

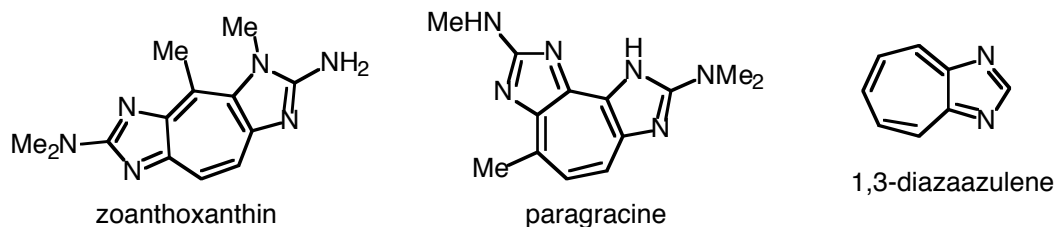
NOVEL HETEROCYCLIC TROPONOIDS: SYNTHESIS OF PYRIDO-IMIDAZOTROPOLONES AND RELATED COMPOUNDS BY THE REACTION OF 5-NITROSOTROPOLONE WITH SEVERAL AZINES

Ohki Sato,* Kouichiro Tsurumaki, Syunnichi Tamaru, and Josuke Tsunetsugu*

Department of Chemistry, Faculty of Science, Saitama University, Sakura-ku, Saitama 338-8570, Japan

Abstract – Novel heterocyclic troponoids, such as pyridoimidazotropolones (**3–4**, **5–11**, **12–13**, **14–15** and **16**) were synthesized by the reaction of 5-nitrosotropolone (**1**) with azines as pyridine, *m*- and *p*-substituted pyridines, pyridazine, isoquinoline and phthalazine. Similarly, thiazol afforded **17**. The reaction mechanism involves multi-step reactions; acetylation of **1**, Michael addition of azines to nitrosotropolone acetate (**2**), cyclization and deacetoxylation. The scope and limitation of this method are also discussed.

Non-benzenoid heterocyclic compounds containing a seven-membered ring have been receiving attentions for their biological activities, as well as physical and chemical properties. Among them azaazulenes and related compounds are most extensively studied family.^{1,2} Natural products having 1,3-diazaazulene moieties such as zoanthoxanthins (from *Parazoanthus cfr. axinellae*)^{3,4a} and paragraccines (from *Parazoanthus gracilis*)^{3,4b} were found. However, not so many synthetic methods of polycyclic azines with a 1,3-diazaazulene moiety have been investigated.^{1,2}

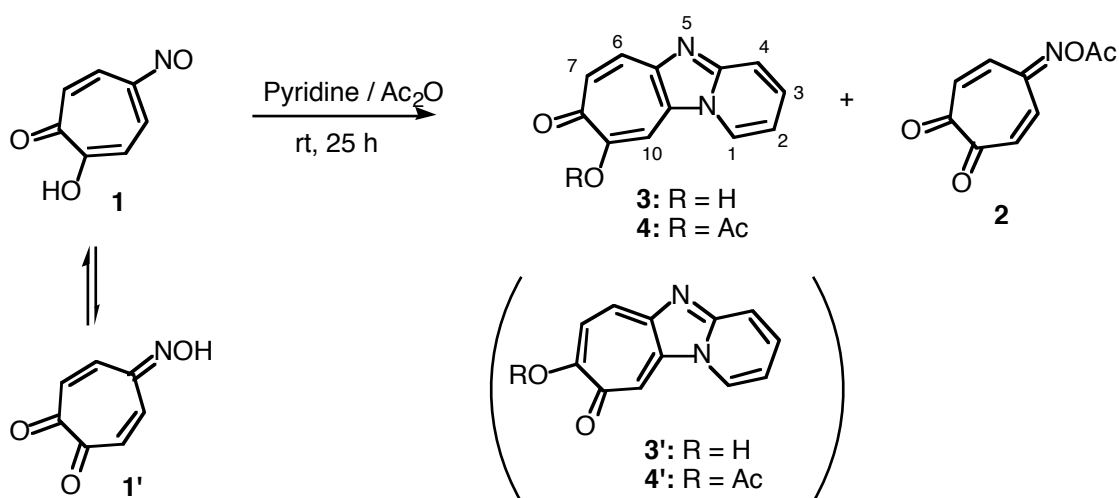


Here we report a new approach for the synthesis of novel heterocycle-fused troponoids, pyridoimidazotropolones, which could be classified into 1,3-diazaazulenes, by the reaction of 5-nitrosotropolone (**1**) and/or its acetate (**2**) with several azines.

RESULTS and DISCUSSION

5-Nitrosotropolone (**1**)^{5,6} is known to exist as an equilibrium mixture between an enol-form (**1**) and its diketone-one (**1'**), and reacted with various amines to give quinoxaline,⁶ aniline-adducts⁷ and oxazoles.⁸

To investigate the reaction in the presence of azines, **1** was treated with 1.5 molar equivalents of pyridine in acetic anhydride at room temperature for 25 hours to give pyrido[1',2':1,2]imidazo[4,5-*e*]tropolone (**3**) and its acetate (**4**) and nitrosotropolone acetate (**2**) in 30, 12 and 10 % yields respectively (Scheme 1). When **2** was treated with 10 molar equivalents of pyridine at room temperature for 34 hours, **3** was obtained in 35 % yield, which exemplified the former is the precursor of the latter in the reaction of **1** with pyridine in the presence of acetic anhydride. The ^1H NMR spectrum of **3** showed two protons at δ 7.33 and 8.10 with a characteristic coupling constant (d , $J = 12.2$ Hz) as a seven-membered ring. This J value indicates the double bond character of seven-membered ring, eliminating possible isomeric structure (**3'**). Calculated heats of formation for **3** and **3'** by PM3⁹ are 8.79 and 18.46 kcal/mol respectively, supporting the stability of the former. ^{13}C NMR spectrum showed seven tertiary carbons and five quarternary carbons, of which δ 178.6 and 156.0 were assigned to carbonyl and hydroxyl-attached carbons respectively. IR absorption band of ν 3235 cm^{-1} is assigned to a hydrogen bonded hydroxyl group of tropolone moiety. The MS spectrum showed strong molecular ion (m/z 212, M^+) and $\text{M}^+ - \text{CO}$ ion peaks. The longest wave-maximum of UV-VIS spectrum in H_2O appeared at 426 nm, whereas in acidic solution (0.5 M *aq.* HCl) did at 406 nm with the characteristic hypsochromic shift of tropolone derivatives. Together with the result of elemental analysis, those spectral data supported the proposed structure.

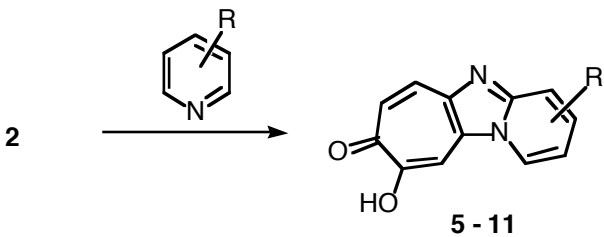
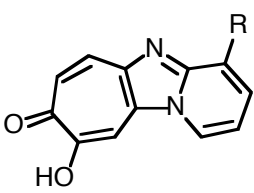
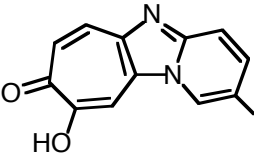
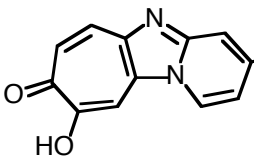
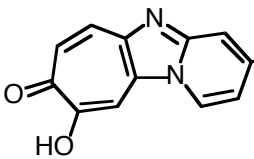


Scheme 1

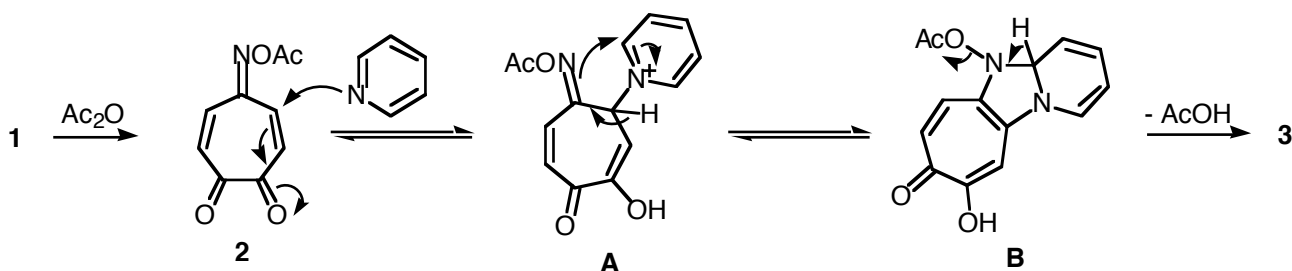
The results of the similar reactions with using several *o*-, *m*- and *p*-substituted pyridines are shown in Table 1. 2-Methoxypyridine did not react by some sterical reason, which will be discussed later. 3-Methoxypyridine afforded single isomer (**5a**), while 3-methyl-, 3-phenyl- and 3-bromopyridines afforded two inseparable isomeric pyridoimidazotropolones (**6**, **7** and **8**) of **a**- and **b**-series, of which the formers are obtained in dominant yields. Those structures were easily discriminated by their ^1H NMR spectral patterns. Sterically unfavorable **a**-series compounds became predominant, suggesting that the reaction proceeded by way of a kinetically controlled pathway. 3-Cyanopyridine did not react because of the paucity of nucleophilicity. In the case of 4-substituted pyridines (4-methoxy-, 4-methyl- and 4-phenylpyridines), pyridoimidazotropolones (**9**, **10** and **11**) were obtained in moderate yields respectively. The plausible reaction mechanism is shown in Scheme 2. Acetylation of 5-nitrosotropolone (**1**) affords

acetate (**2**), to which Michael addition of pyridine occurs to form addition product (**A**), cyclization of which affords a tricyclic intermediate (**B**), and successive elimination of acetic acid gives pyridoimidazolotropolone (**3**).

Table 1. Reaction of **2** with substituted pyridines

				
Substituted pyridine R (mol eq.)	Conditions	Yield (%)	5a: R = OMe 6a: R = Me 7a: R = Ph 8a: R = Br	
2-OMe (1.5)	CH ₂ Cl ₂ / rt / 113 h	No Reaction		
3-OMe (1.5)	CH ₂ Cl ₂ / reflux / 7 d	5a (28)		
3-Me (10)	neat / rt / 3 d	6a (29) 6b (7)		
3-Ph (1.5)	CH ₂ Cl ₂ / rt / 8 d	7a (19) 7b (7)		
3-Br (10)	neat / 70 °C / 27 h	8a (4) 8b (1)		
3-CN (1.5)	CH ₂ Cl ₂ / rt / 76 h	No reaction		
4-OMe (1.5)	CH ₂ Cl ₂ / reflux / 69 h	9 (46)	9: R = OMe 10: R = Me 11: R = Ph	
4-Me (10)	neat / rt / 21 h	10 (27)		
4-Ph (1.5)	CH ₂ Cl ₂ / rt / 6 d	11 (47)		

When trifluoroacetic anhydride was used instead of acetic anhydride in the reaction of **1** and pyridine, the reaction completed in 4.5 hours at room temperature and the yield of **3** was 22 %. Although the reaction rate is faster on the process from **2** to **A** because of strong electron withdrawing force of fluorine atoms, on the process from **A** to **B** electron donation from nitrogen atom of trifluoroacetoxime is weaker, resulting to give **3** in less yield, as a whole. In the case of 2-methoxypyridine steric hindrance in the formation of **A** is considered to be unfavorable. Calculated heats of formation by PM3 are always larger for predominant **a**-series compounds derived from 3-substituted-pyridines than that for **b**-series (e.g., **8a** vs. **8b**: 19.94 vs. 17.75 kcal/mol), indicating that the direction of cyclizaion is not controlled thermodynamically but kinetically.

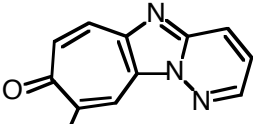
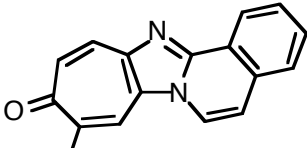
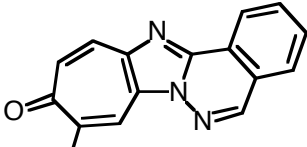
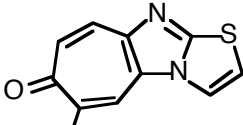


Scheme 2

The reaction of 5-nitrosotropolone (**1**) with diazines such as pyrimidine and pyrazine in acetic anhydride

did not occur but with pyridazine afforded a new heterocycle (**12**) and its acetate (**13**) in good yields as a whole (Table 2). The structure of **12** has been determined by X-Ray crystallography and the ORTEP diagrams are presented in Figure 1. The molecule (**12**) is almost flat (intramolecular torsion angle of C(5)-N(1)-C(8)-C(9): 178.5(2)°; N(1)-C(5)-C(6)-C(7): 178.1(2)°) and the tropolone ring moiety is not delocalized (bond length of C(1)-O(1): 1.248(1)Å; C(2)-O(2): 1.348(1)Å). Pyrimidine and pyrazine gave an unidentifiable complex mixture under refluxed conditions, while at room temperature the latter afforded only nitrosotropolone acetate (**2**). The reaction with condensed azines such as isoquinoline and phthalazine afforded single isomeric heterocycles (**14**, **15** and **16**) in high yields respectively but quinoline did not react because of steric hindrance on the reaction pathway. A mixture of **14** and **15** in CH₂Cl₂-MeOH-H₂O solution was boiled for 68 hours to afford deacetyl compound (**14**) in 86 % yield. The reaction of **2** with thiazole gave a thiazole-condensed heterocycle (**17**).

Table 2. Reactions of **1** and **2** with diazines, condensed azines and thiazole

Substrate	Azine and thiazole (mol eq.)	Conditions	Products and yield (%)
1	Pyridazine (1.5)	Ac ₂ O / rt / 24 h	 12 : R = H (32) 13 : R = Ac (54)
1	Pyrimidine (1.5)	Ac ₂ O / rt / 28 h Ac ₂ O / reflux / 8 h	No reaction Complex mixture
1	Pyrazine (1.5)	Ac ₂ O / rt / 27 h Ac ₂ O / reflux / 13 h	2 (93) Complex mixture
1	Isoquinoline (1.5)	Ac ₂ O / rt / 56 h	 14 : R = H (17) 15 : R = Ac (66)
2	Quinoline (10)	neat / rt / 55 h	Complex mixture
1	Phthalazine (1.5)	Ac ₂ O / rt / 72 h	 16 (77)
2	Thiazole (10)	neat / 70 °C / 27 h	 17 (13)

Nucleophilicity is not parallel with p*K*_a value, of course, but in such a case as this where the multi-step

equilibria are considered both factors could be correlated loosely. When the pK_a value of azine is less than 2 like pyrimidine (1.31), pyrazine (0.65), 3-cyanopyridine (1.50) the reaction did not occur. On the other hand, when that is more than 2 (*e.g.*, pK_a : 5.23 for pyridine, 4.80 for 3-phenylpyridine, 6.62 for 4-methoxypyridine, 2.33 for pyridazine, 2.50 for thiazole), the reaction occurred.

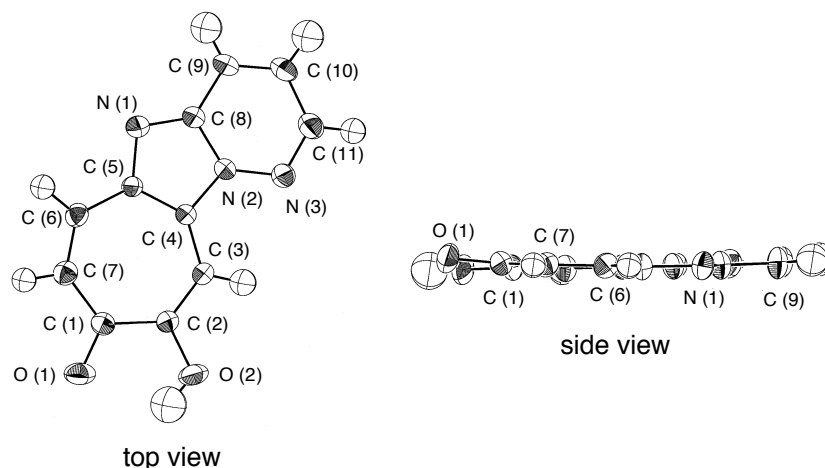


Figure 1. ORTEP diagrams of **12**

Although the reaction has not been optimized well yet, it appears that this method is governed by both steric and nucleophilic factors of azines. The wider application and development of the reaction is now under investigation.

EXPERIMENTAL

Mps were determined with a Mitamura air-bath apparatus and are uncorrected. ^1H and ^{13}C NMR spectra were determined with Bruker AM-400, AC-300 and/or AC-200 spectrometers. IR spectra were determined with a Perkin Elmer System 2000 FT instrument and electronic spectra (UV-VIS) with a JASCO V-560 spectrophotometer. MS spectra were determined with JEOL JMS-DX 303 spectrometer. Unless otherwise stated the spectra were taken in the following solvents/media: IR, KBr; UV-VIS, CH_2Cl_2 and H_2O ; ^1H and ^{13}C NMR, $\text{DMSO}-d_6$; MS spectra were taken by electron impact (EI) and fast atom bombardment (FAB) methods. The progress of most reactions was monitored by TLC using Merck Kieselgel 60F₂₅₄.

Typical experimental procedure for the reaction of 5-nitrosotropolone (1) with azines in acetic anhydride: A solution of **1** (517 mg, 3.42 mmol) and 1.5 molar equivalents of pyridine (406 mg, 5.13 mmol) in acetic anhydride (25 mL) was stirred at rt for 25 h. The insoluble nitrosotropolone acetate (**2**, 68 mg, 10 % yield) was removed by filtration and the filtrate was evaporated under reduced pressure. The residue was purified by recrystallization from CH_2Cl_2 to give pyrido[1',2':1,2]imidazo[4,5-*e*]tropolone (**3**, 216 mg, 30 % yield) and its acetate (**4**, 100 mg, 12 % yield). Compounds (**3** and **4**) could not be purified by column chromatography because of their lability to silica gel and aluminum oxide.

Typical experimental procedure for the reaction of nitrosotropolone acetate (2) with azines: a) A solution of **2** (500 mg, 2.59 mmol) and 1.5 molar equivalents of 4-methoxypyridine (426 mg, 3.90 mmol) in CH_2Cl_2 (19 mL) was refluxed for 69 h. The solvent was removed *in vacuo* and the residue was purified by recrystallization from acetonitrile to give **9** (291 mg, 46 % yield). b) A mixture of **2** (501 mg,

2.59 mmol) and 10 molar equivalents of 3-methylpyridine (2.41 g, 25.9 mmol) was stirred at rt for 72 h. The reactant was purified by recrystallization from CH₂Cl₂ to give **6a** and **6b** (211 mg, 29 % and 7 % yields calcd by the ¹HNMR spectrum) as an inseparable mixture.

Typical experimental procedure for the transformation to pyridoimidazotropolones from their acetates: A mixture of **14** and **15** (256 mg, **14** : **15** = 1 : 3.9 by ¹HNMR spectrum) in CH₂Cl₂ (40 mL), MeOH (80 mL) and H₂O (20 mL) was refluxed for 68 h. The solvent was removed *in vacuo* and the residue was purified by recrystallization from benzene to give **14** (196 mg, 86 % yield). All synthetic acetates (**4**, **13** and **15**) are relatively unstable and a part of them were converted into deacetyl compounds (**3**, **12** and **14**) respectively during the period of recrystallization. The structure of those acetates was finally established by the transformation.

Physical data of synthetic heterocycles (3–17): **3**: yield 30 %; yellow fine needles; mp 230 °C (sub.); ¹HNMR (300 MHz, DMSO-*d*₆, δ 2.50) δ_{H} 7.15 (1H, dd, *J* = 7.4, 6.2, H-2), 7.33 (1H, d, *J* = 12.2, H-7), 7.58 (1H, dd, *J* = 9.2, 7.4, H-3), 7.75 (1H, d, *J* = 9.2, H-4), 8.10 (1H, d, *J* = 12.2, H-6), 8.35 (1H, s, H-10), 9.14 (1H, d, *J* = 6.2, H-1), 9.54 (1H, br s, OH); ¹³CNMR (50 MHz, DMSO-*d*₆, δ 39.7) δ_{C} 102.7, 113.1, 117.7, 126.5, 127.4, 129.5, 129.6, 134.0, 142.1, 146.5, 156.0, 178.6; IR (KBr, cm⁻¹) ν_{max} 3235, 1642, 1586, 1564, 1533, 1460, 1404, 1353, 1283, 1207; MS (EI (+), %) *m/z* 212 (M⁺, 100), 184 (M⁺-CO, 100); UV-VIS (CH₂Cl₂, nm, log ϵ ν_{max} 253 (4.56), 262 (4.55), 288 (4.44), 299 (4.58), 312 (4.58), 371 (4.06), 394 (4.19), 410 (4.35), 434 (4.25); UV-VIS (H₂O, nm, log ϵ ν_{max} 243 (4.20), 261 (4.18), 300 (4.17), 311 (4.21), 407 (4.00), 426 (3.95); UV-VIS (0.5M aq. HCl, nm, log ϵ ν_{max} 251 (4.41), 283 (4.04), 296 (4.05), 345 (3.76), 387 (4.05), 406 (4.02); Anal. Calcd for C₁₂H₈N₂O₂: C, 67.92; H, 3.80; N, 13.20. Found: C, 67.82; H, 3.73; N, 13.18. **4**: yield 12 %; brown powder; mp 216–219 °C (sub.); ¹HNMR (300 MHz, DMSO-*d*₆, δ 2.50) δ_{H} 2.32 (3H, s, Ac), 7.20 (1H, d, *J* = 12.7, H-7), 7.26 (1H, dd, *J* = 7.4, 7.0, H-2), 7.66 (1H, dd, *J* = 8.7, 7.4, H-3), 7.84 (1H, d, *J* = 8.7, H-4), 8.00 (1H, d, *J* = 12.7, H-6), 8.69 (1H, s, H-10), 9.16 (1H, d, *J* = 7.0, H-1); IR (KBr, cm⁻¹) ν_{max} 1746, 1642, 1599, 1525, 1520, 1201, 1079, 927, 857, 765; MS (FAB (+), NBA, %) *m/z* 255 (MH⁺, 56). **5a**: yield 28 %; yellow fine needles; mp 232 °C (sub.); ¹HNMR (300 MHz, DMSO-*d*₆, δ 2.50) δ_{H} 4.00 (3H, s), 6.95 (1H, d, *J* = 7.4), 7.06 (1H, dd, *J* = 7.4, 6.2), 7.31 (1H, d, *J* = 12.3), 8.10 (1H, d, *J* = 12.3), 8.30 (1H, s), 8.73 (1H, d, *J* = 6.2); IR (KBr, cm⁻¹) ν_{max} 3267, 1566, 1456, 1399, 1331, 1282, 1225, 830, 728; MS (EI (+), %) *m/z* 242 (M⁺, 100), 214 (M⁺-CO, 100); UV-VIS (CH₂Cl₂, nm, log ϵ ν_{max} 244 (4.61), 264 (4.42), 306 (4.55), 317 (4.64), 402 (4.29), 421 (4.20); Anal. Calcd for C₁₃H₁₀N₂O₃: C, 64.46; H, 4.16; N, 11.56. Found: C, 64.42; H, 4.09; N, 11.49. **6a** and **6b**: yields 29 and 7 % (calcd by the ¹HNMR spectrum); brownish yellow powder; ¹HNMR (300 MHz, DMSO-*d*₆, δ 2.50) for **6a** δ_{H} 2.57 (3H, s, Me), 7.06 (1H, dd, *J* = 7.0, 6.6, H-2), 7.31 (1H, d, *J* = 12.2, H-7), 7.38 (1H, d, *J* = 7.0, H-3), 8.14 (1H, d, *J* = 12.2, H-6), 8.32 (1H, s, H-10), 8.99 (1H, d, *J* = 6.6, H-1), 9.54 (1H, br s, OH); ¹HNMR (300 MHz, DMSO-*d*₆, δ 2.50) for **6b** δ_{H} 2.38 (3H, s, Me), 7.30 (1H, d, *J* = 12.1, H-7), 7.45 (1H, d, *J* = 9.1, H-3), 7.66 (1H, d, *J* = 9.1, H-4), 8.07 (1H, d, *J* = 12.1, H-6), 8.28 (1H, s, H-10), 8.99 (1H, s, H-1), 9.54 (1H, br s, OH); MS (EI (+), %) *m/z* 226 (M⁺, 100), 198 (M⁺-CO, 100); HRMS (EI(+)) Calcd for C₁₃H₁₀N₂O₂: 226.0742, Found: 226.0728. **7a** and **7b**: yields 19 and 7 % (calcd by the ¹HNMR spectrum); brownish yellow powder; ¹HNMR (300 MHz, DMSO-*d*₆, δ 2.50) for **7a** δ_{H} 7.26 (1H, t, *J* = 7.0), 7.31 (1H, d, *J* = 12.5), 7.55 (3H, m), 7.76 (1H, d,

$J = 7.0$), 8.10 (2H, d, $J = 7.0$), 8.15 (1H, d, $J = 12.5$), 8.38 (1H, s), 9.16 (1H, d, $J = 7.0$), 9.58 (1H, br s, OH); $^1\text{HNMR}$ (300 MHz, $\text{DMSO-}d_6$, $\Delta 2.50$) for **7b** Δ_{H} 7.34 (1H, d, $J = 12.1$), 7.47 (3H, m), 7.84 (1H, d, $J = 9.6$), 7.92 (2H, d, $J = 7.4$), 7.97 (1H, d, $J = 9.6$), 8.08 (1H, d, $J = 12.1$), 8.62 (1H, s), 9.44 (1H, s), 9.58 (1H, br s, OH); MS (EI (+), %) m/z 288 (M^+ , 100), 260 ($\text{M}^+ - \text{CO}$, 100); HRMS (EI(+)) Calcd for $\text{C}_{18}\text{H}_{12}\text{N}_2\text{O}_2$: 228.0899, Found: 228.0896. **8a** and **8b**: yields 4 and 1 % (calcd by the $^1\text{HNMR}$ spectrum); reddish brown powder; $^1\text{HNMR}$ (300 MHz, $\text{DMSO-}d_6$, $\Delta 2.50$) for **8a** Δ_{H} 7.06 (1H, t, $J = 7.4$), 7.33 (1H, d, $J = 12.1$), 7.92 (1H, d, $J = 7.4$), 8.16 (1H, d, $J = 12.1$), 8.30 (1H, s), 9.17 (1H, d, $J = 7.4$); $^1\text{HNMR}$ (300 MHz, $\text{DMSO-}d_6$, $\Delta 2.50$) for **8b** Δ_{H} 7.32 (1H, d, $J = 12.2$), 7.66–7.70 (2H, m), 8.09 (1H, d, $J = 12.2$), 8.38 (1H, s), 9.51 (1H, s); MS (EI (+), %) m/z 292 ($\text{M}^+ + 2$, 100), 290 (M^+ , 100), 264 ($\text{M}^+ + 2 - \text{CO}$, 80), 262 ($\text{M}^+ - \text{CO}$, 79); HRMS (EI(+)) Calcd for $\text{C}_{12}\text{H}_7^{79}\text{BrN}_2\text{O}_2$: 289.9691, Found: 289.9680. **9**: yield 46 %; yellow fine needles; mp 238 °C (sub.); $^1\text{HNMR}$ (300 MHz, $\text{DMSO-}d_6$, $\Delta 2.50$) Δ_{H} 3.92 (3H, s), 6.87 (1H, d, $J = 7.7$), 7.07 (1H, s), 7.30 (1H, d, $J = 12.3$), 8.02 (1H, d, $J = 12.3$), 8.31 (1H, s), 9.01 (1H, d, $J = 7.7$); IR (KBr, cm^{-1}) Δ_{max} 3226, 1652, 1538, 1463, 1404, 1218, 1018, 843; MS (EI (+), %) m/z 242 (M^+ , 100), 214 ($\text{M}^+ - \text{CO}$, 100); UV-VIS (CH_2Cl_2 , nm, log Δ Δ_{max} 257 (4.47), 298 (4.29), 310 (4.26), 411 (4.21), 433 (4.15); Anal. Calcd for $\text{C}_{13}\text{H}_{10}\text{N}_2\text{O}_3$: C, 64.46; H, 4.16; N, 11.56. Found: C, 64.25; H, 4.11; N, 11.42. **10**: yield 27 %; mp 230 °C (sub.); brownish yellow powder; $^1\text{HNMR}$ (300 MHz, $\text{DMSO-}d_6$, $\Delta 2.50$) Δ_{H} 2.44 (3H, s), 7.02 (1H, d, $J = 7.0$), 7.32 (1H, d, $J = 12.1$), 7.53 (1H, s), 8.07 (1H, d, $J = 12.1$), 8.32 (1H, s), 9.04 (1H, d, $J = 7.0$); IR (KBr, cm^{-1}) Δ_{max} 3250, 1655, 1561, 1541, 1459, 1259, 1214, 805; MS (EI (+), %) m/z 226 (M^+ , 83), 198 ($\text{M}^+ - \text{CO}$, 100); Anal. Calcd for $\text{C}_{13}\text{H}_{10}\text{N}_2\text{O}_2$: C, 69.02; H, 4.46; N, 12.38. Found: C, 68.75; H, 4.35; N, 12.17. **11**: yield 47 %; yellow fine needles; mp 248 °C (sub.); $^1\text{HNMR}$ (300 MHz, $\text{DMSO-}d_6$, $\Delta 2.50$) Δ_{H} 7.35 (1H, d, $J = 12.1$), 7.49 (1H, dd, $J = 7.2, 1.1$), 7.53–7.59 (3H, m), 7.95 (2H, d, $J = 7.7$), 8.07 (1H, d, $J = 1.1$), 8.11 (1H, d, $J = 12.1$), 8.40 (1H, s), 9.22 (1H, d, $J = 7.2$); IR (KBr, cm^{-1}) Δ_{max} 3224, 1588, 1568, 1538, 1460, 1400, 1356, 1269, 866, 842, 753; MS (EI (+), %) m/z 288 (M^+ , 100), 260 ($\text{M}^+ - \text{CO}$, 100); UV-VIS (CH_2Cl_2 , nm, log Δ Δ_{max} 282 (4.63), 304 (4.57), 316 (4.50), 425 (4.40), 449 (4.33); Anal. Calcd for $\text{C}_{18}\text{H}_{12}\text{N}_2\text{O}_2$: C, 74.99; H, 4.20; N, 9.72. Found: C, 74.79; H, 4.15; N, 9.57. **12**: yield 32 %; orange plates; mp 207 °C (sub.); $^1\text{HNMR}$ (300 MHz, $\text{DMSO-}d_6$, $\Delta 2.50$) Δ_{H} 7.32 (1H, d, $J = 12.1$), 7.52 (1H, dd, $J = 9.2, 6.4$), 7.96 (1H, s), 8.12 (1H, d, $J = 12.1$), 8.30 (1H, dd, $J = 9.2, 1.5$), 8.77 (1H, dd, $J = 6.4, 1.5$), 9.85 (1H, br s, OH); $^{13}\text{CNMR}$ (50 MHz, $\text{DMSO-}d_6$, $\Delta 39.7$) Δ_{C} 101.0, 121.8, 126.7, 129.2, 130.2, 134.2, 140.3, 141.1, 145.0, 157.0, 179.4; IR (KBr, cm^{-1}) Δ_{max} 3202, 1585, 1538, 1463, 1344, 1271, 1224, 1173, 880, 800; MS (EI (+), %) m/z 213 (M^+ , 100), 185 ($\text{M}^+ - \text{CO}$, 100); UV-VIS (CH_2Cl_2 , nm, log Δ Δ_{max} 251 (4.84), 271 (4.72), 293 (4.69), 302 (4.63), 339 (4.16), 355 (4.20), 422 (4.50), 445 (4.34); Anal. Calcd for $\text{C}_{11}\text{H}_7\text{N}_3\text{O}_2$: C, 61.97; H, 3.31; N, 19.71. Found: C, 61.85; H, 3.23; N, 19.56; Crystal data: $\text{C}_{11}\text{H}_7\text{N}_3\text{O}_2$, monoclinic, space group C2/c, $a = 13.3320(7)$, $b = 7.3900(5)$, $c = 19.7090(10)$ Å, $\beta = 90$, $\alpha = 109.543(4)$, $\gamma = 90$ °, $V = 1829.9(2)$ Å³, $Z = 8$, $\rho = 1.55$ g cm⁻³, μ (Mo-K α) = 0.711 cm⁻¹, $F(000) = 880$, $R = 0.048$, $\text{WR2} = 0.125$, $\text{GOF} = 2.722$. **13**: yield 54 %; brownish yellow powder; mp 185 °C (sub.); $^1\text{HNMR}$ (300 MHz, $\text{DMSO-}d_6$, $\Delta 2.50$) Δ_{H} 2.31 (3H, s), 7.22 (1H, d, $J = 12.2$), 7.61 (1H, dd, $J = 9.2, 6.4$), 8.04 (1H, d, $J = 12.2$), 8.34 (1H, s), 8.40 (1H, dd, $J = 9.2, 1.5$), 8.85 (1H, dd, $J = 6.4, 1.5$); IR (KBr, cm^{-1}) Δ_{max} 1762, 1608, 1549, 1332, 1205, 1194, 1077, 804; MS (FAB (+), NBA, %) m/z 256 (MH^+ , 7.6). **14**: yield 17 %; yellow powder; mp 258 °C (sub.); $^1\text{HNMR}$ (300 MHz,

DMSO- d_6 , δ 2.50) δ_{H} 7.33 (1H, d, $J = 12.1$), 7.48 (1H, d, $J = 7.7$), 7.74–7.82 (2H, m), 7.99 (1H, d, $J = 8.1$), 8.21 (1H, d, $J = 12.1$), 8.35 (1H, s), 8.62 (1H, d, $J = 8.8$), 8.91 (1H, d, $J = 7.7$); IR (KBr, cm^{-1}) ν_{max} 3236, 1640, 1586, 1532, 1463, 1398, 1257, 1210; MS (EI (+), %) m/z 262 (M^+ , 100), 234 ($\text{M}^+ - \text{CO}$, 100); UV-VIS (CH_2Cl_2 , nm, log ϵ) ϵ_{max} 231 (4.17), 269 (4.63), 279 (4.69), 291 (4.60), 303 (4.69), 393 (4.47), 412 (4.46); Anal. Calcd for $\text{C}_{16}\text{H}_{10}\text{N}_2\text{O}_2$: C, 73.27; H, 3.84; N, 10.68. Found: C, 73.05; H, 3.80; N, 10.71. **15**: yield 66 % brownish yellow powder; mp 235 °C (sub.); ^1H NMR (300 MHz, DMSO- d_6 , δ 2.50) δ_{H} 2.34 (3H, s), 7.20 (1H, d, $J = 12.5$), 7.58 (1H, d, $J = 7.4$), 7.77–7.85 (2H, m), 8.00 (1H, d, $J = 8.0$), 8.10 (1H, d, $J = 12.5$), 8.63 (1H, d, $J = 8.5$), 8.69 (1H, s), 8.90 (1H, d, $J = 7.4$); IR (KBr, cm^{-1}) ν_{max} 1755, 1652, 1557, 1538, 1520, 1455, 1212, 1092, 857; MS (FAB (+), NBA, %) m/z 305 (MH^+ , 13). **16**: yield 77 %; yellow powder; mp 250 °C (sub.); ^1H NMR (300 MHz, DMSO- d_6 , δ 2.50) δ_{H} 7.32 (1H, d, $J = 12.2$), 7.97–8.09 (2H, m), 8.00 (1H, s), 8.19 (1H, d, $J = 12.2$), 8.26 (1H, d, $J = 7.5$), 8.59 (1H, d, $J = 7.8$), 9.23 (1H, s); IR (KBr, cm^{-1}) ν_{max} 3255, 1586, 1540, 1467, 1378, 1253, 888, 847; MS (EI (+), %) m/z 263 (M^+ , 100), 235 ($\text{M}^+ - \text{CO}$, 100); UV-VIS (CH_2Cl_2 , nm, log ϵ) ϵ_{max} 279 (4.81), 292 (4.76), 304 (4.69), 368 (4.42), 400 (4.47), 419 (4.38); Anal. Calcd for $\text{C}_{15}\text{H}_9\text{N}_3\text{O}_2$: C, 68.44; H, 3.45; N, 15.96. Found: C, 68.29; H, 3.34; N, 15.87. **17**: yield 13 %; reddish brown powder; mp 169 °C (sub.); ^1H NMR (300 MHz, DMSO- d_6 , δ 2.50) δ_{H} 7.21 (1H, d, $J = 12.1$), 7.53 (1H, d, $J = 4.6$), 7.98 (1H, d, $J = 12.1$), 8.21 (1H, s), 8.55 (1H, d, $J = 4.6$); IR (KBr, cm^{-1}) ν_{max} 3167, 1683, 1557, 1538, 1455, 1257, 1204, 851, 672; MS (EI (+), %) m/z 218 (M^+ , 100), 190 ($\text{M}^+ - \text{CO}$, 100); Anal. Calcd for $\text{C}_{10}\text{H}_6\text{N}_2\text{O}_2\text{S}$: C, 55.04; H, 2.77; N, 12.84. Found: C, 54.82; H, 2.63; N, 12.65.

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