HETEROCYCLES, Vol. 87, No. 11, 2013. pp. 2343 - 2350. © 2013 The Japan Institute of Heterocyclic Chemistry
Received, 23rd August, 2013, Accepted, 17th Spetember, 2013, Published online, 3rd October, 2013
DOI: 10.3987/COM-13-12822

SYNTHESIS OF SOME PYRAZOLE-FUSED PYRIDO[3,2-*a*]AZULENES

Dao-Lin Wang,* Zhe Dong, Qing-Tao Cui, Fei-Fei Yang, and Wei Zhao

Liaoning Key Laboratory of Synthesis & Application of Functional Compound, College of Chemistry & Chemical Engineering, Bohai University, Jinzhou 121001, P. R. China

Abstract — Facile synthesis of 11*H*(2*H*)-4-oxopyrazolo[3',4':6,5]pyrido-[3,2-*a*]azulene-10-carboxylates (**3**) via a domino reaction of 3-(dimethyl-amino)-2-(2-methoxy-1-ethoxycarbonylazulen-3-oyl)acrylonitrile (**1**) with hydrazines (**2**) in moderate to good yields. This reaction provides a new procedure for synthesis of pyridinone-fused azulenes.

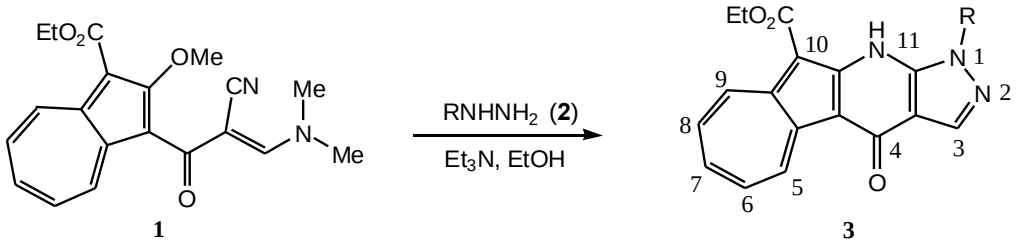
Various types of heterocycle-fused azulenes have so far been obtained on the viewpoints of chemical properties and physiological activities by several synthetic methods.[1-9] In recent years, the azuleno[2,1-*d*]pyrimidines,[10] azuleno[2,1-*d*]pyrimidinones,[11] and azuleno[2,1-*b*]pyrans[12] have been successfully prepared by our group.

As it is very well known that pyridin-4-(*1H*)-ones are key structural elements in medicinal chemistry and versatile intermediates in organic synthesis.[13] Many derivatives have been studied as potential treatments for a range of diseases because of their important biological properties, such as antibacterial[14] antiviral,[15] antiplatelet,[16] antitumor,[17] and other pharmacological activities.

On the other hand, the domino reactions have emerged as a powerful tool for the effective creation and expansion of molecular diversity.[18] Carbon–carbon and carbon–heteroatom bond-forming reactions are crucial to organic synthesis. Domino processes are important for generating high levels of diversity and complexity giving rise to complex structures by simultaneous formation of two or more bonds from simple substrates. These advantages are of particular interest in pharmaceutical research for the construction of libraries of biologically active compounds. Thus, developing new, environmentally benign domino reactions is an important topic of green chemistry.[19]

As part our work concerning the synthesis of heterocycle-fused azulenes with potential therapeutic

interest, we recently reported a three-step synthesis of azuleno[2,1-*b*]pyridin-4(*1H*)-one derivatives from ethyl 2-methoxyazulene-3-carboxylate involving conversion to a *β*-enaminone followed by reaction with a primary amine *via* tandem addition-elimination-S_NAr reaction.[20] Herein, we report on the synthesis of 11*H*(2*H*)-4-oxopyrazolo[3',4':6,5]pyrido[3,2-*a*]azulene-10-carboxylate derivatives (**3**) *via* a domino reaction of 3-(dimethylamino)-2-(2-methoxy-1-ethoxycarbonylazulen-3-oyl)acrylonitrile (**1**) with hydrazines (**2**) (Scheme 1).



1 **3**

Scheme 1

In this study, we first optimized the reaction of 3-(dimethylamino)-2-(2-methoxy-1-ethoxycarbonyl-azulen-3-oyl)acrylonitrile (**1**) with phenylhydrazine (**2a**) as model substrates. In our preliminary experiments 1 mmol **1** was treated with 1.1 mmol **2a** in EtOH at reflux. The reaction was complete in 4 h. After work-up of the reaction mixture, ethyl 11*H*(2*H*)-4-oxo-1-phenylpyrazolo[3',4':6,5]pyrido [3,2-*a*]-azulene-10-carboxylate (**3a**) was obtained in 76% as orange needles (mp 224-226 °C). Its structure was determined from the spectral data as well as elemental analysis ($C_{23}H_{17}N_3O_3$). In the ir spectrum, two carbonyl signals at 1661 and 1622 cm^{-1} and NH signals at 3413 cm^{-1} are observed. The ^1H NMR spectrum shows singlet peak at *δ* 8.30 (1H, s) for pyrazole-3-H, and seven-membered protons are seen at signals at *δ* 7.82 (1H, dd, *J* = 9.6, 9.6 Hz), 7.97-8.04 (2H, m), 9.19 (1H, d, *J* = 10.0 Hz), and 10.39 (1H, d, *J* = 9.6 Hz), together with ethoxycarbonyl protons at *δ* 1.35 (3H, t, *J* = 7.2 Hz, $OCH_2\underline{CH_3}$), 4.41 (2H, q, *J* = 7.2 Hz, $CO_2\underline{CH_2}CH_3$), NH protons at *δ* 9.11 (1H, s), and phenyl at *δ* 6.44-7.14 (5H, m). In the ^{13}C NMR spectrum, two carbonyl signals at 163.6 and 171.2 are observed.

In an initial endeavor, we carried out the reaction of 3-(dimethylamino)-2-(2-methoxy-1-ethoxycarbonylazulen-3-oyl)acrylonitrile (**1**) and phenylhydrazine (**2a)** using the different solvents (Table 1). We screened different solvents such as ethanol, methanol, dichloromethane, tetrahydrofuran, acetonitrile, chloroform and *N*,*N*-dimethylformamide at reflux condition. As shown in the Table 1, the best yield was obtained when ethanol was used as a solvent. In case of the protic solvents the yields are better than aprotic solvent.

Table 1. Effect of various solvent on the model reaction[a]

Entry	Solvent	Time[b] (h)	Yield[c] (%)
1	EtOH	4	76
2	MeOH	4	72
3	CH_2Cl_2	6	54
4	$CHCl_3$	4	65
5	MeCN	4	70
6	THF	6	47
7	DMF	2	64

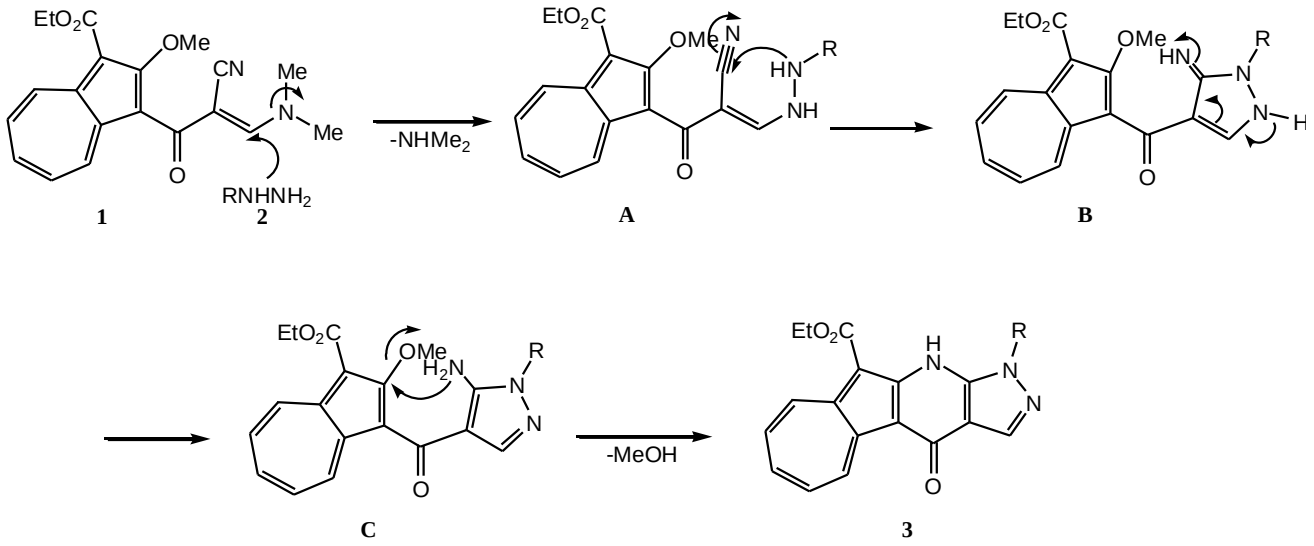
[a] Reaction conditions: 3-(dimethylamino)-2-(2-methoxy-1-ethoxycarbonylazulen-3-oyl)acrylonitrile (**1**, 1 mmol), phenylhydrazine (**2a**, 1.1 mmol), solvent (30 mL), at reflux temperature.
[b] Reaction progress monitored by TLC.
[c] Isolated yield.

Under the optimized conditions, a wide range of substituted aromatic hydrazines (**2**) underwent this one-pot condensation with 3-(dimethylamino)-2-(2-methoxy-1-ethoxycarbonylazulen-3-oyl)acrylonitrile (**1**) to give the corresponding pyrazolo[3',4':6,5]pyrido[3,2-*a*]azulene-10-carboxylates (**3**). The results are summarized in Table 2. For hydrazines bearing either electron-donating or electron-withdrawing substituents, the reaction proceeded smoothly in all cases. However, aromatic hydrazines with electron-withdrawing groups (Entries 6-8) reacted more rapidly and the products were obtained in good yields, while substitution of electronrich groups (Entries 2-5) on the benzene ring decreased the reactivity, requiring longer reaction times. Similarly, hydrazine hydrate (**2i**) and 2-hydrazinylethanol (**2j**) also participated in the reaction with **1** to give the corresponding products **3i** and **3j**, in 62 and 66% yields (Entries 9 and 10), respectively.

Table 2. Synthesis of 11*H*(2*H*)-4-oxopyrazolo[3',4':6,5]pyrido[3,2-*a*]azulene-10-carboxylates (**3**)

Entry	**2**/R		Time/h	Product	Yield/%
1	**2a**	C_6H_5	4	**3a**	76
2	**2b**	2-MeC_6H_4	4	**3b**	74
3	**2c**	4-MeC_6H_4	5	**3c**	70
4	**2d**	2,4-$Me_2C_6H_3$	4	**3d**	66
5	**2e**	4-$MeOC_6H_4$	4	**3e**	72
6	**2f**	4-FC_6H_4	2	**3f**	78
7	**2g**	4-ClC_6H_4	2	**3g**	83
8	**2h**	4-BrC_6H_4	2	**3h**	85
9	**2i**	H	5	**3i**	62
10	**2j**	CH_2CH_2OH	6	**3j**	66

The proposed mechanism of the process is summarized in Scheme 2. The sequence involves an initial conjugate addition of the hydrazine (**2**) to enaminone (**1**) followed by elimination of the dimethylamino group to give adduct **A.** This then undergoes domino cyclizations of the 2-methoxy of azulenyl group by attack of NH group leads to yield the tetracyclic system (**3**).



Scheme 2

In conclusion, we have successfully developed facile and efficient method to prepare a series of 11*H*(2*H*)-4-oxopyrazolo[3',4':6,5]pyrido[3,2-*a*]azulene-10-carboxylate derivatives *via* a domino reaction of 3-(dimethylamino)-2-(2-methoxy-1-ethoxycarbonylazulen-3-oyl)acrylonitrile with hydrazines in moderate to good yields. Further investigations to elaborate the scope of this methodology and to show the synthetic utility of the heterocycle-fused azulene derivatives obtained are currently in progress in our laboratory.

EXPERIMENTAL

All melting points were determined on a Yanako MP-3 apparatus and are uncorrected. NMR spectra were recorded on a Bruker spectrometer (400 MHz). IR spectra were measured on Shimadzu IR-740 spectrophotometer. Elemental analyses were performed on EA 2400 II elemental analyzer (Perkin-Elmer).

Preparation of 11*H*(2*H*)-4-oxopyrazolo[3',4':6,5]pyrido[3,2-*a*]azulene-10-carboxylates.

General procedure: A mixture of 3-(dimethylamino)-2-(2-methoxy-1-ethoxycarbonylazulen-3-oyl)-acrylonitrile[20] (**1**) (1.0 mmol), hydrazines (**2**) **(**1.1 mmol) and triethylamine (0.5 mL) in EtOH (30 mL) was heated to reflux under stirring for the given time (Table 2). After completion (by TLC), the reaction

mixture was cooled to room temperature, then water (20 mL) was added to the mixture and stirred for 15 min. The solid was filtered and recrystallized to afford the corresponding products. The physical and spectra data of the compounds **3a-j** are as follows:

Ethyl 1-Phenyl-*11H*(2*H*)-4-oxopyrazolo[3',4':6,5]pyrido[3,2-*a*]azulene-10-carboxylate (3a): Orange needles (from EtOH). mp 224-226 °C; IR (KBr, cm^{-1}): *v* 3413 (NH), 1661 (C=O), 1622 (C=O). ^{1}H-NMR (DMSO-d_6): δ 1.35 (3H, t, *J* = 7.2 Hz, $OCH_2\underline{CH_3}$), 4.41 (2H, q, *J* = 7.2 Hz, $CO_2\underline{CH_2}CH_3$), 6.44-6.46 (2H, m), 6.90-6.6.95 (1H, m), 7.12-7.14 (2H, m), 7.82 (1H, dd, *J* = 9.6, 9.6 Hz), 7.97-8.04 (2H, m), 8.30 (1H, s), 9.11 (1H, s, NH), 9.19 (1H, d, *J* = 10.0 Hz), 10.39 (1H, d, *J* = 9.6 Hz); ^{13}C-NMR (DMSO-d_6): δ 12.0, 59.9, 97.9, 106.0, 111.2, 111.8, 114.1, 119.8, 127.9, 130.5, 131.0, 134.6, 135.9, 136.5, 139.0, 139.1, 144.9, 145.7, 150.2, 163.6, 171.2. *Anal*. Calcd for $C_{23}H_{17}N_3O_3$: C 72.05, H 4.47, N 10.96. Found: C 72.18, H 4.62, N 10.87.

Ethyl 1-(2-Methylphenyl)-11*H*(2*H*)-4-oxopyrazolo[3',4':6,5]pyrido[3,2-*a*]azulene-10-carboxylate (3b): Orange needles (from EtOH). mp 222-224 °C; IR (KBr, cm^{-1}): *v* 3412 (NH), 1662 (C=O), 1625 (C=O). ^{1}H-NMR (DMSO-d_6): δ 1.21 (3H, t, *J* = 7.2 Hz, $OCH_2\underline{CH_3}$), 2.39 (3H, s, CH_3), 4.29 (2H, q, *J* = 7.2 Hz, $CO_2\underline{CH_2}CH_3$), 6.36-6.6.37 (1H, m), 6.82-6.84 (2H, m), 7.12-7.14 (1H, m), 7.83 (1H, dd, *J* = 9.6, 9.6 Hz), 7.97-8.04 (2H, m), 8.24 (1H, s), 9.01 (1H, s, NH), 9.15 (1H, d, *J* = 10.4 Hz), 10.41 (1H, d, *J* = 9.6 Hz); ^{13}C-NMR (DMSO-d_6): δ 13.6, 17.4, 61.2, 99.6, 107.9, 112.1, 113.0, 116.0, 121.5, 123.3, 127.3, 130.9, 132.2, 132.8, 136.3, 137.6, 138.2, 140.7, 140.8, 144.6, 147.5, 152.3, 165.5, 173.0. *Anal*. Calcd for $C_{24}H_{19}N_3O_3$: C 72.53, H 4.82, N 10.57. Found: C 72.71, H 4.99, N 10.58.

Ethyl 1-(4-Methylphenyl)-11*H*(2*H*)-4-oxopyrazolo[3',4':6,5]pyrido[3,2-*a*]azulene-10-carboxylate (3c): Orange needles (from EtOH). mp 216-218 °C; IR (KBr, cm^{-1}): *v* 3423 (NH), 1660 (C=O), 1623 (C=O). ^{1}H-NMR (DMSO-d_6): δ 1.35 (3H, t, *J* = 7.2 Hz, $OCH_2\underline{CH_3}$), 2.16 (3H, s, CH_3), 4.42 (2H, q, *J* = 7.2 Hz, $CO_2\underline{CH_2}CH_3$), 6.34 (2H, d, *J* = 7.2 Hz), 6.92 (2H, d, J = 7.2 Hz), 7.92 (1H, dd, *J* = 9.6, 9.6 Hz), 7.96-8.03 (2H, m), 8.28 (1H, s), 9.01 (1H, s, NH), 9.15 (1H, d, *J* = 10.0 Hz), 10.36 (1H, d, *J* = 9.6 Hz); ^{13}C-NMR (DMSO-d_6): δ 12.1, 18.8, 59.9, 97.8, 106.0, 111.2, 112.1, 114.2, 128.8, 130.5, 131.0, 134.6, 135.9, 136.4, 139.0, 139.1, 142.6, 145.8, 150.0, 150.1, 163.5, 171.2. *Anal*. Calcd for $C_{24}H_{19}N_3O_3$: C 72.53, H 4.82, N 10.57. Found: C 72.68, H 4.97, N 10.76.

Ethyl 1-(2,4-Dimethylphenyl)-11*H*(2*H*)-4-oxopyrazolo[3',4':6,5]pyrido[3,2-*a*]azulene-10-carboxylate (3d): Orange needles (from EtOH). mp 200-202 °C; IR (KBr, cm^{-1}): *v* 3425 (NH), 1661 (C=O), 1620 (C=O). ^{1}H-NMR (DMSO-d_6): δ 1.23 (3H, t, *J* = 7.2 Hz, $OCH_2\underline{CH_3}$), 2.15 (3H, s, CH_3), 2.24 (3H, s, CH_3), 4.32 (2H, q, *J* = 7.2 Hz, $CO_2\underline{CH_2}CH_3$), 6.62 (1H, d, *J* = 8.0 Hz), 6.94 (1H, s), 7.14 (1H, d, *J* = 8.0 Hz), 7.83 (1H, dd, *J* = 9.6, 9.6 Hz), 7.98-8.02 (2H, m), 8.23 (1H, s), 8.94 (1H, s, NH), 9.14 (1H, d, *J* = 10.0

Hz), 10.39 (1H, d, *J* = 9.6 Hz); ^{13}C-NMR (DMSO-d_6): δ 12.1, 12.3, 18.8, 59.9, 97.8, 106.0, 111.3, 112.1, 114.2, 128.7, 128.8, 130.5, 131.0, 134.6, 135.9, 136.4, 139.0, 139.1, 142.6, 145.8, 150.0, 150.1, 154.2, 163.6, 171.2. *Anal*. Calcd for $C_{25}H_{21}N_3O_3$: C 72.98, H 5.14, N 10.21. Found: C 73.14, H 5.25, N 10.36.

Ethyl 1-(4-Methoxyphenyl)-11*H*(*2H*)-4-oxopyrazolo[3',4':6,5]pyrido[3,2-*a*]azulene-10-carboxylate (3e): Orange needles (from EtOH). mp 148-150 °C; IR (KBr, cm^{-1}): *v* 3433 (NH), 1658 (C=O), 1632 (C=O). ^{1}H-NMR (DMSO-d_6): δ 1.37 (3H, t, *J* = 7.2 Hz, $OCH_2\underline{CH_3}$), 3.88 (3H, s, OCH_3), 4.43 (2H, q, *J* = 7.2 Hz, $CO_2\underline{CH_2}CH_3$), 7.06 (2H, d, *J* = 8.4 Hz), 7.39 (2H, d, *J* = 8.4 Hz), 7.76 (1H, dd, *J* = 9.6, 9.6 Hz), 7.93-7.98 (2H, m), 8.30 (1H, s), 8.89 (1H, d, *J* = 10.0 Hz), 9.06 (1H, s, NH), 10.25 (1H, d, *J* = 9.6 Hz); ^{13}C-NMR (DMSO-d_6): δ 15.4, 18.8, 59.9, 97.8, 106.0, 111.2, 112.1, 114.2, 128.3, 128.8, 130.5, 131.0, 134.6, 135.9, 136.4, 139.0, 139.1, 145.8, 150.0, 150.1, 163.6, 171.2. *Anal*. Calcd for $C_{24}H_{19}N_3O_4$: C 69.72, H 4.63, N 10.16. Found: C 69.91, H 4.77, N 10.30.

Ethyl 1-(4-Fluorophenyl)-11*H*(*2H*)-4-oxopyrazolo[3',4':6,5]pyrido[3,2-*a*]azulene-10-carboxylate (3f): Orange needles (from EtOH). mp 232-234 °C; IR (KBr, cm^{-1}): *v* 3436 (NH), 1667 (C=O), 1622 (C=O). ^{1}H-NMR (DMSO-d_6): δ 0.99 (3H, t, *J* = 7.2 Hz, $OCH_2\underline{CH_3}$), 4.11 (2H, q, *J* = 7.2 Hz, $CO_2\underline{CH_2}CH_3$), 6.66 (2H, d, *J* = 8.6 Hz), 7.28 (2H, d, *J* = 8.6 Hz), 7.92 (1H, dd, *J* = 9.6, 9.6 Hz), 8.04 (1H, dd, *J* = 9.2, 9.6 Hz), 8.16 (1H, dd, *J* = 9.6, 9.6 Hz), 8.67 (1H, d, *J* = 9.6 Hz), 9.01 (1H, s), 9.87 (1H, s, NH), 10.01 (1H, d, *J* = 9.2 Hz); ^{13}C-NMR (DMSO-d_6): δ 12.2, 59.9, 98.0, 105.9, 111.3, 113.6, 114.6, 130.4, 131.0, 134.6, 135.8, 136.5, 139.0, 139.1, 145.6, 149.9, 150.0, 154.7, 157.1, 163.6, 171.2. *Anal*. Calcd for $C_{23}H_{16}FN_3O_3$: C 68.82, H 4.02, N 10.47. Found: C 68.99, H 4.16, N 10.58.

Ethyl 1-(4-Chlorophenyl)-11*H*(*2H*)-4-oxopyrazolo[3',4':6,5]pyrido[3,2-*a*]azulene-10-carboxylate (3g): Orange needles (from MeOH). mp 265-267 °C; IR (KBr, cm^{-1}): *v* 3419 (NH), 1681 (C=O), 1628 (C=O). ^{1}H-NMR (DMSO-d_6): δ 0.99 (3H, t, *J* = 7.2 Hz, $OCH_2\underline{CH_3}$), 4.11 (2H, q, *J* = 7.2 Hz, $CO_2\underline{CH_2}CH_3$), 6.66 (2H, d, *J* = 8.6 Hz), 7.28 (2H, d, *J* = 8.6 Hz), 7.92 (1H, dd, *J* = 9.6, 9.6 Hz), 8.04 (1H, dd, *J* = 9.2, 9.6 Hz), 8.16 (1H, dd, *J* = 9.6, 9.6 Hz), 8.67 (1H, d, *J* = 9.6 Hz), 9.01 (1H, s), 9.87 (1H, s, NH), 10.01 (1H, d, *J* = 9.2 Hz); ^{13}C-NMR (DMSO-d_6): δ 13.9, 61.8, 99.9, 107.7, 111.4, 113.1, 115.4, 115.9, 125.2, 129.5, 132.3, 132.9, 136.5, 137.6, 138.3, 140.9, 145.7, 147.3, 151.8, 165.3, 172.9. *Anal*. Calcd for $C_{23}H_{16}ClN_3O_3$: C 66.11, H 3.86, N 10.06. Found: C 66.23, H 3.98, N 10.23.

Ethyl 1-(4-Bromophenyl)-11*H*(*2H*)-4-oxopyrazolo[3',4':6,5]pyrido[3,2-*a*]azulene-10-carboxylate (3h): Orange needles (from MeOH). mp 237-239 °C; IR (KBr, cm^{-1}): *v* 3433 (NH), 1671 (C=O), 1612 (C=O). ^{1}H-NMR (DMSO-d_6): δ 0.98 (3H, t, *J* = 7.2 Hz, $OCH_2\underline{CH_3}$), 4.01 (2H, q, *J* = 7.2 Hz, $CO_2\underline{CH_2}CH_3$), 6.62 (2H, d, *J* = 8.4 Hz), 7.40 (2H, d, *J* = 8.4 Hz), 7.91 (1H, dd, *J* = 9.2, 9.6 Hz), 8.03 (1H, dd, *J* = 9.2, 9.2 Hz), 8.15 (1H, dd, *J* = 9.2, 9.2 Hz), 8.65 (1H, d, *J* = 10.0 Hz), 8.99 (1H, s), 9.96 (1H, s,

NH), 10.02 (1H, d, *J* = 9.2 Hz); ^{13}C-NMR (DMSO-d_6): δ 12.1, 59.9, 98.1, 105.9, 111.8, 114.1, 119.8, 127.9, 130.5, 131.1, 134.6, 135.8, 136.5, 139.1, 144.3, 144.9, 145.5, 150.0, 163.5, 163.6, 171.1. *Anal*. Calcd for $C_{23}H_{16}BrN_3O_3$: C 59.76, H 3.49, N 9.09. Found: C 59.92, H 3.64, N 9.23.

Ethyl 11*H*(2*H*)-4-Oxopyrazolo[3',4':6,5]pyrido[3,2-*a*]azulene-10-carboxylate (3i): Orange needles (from EtOH). mp 231-233 °C; IR (KBr, cm^{-1}): *v* 3423 (NH), 1669 (C=O), 1628 (C=O). ^{1}H-NMR (DMSO-d_6): δ 1.41 (3H, t, *J* = 7.2 Hz, $OCH_2\underline{CH_3}$), 4.46 (2H, q, *J* = 7.2 Hz, $CO_2\underline{CH_2}CH_3$), 6.72 (2H, m), 7.92-8.04 (2H, m), 8.14 (1H, dd, *J* = 9.6, 9.6 Hz), 8.71 (1H, s), 8.90 (1H, d, *J* = 9.6 Hz), 10.02 (1H, d, *J* = 9.6 Hz); ^{13}C-NMR (DMSO-d_6): δ 12.7, 59.9, 95.4, 105.7, 111.5, 114.7, 130.6, 131.2, 134.7, 136.1, 136.3, 138.9, 139.7, 146.5, 149.7, 163.9, 171.1. *Anal*. Calcd for $C_{17}H_{13}N_3O_3$: C 66.44, H 4.26, N 13.67. Found: C 66.57, H 4.42, N 13.83.

Ethyl 1-(2-Hydroxyethyl)-11*H*(2*H*)-4-oxopyrazolo[3',4':6,5]pyrido[3,2-*a*]azulene-10-carboxylate (3j): Orange needles (from EtOH). mp 210-212 °C; IR (KBr, cm^{-1}): *v* 3423 (NH), 3318 (OH), 1655 (C=O), 1620 (C=O). ^{1}H-NMR (DMSO-d_6): δ 1.40 (3H, t, *J* = 7.2 Hz, $OCH_2\underline{CH_3}$), 3.16 (2H, d, *J* = 5.2 Hz, CH_2), 3.54 (2H, d, *J* = 5.2 Hz, CH_2), 4.45 (2H, q, *J* = 7.2 Hz, $CO_2\underline{CH_2}CH_3$), 4.79 (1H, s, OH), 7.11 (1H, s), 7.91 (1H, dd, *J* = 9.6, 9.6 Hz), 7.99 (1H, dd, *J* = 9.6, 9.6 Hz), 8.09 (1H, dd, *J* = 9.6, 9.6 Hz), 8.73 (1H, d, *J* = 10.2 Hz), 8.90 (1H, s, NH), 9.96 (1H, d, *J* = 9.6 Hz); ^{13}C-NMR (DMSO-d_6): δ 12.7, 51.9, 56.8, 60.1, 96.1, 106.1, 111.3, 114.7, 130.2, 130.8, 134.3, 135.9, 136.1, 138.6, 138.9, 145.1, 148.7, 164.2, 171.2. *Anal*. Calcd for $C_{19}H_{17}N_3O_4$: C 64.95, H 4.88, N 11.96. Found: C 65.11, H 4.96, N 12.13.

ACKNOWLEDGEMENT

This work was partially supported by Science and Technology Department of Liaoning Province (No. 2011220022).

REFERENCES

1. T. Morita, T. Nakadate, and K. Takase, *Heterocycles*, 1981, **15**, 835.
2. K. Fujimori, T. Fujita, K. Yamane, M. Yasunami, and K. Takase, *Chem. Lett*., 1983, **12**, 1721.
3. K. Yamane, K. Fujimori, S. Ichikawa, S. Miyoshi, and K. Hashizume, *Heterocycles*, 1983, **20**, 1263.
4. K. Fujimori, H. Fukazawa, Y. Nezu, K. Yamane, M. Yasunami, and K. Takase, *Chem. Lett*., 1986, **15**, 1021.
5. D.-L. Wang and K. Imafuku, *Heterocycles*, 2001, **54**, 647.
6. K. Imafuku and D.-L. Wang, *Heterocycles*, 2002, **58**, 405.
7. H. Matsuo, K. Fujimori, A. Ohta, A. Kakehi, M. Yasunami, and T. Nozoe, *Heterocycles*, 2003, **61**,

271.

8. M. Nishiura, I. Ueda, and K. Yamamura, *Heterocycles*, 2007, **74**, 951.
9. S. Ito, T. Okujima, S. Kikuchi, T. Shoji, N. Morita, T. Asao, T. Ikoma, S. Tero-Kubota, J. Kawakami, and A. Tajiri, *J. Org. Chem*., 2008, **73**, 2256.
10. D.-L. Wang, Z. Gu, S. Han, and J. Xu, *Synth. Commun.*, 2009, **39**, 2329.
11. D.-L. Wang, Y.-F. Li, J. Xu, W. Li, S.-F. Li, and L.-N. Lin, *Heterocycles*, 2011, **83**, 365.
12. D.-L. Wang, S.-S. Feng, Q.-T. Cui, and J.-Y. Yu, *Heterocycles*, 2012, **85**, 441.
13. P. M. Weintraub, J. S. Sabol, J. M. Kane, and D. R. Borcherding, *Tetrahedron*, 2003, **59**, 2953.
14. D. D. Erol and N. Yulug, *Eur. J. Med. Chem*., 1994, **29**, 893.
15. R. P. Frutos, N. Haddad, I. N. Houpis, M. Johnson, L. L. Smith-Keenan, V. Fuchs, N. K. Yee, V. Farina, A. M. Faucher, C. Brochu, B. Haché, J. S. Duceppe, and P. Beaulieu, *Synthesis*, 2006, 2563.
16. L. J. Huang, M. C. Hsieh, C. M. Teng, K. H. Lee, and S. C. Kuo, *Bioorg. Med. Chem*., 1998, **6**, 1657.
17. C. T. Chen, M. H. Hsu, Y. Y. Cheng, C. Y. Liu, L. C. Chou, L. J. Huang, T. S. Wu, X. M. Yang, K. H. Lee, and S. C. Kuo, *Eur. J. Med. Chem*., 2011, **46**, 6046.
18. a) L.-F. Tietze, *Chem. Rev*., 1996, **96**, 115; b) L.-F. Tietze, G. Brasche, and K. Gericke, *Domino Reactions in Organic Synthesis*; Wiley–VCH: Weinheim, 2006. p. 160.
19. a) B. T. Barry and G. H. Dennis, *Chem. Rev*., 2009, **109**, 4439; b) N. R. Candeias, L. F. Veiros, C. A. M. Afonso, and P. M. P. Gois, *Eur. J. Org. Chem*., 2009, 1859.
20. D.-L. Wang, Q.-T. Cui, S.-S. Feng, and J.-Y. Yu, *Heterocycles*, 2012, **85**, 697.