Chemistry of Heterocyclic Compounds, Vol. 36, No. 8, 2000

DERIVATIVES OF 1,4-DIARYL-5,6,7,8-TETRAHYDRO-2,2a,8a-TRIAZACYCLOPENTA[*c,d*]AZULENE

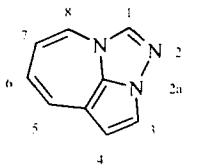
A. M. Demchenko

Derivatives of the previously unknown heterocyclic system 2,2a,8a-triazacyclopenta[c,d]azulene were synthesized by condensation of 3-aryl-4,5-pentamethylene-1,2,4-triazoles or 2-(β-aroylhydrazin)-1-aza-Δ¹-cycloheptene with α-halogeno ketones, followed by cyclization of the intermediate products in alkaline media.

Keywords: 3-aryl-4,5-pentamethylene-1,2,4-triazoles, α-halogeno ketones, 2,2a,8a-triazacyclopenta[*c,d*]-azulene, correlation dependence of proton chemical shifts, cyclization in alkaline media, quaternary phenacylium salts.

Derivatives of 2a,4a-diazacyclopenta[*c,d*]azulene were synthesized earlier and their properties were studied [1, 2]. These heterocyclic systems were obtained by cyclization in alkaline media of the condensation products of 1,2-pentamethylenimidazoles with substituted phenacyl bromides.

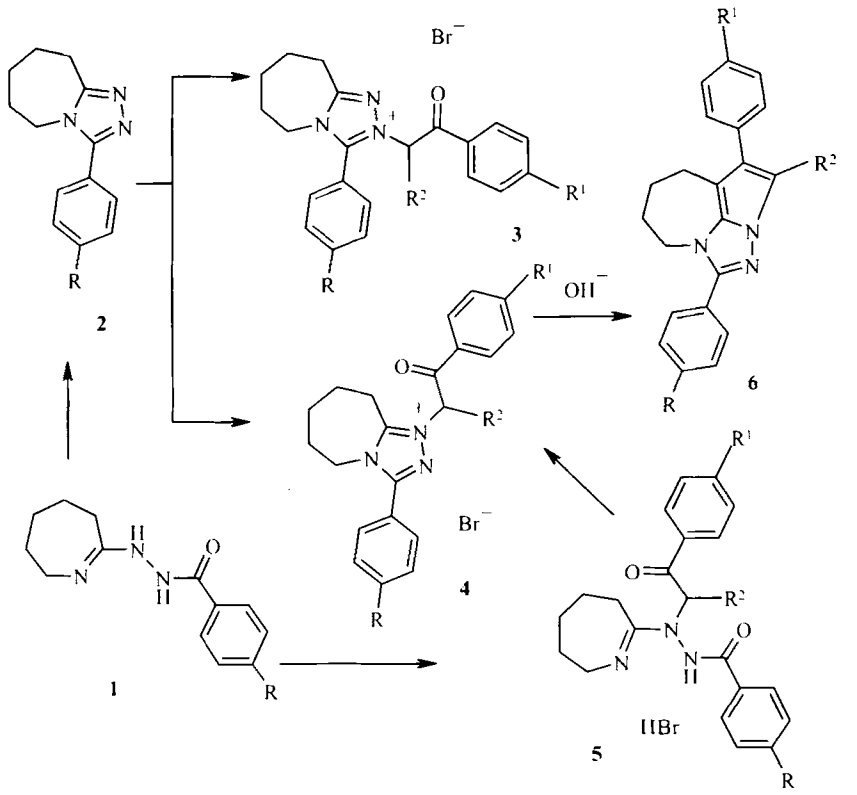
In the present work it was proposed to prepare examples of the new heterocyclic system 2,2a,8a-triazacyclopenta[*c,d*]azulene by condensation of 3-aryl-4,5-pentamethylen-1,2,4-triazoles with α-halogeno ketones with subsequent cyclization of the intermediate salts in alkaline medium.



Alkylation of 3-aryl-4,5-pentamethylen-1,2,4-triazoles **2** with α-halogeno ketones by boiling equimolar amounts of the reagents in polar solvents (ethanol or acetone) gave a mixture of compounds **3** and **4** in a 4:1 ratio (to judge from ratio of the integrated intensities of the methylene groups of the phenacyl residues in the ^{1}H NMR spectra). Separation of the mixture by crystallization from various solvents was unsuccessful. Because in most cases the mixture of compounds **3** and **4** obtained was a viscous, non-crystallizing oil, further reactions were carried out without further purification. Boiling solutions of the mixtures of quaternary phenacylium salts **3** and **4** in water in the presence of base (sodium hydroxide, sodium carbonate, or potash) was accompanied by cyclization to the derivatives of 1,4-diaryl-5,6,7,8-tetrahydro-2,2a,8a-triazacyclopenta[*c,d*]azulene (**6**). Considering that the latter is formed only from the quaternary salt **4**, the yield of the required products was relatively low, reaching 30–45%. Compounds **6** are light yellow crystals, stable on storage under normal conditions (Table 1). In the ^{1}H NMR spectra of compounds **6**, the protons of the 6- and 7-CH_2 groups appeared as a broad singlet at high field

T. G. Shevchenko Chernigov Pedagogical University, Chernigov 250037, Ukraine; e-mail: chspu@mail.cn.ua. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 8, pp. 1123-1127, August, 2000. Original article submitted January 11, 1999.

0009-3122/00/3608-0985$25.00©2000 KluwerAcademic/Plenum Publishers



1, **2**, **6 a** R = OCH_3, $R^1 = R^2 = H$; **b** R = CH_3, $R^1 = R^2 = H$; **c** R = Br, $R^1 = R^2 = H$; **d** R = Br, $R^1 = OCH_3$, $R^2 = H$; **e** R = Br, $R^1 = OC_2H_5$, $R^2 = H$; **f** R = R^1 = Br, $R^2 = H$; **g** R = Cl*, R^1 = Cl, $R^2 = H$; **h** R = Cl*, R^1 = Br, $R^2 = H$; **i** R = Br, $R^1 = CH_3$, $R^2 = H$; **j** R = Br, $R^1 = OCH_3$, $R^2 = CH_3$

* Substituent in the *ortho* position.

in the region 1.99-2.08 ppm, while the singlet signals of the 8- and 5-CH_2 groups appeared in the regions 2.72-2.92 and 3.72-4.07 ppm respectively. The signals of the 3-H protons may be identified among the absorptions of other aromatic protons in the 7.16-7.43 ppm region. It should be noted that for compounds **6c,d,e,f,i** (in which R = Br) there is a correlation of the chemical shifts of the protons in positions 3 of the systems with the electronic effects of the *para* substituents R^1 (in particular on the Hammet σ_{para} constant [3]) which can be expressed by the equation:

$$\delta \text{ ppm} = 0.348\sigma_{para} + 7.275$$

In the case of compound **6j** the signal of this proton is absent, but it is replaced by a three-proton singlet of a methyl group at 2.36 ppm.

In order to increase the yields of compounds **6a-j** the alkylation of 2-(β-aroylhydrazin)-1-aza-Δ^1-cycloheptene with α-halogeno ketones in polar solvents (ethanol or acetone) was studied. Salts **5** obtained by boiling equimolar amounts of the reagents in ethanol were oils and their crystallization for later identification was unfortunately unsuccessful. Consequently salts **5** without isolation were treated with acetic anhydride and 10% aqueous sodium hydroxide to give compounds **6**. Because the intermediate stage of formation of the by-products **3** was avoided by this synthetic route, the yields of the required products were increased to 63%. Compound **6b** was

TABLE 1. Physicochemical Characteristics of Compounds **6a-j**

Compound	Empirical formula	Found, % / Calculated, %		mp, °C	^{1}H NMR spectra, δ, ppm						Yield, %
		N	Hal		6- and 7-CH_2 s	5-CH_2 s	8-CH_2 s	3-H s	H_{arom}	Other protons	
6a	$C_{22}H_{21}N_3O$	12.1 / 12.2		212-213	2.08	2.92	4.02	7.18	7.00-7.63 (9H)	3.87 (3H, s, OCH_3)	38
6b	$C_{22}H_{21}N_3$	13.6 / 13.8		201-202	2.01	2.82	4.05	7.25	7.16-7.68 (9H)	2.40 (3H, s, CH_3)	45
6c	$C_{21}H_{18}BrN_3$	10.6 / 10.7	20.3 / 20.4	185-186	2.01	2.81	4.07	7.30	7.17-7.78 (9H)		63
6d	$C_{22}H_{20}BrN_3O$	9.85 / 9.94	18.7 / 18.9	213	2.00	2.77	4.07	7.20	6.92-7.76 (8H)	3.76 (3H, s, OCH_3)	58
6e	$C_{23}H_{22}BrN_3O$	9.56 / 9.63	18.1 / 18.3	230	2.01	2.77	4.06	7.16	6.90-7.74 (8H)	1.33 t (3H); 4.05 q (2H)	55
6f	$C_{21}H_{17}Br_2N_3$	8.83 / 8.91	33.8 / 34.0	246-48	2.01	2.79	4.07	7.34	7.42-7.78 (8H)		49
6g	$C_{21}H_{17}Cl_2N_3$	10.8 / 11.0	18.3 / 18.6	204-205	1.99	2.80	3.72	7.37	7.35-7.74 (8H)		36
6h	$C_{21}H_{17}BrClN_3$	9.71 / 9.84		189-190	2.00	2.80	3.74	7.43	7.39-7.75 (8H)		41
6i	$C_{22}H_{20}BrN_3O$	9.79 / 9.95	18.7 / 19.0	197-198	2.01	2.79	4.06	7.21	7.15-7.77 (8H)	2.30 (3H, s, CH_3)	59
6j	$C_{23}H_{22}BrN_3O$	9.59 / 9.63	18.4 / 18.3	203-204	1.95	2.60	4.03	2.36 (3H)*	6.95-7.76 (8H)	3.77 (3H, s, OCH_3)	30

* Signal of the 3-Me group.

synthesized by method A from 3-(4'-bromophenyl)-4,5-pentamethylen-1,2,4-triazole (**2**) and by method B from 2-[β-(4'-bromobenzoyl)hydrazin]-1-aza-Δ'-cycloheptene (**1**). A mixed melting point of the samples obtained by different methods gave no depression and their ^{1}H NMR spectra were identical. These observation permit the conclusion that compounds of type **1** with a complex amide structure and theoretically with three reactive centers are alkylated at the nitrogen atom outside the ring, alongside the cycloheptene portion of the molecule.

EXPERIMENTAL

^{1}H NMR spectra were recorded with a Bruker VXR-300 spectrometer with a working frequency of 299.945 MHz with TMS as internal standard. The purity of the compounds synthesized was monitored by TLC on Silufol UV-254 plates with 9:1 chloroform–methanol as eluant.

2-(β-Aroylhydrazin)-1-aza-Δ'-cycloheptenes (**1**) and 3-aryl-4,5-pentamethylen-1,2,4-triazoles (**2**) were synthesized by known methods [4, 5] and α-bromoacetophenones were synthesized as described previously [6].

1-(4'-Methoxyphenyl)-4-phenyl-5,6,7,8-tetrahydro-2,2a,8a-triazacyclopenta[*c,d*]azulene (6a). A mixture of 3-(4'-methoxyphenyl)-4,5-pentamethylen-1,2,4-triazole **2a** (2.43 g, 0.01 mol) and phenacyl bromide (1.99 g, 0.01 mol) was boiled in acetone (100 ml) for 5 h. After cooling, the solvent was decanted, the viscous mass formed was washed with ether, 10% NaOH solution was added and the mixture was boiled for 3 h. After cooling, the residue was filtered off, washed with water, dried, and recrystallized from benzene.

1-(4'-Tolyl)-4-phenyl-5,6,7,8-tetrahydro-2,2a,8a-triazacyclopenta[*c,d*]azulene (6b) was made analogously to compound **6a** from equimolar quantities of 3-(4'-tolyl)-4,5-pentamethylen-1,2,4-triazole (**2b**) and phenacyl bromide. It was recrystallized from propanol-2.

1-(4'-Bromophenyl)-4-phenyl-5,6,7,8-tetrahydro-2,2a,8a-triazacyclopenta[*c,d*]azulene (6c). A. This compound was obtained analogously to compound **6a** from equimolar quantities of 3-(4'-bromophenyl)-4,5-pentamethylen-1,2,4-triazole (**2c**) and phenacyl bromide. It was recrystallized from pyridine.

B. A mixture of 2-[β-(4'-bromobenzoyl)hydrazin]-1-aza-Δ'-cycloheptene **1** (3.1 g, 0.01 mol) and phenacyl bromide (1.99 g, 0.01 mol) was boiled in ethanol (100 ml) for 5 h, the solvent was evaporated in vacuum, the residue was washed with ether, acetic anhydride (20 ml) was added and the mixture was boiled for 30 min. After removal of acetic anhydride in vacuum, 10% NaOH solution (40 ml) was added and the mixture was boiled for 3 h. After cooling, the residue was filtered off, washed with water and dried.

Compounds **6d,e,f,i,j** were prepared analogously to compound **6c**. Compound **6f** was recrystallized from ethanol, the others from benzene.

1-(2'-Chlorophenyl)-4-phenyl-5,6,7,8-tetrahydro-2,2a,8a-triazacylopenta[*c,d*]-azulene (6g) was prepared analogously to compound **6a** from equimolar amounts of 3-(2'-chlorophenyl)-4,5-pentamethylen-1,2,4-triazole **2g** and phenacyl bromide. It was recrystallized from benzene.

Compound **6h** was prepared analogously to compound **6g**. It was recrystallized from propanol-2.

REFERENCES

1. V. A. Kovtunenko, K. G. Nazarenko, and A. M. Demchenko, *Tetrahedron*, **52**, 9835 (1996).
2. V. A. Kovtunenko, K. G. Nazarenko, and A. M. Demchenko, *Khim. Geterotsikl. Soedin.*, No. 8, 1072 (1996).
3. A. Gordon and R. Ford, *The Chemist's Companion* [Russian translation], Mir, Moscow (1976), 541.
4. S. Petersen and E. Tietze, *Chem. Ber.*, **90**, 909 (1957).
5. S. Petersen, E. Tietze, and W. Wirth, US Pat. 2913454; *Chem. Abstr.*, **54**, 9960 (1960).
6. A. V. Dombrovskii, M. I. Shevchuk, and V. P. Kravets, *Zh. Obshch. Khim.*, **32**, 2278 (1962).