

Supplementary Information

Sandmeyer Synthesis of Isatins: Preparation and Cyclization of Isonitrosoacetanilides

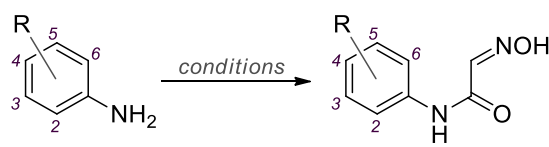
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Table S1. Conditions for the preparation of isonitrosoacetanilides

				
№	R	Conditions, yields	Melting point	Note
1	H	reflux 1–2 min, 80–95%; ^{1,2}	175; ^{1,3}	— ^a
2	2-Me	55°C, overnight; ⁴ reflux 30 min; ⁵ reflux 2 min, 72%; ⁶ 86%; ⁷ CCl ₃ CH(OEt)OH, EtOH–H ₂ O, 80°C, 3 h, 50%; ⁸	117–118; ⁶ 116–119; ⁷ 126–128; ⁸	recr. EtOH–H ₂ O; ⁸
3	2-Et	55°C, overnight; ⁴ reflux 2 min, 69%; ⁹ 45°C, 6.5 h, 86%; ¹⁰	107–108; ⁹ 105–106; ¹⁰	recr. H ₂ O; ¹⁰
4	2- <i>i</i> -Pr	55°C, overnight; ⁴ reflux 2 min, 89%; ⁹ reflux 40 min, 59%; ¹¹ 1. (AcO) ₂ CHCOCl, KHCO ₃ , CH ₂ Cl ₂ , –10–0°C; 2. NH ₂ OH·HCl, EtOH–H ₂ O, reflux 2 h, 72%; ¹²	109–110; ⁹ 104–108; ¹¹	extr. Et ₂ O; ¹¹ recr. Et ₂ O–hexane; ¹¹
5	2- <i>s</i> -Bu	55°C, overnight; ⁴ N ₂ –atm., 55°C, 18 h; ¹³	sticky oil; ^{4,13}	extr. EtOAc; ¹³
6	2- <i>t</i> -Bu	55°C, overnight; ⁴ reflux 2 min, 47%; ⁹ reflux 40 min; ¹¹ CCl ₃ CH(OEt)OH, reflux 40 min, 41%; ¹⁴	156–157; ⁹ 151–152; ¹¹	extr. EtOAc, flash chromatogr.; ¹⁴ recr. PhH–Et ₂ O; ¹¹
7	2-Ph	reflux 1–2 min, 42%; ¹⁵ 1. (AcO) ₂ CHCOCl, KHCO ₃ , CH ₂ Cl ₂ , –10–0°C; 2. NH ₂ OH·HCl, EtOH–H ₂ O reflux 2 h, 90%; ¹⁶	125–126; ¹⁵	recr. NaOH/AcOH; ¹⁶
8	2-CF ₃	NH ₂ OH·H ₂ SO ₄ , H ₂ O–EtOH, 60–80°C, 6 h, 93–97%; ¹⁷ reflux 1–2 min, 64%; ¹⁸ reflux 8 h, 35%; ¹⁹ reflux 30 min, 56%; ²⁰	oil; ¹⁷ 79–80°C; ¹⁸ 78; ²⁰ 82–84; ²¹	recr. CHCl ₃ ; ¹⁸ recr. NaOH/HCl; ¹⁹
9	2-F	55°C, overnight, 71%; ⁴ 75°C, 3 h, 75%; ²² CCl ₃ CH(OEt)OH, reflux 1–2 min, 86%; ²³ reflux 15 min, 67%; ²⁰	116–117; ²³ 118; ²⁰	— ^a
10	2-Cl	reflux 1–2 min, 94%; ² reflux 50 min, 47%; ^{24,20} NH ₂ OH·H ₂ SO ₄ , H ₂ O–EtOH, 60–80°C, 6 h, 85–89%; ¹⁷ 1. (AcO) ₂ CHCOCl, KHCO ₃ , CH ₂ Cl ₂ , –10–0°C; 2. NH ₂ OH·HCl, EtOH–H ₂ O, reflux 2 h, 81%; ¹⁶	150; ³ 152; ^{24,20}	recr. NaOH/HCl; ²⁴
11	2-Br	55°C, overnight, 85%; ⁴ Cl ₃ CCH(OEt)OH, 45°C, 4.5 h, 91%; ²⁵ 80°C, 1 h, 72%; ²⁶ 90°C, 2.5 h, 73%; ²⁷ reflux 40–60 min, 29%; ²⁰	170; ²⁷ 157; ²⁰	— ^a
12	2-I	55°C, overnight, 83%; ^{4,28} 1. (AcO) ₂ CHCOCl, KHCO ₃ , CH ₂ Cl ₂ , –10–0°C; 2. NH ₂ OH·HCl, EtOH–H ₂ O, reflux 2 h, 85%; ¹⁶ 80°C, 1 h, 76%; ²⁹ 20–45°C, 4.5 h, 82%; ¹⁰ reflux 10 min, 62%; ²⁰	157–158; ²⁹ 167–168; ¹⁰ 160; ²⁰	recr. EtOH; ¹⁰

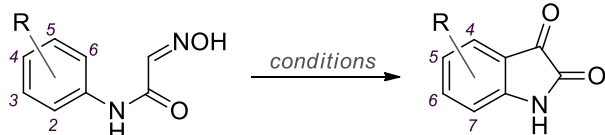
13	2-OMe	1. (AcO) ₂ CHCOCl, KHCO ₃ , CH ₂ Cl ₂ , –10–0°C; 2. NH ₂ OH·HCl, EtOH–H ₂ O, reflux 2 h, 82%; ¹⁶ 80–90°C, 1 h, 57%; ³⁰	118–120; ³¹ 140; ³ 146–147; ³² 144–145; ³⁰	recr. NaOH/HCl; ³⁰
14	2-OCF ₃	55°C, overnight, 85%; ⁴ reflux 8 h, 49%; ¹⁹	— ^a	recr. NaOH/HCl; ¹⁹
15	2-NO ₂	Ar–atm., 55°C, 24 h, 88%; ³³ 65°C, overnight, 83%; ³⁴ 1. (AcO) ₂ CHCOCl, KHCO ₃ , CH ₂ Cl ₂ , –10–0°C; 2. NH ₂ OH·HCl, EtOH–H ₂ O, reflux 2 h, 55%; ¹⁶ reflux 30 min, 20%; ³⁵	145.5–146; ³⁶ 142; ³⁵	recr. H ₂ O; ³⁵
16	2-CO ₂ H	1 equiv. of (NH ₄)SO ₄ , 49%; ³⁷	208; ³ 215; ³⁷	recr. EtOH; ³⁷
17	3-Me	reflux 1 min, 90%; ³⁸ N ₂ –atm., 55°C, overnight, 87%; ¹³ CCl ₃ CH(OEt)OH, EtOH–H ₂ O, 80°C, 3 h, 62%; ⁸	145; ^{38,39} 152–156; ⁸	recr. EtOH–H ₂ O; ⁸
18	3- <i>i</i> -Pr	55°C, overnight, 72%; ⁴	— ^a	— ^a
19	3-Ph	55°C, overnight, 88%; ⁴	— ^a	— ^a
20	3-CF ₃	reflux 1–2 min, 89%; ¹⁸ reflux 30 min, 83%; ³⁸ 20–90°C, 2 h, 80%; ⁴⁰	143; ¹⁸ 140; ³⁸	recr. CHCl ₃ ; ¹⁸
21	3-F	reflux 1 min, 87%; ^{38,20} 20–90°C, 2 h, 83%; ⁴⁰	175; ^{38,20}	— ^a
22	3-Cl	reflux 1–2 min, 40%; ^{24,38,20} 93%; ⁴¹ 20–90°C, 2 h, 85%; ⁴⁰	154; ³ 146; ^{24,38,20}	recr. NaOH/HCl; ²⁴ extr. Et ₂ O; ⁴¹
23	3-Br	reflux 15 min, 55%; ^{38,20} 20–90°C, 2 h, 92%; ⁴⁰ 20–90°C, 5 h, 95%; ⁴²	165; ^{38,20}	— ^a
24	3-I	80–90°C, 2 h, 87%; ⁴³ reflux 1 min, 74%; ^{38,20}	157; ^{38,20}	— ^a
25	3-OMe	reflux 1 min, 42%; ³⁸ reflux 20 min, 85%; ⁴⁵ 55°C, overnight, 71%; ⁴⁴ 1. (AcO) ₂ CHCOCl, KHCO ₃ , CH ₂ Cl ₂ , –10–0°C; 2. NH ₂ OH·HCl, EtOH–H ₂ O, reflux 2 h, 63%; ¹⁶	172; ³⁸ 170–172; ⁴⁴	recr. Et ₂ O–MeOH; ⁴⁴
26	3-OCF ₃	95°C, 30 min, 87%; ⁴⁶ H ₂ O–EtOH, reflux 15 min, 86%; ⁴⁷	140; ⁴⁶	— ^a
27	3-NO ₂	reflux 1 min, 48%; ³⁸ 20–90°C, 2 h, 88%; ⁴⁰ reflux 30 min, 80%; ³⁵	168; ³⁸ 172; ⁴⁸ 181; ³⁵	recr. EtOH; ^{48,35}
28	4-Me	reflux 1–2 min, 83–86%; ¹ 78%; ²⁰ NH ₂ OH·H ₂ SO ₄ , 60–80°C, 2 h, 96–99%; ¹⁷ CCl ₃ CH(OEt)OH, EtOH–H ₂ O, 80°C, 3 h, 64%; ⁸ 90°C, 2.5 h, 89%; ⁴⁹	162; ^{1,20,50} 161; ³⁹ 149–151; ⁸	recr. EtOH–H ₂ O; ⁸
29	4-Et	90°C, 2.5 h, 92%; ⁴⁹ 70°C, 6–8 h; ⁵² reflux 2 h, 75%; ⁵¹	— ^a	— ^a
30	4- <i>i</i> -Pr	55°C, overnight; ^{4,53} reflux 2 min; ⁵⁴	— ^a	— ^a
31	4- <i>t</i> -Bu	reflux 1 min; ⁵⁵ reflux 10 min, 93%; ⁵⁶	110–112; ⁵⁶	— ^a
32	4-CF ₃	reflux 1–2 min, 76%; ¹⁸ reflux 10 min; ⁵⁷	148.5; ¹⁸	recr. CHCl ₃ ; ¹⁸
33	4-F	reflux 2 min, 97%; ⁵⁸ reflux 1–2 min, 92%; ⁵⁹ reflux 1 min, 88%; ²⁰ 90°C, 2.5 h, 95%; ⁴⁹ 65°C, 2 h, 86%; ⁶⁰	160; ^{59,58} 161–164; ⁶⁰ 159; ²⁰	recr. EtOH–H ₂ O; ⁵⁹ recr. EtOAc; ⁶⁰

34	4-Cl	NH ₂ OH·H ₂ SO ₄ , 70–80°C, 3 h, 96–99%; ¹⁷ 90°C, 2.5 h, 84%; ⁴⁹ reflux 30 min, 86%; ⁶¹ NH ₂ OH·H ₂ SO ₄ , reflux 45 min, 72%; ³	160; ⁶¹ 165; ³	recr. EtOH; ⁶¹ recr. NaOH/HCl; ³
35	4-Br	60°C, overnight, 66%; ⁶² reflux 1 h, 91%; ⁶³ reflux 10 min, 66%; ⁶⁴ 100°C, 4 h, 83%; ⁶⁵ 1. (AcO) ₂ CHCOCl, KHCO ₃ , CH ₂ Cl ₂ , –10–0°C; 2. NH ₂ OH·HCl, EtOH–H ₂ O reflux 2 h, 80%; ¹⁶	172; ⁶² 174; ⁶⁴	— ^a
36	4-I	reflux 45 min; ⁶⁶ H ₂ SO ₄ –H ₂ O, reflux 30 min; ⁶⁷	180–182; ⁶⁶	recr. NaOH/HCl, MeOH; ⁶⁶
37	4-OMe	60°C, overnight, 59%; ⁶² 75°C, 63%; ⁶⁸ reflux 5 min, 63%; ⁶⁴ reflux 1 h, 85%; ⁶⁹	184–185; ^{64,68} 185; ⁶⁹ 181–182; ²¹	— ^a
38	4-OCF ₃	H ₂ O–EtOH, reflux 15 min, 90%; ⁷⁰ 80°C, 1.5 h; ⁷¹ 95°C; ⁷²	— ^a	— ^a
39	4-NO ₂	reflux 1 h; ² reflux 30 min, 77%; ³⁵ 1. (AcO) ₂ CHCOCl, KHCO ₃ , CH ₂ Cl ₂ , –10–0°C; 2. NH ₂ OH·HCl, EtOH–H ₂ O, reflux 2 h, 82%; ¹⁶	204–206; ³⁵ 184; ⁴⁸ 211–213; ²¹	recr. EtOH; ^{48,35}
40	4-CO ₂ H	H ₂ SO ₄ –H ₂ O, 90°C, 30 min, 64%; ⁷³ (NH ₄)SO ₄ , 81%; ³⁷	147; ³⁷	recr. EtOH; ³⁷
41	4-CO ₂ Et	1. (AcO) ₂ CHCOCl, KHCO ₃ , CH ₂ Cl ₂ , –10–0°C; 2. NH ₂ OH·HCl, EtOH–H ₂ O, reflux 2 h, 85%; ¹⁶ (NH ₄)SO ₄ , 80%; ³⁷ CCl ₃ CH(OEt)OH, H ₂ SO ₄ –H ₂ O, reflux 2 min, 90%; ⁷⁴ 75°C, 4 h, 94%; ⁷⁵	100; ³⁷	recr. EtOH; ³⁷
42	2,3-Me ₂	N ₂ –atm., 75°C, 195 min, 87%; ¹³ NH ₂ OH·H ₂ SO ₄ , 75°C, 195 min, 87%; ⁷⁶ reflux 3 min, 64%; ⁷⁷ 62–65°C, 1 h, 88%; ⁷⁸	131–132; ⁷⁷ 130–132; ⁷⁶ 122–126; ⁷⁸	recr. MePh; ⁷⁷
43	2,4-Me ₂	reflux 8 min, 55%; ⁷⁷ 20–80°C, 3 h, 64%; ⁷⁹ 67%; ⁷⁸ reflux 1 min, 74%; ²⁰	158–159; ⁷⁷ 159; ⁸⁰ 162; ²⁰ 173–175; ⁷⁸	recr. EtOAc– hexane; ⁷⁹ recr. PhH–EtOH; ⁷⁸
44	2,5-Me ₂	100°C, 1 h, 92%; ⁸¹ 70°C, 6–8 h; ⁵² reflux 5 min, 78%; ⁸² 33%; ⁷⁷ 1. (AcO) ₂ CHCOCl, KHCO ₃ , CH ₂ Cl ₂ , –10–0°C; 2. NH ₂ OH·HCl, EtOH–H ₂ O, reflux 2 h, 78%; ¹⁶	151–153; ⁷⁷ 149; ⁸⁰ 155–160; ⁸² 151; ³	recr. MePh; ⁷⁷
45	3,4-Me ₂	reflux 2 min, 84%; ⁷⁷ 90°C, 5 h; ⁸⁴	179–180; ⁷⁷	recr. EtOAc– heptane; ⁷⁷
46	3,5-Me ₂	45°C, 1.5 h, 75°C, 1 h, 84–86%; ^{85,86} 90°C, 5 h; ⁸⁴ 70°C, 6–8 h; ⁵² reflux 5 min, 33%; ⁷⁷	— ^a	— ^a
47	2,3-F ₂	60°C, 2 h, 64%; ⁸⁷ 100°C, 1 h; ⁸⁹ 50°C, 10 h; ⁸⁸ 50°C, overnight, 91%; ⁹⁰	— ^a	— ^a
48	2,4-F ₂	75°C, 3 h, 79%; ²² H ₂ SO ₄ –H ₂ O, 130°C, 30 min; ⁹¹	— ^a	— ^a
49	2,5-F ₂	reflux 1 min, 80%; ⁹²	— ^a	— ^a
50	3,4-F ₂	reflux 2 min, 94%; ⁵⁸	156; ⁵⁸	— ^a
51	3,5-F ₂	reflux 30–60 min, 91%; ⁹³ 45–55°C, 10 h, 63%; ⁹⁴	190–192; ⁹³	— ^a

52	2,3-Cl ₂	reflux 30 min, 13%; ^{24,20}	172; ^{24,20}	recr. NaOH/HCl; ²⁴
53	2,4-Cl ₂	70°C, 6–8 h; ⁵²	169; ⁹⁵	recr. EtOH; ⁹⁵
54	2,5-Cl ₂	reflux 15 min, 22%; ⁷⁷ reflux 30 min, 42%; ²⁰ EtOH–H ₂ O, 55°C, 12 h, 87%; ⁹²	163; ³ 167; ²⁰ 166–168; ⁷⁷	recr. NaOH/HCl; ²⁴
55	3,4-Cl ₂	reflux 1 min, 50%; ^{24,20} 80–90°C, 2 h; ⁹⁶	158; ³ 154; ^{24,20}	recr. NaOH/HCl; ²⁴
56	3,5-Cl ₂	reflux 15 min, 31%; ^{24,20} H ₂ O–dioxane, reflux 50 min, 89%; ^{97,98}	185; ³ 230; ^{24,20} 196–197; ^{97,98}	recr. NaOH/HCl; ²⁴
57	2,4-Br ₂	65–70°C, 2–5 h; ⁹⁹ reflux 1 min; ⁵⁰	215; ^{3,50}	— ^a
58	2,5-Br ₂	EtOH–H ₂ O, 80°C, 12 h, 72%; ^{100,101} EtOH–H ₂ O, reflux, 12 h, 84%; ¹⁰² MeOH–H ₂ O, reflux 12 h, 86%; ¹⁰³	148–150; ²¹	— ^a
59	3,5-Br ₂	EtOH–H ₂ O, 70–80°C, 3.5 h, 82–88%; ¹⁷ reflux 15 min, 11%; ⁷⁷	196–200; ¹⁷ 197–200; ⁷⁷ 196–198; ²¹	recr. NaOH/HCl; ⁷⁷
60	1-Aminotetralin	NH ₂ OH·H ₂ SO ₄ , reflux, 50%; ³⁹ 55°C, 18 h, 94%; ¹³	179; ³⁹	recr. EtOH; ³⁹
61	2-Aminotetralin	NH ₂ OH·H ₂ SO ₄ , reflux; ³⁹ N ₂ –atm., 50°C, overnight, 94%; ¹²⁷	168; ³⁹	recr. EtOH–H ₂ O; ³⁹
62	1-Naphthylamine	NH ₂ OH·H ₂ SO ₄ , reflux; ¹²⁸ N ₂ –atm., 50°C, overnight, 47%; ¹²⁷ reflux 1–2 min; ¹²⁹	— ^a	— ^a
63	2-Naphthylamine	reflux 1–2 min, 63%; ¹³⁰ reflux 4 h, 91%; ¹³¹	>185; ¹³⁰	— ^a

^a No data available

Table S2. Conditions for cyclization of isonitrosoacetanilides, yields and characteristics of the corresponding isatins

						
№	Isatin	Acet-anilide	Conditions for cyclization, yields	Melting point	State	Note
1	H	H	conc. H ₂ SO ₄ , 60–80°C, 10 min, 71–78%; ¹ conc. H ₂ SO ₄ , 60–80°C, 10 min, 67% (2 steps); ¹⁰⁴	189–192 (techn.), 196–197 (purified); ¹ 200–202; ¹⁰⁵ 201–204; ¹⁰⁴	brown-red crystals; ¹ orange red crystals; ¹⁰⁴	recr. NaOH/H ⁺ or AcOH; ¹ recr. PhH; ¹⁰⁵
2	5-Me	4-Me	conc. H ₂ SO ₄ , 60–80°C, 10 min, 90–94%; ¹ 95% H ₂ SO ₄ , rt 5 min, 80°C, 4 h, 65% (2 steps); ⁵²	187; ¹ 185–187; ¹⁰⁵ 180; ¹⁰⁶ 184–187; ⁵² 183–184; ¹⁰⁷	dark orange; ¹⁰⁴ red needles; ^{105,106} reddish brown solid; ⁵²	recr. EtOH; ^{105,106} recr. NaOH/H ⁺ or AcOH; ¹
3	5-Et	4-Et	conc. H ₂ SO ₄ , 60°C, 60 min, 74%; ⁵¹ 48%; ¹⁰⁸ 95% H ₂ SO ₄ , rt 5 min, 80°C, 4 h, 53% (2 steps); ⁵²	131–133; ⁵²	bright orange solid; ⁵¹ red solid; ^{52,108}	recr. MeOH; ¹⁰⁹ chromatogr.; ⁵¹
4	5- <i>i</i> -Pr	4- <i>i</i> -Pr	80°C, 10 min, 71% (2 steps); ^{4,53}	137; ¹⁰⁹	yellow solid; ¹⁰⁹	— ^a
5	5- <i>t</i> -Bu	4- <i>t</i> -Bu	80°C, 10 min, 51%; ^{53,56} 80°C, 10 min, 65% (2 steps); ⁵⁵	142–143; ⁵⁵ 110–111; ⁵⁶	red crystals; ⁵⁵ dark red solid; ⁵⁶	chromatogr.; ^{55,56}
6	5-CF ₃	4-CF ₃	conc. H ₂ SO ₄ , 85–90°C, 15 min, 45%; ¹⁸ 98.5%–H ₂ SO ₄ , 80°C, 2 h, 42% (2 steps); ⁵⁷	246; ¹⁸ 191–193; ¹⁰⁵ 244–245; ⁵⁷	light brown crystals; ¹⁸ yellow needles; ¹⁰⁵ brown crystals; ⁵⁷	recr. AcOH, MeOH; ¹⁸ recr. PhH; ¹⁰⁵ recr. EtOH; ⁵⁷
7	5-F	4-F	conc. H ₂ SO ₄ , 80°C, 20 min, 56%; ⁵⁸ conc. H ₂ SO ₄ , 85°C, 3 h, 55% (2 steps); ⁹¹ conc. H ₂ SO ₄ , 70–80°C, 10 min, 72%; ⁵⁹ conc. H ₂ SO ₄ , 75°C, 20 min, 88%; ⁶⁰ conc. H ₂ SO ₄ , 65°C, 1 h, 74%; ²	227; ⁵⁸ 223–225; ¹¹⁰ 225; ⁵⁹ 223–226; ⁶⁰ 221–224; ² 226–228; ⁵²	brick red needles; ⁵⁸ orange solid; ⁹¹ golden yellow solid; ^{110,59} brownish solid; ⁶⁰ red solid; ² dark red colored solid; ⁵²	recr. AcOH–H ₂ O; ⁵⁸ extr. EtOAc, chromatogr.; ⁹¹ recr. EtOH, AcOH; ⁵⁹
8	5-Cl	4-Cl	conc. H ₂ SO ₄ , 95–100°C, 15 min, 92%; ⁶¹ conc. H ₂ SO ₄ , 90°C, 30 min, 90%; ¹¹¹ conc. H ₂ SO ₄ , 105°C, 10–15 min, 90%; ³	248–251; ¹⁰⁵ 250; ⁶¹ 237–239; ¹¹¹ 225–227; ⁷² 256–258; ¹⁰⁷ 245–247; ⁵²	dark brown solid; ¹¹² yellow solid; ⁷² orange solid; ¹⁰⁷ dark orange solid; ⁵²	recr. EtOH; ¹⁰⁵ recr. AcOH–H ₂ O; ⁶¹ recr. NaOH/H ⁺ ; ⁷²
9	5-Br	4-Br	85% H ₂ SO ₄ , 80°C, 10 min, 96%; ⁶² conc. H ₂ SO ₄ , 80°C, 10 min, 67% (2 steps); ¹⁰⁴ 98% H ₂ SO ₄ , 80°C, 10 min, 80%; ⁶³ conc. H ₂ SO ₄ , 1 h, 80°C, 10 min, 96%; ⁶⁴	252; ^{62,64} 271–273; ¹⁰⁴ 247–250; ^{113,107}	yellow color; ¹⁰⁴ pale yellow solid; ¹⁰⁷ orange solid; ⁵²	— ^a

10	5-I	4-I	conc. H ₂ SO ₄ , 70°C, 1 h; ⁶⁷ conc. H ₂ SO ₄ , 100°C, 15 min; ⁶⁶	276–280; ¹¹³ 264–265; ⁶⁶ 281–282; ¹¹⁴ 248–250; ¹⁰⁷	red prisms; ¹¹⁴ red solid; ¹⁰⁷	extr. EtOAc, chromatogr.; ⁶⁷ recr. EtOH; ⁶⁶
11	5-OMe	4-OMe	85% H ₂ SO ₄ , 80°C, 10 min, 88%; ⁶² 90% H ₂ SO ₄ , 80°C, 10 min, 69%; ⁸³ 90% H ₂ SO ₄ , 65–80°C, 1.5–2 h, 88%; ⁶⁸ 90% H ₂ SO ₄ , 110°C, 5 min, 71%; ⁶⁹	202–204; ¹⁰⁵ 201–205; ^{64,62,68} 201; ⁶⁹ 196–198; ¹⁰⁷ 201–203; ⁸³	brown-red solid; ⁶⁸ red solid; ⁶⁹ yellow solid; ¹⁰⁷	recr. PhH; ¹⁰⁵ recr. AcOH; ⁶⁸ recr. H ₂ O; ⁸³
12	5-OCF ₃	4-OCF ₃	conc. H ₂ SO ₄ , 100°C, 1 h, 46%; ⁷⁰ conc. H ₂ SO ₄ , 70°C, 5 h, 29% (2 steps); ⁷¹ conc. H ₂ SO ₄ , 80°C, 10 min, 67% (2 steps); ¹⁰⁴ conc. H ₂ SO ₄ , 80°C, 30 min, 68% (2 steps); ⁷²	238–240; ¹⁰⁴ 191–193; ⁷² 168–170; ¹⁰⁷	yellow solid; ^{104,72,107}	extr. EtOAc, chromatogr.; ⁷¹ recr. NaOH/H ⁺ ; ⁷²
13	5-NO ₂	4-NO ₂	conc. H ₂ SO ₄ , 50°C, 20 min, 65°C, 1 h, 76%; ² conc. H ₂ SO ₄ , 80°C, 10 min, 48%; ¹⁰⁴	254–257; ² 252–254; ¹⁰⁵ 251; ¹¹³	pale yellow crystals; ² dark orange; ¹⁰⁴	recr. EtOH; ¹⁰⁵
14	5-CO ₂ H	4-CO ₂ H	conc. H ₂ SO ₄ , 95°C, 1 h, 65%; ⁷³ 89.5% H ₂ SO ₄ , 75–78°C, 10–15 min, 79%; ³⁷	274–275; ⁷³ 265–267; ³⁷	yellow crystals; ³⁷	recr. Me ₂ CO; ³⁷
		4-CO ₂ Et	conc. H ₂ SO ₄ , 90°C, 30 min, 52%; ⁷⁴ N ₂ -atm, conc. H ₂ SO ₄ , 80°C, 30 min, 95%; ⁷⁵			
15	5-CO ₂ Et	4-CO ₂ Et	89.5% H ₂ SO ₄ , 75–78°C, 10–15 min, 75%; ³⁷	205–207; ¹⁰⁵ 150; ³⁷	yellow solid; ¹⁰⁵	recr. Et ₂ O; ¹⁰⁵
16	7-Me	2-Me	86% H ₂ SO ₄ , 75°C, 30 min, 61– 78%; ¹¹⁵ conc. H ₂ SO ₄ , 50–80°C, 30 min, 38% (2 steps); ⁵ conc. H ₂ SO ₄ , 50–80°C, 20 min, 32%; ⁶	267–269; ¹⁰⁵ 267; ¹⁰⁶ 273; ⁶ 270–273; ⁵	deep-red crystals (AcOH); ¹¹⁵ orange-red needles (AcOH); ¹⁰⁶ orange solid; ⁶	recr. MeOH; ¹⁰⁵ recr. AcOH; ^{115,106}
17	7-Et	2-Et	86% H ₂ SO ₄ , 55°C, 25 min, 70°C, 20 min, 81%; ¹⁰ conc. H ₂ SO ₄ , 90–105°C, 15 min, 27%; ¹³ 93% H ₂ SO ₄ , 60–70°C, 10 min, 81%; ⁹	189–190; ¹⁰ 193–194; ⁹	orange-brown precipitate; ¹³ rust colored crystals; ¹⁰	recr. MeOH; ¹⁰
18	7- <i>i</i> -Pr	2- <i>i</i> -Pr	95% H ₂ SO ₄ , 65°C, 10 min, 80°C, 10 min, 95%; ¹¹ 93% H ₂ SO ₄ , 60–70°C, 10 min, 89%; ⁹	189–191; ¹¹ 196–198; ⁹	orange solid; ¹¹	— ^a
19	7- <i>s</i> -Bu	2- <i>s</i> -Bu	95% H ₂ SO ₄ , 65°C, 10 min, 80°C, 10 min; ¹¹ conc. H ₂ SO ₄ , 80°C, 30 min, 52%; ¹³	130–132; ¹¹	— ^a	— ^a
20	7- <i>t</i> -Bu	2- <i>t</i> -Bu	95% H ₂ SO ₄ , 65°C, 10 min, 80°C, 10 min; ¹¹ 93% H ₂ SO ₄ , 60–70°C, 10 min, 98%; ⁹	227–230; ¹¹ 236–238; ⁹	— ^a	— ^a
21	7-Ph	2-Ph	conc. H ₂ SO ₄ , 0–20°C, 4 h, 88%; ¹⁵	184–184.5; ¹⁵ 185–186; ²⁹	orange crystals; ¹⁵ orange solid; ²⁹	recr. DCM– MeOH; ¹⁵

22	7-CF ₃	7-CF ₃	conc. H ₂ SO ₄ , 30 min, 75–90°C, 45 min, 60%; ¹⁸ conc. H ₂ SO ₄ , 60–70°C, 80°C, 3 h, 78%; ¹⁹ conc. H ₂ SO ₄ , 90°C, 15 min, 52%; ²⁰	189–190; ¹⁸ 192; ²⁰	reddish-brown crystals; ¹⁸ red solid; ¹⁹ orange crystals; ²⁰	recr. EtOH; ²⁰
23	7-F	2-F	conc. H ₂ SO ₄ , 70°C, 1 h, 70–90°C, 1 h, 47–57%; ²² 95% H ₂ SO ₄ , 80°C, 4 h, 52% (2 steps); ⁵²	186–190; ²² 192–194; ⁵²	orange powder; ²² yellowish orange solid; ⁵²	extr. EtOAc; ^{22,52} recr. Me ₂ CO–H ₂ O; ²²
24	7-Cl	2-Cl	conc. H ₂ SO ₄ , 95°C, 10–15 min, 35%; ^{3,20} conc. H ₂ SO ₄ , 65°C, 1 h, 78%; ² conc. H ₂ SO ₄ , 70–100°C, 30 min, 70%; ³¹	175; ^{3,20} 176–178; ¹⁰⁷ 152–154; ² 183–185; ³¹	reddish brown; ³ yellow solid; ¹⁰⁷ orange needles; ²⁰ red solid; ² orange solid; ³¹	recr. AcOH; ²⁰
25	7-Br	2-Br	conc. H ₂ SO ₄ , 70°C, 20 min, 81%; ²⁵ conc. H ₂ SO ₄ , 80°C, 15 min, 48%; ²⁶ conc. H ₂ SO ₄ , 60–80°C, 45 min, 65%; ²⁷	195–200; ²⁷ 195; ²⁰	red amorphous solid; ²⁶ orange-red needles; ²⁰	extr. EtOAc, flash chromatogr.; ²⁶ recr. H ₂ O; ²⁷ recr. AcOH; ²⁰
26	7-I	2-I	86% H ₂ SO ₄ , 70°C, 20 min, 80%; ¹⁰ conc. H ₂ SO ₄ , 80°C, 10–15 min, 50%; ²⁹ 80%; ²⁸	208; ²⁹ 221–222; ¹⁰ 214; ²⁰	red; ²⁹ dark red powder; ²⁸ bright red crystals; ¹⁰ deep red needles; ²⁰	recr. MeOH; ¹⁰ recr. AcOH; ²⁰
27	7-OMe	2-OMe	85% H ₂ SO ₄ , 85°C, 15 min, 18%; ³¹ PPA, 100°C, 22%; ¹¹⁶	240–242; ³¹ 242–243; ¹¹⁶	— ^a	extr. CHCl ₃ ; ³¹ recr. CHCl ₃ ; ¹¹⁶
28	7-OCF ₃	2-OCF ₃	conc. H ₂ SO ₄ , 80°C, 3 h, 89%; ¹⁹ conc. H ₂ SO ₄ , 80°C, 10 min, 70%; ⁴	— ^a	red solid; ¹⁹	— ^a
29	7-NO ₂	2-NO ₂	conc. H ₂ SO ₄ , 60°C, 3 h, 89%; ³³ conc. H ₂ SO ₄ , 90°C, 150 min, 91%; ³⁴ conc. H ₂ SO ₄ , 95–100°C, 15 min, 68%; ³⁶	232–233; ³⁶	brick red powder; ³⁴ tan powder; ³⁶	recr. AcOH; ³⁶
30	7-CO ₂ H	2-CO ₂ H	89.5% H ₂ SO ₄ , 75–78°C, 10–15 min, 90%; ³⁷ conc. H ₂ SO ₄ , 95–110°C, 10–15 min; ³	245; ³⁷ 235; ³	yellow crystals; ³⁷ brownish yellow; ³	recr. Me ₂ CO; ³
31	4-Me + 6-Me	3-Me	90% H ₂ SO ₄ , 60–70°C, 30 min, (4-isomer, 16%; 6-isomer, 14%); ³⁸ PPA, 60°C, 6 h (mixture of isomers, 81%; 4-isomer, 26%); ¹¹⁷ MsOH, 80°C, 10 min (mixture of isomers 30/70); ¹¹⁸	<u>4-Isomer</u> : 193; ³⁸ 189; ¹¹⁹ 188–192; ¹¹⁷ <u>6-Isomer</u> : 189; ³⁸ 180–185; ¹¹⁷	<u>4-Isomer</u> : red needles; ³⁸ orange-red leaves; ¹¹⁹ <u>6-Isomer</u> : orange needles; ³⁸	separation; ^{119,117} recr. EtOH; ^{38,119}
32	4- <i>i</i> -Pr + 6- <i>i</i> -Pr	3- <i>i</i> -Pr	conc. H ₂ SO ₄ , 55–70°C, 80°C, 10 min (mixture of isomers, 78%; 6-isomer, 59%); ⁴	— ^a	<u>6-Isomer</u> : dark brown solid; ⁴	— ^a
33	4-CF ₃ + 6-CF ₃	3-CF ₃	conc. H ₂ SO ₄ , 85–90°C, 15 min (4-isomer, 47%); ¹⁸ conc. H ₂ SO ₄ , 90–95°C, 30 min (4-isomer, 17%); ³⁸ 86% H ₂ SO ₄ , 85°C, 15 min (4-isomer, 26%; 6-isomer, 11%); ⁴⁰	<u>4-Isomer</u> : 212–212.5; ¹⁸ 224; ³⁸	<u>4-Isomer</u> : yellow plates; ³⁸	recr. AcOH, then MeOH; ¹⁸ separation chromatogr.; ⁴⁰ recr. NaOH/H ⁺ ; ⁸⁰

34	4-F + 6-F	3-F	86% H ₂ SO ₄ , 85°C, 15 min (4-isomer, 6%; 6-isomer, 88%); ⁴⁰ conc. H ₂ SO ₄ , 90–95°C, 30 min (4-isomer, traces; 6-isomer, 69%); ^{38,20} conc. H ₂ SO ₄ , 65–80°C, 45 min (4-isomer, 64%; 6-isomer, 14%); ⁸⁰	<u>4-Isomer:</u> 212; ³⁸ <u>6-Isomer:</u> 197; ^{38,20}	<u>4-Isomer:</u> orange plates; ³⁸ <u>6-Isomer:</u> yellow needles; ^{38,20}	recr. EtOH, AcOH; ^{38,20} separation; ^{40,80}
35	4-Cl + 6-Cl	3-Cl	conc. H ₂ SO ₄ , 90–95°C, 30 min (4-isomer, 33%; 6-isomer, 31–35%); ^{24,38,20} conc. H ₂ SO ₄ , 90–95°C, 15 min (4-isomer, 46%; 6-isomer, 30%); ⁴¹ 86% H ₂ SO ₄ , 85°C, 15 min (4-isomer, 53%; 6-isomer, 32%); ⁴⁰ conc. H ₂ SO ₄ , 60–65°C, 30 min, 80°C, 15 min (4-isomer, 59%; 6-isomer, 22%); ⁸⁰	<u>4-Isomer:</u> 256; ^{24,38,20} 256–258.5; ⁴¹ <u>6-Isomer:</u> 263; ^{24,38,20} 258–259; ⁴¹ 260; ¹⁰⁶	<u>4-Isomer:</u> orange red needle; ^{24,38,20} red needles; ⁴¹ <u>6-Isomer:</u> yellow plates; ^{24,38,20} golden yellow needles (AcOH); ¹⁰⁶	separation; ^{24,38,20,40} , ^{80,41} recr. AcOH; ^{41,38,20}
36	4-Br + 6-Br	3-Br	conc. H ₂ SO ₄ , 90–95°C, 30 min (4-isomer, 46%; 6-isomer, 29%); ^{38,20} 86% H ₂ SO ₄ , 85°C, 15 min (4-isomer, 41%; 6-isomer, 28%); ⁴⁰ conc. H ₂ SO ₄ , 80°C, 15 min (4-isomer, 56%; 6-isomer, 27%) 56%; ⁸⁰	<u>4-Isomer:</u> 267; ³⁸ <u>6-Isomer:</u> 270; ³⁸	<u>4-Isomer:</u> orange-red needles; ^{38,20} <u>6-Isomer:</u> yellow plates; ^{38,20}	recr. AcOH; ^{38,20} separation; ^{40,80}
37	4-I + 6-I	3-I	conc. H ₂ SO ₄ , 90–95°C, 30 min (4-isomer, 45%; 6-isomer, 15%); ^{38,20} conc. H ₂ SO ₄ , 80°C, 15 min (4-isomer, 53%; 6-isomer, 29%); ⁸⁰	<u>4-Isomer:</u> 260; ^{38,20} <u>6-Isomer:</u> 274; ^{38,20}	<u>4-Isomer:</u> red needles; ^{38,20} <u>6-Isomer:</u> yellow plates; ^{38,20}	recr. AcOH; ^{38,20} separation; ⁸⁰
38	6-OMe	3-OMe	PPA, 55°C, 6 h, 93%; ⁴⁵ PPA, 55°C, 1 h, 82%; ⁴⁴ 90% H ₂ SO ₄ , 60–70°C, 30 min, 23%; ³⁸	230; ³⁸ 235–237; ⁴⁴	amber plates; ³⁸ red solid; ⁴⁴	recr. EtOH; ³⁸ recr. hexane– THF; ⁴⁴ extr. EtOAc; ⁴⁴
39	6-OPh	3-OPh	BF ₃ ·Et ₂ O, 85°C, 45 min, 13%; ^{120,121}	— ^a	— ^a	— ^a
40	6-OCF ₃	3-OCF ₃	conc. H ₂ SO ₄ , 90°C, 50 min, 60%; ⁴⁶ conc. H ₂ SO ₄ , 100°C, 1 h, 38%; ⁴⁷	169–170; ⁴⁶	brown solid; ⁴⁷	extr. EtOAc, chromatogr.; ⁴⁶
41	4-NO ₂	3-NO ₂	conc. H ₂ SO ₄ , 80°C, 10 min, 26%; ⁴⁰	248–250; ¹⁰⁵	— ^a	recr. EtOH; ¹⁰⁵ extr. EtOAc, chromatogr.; ⁴⁰
42	6,7-Me ₂	2,3-Me ₂	86% H ₂ SO ₄ , 75°C, 30 min, 61–78%; ¹¹⁵ MeSO ₃ H, 70–80°C, 75 min, 65%; ⁷⁶ 70%; ¹³ 100% HF rt 15–20 min, 93%; ⁷⁸	252–253; ⁷⁶ 230–232; ⁷⁷ 255–258; ⁷⁸ 250–255; ¹¹⁵	orange-red solid; ⁷⁶ orange; ^{77,78} deep-red crystals (AcOH); ¹¹⁵	recr. NaOH/H ⁺ ; ^{13,115,76,7} _{7,78}
43	5,7-Me ₂	2,4-Me ₂	86–88% H ₂ SO ₄ , 75°C, 30 min, 61–78%; ¹¹⁵ 90%; ⁷⁹ 100% HF, rt 15–20 min, 89%; ⁷⁸	249–251; ⁷⁸ 247–249; ¹¹⁵ 228–231; ⁷⁷ 243; ^{106,20} 239–241; ¹²²	deep-red crystals; ^{115,20} red needles (AcOH); ¹⁰⁶ orange solid; ¹²²	recr. AcOH; ^{115,106} recr. EtOH; ²⁰
44	4,7-Me ₂	2,5-Me ₂	86% H ₂ SO ₄ , 80°C, 1 h; ¹²³ 95% H ₂ SO ₄ , 80°C, 4 h, 42% (2 steps); ⁵² conc. H ₂ SO ₄ , 70°C, 30 min, 19%; ⁸¹ 86% H ₂ SO ₄ , 75°C, 10 min, 72%; ⁸²	250; ³ 267; ¹⁰⁶ 265–270; ⁸² 260–264; ⁷⁷ 190–192; ⁵²	orange-yellow; ³ orange-red needles (AcOH); ¹⁰⁶ red-orange solid; ⁸² orange; ⁷⁷	— ^a

45	4,5-Me ₂ + 5,6-Me ₂	3,4-Me ₂	91% H ₂ SO ₄ , 75°C, 10 min (4,5-isomer, 17–25%; 5,6-isomer, 34–46%); ^{77,124,84}	<u>4,5-Isomer:</u> 225–226; ^{77,125} <u>5,6-Isomer:</u> 214–215; ^{77,126} 217–218; ¹²⁵	<u>4,5-Isomer:</u> red; ⁷⁷ orange solid; ⁸³ <u>5,6-Isomer:</u> red; ⁷⁷ orange needles; ¹²⁶ crystalline red solid; ¹²⁴	separation; ^{77,124} recr. EtOH; ¹²⁶
46	4,6-Me ₂	3,5-Me ₂	conc. H ₂ SO ₄ , 80°C, 30 min, 50%; ⁸⁵ 44%; ⁸⁶ conc. H ₂ SO ₄ , 55°C, 30 min; ⁸⁴ 95% H ₂ SO ₄ , 80°C, 4 h, 45% (2 steps); ⁵²	228–231; ⁵²	orange solid; ⁸⁶ red solid; ⁵²	extr. EtOAc; ⁵²
47	6,7-F ₂	2,3-F ₂	conc. H ₂ SO ₄ , 80°C, 3 h, 55%; ⁸⁷ conc. H ₂ SO ₄ , 70–90°C, 1 h; ⁸⁸ conc. H ₂ SO ₄ , 80°C, 40 min, 57%; ⁸⁹ conc. H ₂ SO ₄ , 80°C, 3 h, 55% (2 steps); ⁹⁰	— ^a	brown solid; ⁸⁷ yellow solid; ⁸⁹ dark green solid; ⁹⁰	extr. EtOAc; ⁸⁸ chromatogr.; ⁸⁹
48	5,7-F ₂	2,4-F ₂	conc. H ₂ SO ₄ , 85°C, 3 h, 11% (2 steps); ⁹¹	— ^a	orange solid; ⁹¹	extr. EtOAc, chromatogr.; ⁹¹
49	4,7-F ₂	2,5-F ₂	conc. H ₂ SO ₄ , 90°C, 1 h, 76%; ⁹²	— ^a	— ^a	chromatogr.; ⁹²
50	5,6-F ₂	3,4-F ₂	conc. H ₂ SO ₄ , 80°C, 20 min, 55%; ⁵⁸	226; ⁵⁸	shiny red needles; ⁵⁸	recr. AcOH– H ₂ O; ⁵⁸
51	4,6-F ₂	3,5-F ₂	96% H ₂ SO ₄ , 58–62°C, 5 h, 75%; ⁹³	— ^a	yellow solid; ⁹³	— ^a
52	6,7-Cl ₂	2,3-Cl ₂	conc. H ₂ SO ₄ , 120°C, 10 min, 64%; ²⁰	204; ²⁰	yellow–orange needles; ²⁰	recr. AcOH; ²⁰
53	5,7-Cl ₂	2,4-Cl ₂	95% H ₂ SO ₄ , 80°C, 4 h, 52% (2 steps); ⁵²	221–223; ⁵²	reddish yellow solid; ⁵²	— ^a
54	4,7-Cl ₂	2,5-Cl ₂	conc. H ₂ SO ₄ , 90–95°C, 30 min, 37%; ^{24,20} conc. H ₂ SO ₄ , 80°C, 20 min, 98%; ⁹²	245; ^{24,20}	light orange needles; ^{24,20} red solid; ⁹²	separation; ^{24,20}
55	4,5-Cl ₂ + 5,6-Cl ₂	3,4-Cl ₂	conc. H ₂ SO ₄ , 90–95°C, 30 min (4,5-isomer, 41%; 5,6-isomer, 10%); ^{24,20} conc. H ₂ SO ₄ , 80°C, 15 min (4,5-isomer, 49%; 5,6-isomer, 33%); ^{80,96}	<u>4,5-Isomer:</u> 250; ^{24,20} 245–247; ⁷⁷ <u>5,6-Isomer:</u> 278; ²⁴	<u>4,5-Isomer:</u> red plate; ^{24,20} deep red crystals (AcOH); ⁷⁷ <u>5,6-Isomer:</u> orange red needles; ^{24,20}	separation; ⁸⁰ recr. EtOH; ^{24,20} recr. AcOH; ⁷⁷
56	4,6-Cl ₂	3,5-Cl ₂	conc. H ₂ SO ₄ , 90–95°C, 30 min, 30%; ^{24,20} conc. H ₂ SO ₄ , 90°C, 1 h, 96%; ⁹⁷ conc. H ₂ SO ₄ , 90°C, 10 min, 96%; ⁹⁸	251; ^{24,20} 250; ³ 228–230; ^{97,98}	yellow needles; ^{24,20} lemon yellow; ³ orange colored solid; ⁹⁸	separation; ^{24,20}
57	4,7-Br ₂	2,5-Br ₂	86% H ₂ SO ₄ , 100°C, 15 min, 63%; ¹⁰³ 47%; ¹⁰² conc. H ₂ SO ₄ , 100°C, 30 min, 56%; ¹⁰⁰ 96%; ¹⁰¹	— ^a	light orange solid; ¹⁰⁰ bright orange crystals; ¹⁰²	— ^a
58	4,6-Br ₂	3,5-Br ₂	86% H ₂ SO ₄ , 60–110°C, 80–86%; ¹⁷	259–260; ¹⁷ 254–256; ⁷⁷	orange; ⁷⁷	recr. EtOH; ^{17,77}
59	6,7- (CH ₂) ₃ -	1- Aminote tralin	90% H ₂ SO ₄ ; ³⁹ MsOH, 25°C, 1 h, 73%; ¹³² conc. H ₂ SO ₄ , 85°C, 10 min; ¹²⁷	— ^a	orange-brown; ^{132,127}	extr. EtOAc; ¹²⁷

60	benzo[<i>g</i>]	1-Naphthylamine	conc. H ₂ SO ₄ , 85°C, 10 min, 34%; ^{127–129}	— ^a	black; ¹²⁷	extr. EtOAc; ¹²⁷
61	benzo[<i>e</i>]	2-Naphthylamine	conc. H ₂ SO ₄ , 80°C, 10 min, 28%; ¹³⁰ MsOH, 110°C, 40 min, 87%; ¹³¹	254–256; ¹³⁰ 248–249; ¹³²	dark red; ¹³¹	chromatogr. ¹³¹

^a No data available

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