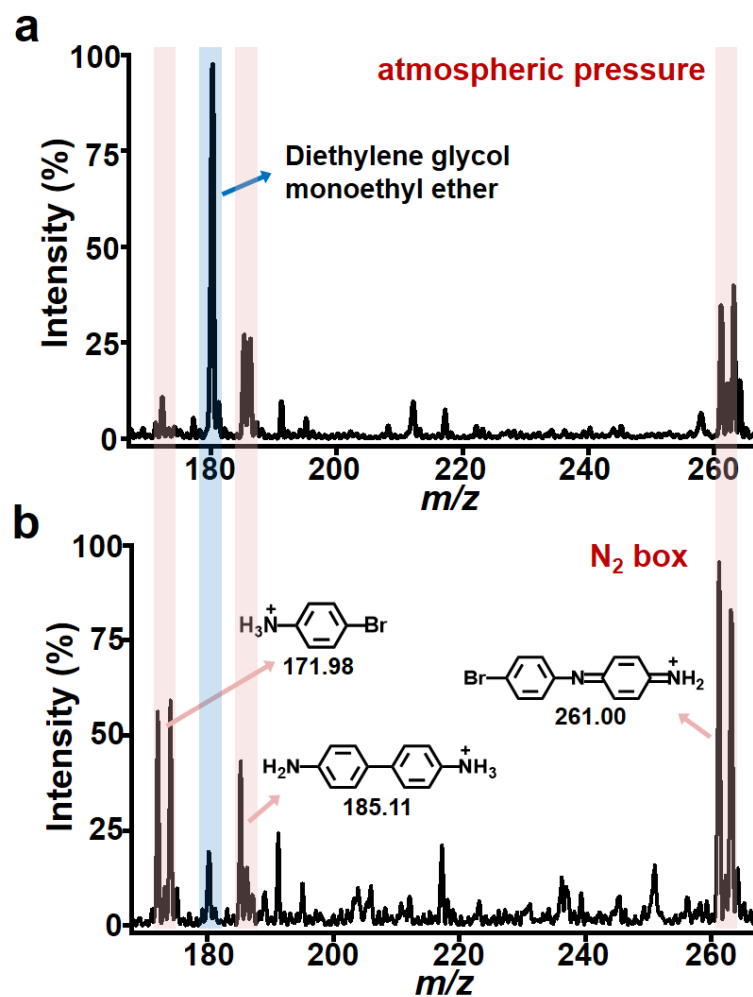
Supplementary Fig. 47. MS² spectrum of the peak at m/z 280.12 shown in Fig. S46.



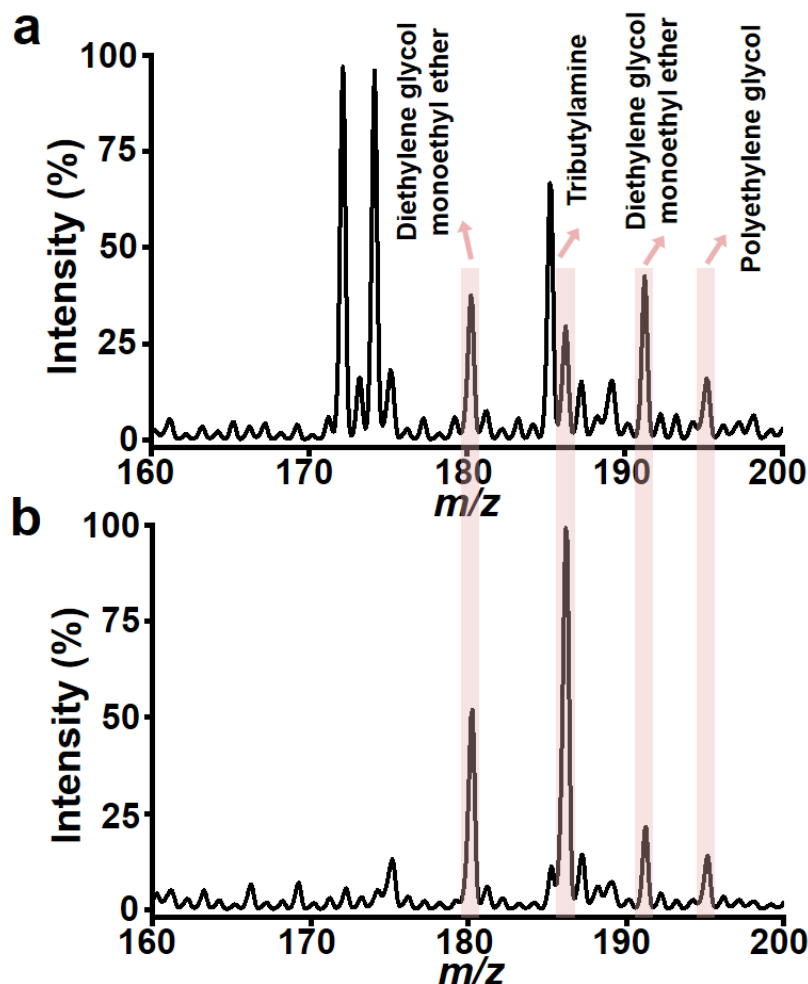
Supplementary Fig. 48. Mass spectrum of the MeOH/H₂O microdroplets containing both 4-bromo-N,N-dimethylaniline and p-toluenethiol.



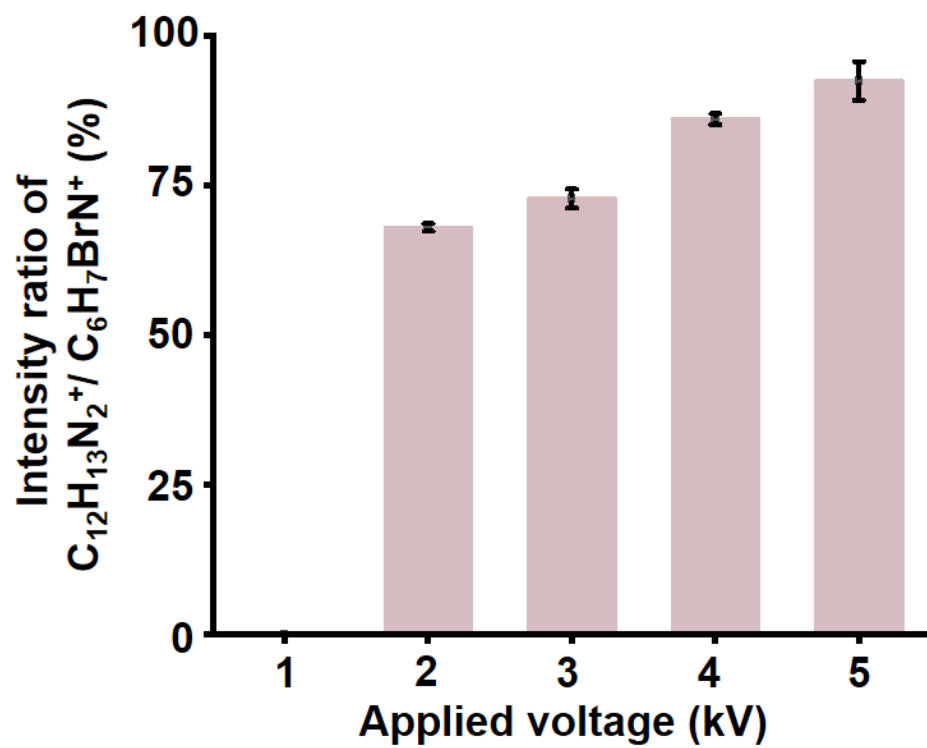
Supplementary Fig. 49. MS² spectrum of the peak at m/z 244.12 shown in Fig. S48.



Supplementary Fig. 50. (a) Mass spectrum of 4-bromoaniline-containing MeOH/H₂O microdroplets using N₂ as the nebulizing gas at atmospheric pressure; (b) Mass spectrum of the same microdroplets generated using N₂ as the nebulizing gas inside a N₂ box.



Supplementary Fig. 51. (a) Mass spectrum of 4-bromoaniline-containing MeOH/H₂O microdroplets using N₂ as the nebulizing gas; (b) Mass spectrum of blank MeOH/H₂O microdroplets using N₂ as the nebulizing gas. The peaks at m/z 180.16, 186.22, 191.09, and 195.12 are common background contaminants in mass spectrometry, corresponding to diethylene glycol monoethyl ether [C₆H₁₄O₃+NH₄]⁺, tributylamine [C₁₂H₂₇N+H]⁺, 1,8-diazabicyclo[5.4.0]undec-7-ene [C₉H₁₆N₂+K]⁺, and polyethylene glycol [C₈H₁₈O₅+H]⁺, respectively.



Supplementary Fig. 52. Optimization of the applied voltage on the sprayer.

Table S1. Mulliken charge and spin densities of TS (C-C).

ATOM	Mulliken charges	spin densities
C	0.181717	0.137869
C	-0.13346	0.014223
C	-0.12915	0.014559
C	-0.18672	0.03215
H	0.171632	-0.00159
Br	-0.09908	0.004444
C	-0.18691	0.009087
H	0.176063	-0.00071
C	0.26329	0.042959
H	0.172717	-0.00046
H	0.17271	0.000109
C	0.217022	-0.01308
C	-0.1706	0.230369
C	-0.18019	0.214338
Br	-0.12911	0.048658
C	-0.20582	-0.04098
H	0.164572	-0.00731
C	-0.20854	-0.03918
H	0.171611	-0.00666
C	0.268784	0.222222
H	0.166031	0.003718
H	0.165986	0.003333
N	-0.22711	1.055135
H	0.232489	-0.001
N	-0.13775	0.083111
Total	1	2

Table S2. Bond length of TS (C-C).

ATOM	Bond length (Å)
R(1,2)	1.4584
R(1,3)	1.4626
R(1,6)	1.9736
R(1,12)	1.9341
R(2,4)	1.353
R(2,5)	1.0817
R(3,7)	1.3502
R(3,8)	1.0826
R(4,9)	1.4364
R(4,10)	1.0838
R(7,9)	1.4391
R(7,11)	1.0837
R(9,25)	1.3195
R(12,13)	1.4517
R(12,14)	1.4529
R(12,15)	2.0053
R(13,16)	1.3671
R(13,17)	1.0815
R(14,18)	1.3654
R(14,19)	1.0824
R(16,20)	1.4198
R(16,21)	1.0831
R(18,20)	1.422
R(18,22)	1.0831
R(20,23)	1.3792
R(23,24)	1.0283

Table S3. Mulliken charge and spin densities of TS (C-N).

ATOM	Mulliken charges	spin densities
C	-0.004827	0.027619
C	-0.085646	-0.012701
C	-0.077324	-0.010545
C	-0.189234	0.025358
H	0.165705	0.000634
Br	-0.08169	0.003492
C	-0.219427	0.024544
H	0.166618	0.00042
C	0.145382	-0.007007
H	0.165204	-0.00056
H	0.180451	-0.001112
C	0.234568	0.036721
C	-0.146997	0.231498
C	-0.209357	0.232313
Br	-0.090975	0.060083
C	-0.183853	-0.036602
H	0.175153	-0.006693
C	-0.178606	-0.036117
H	0.1829	-0.007278
C	0.251769	0.265384
H	0.172548	0.00201
H	0.172439	0.001922
N	-0.224206	1.073655
H	0.237005	0.004921
N	0.004634	0.131606
Total	1	2

Table S4. Bond length of TS (C-N).

ATOM	Bond length (Å)
R(1,2)	1.3922
R(1,3)	1.3928
R(1,6)	1.9192
R(2,4)	1.3911
R(2,5)	1.082
R(3,7)	1.3904
R(3,8)	1.082
R(4,9)	1.3951
R(4,10)	1.0832
R(7,9)	1.3958
R(7,11)	1.0834
R(9,25)	1.4345
R(12,13)	1.4502
R(12,14)	1.4489
R(12,15)	1.9831
R(12,25)	1.8511
R(13,16)	1.3652
R(13,17)	1.0831
R(14,18)	1.3657
R(14,19)	1.0822
R(16,20)	1.4223
R(16,21)	1.0829
R(18,20)	1.4222
R(18,22)	1.0831
R(20,23)	1.3762
R(23,24)	1.0285

Appendix: Cartesian coordinates and energies of TS

TS (C-C)

UB3LYP SCF Energy: -5721.54295119 a.u.

UB3LYP enthalpy: -5721.335163 a.u.

UB3LYP free energy: -5721.396053 a.u.

Imaginary frequency: -456.27 cm⁻¹

Cartesian coordinates:

ATOM	x	y	z
C	0.059618	-0.006994	0.015029
C	-0.426173	1.293937	0.460556
C	-0.331266	-0.413827	-1.334365
C	-0.966587	2.178489	-0.408943
H	-0.297671	1.567811	1.499041
Br	-0.403709	-1.413346	1.319982
C	-0.881230	0.463184	-2.201204
H	-0.112730	-1.425317	-1.652442
C	-1.183335	1.805394	-1.779012
H	-1.270038	3.167021	-0.084498
H	-1.116188	0.172014	-3.218223
C	1.990887	0.085707	-0.032731
C	2.486651	-1.246484	-0.327684
C	2.342241	1.127602	-0.982452
Br	2.489738	0.625960	1.832769
C	3.037261	-1.541363	-1.543839
H	2.375916	-2.024685	0.415082
C	2.902350	0.821382	-2.189331
H	2.112537	2.157515	-0.741631
C	3.219282	-0.525210	-2.518477
H	3.359603	-2.551725	-1.763859
H	3.121956	1.606570	-2.902274
N	3.825886	-0.818660	-3.721883
H	3.149572	-1.051505	-4.460648
N	-1.683205	2.674984	-2.636330
H	-1.906647	3.620689	-2.349137

TS (C-N)

UB3LYP SCF Energy: -5721.56892910 a.u.

UB3LYP enthalpy: -5721.352026 a.u.

UB3LYP free energy: -5721.413703 a.u.

Imaginary frequency: -357.39 cm⁻¹

Cartesian coordinates:

ATOM	x	y	z
C	-1.832023	3.725056	0.365505
C	-1.620568	2.964835	1.512436
C	-1.417767	3.286013	-0.889743
C	-0.969350	1.740662	1.401099
H	-1.958987	3.306682	2.481594
Br	-2.731958	5.413667	0.513942
C	-0.769661	2.060580	-0.996809
H	-1.598811	3.877697	-1.777367
C	-0.547089	1.294511	0.148531
H	-0.816500	1.131955	2.284008
H	-0.455130	1.697296	-1.967822
C	1.987390	0.014052	-0.027938
C	2.304241	-1.401116	-0.028428
C	2.372555	0.786733	-1.191496
Br	2.456674	0.908039	1.678877
C	2.825313	-1.997339	-1.140559
H	2.097147	-1.986127	0.859267
C	2.896897	0.170865	-2.291866
H	2.221905	1.858362	-1.187131
C	3.137509	-1.230822	-2.297302
H	3.031586	-3.060448	-1.137393
H	3.159589	0.755868	-3.164680
N	3.600099	-1.851130	-3.435379
H	4.625884	-1.911696	-3.480230
N	0.137518	0.039205	0.033717
H	-0.095092	-0.596511	0.799247