REACTIONS OF 2-ALKYLAMINO- AND 2-DIALKYLAMINO-1-AZAAZULENES WITH DIPHENYLCYCLOPROPENONE

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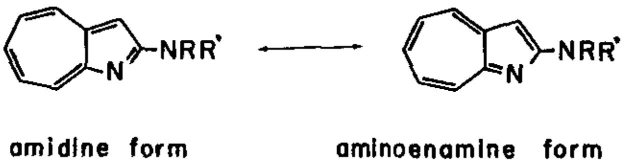
Abstract - Reaction of 2-alkylamino-1-azaazulenes with DPP gave 1,2-diphenyl-3*H*-9-azacyclopent[*a*]azulen-3-one and *N*-alkyl-*N*-(1-azaazulen-2-yl)-2,3-diphenyl-2-propenamides. Reaction of 2-dialkylamino-1-azaazulenes with DPP gave 2-dialkylamino-4,5-diphenyl-7*H*-1-azacyclopent[*e*]azulen-7-ones 2-dialkylamino-3,4-diphenyl-5*H*-1-azabenz[*cd*]azulen-5-ones. Some structures of the products were determined by single-crystal X-ray structure analyses.

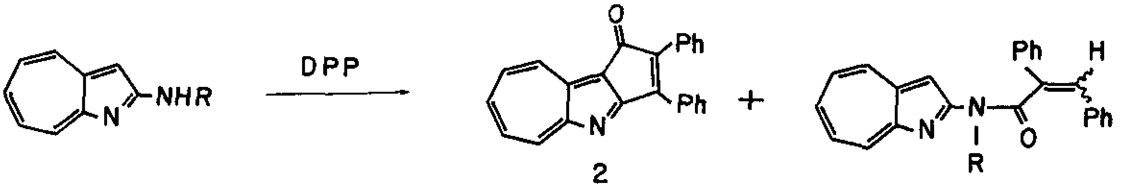
Cycloaddition reactions of diphenylcyclopropenone (DPP) with heterocycles are interesting for the construction of novel heterocycles; especially the reactions of DPP with 2-amino-substituted heterocycles are intensively studied.[1-10] We have also reported on the cycloaddition of 2-hydrazino-1-azaazulenes[11] and 2-amino-1-azaazulenes with DPP.[12] It is considered that 2-alkylamino-1-azaazulenes have a resonance contribution of amidine form and aminoenamine form. Therefore, it is expected that reaction of 2-(substituted amino)-1-azaazulenes with DPP would occur at 3-C or 1-N, or else at 2-amino group at first, giving some varieties of cycloadducts. We expanded the reactions to 2-alkylamino- and 2-



dialkylamino-1-azaazulenes with DPP and obtained interesting results, in which novel cyclizations were observed.

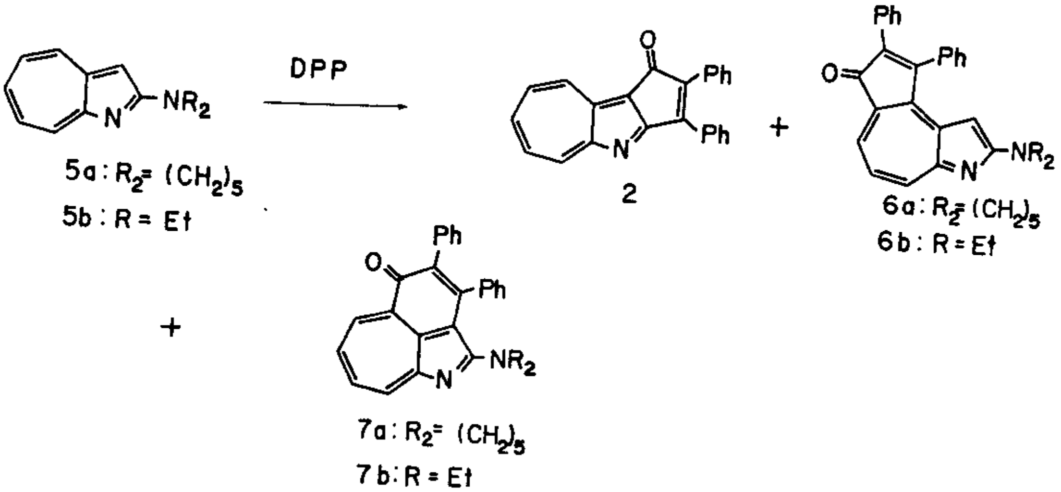
As the typical example, the reaction of 2-ethylamino-1-azaazulene (**1a**) with 1 equivalent of DPP in refluxing acetonitrile for 2 h gave 1,2-diphenyl-3*H*-9-azacyclopent[*a*]azulen-3-one (**2**) (11%) and a mixture of (*Z*)- and (*E*)-*N*-(1-azaazulen-2-yl)-*N*-ethyl-2,3-diphenyl-2-propenamides (**3a** : **4a** = 3 : 1 by ^{1}H nmr) (47%), along with recovered **1a** (29%). From the mixture of **3a** and **4a**, only **3a** was isolated in pure form by fractional recrystallization, but **4a** was not. When the reaction was performed in refluxing xylene, a mixture of **3a** and **4a** (67%) was obtained, but **2** was not. Some of the results are listed in Table 1. The structures of **2** and **3b** were deduced by X-ray structural analyses (Figures 1 and 2),[13-15] and **3a** was deduced by comparison with its spectral features with those of **3b**.

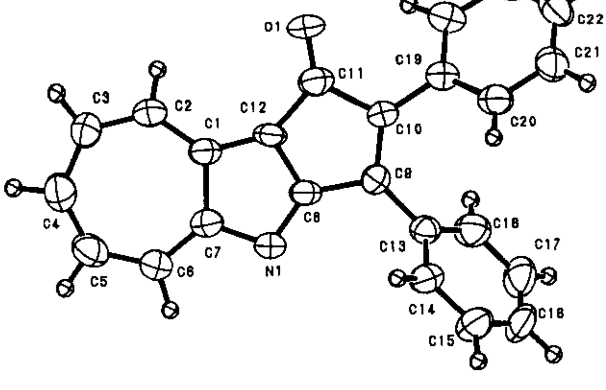
Reaction of dialkylamino-1-azaazulenes with DPP proceeded rather slow and gave distinct results from that of alkylamino-1-azaazulenes; thus treatment of 2-piperidino-1-azaazulene (**5a**) with DPP in acetonitrile for 7 d yielded **2** (0.5%), 8,9-diphenyl-2-piperidino-7*H*-1-azacyclopent[*e*]azulen-7-one (**6a**) (5%), and 3,4-diphenyl-2-piperidino-5*H*-1-azabenz[*cd*]azulen-5-one (**7a**) (3.5%) as cycloadducts; mainly starting compound (**5a**) was recovered (79.5%). Some of the results are listed in Table 1. Treatment at higher temperature, such as in refluxing xylene, did not improved results. The structures of **6b** and **7a** were deduced by X-ray structural analyses (Figures 3 and 4),[13,16,17] and **6a** and **7b** were characterized by comparison with their spectral features with those of **6b** and **7a**, respectively.



1a: R=Et
1b: R=*i*-Pr

3a: (*Z*)-form, R=Et
3b: (*Z*)-form, R=*i*-Pr
4a: (*E*)-form, R=Et
4b: (*E*)-form, R=*i*-Pr





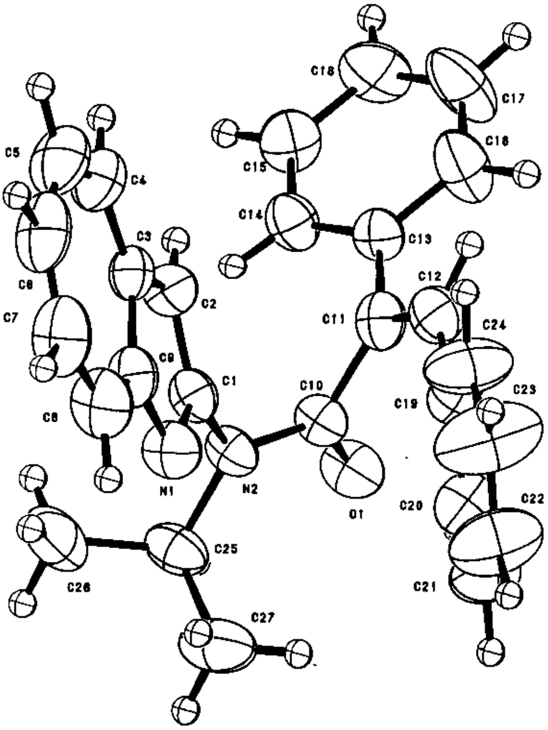


Figure 1. ORTEP drawing of **2**.

Figure 2. ORTEP drawing of **3b**.

Table 1. Reactions of **1a**, **1b**, **5a**, and **5b** with DPP.

Compounds	Conditions		Products (%)			Recovery (%)
1a	MeCN reflux	2 h	**2** (11)	**3a** + **4a** (3:1) (47)		**1a** (29)
1a	xylene reflux	1 h	**2** (-)	**3a** + **4a** (3:1) (67)		**1a** (20)
1b	MeCN reflux	2 h	**2** (9.5)	**3b** + **4b** (3:1) (57)		**1b** (13)
1c	xylene reflux	1 h	**2** (-)	**3b** + **4b** (3:1) (85)		**1b** (-)
5a	MeCN reflux	7 d	**2** (0.5)	**6a** (5)	**7a** (3)	**5a** (79.5)
5a	benzene reflux	10 d	**2** (2)	**6a** (2)	**7a** (5)	**5a** (90)
5a	xylene reflux	4 d	**2** (-)	**6a** (0.6)	**7a** (1)	**5a** (93)
5b	MeCN reflux	10 d	**2** (-)	**6b** (10)	**7b** (6)	**5b** (75)
5b	benzene reflux	10 d	**2** (-)	**6b** (3)	**7b** (4)	**5b** (90)
5b	xylene reflux	4 d	**2** (-)	**6b** (3)	**7b** (2)	**5b** (93.5)

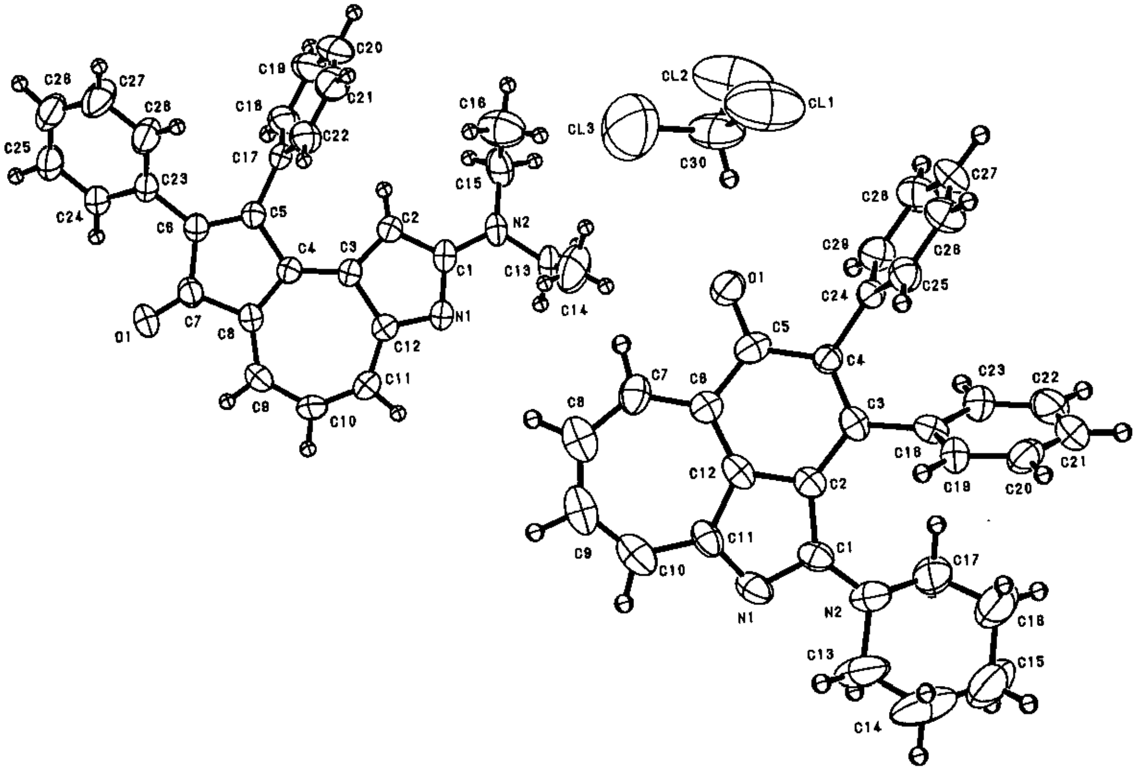
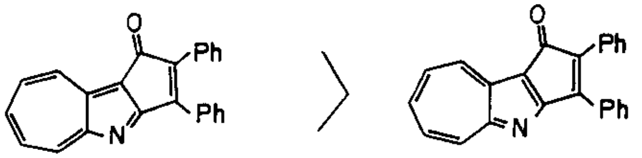


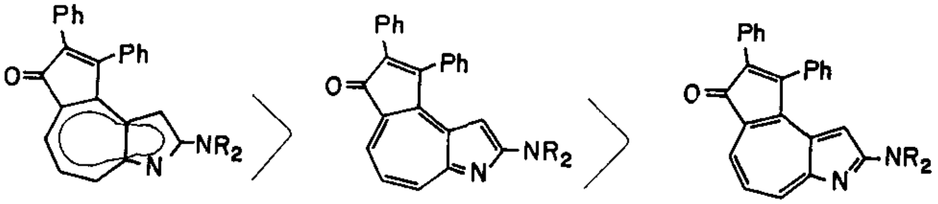
Figure 3. ORTEP drawing of **6b**.

Figure 4. ORTEP drawing of **7a**.

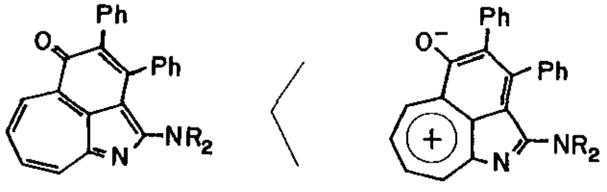
From consulting of the bond distances, in contrast with 1-azaazulenes, a distinct bond alternation of the seven-membered ring of **2** (1.359-1.405 Å) was observed; it is considered that **2** mainly has a contribution of resonance form (**2A**); because of having an unstable antiaromatic cyclopentadienone moiety, a contribution of resonance form (**2B**) is small. The result resembles that of 3*H*-cyclopent[*a*]azulen-3-one.[18] On the other hand, a bond alternation of the seven-membered ring of **6b** is not observed, though small differences of bond distances (1.373-1.405 Å) exist, suggesting that **6b** has a contribution due to the 1-azaazulene moiety and the enone moiety, such as **6A**. This result agreed with a conclusion based on the ^{1}H nmr spectra of **6b**, in which the coupling constants of the protons on the seven-membered ring are equal (J=9.8 Hz).



2A 2B

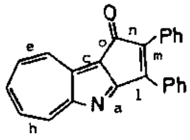


6A 6B 6C

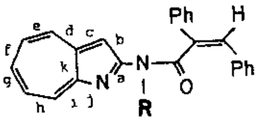


7B 7A

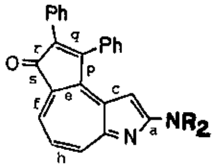
Table 2. Selected Bond Distances (l/Å) of **2**, **3b**, **6b**, and **7a**.



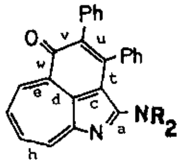
2



3b



6b

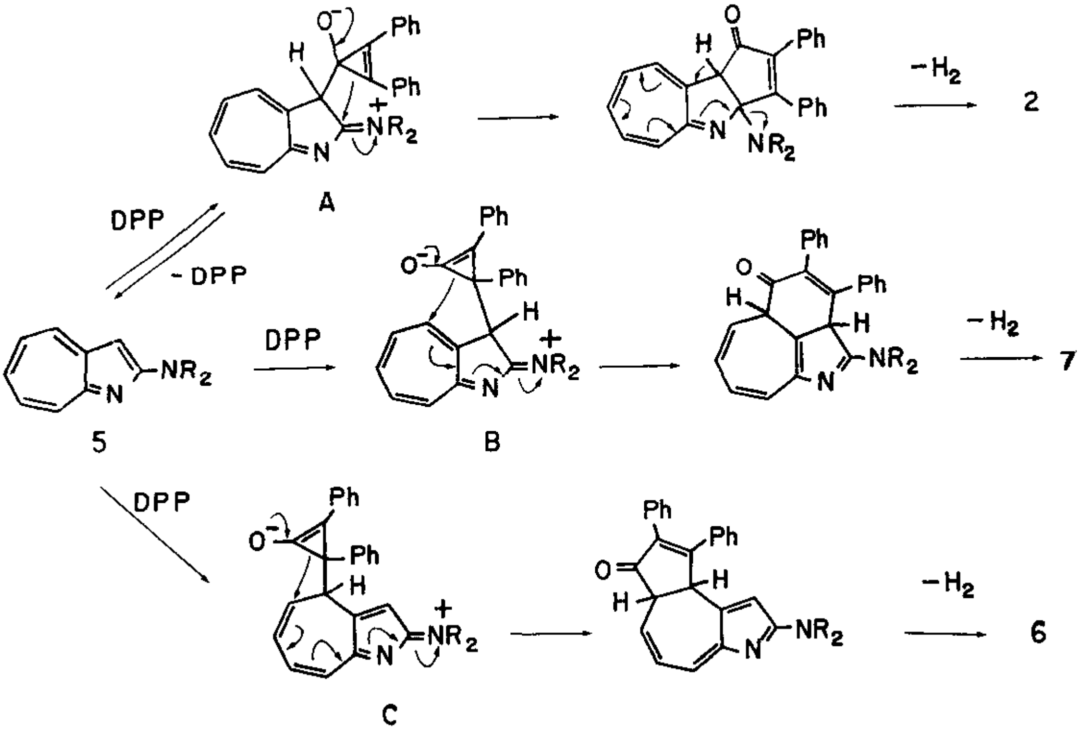


7a

	2	**3b**	**6b**	**7a**
a	1.327 (6)	1.353 (3)	1.363 (5)	1.353 (9)
b	1.402 (6)	1.371 (3)	1.407 (5)	1.46 (1)
c	1.394 (6)	1.393 (3)	1.375 (5)	1.39 (1)
d	1.403 (7)	1.384 (4)	1.405 (5)	1.40 (1)
e	1.372 (8)	1.383 (4)	1.399 (5)	1.41 (1)
f	1.405 (8)	1.397 (5)	1.379 (6)	1.38 (1)
g	1.359 (8)	1.364 (5)	1.392 (6)	1.38 (1)
h	1.396 (8)	1.384 (4)	1.372 (6)	1.38 (1)
i	1.369 (7)	1.393 (3)	1.386 (6)	1.41 (1)
j	1.391 (6)	1.358 (3)	1.348 (5)	1.33 (1)
k	1.482 (6)	1.465 (4)	1.490 (5)	1.46 (1)
l	1.462 (7)			
m	1.533 (7)			
n	1.366 (6)			
o	1.479 (6)			
p			1.508 (5)	
q			1.481 (5)	
r			1.354 (5)	
s			1.501 (5)	
t				1.47 (1)
u				1.47 (1)
v				1.37 (1)
w				1.43 (1)
C=O	1.216 (6)		1.216 (4)	1.253 (9)

A bond alternation of the seven-membered ring of **7a** is not also observed, and the length of C=O bond is slightly long (1.253 Å). The results suggest that **7a** has a contribution of the ionic resonance form as **7A**, which stabilized by tropilium ion moiety.

A reasonable mechanism for the formation of **2**, 6, and **7** was shown in Scheme 1. Kinetically preferential attack of DPP at C-3 position of **5** would give intermediate (**A**). Cyclization of **A** at C-2 followed by successive deamination furnished **2**. When substituent at C-2 was bulky, a Michael type addition would be preferred and intermediate **B** would be produced and successive cyclization and dehydrogenation furnished 6. In these reactions, 2-dialkylamino-1-azaazulenes behaved as enamine and dienamine.



Scheme 1

EXPERIMENTAL

Melting points are uncorrected. ^{1}H Nmr spectra (250 MHz) were recorded on a Hitachi R-250H spectrometer using deuteriochloroform as a solvent with tetramethylsilane as an internal standard. Ir spectra were recorded on a Hitachi 270-5- infrared spectrophotometer for Nujol mulls. Electronic spectra were taken with Hitachi 220A spectrophotometer using ethanol as a solvent. Mass spectra were taken with a JEOL JMS-01SG-2 spectrometer. Kieselgel 60 was used for column chromatography and Kieselgel 60G for preparative thin-layer chromatography.

Reaction of 1 and 5 with DPP. General procedure. A mixture of **1a** (0.344 g, 2.00 mmol) and DPP (0.412 g, 2.00 mmol) in the solvent (50 ml) was refluxed, then the solvent was evaporated. The residue was chromatographed with chloroform to give **2**, **3a**, and **4a**, and recovered 1a, successively. The reaction conditions and the results are listed in Table 1.

2: Red needles (from hexane), mp 212-214 ℃; ^{1}H nmr δ =7.30-7.48 (8H, m), 7.55-7.70 (3H, m), 7.80-7.85 (2H, m), and 8.45-8.55 (2H, m); ir 1684 cm^{-1} (C=O); uv λ_{max}/nm (log ε) 266 (4.13), 317 (4.52), 446 (3.48), 471 (3.51), 525 (sh, 3.05), and 565 (sh, 2.67); Anal. Calcd for $C_{24}H_{15}NO$: C, 86.46; H, 4.54; N, 4.20. Found: C, 86.41; H, 4.62; N, 3.98.

3a: Orange prisms (from hexane), mp 102-104 ℃; ^{1}H nmr δ =0.85-1.10 (3H, m), 4.10-4.50 (2H, m), 6.80-7.80 (14H, m), and 8.10-8.50 (3H, m); ir 1644 cm^{-1} (C=O); ms *m/z* (rel intensity) 378 (M$^+$, 92), 301 (100); Anal. Calcd for $C_{26}H_{22}N_2O$: C, 82.51; H, 5.86; N,7.40. Found: C, 82.63; H, 5.82; N, 7.45.

3b: Orange prisms (from hexane), mp 132-134 ℃; ^{1}H nmr δ =1.34 (6H, d, *J*=6.1 Hz), 5.50-5.70 (1H, m), 6.40-7.70 (14H, m), and 8.10-8.50 (3H, m); ir 1634 cm^{-1} (C=O); Anal. Calcd for $C_{27}H_{24}N_2O$: C, 82.62; H, 6.16; N, 7.14. Found: C, 82.54; H, 6.37; N, 7.31.

6a: Green prisms (from ethanol), mp 205-206 ℃; ^{1}H nmr δ =1.55-1.70 (6H, m), 3.40-3.60 (4H, m), 5.07 (1H, s), 7.20-7.52 (11H, m), 7.69 (1H, d, *J*=9.8 Hz), and 7.90 (1H, d, *J*=10.4 Hz); ir 1700 cm^{-1} (C=O); uv λ_{max}/nm (log ε) 276 (4.26), 360 (4.55), 466 (3.67), 488 (3.74), 520 (3.60), and 663 (3.60); ms *m/z* (rel intensity) 416 (M$^+$, 100), 415 (31), 387 (27), 361 (38), 332 (7), 152 (14), 138 (18), and 77 (4); Anal. Calcd for $C_{29}H_{24}N_2O$: C, 83.63; H, 5.81; N, 6.72. Found: C, 83.58; H, 5.71; N, 6.37.

7a: Violet prisms (from hexane-chloroform), mp 207-208 ℃; ^{1}H nmr δ =1.25-1.40 (6H, m), 3.30-3.40 (4H, m), 6.95-7.25 (10H, m), 7.56 (1H, td, *J*=9.5 and 2.4 Hz), 7.80-8.00 (2H, m), and 8.75 (1H, d,

J=11.0 Hz); ir 1612 cm^{-1} (C=O); uv λ_{max}/nm (log ε) 247 (4.25), 286 (4.30), 309 (4.35), 340 (4.13), 414 (4.10), and 522 (4.04); ms m/z (rel intensity) 416 (M^+, 100), 415 (58), 387 (4), 361 (8), 360 (13), 347 (31), 346 (26), 333 (23), 332 (8), 276 (7), 172 (10), and 77 (4); Anal. Calcd for $C_{29}H_{24}N_2O$: C, 83.63; H, 5.81; N, 6.72. Found: C, 83.47; H, 5.62; N, 6.88.

6b: Green prisms (from ethanol), mp 116-118 ℃; ^{1}H nmr δ=1.05-1.65 (6H, m), 3.10-3.80 (4H, m), 4.96 (1H, s), 7.20-7.55 (11H, m), 7.48 (1H, d, J=9.8 Hz), and 7.91 (1H, d, J=9.8 Hz); ir 1704 cm^{-1} (C=O); uv λ_{max}/nm (log ε) 276 (4.06), 359 (4.35), 445 (3.46), 488 (3.53), 520 (3.360), and 663 (3.42); ms m/z (rel intensity) 404 (M^+, 91), 403 (21), 389 (25), 375 (86), 361 (100), 360 (47), 333 (2), 332 (5), 304 (7), 276 (13), 152 (6), 138 (18), and 77 (9); Anal. Calcd for $C_{28}H_{24}N_2O$: C, 83.14; H, 5.98; N, 6.92. Found: C, 83.25; H, 5.78; N, 6.68.

7b: Violet prisms (from ethanol), mp 203-204 ℃; ^{1}H nmr δ=0.97 (6H, t, J=7.0 Hz), 3.26 (4H, q, J=7.0 Hz), 6.95-7.20 (10H, m), 7.54 (1H, td, J=10.4 and 3.1 Hz), 7.80-8.00 (2H, m), and 8.75 (1H, d, J=10.4 Hz); ir 1614 cm^{-1} (C=O); uv λ_{max}/nm (log ε) 248 (4.17), 285 (4.23), 309 (4.30), 340 (4.06), 414 (4.03), and 522 (3.99); ms m/z (rel intensity) 404 (M^+, 40), 403 (24), 375 (100), 361 (19), 360 (25), 347 (65), 346 (65), 345 (47), 276 (13), 174 (10), 173 (19), 87 (23), and 77 (9); Anal. Calcd for $C_{28}H_{24}N_2O$: C, 83.14; H, 5.98; N, 6.92. Found: C, 83.32; H, 5.91; N, 6.76.

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14. Crystal data **2**: M.W.=333.39, monoclinic space group $C2_1/c$, Z=4, a=9.622(3), b=10.235(4), c=17.801(3) Å, β=101.28(2)°, V=1719.0(9) $Å^3$, D_{calcd}=1.288 g/cm^3, R=0.050, Rw=0.052 for total 4421 reflections.
15. Crystal data **3b**: M.W.=392.50, triclinic space group $P\bar{1}$, Z=2, a=11.426(4), b=11.289(5), c=9.679(4) Å, α=118.28(3)°, β=104.27(3)°, γ=65.74(2)°, V=1103.3(8) $Å^3$, D_{calcd}=1.181 g/cm^3, R=0.053, Rw=0.058 for total 5308 reflections.
16. Crystal data **6b**: M.W.=404.51, monoclinic space group $C2_1/a$, Z=4, a=9.56(1), b=19.12(1), c=12.287(5) Å, β=96.95(7)°, V=2230(4) $Å^3$, D_{calcd}=1.205 g/cm^3, R=0.052, Rw=0.055 for total 4771 reflections.
17. Crystal data **7a**: M.W.=535.90, triclinic space group $P\bar{1}$, Z=2, a=11.908(6), b=13.127(4), c=10.062(7) Å, α=92.18(5)°, β=113.84(5)°, γ=109.76(3)°, V=1326(9) $Å^3$, D_{calcd}=1.342 g/cm^3, R=0.063, Rw=0.067 for total 5121 reflections.
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