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SYNTHESIS AND SOME REACTIONS OF 1,8-DIAMINO-1-AZAAZULENIUM SALTS

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Abstract - Amination of 8-amino-3-phenyl-1-azaazulene gave 1,8-diamino-3-phenyl-1-azaazulenium salt (**2**). Reactions of the salt (**2**) with triethyl orthoformate and acetic anhydride gave 1-phenyl-2a,3,5-triazabenz[*cd*]azulene derivatives (**3a** and **3b**). The compound (**3a**) was also obtained by the reaction of **2** with diethyl ethoxymethylenemalonate in the presence of potassium carbonate. The reaction of **2** with ethyl pyruvate gave 4-acetyl-1-phenyl-2a,3,5-triazabenz[*cd*]azulene (**3c**). The structure of **3c** was deduced by X-Ray structure analysis. Reaction of **2** with acetylenic esters in the presence of potassium carbonate gave 2a,3-diazabenz[*cd*]azulene derivatives (**10a**, **b**).

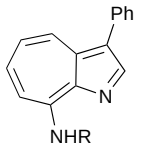
INTRODUCTION

o-Diamino-substituted heterocycles such as 1,2-diaminopyridinium salt are useful for the preparation of fused heterocycles.[1—4] Recently, we reported the synthesis and reactions of 1,2-diamino-1,3-diazaazulenium salt, where some interesting fused heterocycles such 1,3,3a,9-tetraazacyclopent[*a*]azulenes and 1,2a,3-triazabenz[*cd*]azulenes were obtained.[5] 1,8-Diamino-1-azaazulenium salt has peri-situated diamino groups and may enable to synthesize new fused heterocycles. In this paper we report on the synthesis and some reactions of 1,8-diamino-1-azaazulenium *O*-mesitylenesulfonate.

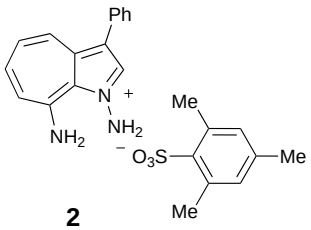
RESULTS AND DISCUSSION

Desired 1,8-diamino-3-phenyl-1-azaazulenium *O*-mesitylenesulfonate (**2**) was synthesized in 79% yield by the treatment of 8-amino-3-phenyl-1-azaazulene (**1a**) with *O*-mesitylenesulfonylhydroxylamine (MSH) in dichloromethane.

It is known that the heterocycles having peri-situated diamino groups such as 8-acetylamino-1-aminoquinolinium salts lead to a variety of bridgehead-nitrogen compounds.[6] Therefore, it is expected that the reaction of the salt (**2**) with triethyl orthoformate or acetic anhydride would give new bridgehead-nitrogen heterocycles. Thus the reaction of **2** with triethyl orthoformate was examined but 1-phenyl-2a,3,5-triazabenz[*cd*]azulene (**3a**) was obtained in poor yield. When the reaction was performed in the presence of molecular sieves 4A in refluxing xylene for 6 h, the yield was improved and **3a** was obtained in 71% yield. Reaction of **2** with acetic anhydride under reflux gave no distinct poroduct. When the reaction was performed in the presence of sodium acetate under refluxed for 1 day, complex mixture was obtained and only 4-methyl-1-phenyl-2a,3,5-triazabenz[*cd*]azulene (**3b**) (15%) was isolated. The compound (**3b**) was also obtained directly by the reaction of 8-acetylamino-3-phenyl-1-azaazulene (**1b**) with MSH in 87% yield. These suggest that the reactions of 8-acylamino-3-phenyl-1-azaazulenes with MSH would be superior to that of **2** with acid anhydride.



1a : R = H
1b : R = Ac



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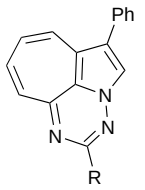
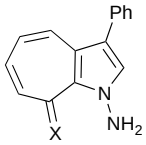


3a : R = H
3b : R = Me
3c : R = Ac

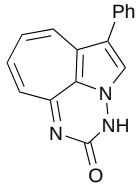


4 : X = NH
5 : X = O

It is thought that treatment of **2** with ion-exchange resin or base would lead to 1-amino-8-imino-3-phenyl-1,8-dihydro-1-azaazulene (**4**). When **2** was treated with IRA-410 ion-exchange resin in acetonitrile, no change occurred. Treatiment of **2** with potassium carbonate in acetonitrile gave unstable yellow compound, which structure was not determined. When the reaction was performed in ethanol, expected **4** was not isolated, instead 1-amino-3-phenyl-1-azaazulen-8(1*H*)-one (**5**), which would be hydrolyzed product of **4**, was obtained in 65% yield. It is known that the reaction of 1,2-diamino-1,3-diazaazulene with diethyl ethoxymethylenemalonate (DEEM) gave 1,3,3a,9-tetraazacyclopent[*a*]azulene.[5] Therefore, we treated the salt **2** with DEEM in the presence of potassium carbonate in acetonitrile, and obtained **3a** in 96% yield. The reaction mechanisum for the formation of **3a** would be resemble to that of 1,3,3a,9-tetraazacyclopent[*a*]azulene.[5]

1-Phenyl-2a,3,5-triazabenz[*cd*]azulen-5(4*H*)-one (**6**) was easily obtained by the treatment of **2** with *N*,*N*'-carbonyldiimidazol in the presence of potassium carbonate in acetonitrile under reflux for 3 days in 68% yield.

As the compound (**4**) derived from **2** has dual reactive functional groups, it is expected that the reaction of **4** with α-keto ester such as ethyl pyruvate would produce triazepinone-fused azaazulene derivative. We



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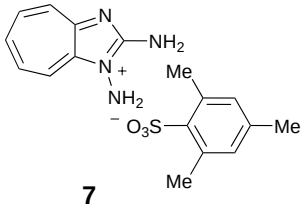

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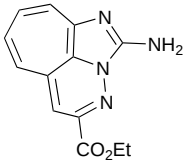

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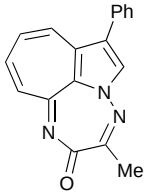

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reported previously that the reaction of 1,2-diamino-1,3-diazaazulenium salt (**7**) with ethyl pyruvate in the presence of potassium carbonate gave ethyl 2-amino-1,2a,3-triazabenz[*cd*]azulene-4-carboxylate (**8**), where the attack of amino group occurred on acetyl moiety of ethyl pyruvate.[5] Thus we treated of **2** with ethyl pyruvate in the presence of potassium carbonate in acetonitrile, and the cyclization product (**3c**) was obtained as violet needles in 25% yield and analyzed as for $C_{18}H_{13}N_3O$. In its ^{1}H NMR spectrum, a methyl signal was seen at δ 2.50 and seven-membered ring protons were at δ 5.74 (1H, dd, *J* 11.6 and 8.5), 6.23 (1H, d, *J* 12.2), 6.39 (1H, dd, *J* 12.2 and 8.5), 6.86 (1H, d, *J* 11.6), and the signals of ethyl ester were not observed. In its IR spectrum, a carbonyl signal was seen at 1710 cm^{-1}. These showed that the attack of amino group of **4** occurred on ester group of ethyl pyruvate. To confirm the structure of **3c**, we performed X-Ray crystal structure analysis. An ORTEP drawing[7] is shown in Figure 1. Where, it is showed that the cyclization product is not 1-phenyl-2a,3,6-triazacyclopenta[*ef*]heptalen-5-one (**9**), but 4-acetyl-1-phenyl-2a,3,5-triazabenz[*cd*]azulene (**3c**).

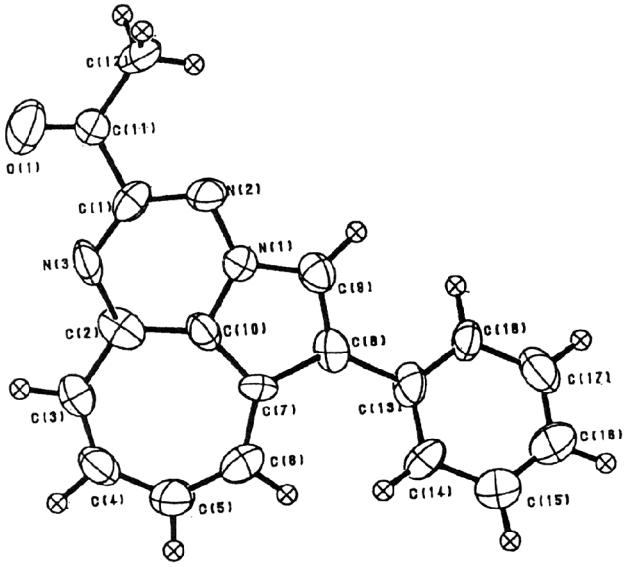
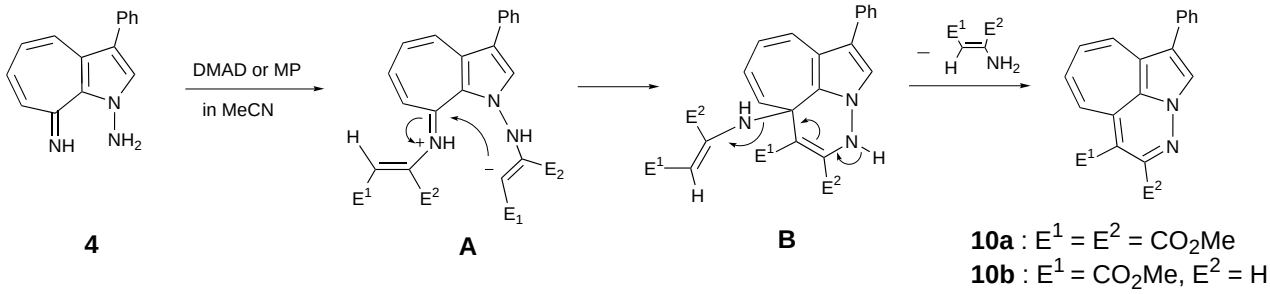


Figure 1 ORTEP drawing of **3c** showing with thermal ellipsoid plot (50% probability)

Since the compound (**4**) derived from **2** has a tropone imine moiety, cycloaddition reactions of **4** with acetylenic esters have aroused interest. Thus we examined the reaction of **2** with dimethyl acetylenedicarboxylate (DMAD) or methyl propiolate (MP) in the presence of potassium carboxylate.

Interestingly, expected 2a,3,5-triazabenz[*cd*]azulene derivatives were not obtained, instead 2a,3-diazabenz[*cd*]azulene derivatives (**10a**, **b**) were obtained in 27% and 50% yield, respectively. In the reactions, the amino group at C-8 in **2** was eliminated. Plausible reaction mechanism is shown in Scheme 1. The Michael reaction of **4** with two equivalent molar of acetylenic esters (DMAD or MP) gives intermediate (**A**). Cyclization of **A** affords **B**, and successive aromatization of **B** accompanied by elimination of diethyl aminomaleate furnishes **10**.



4 **A** **B**

10a : $E^1 = E^2 = CO_2Me$
10b : $E^1 = CO_2Me$, $E^2 = H$

Scheme 1

EXPERIMENTAL

Mps are measured using Yanagimoto micro-melting apparatus and uncorrected. ^{1}H NMR spectra were recorded on Hitachi R-250H spectrometer (250 MHz) and Bruker AVANCE 400S (400 MHz) using deuteriochloroform as a solvent with tetramethylsilane as an internal standard unless otherwise stated; *J* values are recorded in Hz. Electronic spectra were taken with Hitachi 220A spectrophotometer using ethanol as a solvent. IR spectra were recorded for KBr pellets on a Nicolet FT-IR Impact 410. Kieselgel 60 was used for column chromatography.

Synthesis of 1,8-diamino-3-phenyl-1-azaazulenium salt (2)

To the solution of 8-amino-3-phenyl-1-azaazulene (**1a**) (0.881 g, 4.00 mmol) in dichloromethane (100 mL) in ice-water bath was added dropwise over a period of 5 min the solution of *O*-mesitylenesulfonylhydroxylamine (1.29 g, 6.00 mmol) in dichloromethane (10 mL). After being stirred for overnight at rt, the resulted precipitates were collected by filtration and rinsed with dichloromethane, and then dried to give 1,8-diamino-3-phenyl-1-azaazulenium salt (**2**) (1.38 g, 79%), which was recrystallized from methanol to give pale yellow micro-needles, mp 125—127 °C; δ_H (DMSO-d_6) 2.16 (3H, s), 2.49 (6H, s), 6.74 (2H, s), 7.24 (1H, dd, *J* 12.2 and 8.5), 7.36—7.60 (6H, m), 7.81 (1H, dd, *J* 12.2 and 8.5), 7.99 (1H, d, *J* 11.0), 8.15 (1H, s), 9.98 (2H, br s) and 11.07 (2H, br s); ν_{max} / cm^{-1} 3443, 3379, 3253 and 3148 (NH); λ_{max} nm (log ε) 246 (4.40), 306 (4.32) and 398 (3.61). *Anal*. Calcd for $C_{24}H_{25}N_3O_3S \cdot 2H_2O$: C, 61.13; H, 6.20; N, 8.91. Found: C, 61.12; H, 6.09; N, 8.86.

Reaction of 2 with triethyl orthoformate

A mixture of **2** (0.094 g, 0.217 mmol), triethyl orthoformate (0.5 mL) and molecular sieves 4A (1.0 g) in xylene (20 mL) was refluxed for 6 h. The reaction mixture was filtered and the filtrate was evaporated. The residue was chromatographed with chloroform—ethyl acetate (1 : 1) to give 1-phenyl-2a,3,5-triazabenz[*cd*]azulene (**3a**) (0.038 g, 71%). **3a**: Violet needles (from hexane–dichloromethane) mp 138—140 °C; δ_H 5.69 (1H, dd, *J* 11.0 and 8.6), 6.04 (1H, d, *J* 12.2), 6.35 (1H, dd, *J* 12.2 and 8.6), 6.86 (1H, d, *J* 11.0), 7,35 (1H, t, *J* 6.7), 7.36 (2H, t, *J* 6.7), 7.42 (2H, d, *J* 6.7), 7.42 (1H, s) and 7.47 (1H, s); ν_{max} / cm^{-1} 757, 698 (Ph); λ_{max} nm (log ε) 264 (4.32), 328 (3.83, sh), 340 (3.96), 358 (3.95), 450 (2.69, sh), 486 (2.83), 524 (2.93), 572 (2.91), 630 (2.71), 702 (2.22). *Anal*. Calcd for $C_{16}H_{11}N_3$: C, 78.35; H, 4.52; N, 17.13. Found: C, 78.52; H, 4.54; N, 17.03.

Reaction of 2 with diethyl ethoxymethylenemalonate

A mixture of **2** (0.335 g, 0.80 mmol), DEEM (0.260 g, 1.20 mmol) and potassium carbonate (0.691 g, 5.00 mmol) in acetonitrile (150 mL) was refluxed for 2 days. The mixture was filtered and the residue was washed with ethyl acetate. The combined filtrate was evaporated. The residue was chromatographed with chloroform to give **3a** (0.188 g, 96%).

Reaction of 1,8-diamino-3-phenyl-1-azaazulenium salt (2) with potassium carbonate

A mixture of **2** (0.217 g, 0.50 mmol) and potassium carbonate (0.217 g, 2.00 mmol) in ethanol (100 mL) was refluxed for 1 day. The mixture was evaporated and the residue was washed with chloroform. The filtrate was evaporated and the residue was chromatographed with ethyl acetate to give 1-amino-3-phenyl-1-azaazulen-8(1*H*)-one (**5**) (0.072 g, 65%). **5**: Yellow needles (from hexane–dichloromethane) mp 200—202 °C; δ_H 4.3—5.2 (2H, br), 7.07 (1H, t, *J* 9.8), 7.11 (1H, d, *J* 9.8), 7.35 (1H, t, *J* 7.3), 7.49 (2H, t, *J* 7.3), 7.58 (2H, d, *J* 7.3), 7.59 (1H, t, *J* 9.8), 8.26 (1H, s) and 8.35 (1H, d, *J* 9.8); ν_{max} / cm^{-1} 3453, 3296 (NH), 1650 and 1614 (C=O and C=C); λ_{max} nm (log ε) 241 (4.53), 313 (4.62), 424 (3.31). *Anal.* Calcd for $C_{15}H_{12}N_2O$: C, 76.25; H, 5.12; N, 11.86. Found: C, 76.22; H, 5.08; N, 11.91.

Reaction of 2 with acetic anhydride–sodium acetate

A mixture of **2** (0.360 g, 0.86 mmol), acetic anhydride (50 mL) and sodium acetate (0.450 g, 5.5 mmol) was refluxed for 1 day. To the mixture water was added, and the mixture was neutralized with sodium hydrogen carbonate, then extracted with chloroform. The extract was dried over sodium sulfate and evaporated. The residue was chromatographed with chloroform to give 4-methyl-1-phenyl-2a,3,5-triazabenz[*cd*]azulene (**3b**) (0.034 g, 15%). **3b**: Violet needles (from ethyl acetate), mp 134—135 °C; δ_H 2.11 (3H, s), 5.71 (1H, dd, *J* 11.6 and 8.6), 6.10 (1H, d, *J* 12.2), 6.40 (1H, dd, *J* 12.2 and 8.6),

6.90 (1H, d, *J* 11.6), 7.35 (2H, dd, *J* 7.9 and 7.3), 7.40 (1H, t, *J* 7.3), 7.41 (1H, s) and 7.44 (2H, d, *J* 7.9); ν_{max} / cm^{-1} 755, 700 (Ph); λ_{max} nm (log ε) 236 (4.57), 266 (4.53), 328 (4.01), 342 (4.16), 358 (4.16), 452 (2.81, sh), 485 (2.99), 521 (3.09), 566 (3.07), 621 (2.85), 690 (2.85). *Anal*. Calcd for $C_{17}H_{13}N_3$: C, 78.74; H, 5.05; N, 16.20. Found: C, 78.52; H, 5.14; N 16.02.

Reaction of 8-acetylamino-3-phenyl-1-azaazulene (1b) with *O*-mesitylenesulfonylhydroxylamine

The solution of *O*-mesitylenesulfonylhydroxylamine (0.650 g, 3.00 mmol) in dichloromethane (10 mL) was added dropwise over a period of 5 min into the solution of **1b** (0.262 g, 1.00 mmol) in dichloromethane (20 mL) on ice-water bath with stirring. The stirring was continued for 4 days at rt, then the mixture was evaporated. The residue was chromatographed with chloroform to give recovered **1b** (0.030 g, 11%). Elution with acetone gave a mixture of colorless powder and violet crystals. To the mixture hexane–dichloromethane (1 : 1, 10 ml) was added, and the colorless powder was filtered off. Evaporation of the filtrate gave **3b** (0.225 g, 87%).

Reaction of 2 with *N,N'*-carbonyldiimidazol

A mixture of **2** (0.434 g, 1.00 mmol), *N,N'*-carbonyldiimidazol (0.163 g, 1.00 mmol) and potassium carbonate (0.691 g, 5.00 mmol) in acetonitrile (150 mL) was refluxed for 3 days, then the precipitate was filtered. The solid was washed with hot ethanol and the filtrate was evaporated. The residue was recrystallized from ethanol to give 1-phenyl-2a,3,5-triazabenz[*cd*]azulen-5(4*H*)-one (**6**) (0.178 g, 68%).
6: Violet needles (from ethanol) mp 169—170 °C; δ_H (CD_3OD) 5.79 (1H, dd, *J* 11.0 and 8.5), 6.15 (1H, d, *J* 12.2), 6.52 (1H, dd, *J* 12.2 and 8.5), 6.97 (1H, d, *J* 11.0), 7.26 (1H, s) and 7.20—7.45 (5H, m); ν_{max} / cm^{-1} 3150 (NH), 1664 (C=O) and 1640 (C=N); λ_{max} nm (log ε) 264 (4.44), 310 (3.72, sh), 373 (3.89), 490 (2.59, sh), 530 (2.69), 570 (2.66), 628 (2.44, sh), 692 (1.85, sh). *Anal.* Calcd for $C_{16}H_{11}N_3O$: C, 73.55; H, 4.24; N, 16.08. Found: C, 73.47; H, 4.42; N, 15.96.

Reaction of 2 with ethyl pyruvate

A mixture of **2** (0.434 g, 1.00 mmol), ethyl pyruvate (0.348 g, 3.00 mmol) and potassium carbonate (0.691 g, 5.00 mmol) in acetonitrile (200 mL) was stirred for 4 days at rt, then the solvent was evaporated. The residue was washed with chloroform and the filtrate was evaporated. The residue was chromatographed with chloroform to give 4-acetyl-1-phenyl-2a,3,5-triazabenz[*cd*]azulene (**3c**) (0.073 g, 25%). **3c**: Violet needles (from hexane–dichloromethane) mp 169—170 °C; δ_H 2.50 (3H, s), 5.74 (1H, dd, *J* 11.6 and 8.5), 6.23 (1H, d, *J* 12.2), 6.39 (1H, dd, *J* 12.2 and 8.5), 6.86 (1H, d, *J* 11.6), 7.30—7.50 (5H, m) and 7.58 (1H, s); ν_{max} / cm^{-1} 1710 (C=O); λ_{max} nm (log ε) 249 (4.57), 330 (4.02, sh), 341

(4.09), 356 (4.02), 470 (2.39, sh), 500 (2.55), 536 (2.65), 582 (2.64), 638 (2.38), 710 (1.96). *Anal.* Calcd for $C_{18}H_{13}N_3O$: C, 75.25; H, 4.56; N, 14.63. Found: C, 75.21; H, 4.64; N, 14.55.

Reaction of 2 with dimethyl acetylenedicarboxylate

A mixture of **2** (0.335 g, 0.80 mmol), dimethyl acetylenedicarboxylate (0.430 g, 3.00 mmol) and potassium carbonate (0.691 g, 5.00 mmol) in acetonitrile (150 mL) was refluxed for 3 days. The mixture was filtered and the residue was washed with ethyl acetate. The combined filtrate was evaporated. The residue was chromatographed with chloroform to give dimethyl 1-phenyl-2a,3-diazabenz[*cd*]azulene-4,5-dicarboxylate (**10a**) (0.079 g, 27%). **10a**: Dark green needles (from hexane–dichloromethane) mp 143—144 °C; δ_H 3.72 (3H, s), 3.86 (3H, s), 5.43 (1H, dd, *J* 11.0 and 7.9), 6.01 (1H, dd, *J* 12.2 and 7.9), 6.58 (1H, d, *J* 11.0), 6.60 (1H, d, *J* 12.2), 7.29—7.45 (5H, m) and 7.41 (1H, s); ν_{max} / cm^{-1} 1735 and 1685 (C=O); λ_{max} nm (log ε) 262 (4.85), 354 (4.28, sh), 370 (4.41), 390 (4.44), 488 (3.08, sh), 520 (3.27), 562 (3.40), 614 (3.40), 676 (3.23), 736 (2.84, sh). *Anal*. Calcd for $C_{21}H_{16}N_2O_4$: C, 69.99; H, 4.48; N, 7.77. Found: C, 69.56; H, 4.56; N, 7.67.

Reaction of 2 with methyl propiolate

A mixture of **2** (0.434 g, 1.00 mmol), methyl propiolate (0.252 g, 3.00 mmol) and potassium carbonate (0.691 g, 5.00 mmol) in acetonitrile (150 ml) was refluxed for 2 days. The mixture was filtered and the residue was washed with ethyl acetate. The combined filtrate was evaporated. The residue was chromatographed with chloroform to give methyl 1-phenyl-2a,3-diazabenz[*cd*]azulene-5-carboxylate (**10b**) (0.150 g, 50%).

10b: violet needles (from hexane–dichloromethane) mp 163—164 °C; δ_H 3.76 (3H, s), 5.55 (1H, dd, *J* 11.0 and 8.5), 6.18 (1H, dd, *J* 12.2 and 8.5), 6.72 (1H, d, *J* 11.0), 7.20—7.41 (5H, m), 7.42 (1H, s), 7.46 (1H, d, *J* 12.2) and 7.76 (1H, s); ν_{max} / cm^{-1} 1700 (C=O); λ_{max} nm (log ε) 242 (4.51), 270 (4.51), 280 (4.49, sh), 371 (4.34), 392 (4.38), 440 (2.64, sh), 478 (2.91, sh), 512 (3.14), 556 (3.28), 610 (3.29), 676 (3.10), 756 (2.56). Anal. Calcd for $C_{19}H_{14}N_2O_2$: C, 75.48; H, 4.67; N, 9.27. Found: C, 75.62; H, 4.71; N, 9.22.

Crystal data for 3c: violet needles, $C_{18}H_{13}N_3O$, *M*=284.27, orthorhombic, space group Pbca, *a*=27.55(4), *b*=28.766(5), *c*=7.14(3) Å, *V*=5656(23) $Å^3$, *Z*=16, D_{calcd}=1.349 g/cm^3, crystal dimensions 0.06 x 0.20 x 0.64 mm. Data were measured on a Rigaku AFC 5S radiation diffractometer with graphite-monochromated Mo-Kα radiation. A total 5627 reflections were collected using the ω scan technique to a maximum 2θ value of 50.0 °. All calculations were performed using TEXAN structure analysis software.[8] The structure was solved by direct methods and refined by a full-matrix least-squares

method using MITHRIL[9] using 397 variables and 1250 observed reflections ($I > 2\sigma(I)$). The non-hydrogen atoms were refined anisotropically. The weighting scheme $\omega = 4Fo^2/\sigma^2(Fo^2)$ gave satisfactory agreement analysis. The final *R* and *Rw* values were 0.088 and 0.081. The maximum peak and the minimum peak in final difference map were 0.39 $e^-/Å^3$ and –0.36 $e^-/Å^3$.

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