Azulenic β diketones. Synthesis, properties and reactions to form five membered aromatic heterocycles

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Dedicated to Professor Alexandru T. Balaban on the occasion of his 75th birthday
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Abstract
Azulenic β-diketones were synthesized in the reaction of different β-diketones with 1-azulenecarboxylic acid chloride, in the presence of $MgCl_2$ and pyridine, as a result of condensation and subsequent acyl elimination. The obtained dicarbonyl compounds were used for the generation of azulenic pyrazoles and isoxazoles. The structures and some physico-chemical properties of the obtained products were reported.

Keywords: Azulene, β-diketone, pyrazole, isoxazole

Introduction

The high polarizability of the azulene electronic system induces special features in the molecules in which it is present. As an example, the substitution of such a moiety into molecules with low electron density, or even in cations, can stabilize these compounds.[1] The inclusion of such a substituent for compounds with push-pull electronic systems is of increasing interest since many materials with valuable optical properties belong to this compound class.[2]

Until now we have studied heterocyclic derivatives containing azulene and aromatic heterocyclic moieties joined by a double bond such as –N=N-,[3] -CH=N-[4] or -CH=CH-.[5] Our present interest is focused towards the synthesis and properties of compounds having a heterocycle directly substituted by azulene.

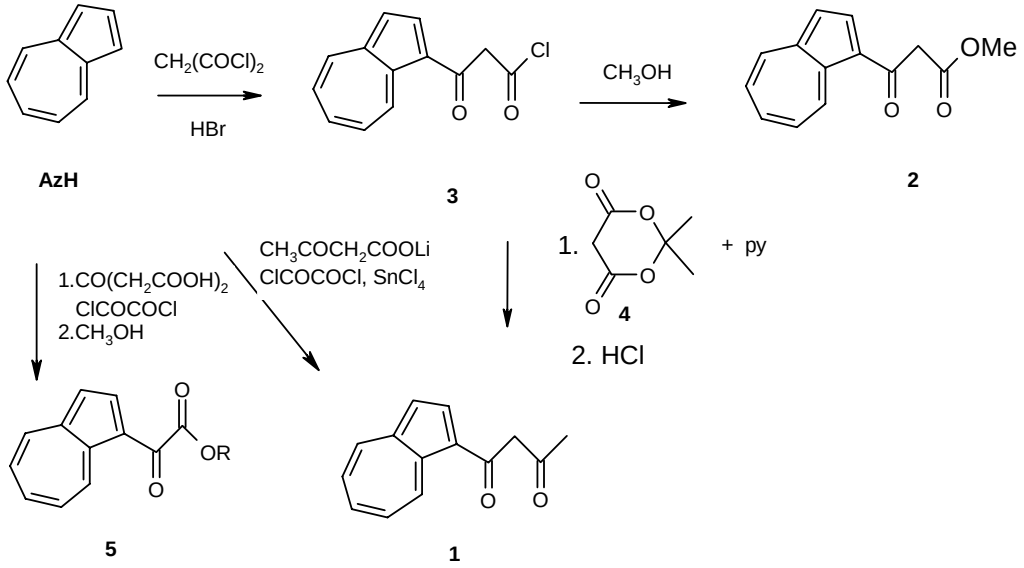
Treibs and Streckenbach[6] obtained 2H-pyrazol-3-ol and 4H-izoxazol-5-one substituted by azulene (at 5 and 3 position, respectively) and Krivun[7] and Dorofeenko[8] synthesized pyrylium salts with the same substituent. The described protocols for the syntheses were incomplete and only the elemental analyses and UV or IR spectra for the obtained products were reported.

In this paper we present results concerning the synthesis of some five-membered aromatic heterocycles and of their synthons, the β-dicarbonylic compounds.

Results and Discussions

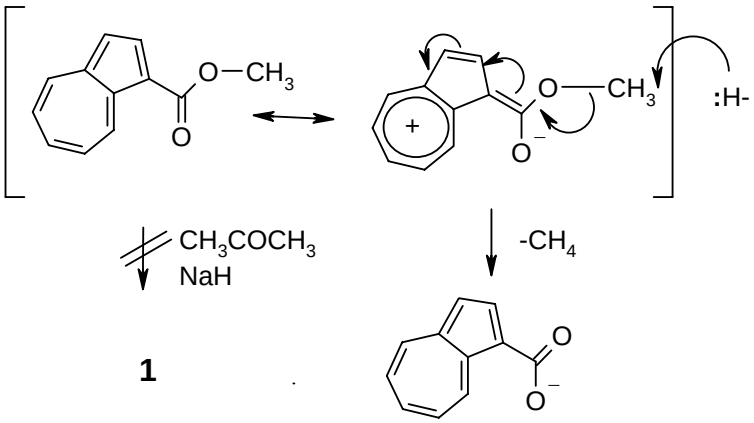
A. Synthesis

Our first attempt to synthesize the diketone **1** is summarized in Scheme 1. For the generation of the intermediate **3** we have followed the same protocol used by Treibs for the ester **2**.[9] We have modified this procedure, replacing the difficultly available malonyl dibromide by a mixture of malonyl dichloride and gaseous HBr. The subsequent reaction of **3** with Meldrum's ester, **4**,[10] yielded the diketone **1** in a low yield (~10 %). A low yield (also under 10%) also was obtained when the lithium salt of acetylacetic acid was reacted with azulene in the presence of oxalyl chloride (Scheme 1). The reaction of azulene with acetonedicarboxylic acid in the presence of oxalyl chloride followed by treatment with methanol afforded the methyl ester of 1-azulenoylcarboxylic acid, **5** (Scheme 1).



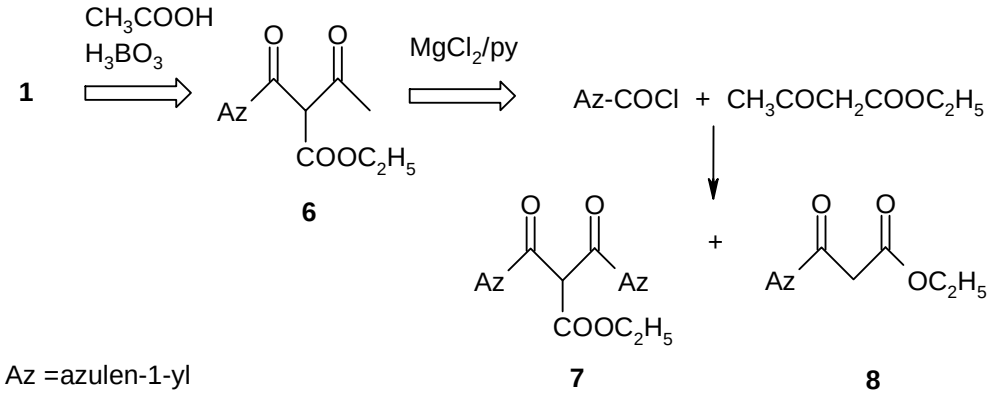
Scheme 1

We hoped that the classical condensation of a ketone with an aromatic ester in the presence of sodium hydride or another strong base could provide access to diketone **1**. Unfortunately, with NaH, the sole reaction product was the sodium salt of 1-azulenecarboxylic acid along with a high amount of unreacted ester. It is possible that the high polarization of the electronic system in the azulenic compound (Scheme 2) allows the nucleophilic displacement of azulenecarboxylate anion by hydride ion.



Scheme 2

Other strong bases promote the nucleophilic substitution of the seven-membered ring in the azulene moiety.[11] To avoid these difficulties we have imagined the synthetic strategy shown in Scheme 3. The procedure is based on the generation of the complex of ethyl acetylacetate with magnesium chloride which can be smoothly acylated by 1-azulenoyl chloride (obtained *in situ* from the acid and oxalyl chloride).[12] The added pyridine promotes the acyl transfer (Scheme 4) and buffers the reaction medium.[13]



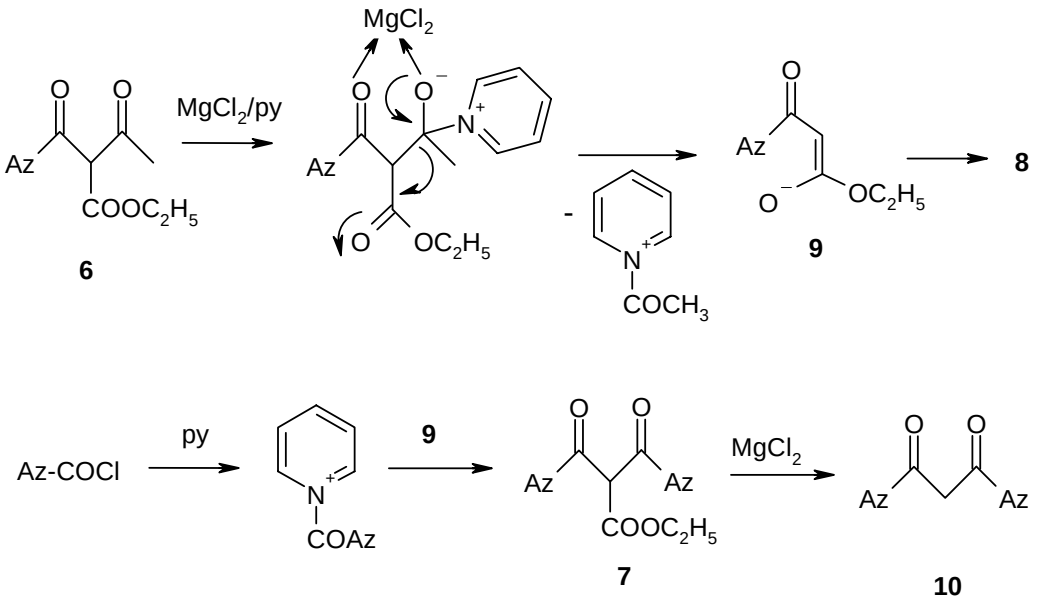
Scheme 3

Unfortunately, instead of compound **1** only the esters **7** and **8** result as products of this reaction in the yields reported in Table 1.

Table 1. Yield of esters **7** and **8** and the amount of recovered 1-azulenecarboxylic acid for the reaction between ethyl acetylacetate and 1-azulenoyl chloride (obtained *in situ* from the acid and oxalyl chloride)

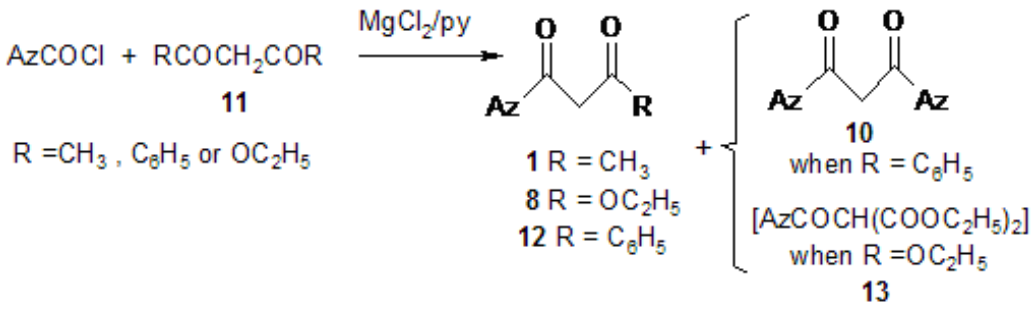
Reaction time (h)	Recovered acid (%)	Yield of diketoester, **7** (%)	Yield of ketoester, **8**, (%)
1.5	28	9	24
3.0	28	12	19
12	29	10	24

Scheme 4 gives a possible explanation for the elimination of the acetyl group and also for generation of ethyl 2,2-di(1-azulenoyl)acetate, **7**. This route for the synthesis of **10**, which cannot be obtained by acylation of azulene with malonyl dichloride, was abandoned when another more favourable source for this compound was discovered.



Scheme 4

We successfully obtained the diketone **1** when ethyl acetylacetate was replaced by acetylacetone, **11** R = CH_3, as in Scheme 5 (Table 2). A possible explanation for this achievement is the reversibility of the reaction between the acid chloride and **11** to generate the rather unstable intermediate, azulenic triketone. Therefore, an excess of acetylacetone displaces the equilibrium towards product **1**. This fact is fairly well suggested by the results in Table 2.



Scheme 5

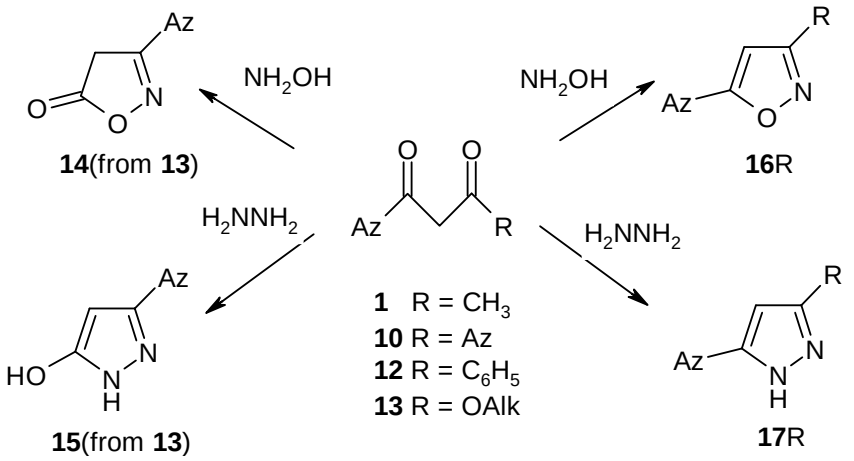
Table 2. Yield of diketone **1** and amount of recovered 1-azulenecarboxylic acid for the reaction between acetylacetone, **11** R = CH_3 and 1-azulenoyl chloride (obtained *in situ* from the acid and oxalyl chloride)

Molar ratio between 1-azulenecarboxylic acid and			Recovered acid (%)	Yield of **1** (%)
oxalyl chloride	$MgCl_2$	pyridine		
1:1	1:1	1:2	72	21
1:1	1:10	1:20	72	64
1:2	1:10	1:20	35	66

We have also used 1-azulenoyl chloride as an acylating reagent for other active methylene compounds such as dibenzoylmethane **11** R = C_6H_5 or diethyl malonate, **11** R = OC_2H_5. The first reaction afforded compound **12** together with **10** in 15 % and 10 % yields, respectively (recovered starting acid 55 %). Therefore, this reaction can be used as a synthetic avenue to both products. When diethyl malonate was used, the acylated product, **13**, conserved both $CO_2C_2H_5$ groups (the yield 12 %; recovered acid 74 %; a small amount of **8** was also detected).

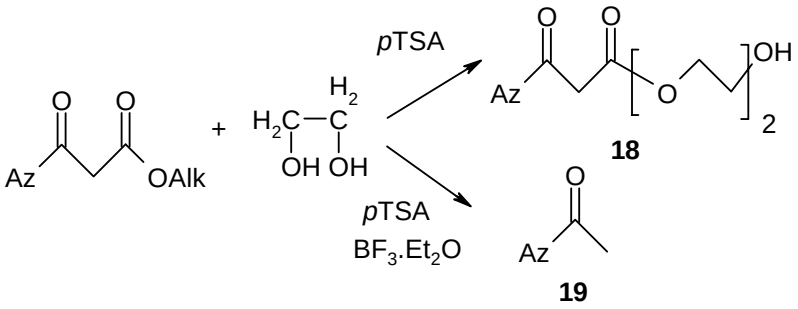
B. Reactions

Treibs has already reported some peculiar chemical properties of azulenic β-ketoesters due to the azulene moiety. Thus, the methylene position cannot be alkylated and the reaction of nitrogen nucleophiles such as hydrazine or hydroxylamine (Scheme 6) occurs slowly.



Scheme 6

With the aim to protect the carbonyl group in the ester **2** for subsequent reactions, we have used ethylene glycol in the presence of *para*-toluenesulfonic acid (*p*-TSA). Instead of the expected ketal, the transesterification product, **18**, was obtained (Scheme 7). When a mixture of *p*-TSA and boron trifluoride etherate was used, only the ketone **19** resulted as the product of ketonic cleavage.



Scheme 7

Our main interest, however, was to synthesize five-membered aromatic heterocyles substituted by azulene starting from the above described β-dicarbonyl compounds (**1**, **10** and **12**) and hydrazine or hydroxylamine. For these reactions we have used the Treibs protocol,[6] modifying the work-up. Thus, we have observed an important increase in the product yields when, after the solvent vaporization, the reaction mixture was heated under vacuum for at least 15 min. The pyrazoles, **17**R, as well as oxazoles, **16**R, with R = CH_3 and C_6H_5 were obtained in good yields (Table 3). For R = 1-azulenyl, however, the results were modest.

Table 3. The reaction of β-dicarbonyl compounds with hydrazine and hydroxylamine in ethanol at reflux

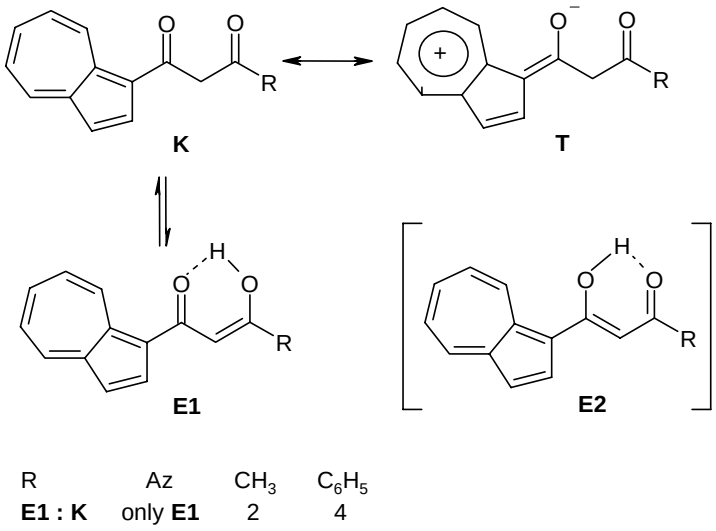
Starting compound	R	Yield of products (%)*	
		16R	**17**R
1	CH_3	60.6	72.0
10	Az	10.0	14.2
12	C_6H_5	53.9	67.3

*The starting materials were completely reacted.

The reaction of diketoester **7** with hydrazine adopted another route. The first step consisted of the ketonic cleavage with the generation of ketoester **13** promoted by the basic medium. The following reaction of **13** gave the same pyrazole **15** obtained by Treibs. We have also prepared heterocycles **14** and **15**, starting from β-ketoesters,[6] in order to characterize the products by comparison with the newly prepared heterocycles **16**R and **17**R (Scheme 6).

C. Structure

As can be shown from Scheme 8, the azulene moiety, due to a strong π-electron releasing effect, stabilizes the neighbouring carbonyl group as in tropylium-like structure **T**. Therefore, a distinct difference between the chemical behaviour of azulenic carbonylic compounds and other corresponding derivatives can be observed. Thus, because of the contribution from structure **T,** compounds having the azulenoyl group as sole enolizable structure, exist only in the ketonic form, **K**.



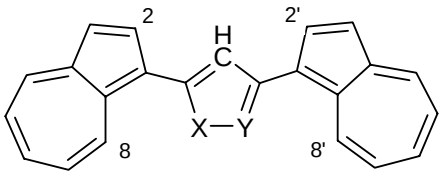
Scheme 8

The high electronic density at oxygen in azulenoyl structure **T** ensures a gain in stability of the enol form for the second carbonyl group present in the β-position of the molecule, **E1**. At the same time, the enol structure **E1** is favoured in comparison to structure **E**2. The difference between the aptitude of a benzoyl and acetyl group to enhance the contribution of the enol structure is maintained also for the azulenic compounds **12** and **1**, respectively (Table 4 and Scheme 8). A significant point here is that the compound **10** with two azulenoyl moieties exists exclusively in the enol form (Table 4). It remains, however, to explain why the diketoester **7** or ketodiester **13** are in ketonic form. It seems that the acidity of enolic OH is surpassed by the acidity of the methyne proton with three activating groups at the carbon atom.

Table 4. Chemical shifts for the methylenic *versus* enolic protons for the compounds X-CH2-Y

Comp.	X	Y	-C*H*$_2$-	=C*H*-
-	CO_2Et	CO_2Et	3.35	-
-	CO_2Me	Ac	3.50	-
-	Ac	Ac	3.60	5.50
-	Ac	Bz	4.06	6.15
8	AzCO	CO_2Me	4.11	-
1	AzCO	Ac	4.19	6.23
12	AzCO	Bz	4.71	6.89
10	AzCO	AzCO	-	6.98
7	$(AzCO)_2CHCO_2Me$		C*H* = 6.44	-
13	$AzCOCH(CO_2Me)_2$		C*H* = 5.43	-

The ^{1}H-NMR spectra recorded for the pyrazole **15** and isoxazole **14** confirm the structures proposed by Treibs, namely a phenolic one for **15** (in pyrazole ring, 4-H: s, 1 H, 6.63 ppm) and a ketonic structure for **14** (for isoxazole ring, 4-H: s, 2 H, 3.94 ppm). The ^{13}C-NMR spectra are also in accord with the structures (C-4 in pyrazole at 87.86 ppm and in isoxazole at 36.00 ppm).



16R=Az; X,Y = O, N 2-H: 8.25 and 8.29 ppm
8-H: 9.23 and 9.51 ppm
17R=Az; X,Y =NH, N both 2-H 8.12 ppm
both 8-H 9.05 ppm

Scheme 9

It is interesting to note that, as shown in Scheme 9, the chemical shifts for the protons in positions 2 and 8 for the two azulenyl substituents are different in isoxazole **16** R = Az but identical in pyrazole **17** R = Az. One might assume that the rapid azolic tautomerization produces symmetry in compound **17** R = Az. Another conclusion, which results from inspection of recorded NMR spectra (Table 5 and 6), refers to the reciprocal influence of heterocyclic rings and azulene in the studied compounds. While the isoxazole protons are slightly more shielded than those of pyrazole, the azulene protons are more deshielded by isoxazole.

Conclusions

The proposed route for the syntheses of azulenic β-diketones, in spite of its moderate yields and low starting material conversions, represents the sole procedure that allows the generation of these important synthons. By the condensation of obtained dicarbonylic synthons with hydrazine or hydroxylamine, valuable aromatic five-membered heterocycles substituted with one or two azulene moieties were obtained. Experimental work is in progress in our laboratory to prepare pyrylium derivatives with one or more azulen-1-yl substituents and will be reported in due course.

Experimental Section

General Procedures. Melting points: Kofler apparatus (Reichert Austria). Elemental analyses: Perkin Elmer CHN 240B. UV spectra in methanol: Beckman DK-2A, UV 5240. IR spectra: Beckman IR 5 A. ^{1}H- and ^{13}C NMR spectra in $CDCl_3$: Bruker 400 DRX (^{1}H: 400 MHz, ^{13}C: 100.63 MHz), TMS was used as internal standard; when necessary, unequivocal signal assignment was confirmed by ^{1}H-^{1}H COSY and ^{1}H-^{13}C HETCOR experiments. Mass spectra: Finnigan MAT 311-A/100 MS. Column chromatography: silica gel (70-230 mesh (ASTM)). Dichloromethane (DCM) was distilled over calcium hydride and ethyl acetate over anhydrous sodium carbonate. Commercial grade of the reagents was used.

General procedure for preparation of dicarbonylic azulenic compounds
In a flame-heated 25 ml round-bottom flask, under an inert atmosphere, freshly calcinated $MgCl_2$ (47.5 mg, 0.5 mmol) and DCM (2 ml) were magnetically stirred. To the resulting heterogeneous mixture β-ketonic compound (0.5 mmol) was added and the flask was cooled in ice. Then pyridine (80 mg, 1.0 mmol) was added, the mixture was stirred 15 min and 1-azulenoyl chloride (obtained from 1-azulenecarboxylic acid (86 mg, 0.5 mmol) and oxalyl chloride (64 mg, 0.5 mmol) in DCM (2 ml)) was finally added. The reaction mixture was stirred 15 min at 0 ^{o}C and then for several hours at room temperature (for the reaction time see Table 1 and 2). The mixture was cooled at 0 ^{o}C, quenched in hydrochloric acid (3 ml, 6 M HCl) and extracted three times

with diethyl ether (3 x about 2 ml). The ethereal solution was dried (Na_2SO_4), the solvent removed in vacuum and the products were separated by column chromatography on silica gel using pentane, DCM and ethyl acetate as eluents. The red or brown fractions were separated as azulencarbonyl derivatives. Azulencarboxylic acid or its magnesium salts, also colored, were eluted in several fractions. Sometimes the last fractions contained also an amount of ketone and, accordingly, they were rechromatographed. The yield of products is reported in Tables 1 and 2.

General procedure for heterocycle synthesis

Carbonyl derivatives were dissolved in methanol at 15-20 ^{o}C and then anhydrous hydrazine or an equimolar mixture of hydroxylamine and its chlorohydrate was added in a huge excess (more than 100 equivalents). The red solution was refluxed for 2 hours; however its color still remained unchanged. Then, the methanol was removed under vacuum heating for 15-30 min on a water bath to eliminate water and excess of hydrazine or hydroxylamine. As a result, the solution turned from brown-red to green or bluish-green. The obtained oil was dissolved in DCM and the products were separated by column chromatography on silica gel using as eluent a mixture of DCM and ethyl acetate (increasing the amount of ester). The different color of the reaction products allowed their easy separation. The yield of products is reported in Table 3.

Product characterization

Table 5 contains relevant physical data for each compound, namely, m.p., molecular ion recorded *via* mass spectrometry and the results of elemental analysis. In Table 6 are listed the chemical shifts for the protons and ^{13}C atoms of the azulen-1-yl moiety as resulting from NMR spectra. In the last section of this part, signals for other protons and ^{13}C as well as the UV and IR spectra are reported.

Table 5. Relevant data for the obtained compounds

Cpd.	Properties, mp (°C)	Molecular formula	MS (ESI)	Calculated (%)/ Found (%)		
				C	H	N
1	Brown crystals, 76	$C_{14}H_{12}O_2$	212 [M, 100]	79.23/79.25	5.70/5.69	-
2	Red crystals, 70[a]	$C_{14}H_{12}O_3$	228 [M, 100]	73.66/73.70	5.30/5.28	-
5	Red oil	$C_{13}H_{10}O_3$	215 [M+1, 100]	72.88/72.88	4.71/4.73	-
7	Red crystals, 178	$C_{26}H_{20}O_4$	397 [M+1, 100]	78.76/78.75	5.09/5.11	-
8	Red oil	$C_{15}H_{14}O_3$	243 [M+1, 100]	74.35/74.31	5.83/5.85	-
10	Brown oil	$C_{23}H_{16}O_2$	325 [M+1, 100]	85.15/85.13	4.98/4.99	-
12	Brown oil	$C_{19}H_{14}O_2$	275 [M+1, 100][e]	83.19/83.18	5.14/5.11	-
13	Red oil	$C_{18}H_{18}O_5$	315 [M+1, 100]	68.76/68.78	5.78/5.78	-
18	Red oil	$C_{17}H_{18}O_5$	303 [M+1, 100]	67.52/67.48	6.00/6.03	-
14	Dark blue-green crystals, 148-150[c]	$C_{13}H_9NO_2$	212 [M+1, 100]	73.91/73.88	4.30/4.31	6.63/6.58
15	Blue crystals, 219[d]	$C_{13}H_{10}N_2O$	210 [M, 100]	74.26/74.28	4.80/4.80	13.33/13.29
16R	R=Me, Green crystals, 134	$C_{14}H_{11}NO$	210 [M+1, 100]	80.35/80.34	5.30/5.38	6.70/6.62
	R=Ph, Green-blue crystals 238	$C_{19}H_{13}NO$	272 [M+1, 100]	84.10/84.05	4.83/4.89	5.17/5.09
	R=Az, Green-blue crystals, 125	$C_{23}H_{15}NO$	322 [M+1, 100]	85.95/85.92	4.71/4.83	4.36/4.31
17R	R=Me, Blue crystals, 78	$C_{14}H_{12}N_2$	209 [M+1, 100]	80.73/80.78	5.81/5.80	13.46/13.42
	R=Ph, Blue oil	$C_{19}H_{14}N_2$	271 [M+1, 100]	84.41/84.43	5.22/5.27	10.37/10.33
	R=Az, Green-blue crystals 190	$C_{23}H_{16}N_2$	321 [M+1, 100]	86.21/86.23	5.04/5.08	8.75/8.69

[a] Lit.[6] 70 °C. [b] Lit[6] 88 °C. [c] Lit.[6] 145-150 °C. [d] Lit.[6] 219-220 °C. [e] The mixture **12 K:E1** is very difficult to separate from dibenzoylmethane by column chromatography, however, it can be purified easily using reverse phase HPLC, solvent MeOH-water.

Table 6. ^{1}H and ^{13}C-NMR for the azulen-1-yl moiety in obtained compounds

Comp.	Positions in azulen-1-yl substituent δ for ^{1}H/δ for ^{13}C									
	2[a]	3[a]	4[b]	5[c]	6[c]	7[c]	8[b]	1	3a	8a
	Spectra of carbonylic compounds									
1K	8.27/ 140.8	7.29/ 118.3	8.51/ 138.9	7.51/ 128.3	7.88/ 139.5	7.68/ 130.2	9.89/ 140.0	-/124.2	-/145.6	-/140.1
1E1	8.21/ 138.1	7.31/ 118.5	8.44/ 138.3	7.44/ 127.1	7.80/ 139.7	7.55/ 128.2	9.81/ 139.2	-/123.0	-/145.9	-/139.7
2	8.25/ 140.3	7.28/ 118.2	8.46/ 138.8	7.52/ 128.1	7.85/ 139.9	7.64/ 130.1	9.89/ 139.7	-/123.7	-/145.7	-/140.9
5	8.42/ 142.6	7.25/ 119.2	8.46/ 138.8	7.57/ 129.4	7.86/ 140.1	7.67/ 130.9	9.8113 9.3	-/120.4	-/147.0	-/142.6
7	8.32/ 139.6	7.21/ 118.6	8.41/ 139.0	7.46/ 128.6	7.93/ 140.2	7.58/ 130.5	9.91/ 140.2	-/123.1	-/146.1	-/141.6
8	8.24/ 140.2	7.25/ 118.7	8.46/ 138.7	7.49/ 128.0	7.82/ 139.8	7.61/ 129.9	9.86/ 139.6	-/123.7	-/145.6	-/140.8
10Az-CH	8.36/ 141.5	7.37/ 118.5	8.42/ 138.6	7.39/ 126.6	7.77/ 139.6	7.52/ 127.8	9.84/ 139.3	-/124.8	-/145.6	-/139.2
Az-CO	8.58/ 137.6	7.29/ 118.3	8.45/ 138.1	7.47/ 126.6	7.82/ 139.5	7.58/ 127.5	9.90/ 139.1	-/123.9	-/145.3	-/141.7
12K	8.41	7.29	8.49	7.48	7.80	7.62	9.87			
12E1	8.35/ 138.2	7.35/ 118.7	8.46/ 138.4	7.42/ 127.8	7.78/ 139.6	7.55/ 128.6	9.89/ 139.2	-/123.9	-/146.1	-/140.8
13	8.17/ 139.6	7.27/ 118.6	8.50/ 139.0	7.56/ 128.6	7.89/ 140.2	7.68/ 130.5	9.90/ 140.2	-/123.1	-/146.1	-/141.6
18	8.25/ 140.3	7.28/ 118.3	8.50/ 138.9	7.54/ 128.3	7.87/ 140.0	7.66/ 130.2	9.87/ 139.8	-/123.7	-/145.8	-/141.0
	Spectra of pyrazoles									
15	8.15/ 135.4	7.44/ 117.5	8.41/ 137.4	7.25/ 123.7	7.72/ 138.7	7.30/ 123.7	8.77/ 135.6	-/119.1	-/141.4	-/133.7
17R=Me	8.01/ 136.3	7.29/ 117.6	8.25/ 137.1	7.11/ 123.4	7.53/ 138.2	7.11/ 123.7	8.89/ 136.2	-/120.9	-/142.0	-/135.3
R=Ph	8.09/ 136.0	7.31/ 117.9	8.34/ 137.6	7.18/ 124.0	7.62/ 138.6	7.25/ 124.2	8.87/ 136.0	-/120.3	-/142.2	-/135.6
R =Az	8.17/ 136.2	7.43/ 117.8	8.36/ 137.5	7.20/ 123.8	7.62/ 138.5	7.23/ 124.1	9.05/ 136.4	-/120.3	-/142.3	-/135.6
	Spectra of isoxazoles									
14	7.81/ 137.9	7.36/ 118.8	8.45/ 138.7	7.44/ 126.9	7.81/ 139.8	7.52/ 127.7	9.40/ 139.1	-/114.5	-/144.6	-/137.1
16R=Me	8.14/ 136.3	7.37/ 118.6	8.35/ 137.9	8.35/ 125.2	7.27/ 139.0	7.68/ 125.5	7.34/ 136.7	-/115.8	-/143.3	-/135.5
R=Ph	8.23/ 136.5	7.44/ 118.8	8.41/ 138.1	7.32/ 125.5	7.73/ 139.2	7.41/ 125.8	9.15/ 136.9	-/115.8	-/143.5	-/135.8
R =Az(3)	8.25/ 137.2	7.45/ 118.7	8.43/ 137.8	7.34/ 124.7	7.74/ 138.8	7.43/ 125.5	9.51/ 137.0	-/115.6	-/143.5	-/136.4
Az(5)	8.29/ 136.5	7.45/ 118.0	8.41/ 138.0	7.33/ 125.3	7.73/ 139.1	7.42/ 125.6	9.23/ 138.1	-/117.2	-/143.2	-/135.8

[a] Doublets with ^{3}J = 4.0-4,4 Hz. [b] Doublets with ^{3}J = 9.6-10.0 Hz.[c] Triplets with ^{3}J = 9.6-10.0 Hz.

Methyl 3-azulen-1-yl-3-oxo-propionate (2). UV, λ_{max}, nm (log ε): 219 (4.25); 233 (4.14); 236 (4.13); 263 (3.88); 306 (4.38); 370 (3.84), 380 (3.88); 512 (2.79). ^{1}H-NMR ($CDCl_3$, δ, ppm): 3.77 (s, 3 H, Me), 4.12 (s, 2 H, CH_2). ^{13}C-NMR ($CDCl_3$ δ, ppm): 48.10 (CH_2), 52.32 (Me), 168.8 (CO_2Me), 188.6 (CO).

Ethyl 3-azulen-1-yl-3-oxo-propionate (8). UV, λ_{max}, nm (log ε): 219 (4.25); 233 (4.14); 236 (4.13); 263 (3.88); 306 (4.38); 370 (3.84), 380 (3.88); 512 (2.79). ^{1}H-NMR ($CDCl_3$ δ, ppm): 1.26 (d, ^3J = 7.2 Hz, 3 H, Me), 4.09 (s, 2 H, CH_2), 4.22 (t, ^3J = 7.2 Hz, 3 H, CH_2CH$_3$). ^{13}C-NMR ($CDCl_3$ δ, ppm): 14.10 (Me), 48.31 (CH_2), 61.14 (CH_2CH_3), 168.3 (CO_2), 188.8 (CO).

2-(2-Hydroxy-ethoxy)-ethyl 3-azulen-1-yl-3-oxo-propionate (18). UV, λ_{max}, nm (log ε): 219 (4.25); 233 (4.14); 236 (4.13); 263 (3.88); 306 (4.38); 370 (3.84), 380 (3.88); 512 (2.79). Numbering for atoms in ester: CO_2-CH_2(1')-CH_2(2')-O-CH_2(3')-CH_2(4')OH. ^{1}H-NMR ($CDCl_3$ δ, ppm): 3.56 (t, ^3J = 4.6 Hz, 2 H, CH_2(4')), 3.69 (t, ^3J = 4.6 Hz, 2 H, CH_2(3')), 3.73 (t, ^3J = 4.6 Hz, 2H, CH_2(2')), 4.16 (s, 2 H, CH_2), 4.37 (t, ^3J = 4.8 Hz, 3H, CH_2(1')). ^{13}C-NMR ($CDCl_3$ δ, ppm): 48.15 (CH_2), 61.69 (C(3')), 64.13 (C(1')), 68.87 (C(2')), 72.37 (C(4')), 168.3 (CO_2), 188.7 (CO).

Ethyl 2-(azulene-1-carbonyl)-3-oxo-3-(azulen-1-yl)-propionate (7). ^{1}H-NMR ($CDCl_3$ δ, ppm): 1.29 (t, ^3J = 7.2 Hz, 3 H, Me), 4.34 (t, ^3J = 7.2 Hz, 2 H, CH_2CH$_3$), 6.46 (s, 1 H, CH). ^{13}C-NMR ($CDCl_3$ δ, ppm): 14.18 (Me), 61.85 (CH_2CH_3), 69.62 (CH), 167.1 (CO_2), 187.3 (CO).

1,3-Di-(azulen-1-yl)-1,3-propanedione (10). UV, λ_{max}, nm (log ε): 220 (4.34); 288 (4.22); 311 (4.27); 388 (3.90), 445 (4.03). 1H-NMR ($CDCl_3$ δ, ppm): ^{1}H-NMR ($CDCl_3$ δ, ppm): 6.98 (s, 1H, CH=). ^{13}C-NMR ($CDCl_3$ δ, ppm): 97.3 (CH=), 183.2 (=COH), 192.5 (CO).

1-(Azulen-1-yl)-1,3-butanedione (1) K : E1. (see Scheme 8) = 1 : 2, UV, λ_{max}, nm (log ε): 219 (4.00); 271 (3.88); 309 (3.94); 393 (3.80), 514 (2.79). ^{1}H-NMR ($CDCl_3$ δ, ppm): 2.10 (s, 3 H, Me(**K**)), 2.29 (s, 3 H, Me(**E1**), 4.19 (s, 2 H, CH_2), 6.23 (s, 1 H, CH=), ^{13}C-NMR ($CDCl_3$ δ, ppm): 24.41 (Me(**E1**), 30.39 (Me(**K**)), 57.37 (CH_2), 98.37 (CH=), 185.7 (Az*C*O(**K**), 187.3 (Az*C*O(**E1**), 203.5 (Me*C*O).

1-(Azulen-1-yl)-3-phenyl-1,3-propanedione (12) K : E1. (see Scheme 8) = 1 : 4, UV, λ_{max}, nm (log ε): 223 (4.14); 278 (3.87); 340 (3.92); 413 (3.96). ^{1}H-NMR ($CDCl_3$ δ, ppm): 4.73 (s, 2 H, CH_2), 6.92 (s, 1 H, CH=), 7.48 (t, ^3J = 7.6 Hz, Ph-H_m(**K** + **E1**)), 7.54 (t, ^3J = 9.8 Hz, Ph-H_p(**K** + **E1**)), 7.99 (d, ^3J = 7.6 Hz, Ph-H_o(**E1**)), 8.11 (d, ^3J = 7.6 Hz, Ph-H_o(**K**)). ^{13}C-NMR ($CDCl_3$ δ, ppm): 53.7 (CH_2), 96.1 (CH=), 127.0 (*m*Ph), 129.0 (*p*Ph), 129.1 (*o*Ph), 187.0 (Az*C*O(**E**)), 192.0 (Az*C*O(**K**)), 196.1 (Ph*C*O).

Diethyl 2-(azulene-1-carbonyl)malonate, 13, UV, λ_{max}, nm (log ε): 219 (4.18); 238 (3.97); 266 (3.88); 309 (4.24); 382 (3.57); 521 (2.79). ^{1}H-NMR ($CDCl_3$ δ, ppm): 1.26 (t, ^3J = 7.2 Hz, 6 H, Me), 4.28 (t, ^3J = 7.2 Hz, 4 H, CH_2CH3), 5.43 (s, 1 H, CH). ^{13}C-NMR ($CDCl_3$ δ, ppm): 14.02 (Me), 62.13 (CH_3CH_2), 64.07 (CH), 165.7 (CO_2), 184.7 (CO). IR (DCM): (ν_{cm-1}) 1642 (s), 1722 (s), 1745 (s).

Methyl 1-(azulen-1-yl)-oxo-acetate (5). UV, λ_{max}, nm (log ε): 219 (4.17); 278 (3.83), 312 (4.19); 389 (3.72); 500 (2.79). ^{1}H-NMR ($CDCl_3$ δ, ppm): 3.99 (s, 3 H, Me). ^{13}C-NMR ($CDCl_3$ δ,

ppm): 52.41 (Me), 164.7 (CO_2), 180.6 (CO). IR (KBr): (ν_{cm-1}) 742 (m), 780 (m), 795 (m), 975 (m), 1095 (m), 1200 (m), 1260 (m), 1395 (m), 1415 (m), 1460 (m), 1495 (m), 1630 (s), 1718 (s).

3-(Azulen-1-yl)-4*H*-isoxazol-5-one (14). UV, λ_{max}, nm (log ε): 220 (4.14); 235 (4.17), 299 (4.31); 370 (3.68); 553 (2.27). ^{1}H-NMR ($CDCl_3$ δ, ppm): 3.98 (s, 2 H, 4-H). ^{13}C-NMR ($CDCl_3$ δ, ppm): 36.00 (C4), 161.1 (C3), 175.0 (C5). IR (KBr): (ν_{cm-1}) 550 (s), 580 (m), 840 (m), 900 (m), 930 (m), 1180 (s), 1300 (m), 1400 (s), 1445 (m), 1460 (m), 1500 (m), 1550 (m), 1775 (s), 2925 (m).

5-(Azulen-1-yl)-2*H*-pyrazol-3-ol (15). ^{1}H-NMR ($CDCl_3$ δ, ppm): 3.46 (s, 1 H, NH), 5.94 (s, 1 H, 4-H). ^{13}C-NMR ($CDCl_3$ δ, ppm): 87.86 (C4), 140.0 (C3), 160.7 (C5).

5-(Azulen-1-yl)-3-methylisoxazole (16) R = CH_3. UV, λ_{max}, nm (log ε): 231 (4.29); 303 (4.38); 377 (3.86); 566 (2.48).^{1}H-NMR ($CDCl_3$ δ, ppm): 2.38 (s, 3 H, CH_3), 6.35 (s, 1 H, 4-H). ^{13}C-NMR ($CDCl_3$ δ, ppm): 11.47 (Me), 100.2 (C4), 168.1 (C5), 159.9 (C3). IR (KBr): (ν_{cm-1}) 730 (m), 765 (m), 855 (m), 905 (m), 1280 (m), 1390 (m), 1455 (m), 1465 (m), 1565 (s), 3200 (b).

5-(Azulen-1-yl)-3-phenylisoxazole (16) R = C_6H_5. UV, λ_{max}, nm (log ε): 240 (4.41); 300 (4.48); 380 (3.79); 570 (2.49). ^{1}H-NMR ($CDCl_3$ δ, ppm): 6.84 (s, 1 H, 4-H), 7.50 (t, ^3J = 7.6 Hz, 1 H, Ph-H_p), 7.49 (dt, ^3J = 7.6 Hz, ^4J = 1.2 Hz, 2 H, Ph-H_m), 7.93 (dd, ^3J = 8.0 Hz, ^4J = 1.2 Hz, 2 H, Ph-H_o). ^{13}C-NMR ($CDCl_3$ δ, ppm): 97.44 (*p*Ph), 126.9 (*o*Ph), 127.7 (C1-Ph), 128.9 (*m*Ph), 129.9 (C4), 169.0 (C5), 162.8 (C3).

3,5-Di(azulen-1-yl)-isoxazole (16) R = Az. UV, λ_{max}, nm (log ε): 231 (4.37); 307 (4.37); 380 (3.82); 573 (2.64). ^{1}H-NMR ($CDCl_3$ δ, ppm): 6.96 (s, 1 H, 4-H). ^{13}C-NMR ($CDCl_3$ δ, ppm): 99.45 (C4), 160.3 (C5), 167.8 (C3). IR (DCM): (ν_{cm-1}) 1567 (s), 1592 (s).

3-(Azulen-1-yl)-5-methyl-1*H*-pyrazole (17) R = CH_3. UV, λ_{max}, nm (log ε): 231 (4.47); 296 (4.49); 364 (3.80); 584 (2.45). ^{1}H-NMR ($CDCl_3$ δ, ppm): 2.26 (s, 3 H, CH_3), 6.36 (s, 1 H, 4-H), 8.59 (s, 1 H, NH). ^{13}C-NMR ($CDCl_3$ δ, ppm): 11.93 (Me), 104.0 (C4), 143.9 (C5), 145.8 (C3). IR (KBr), (ν_{cm-1}) 735 (m), 770 (m), 860 (m), 905 (m), 1135 (m), 1265 (m), 1395 (m), 1430 (m), 1455 (m), 1470 (m), 1500 (m), 1535 (m), 1565 (s), 1695 (m), 2930 (m).

3-(Azulen-1-yl)-5-phenyl-1*H*-pyrazole (17) R = C_6H_5, 3-(Azulen-1-yl)-5-phenyl-1H-pyrazole (17) R = C_6H_5. UV, λ_{max}, nm (log ε): 242 (4.61); 293 (4.61); 367 (3.76); 571 (2.47).^{1}H-NMR ($CDCl_3$ δ, ppm): 6.90 (s, 1H, 4'-H), 7.35 (t, ^3J = 7.6 Hz, 1 H, Ph-H_p), 7.41 (t, ^3J = 7.6 Hz, 2 H, Ph-H_m), 7.83 (d, ^3J = 7.6 Hz, 2 H, Ph-H_o), 8.1 (s, 1 H, NH). ^{13}C-NMR ($CDCl_3$ δ, ppm): 101.9 (C4), 125.7 (*o*Ph), 128.3 (*m*Ph), 128.9 (*p*Ph), 132.3 (C1 Ph), 144.7 (C3), 149.6 (C5).

3,5-Di(azulen-1-yl)-1*H*-pyrazole (17) R = Az. UV, λ_{max}, nm (log ε): 235 (4.43); 301 (4.58); 373 (3.83); 581 (3.34); 581 (2.94). ^{1}H-NMR ($CDCl_3$ δ, ppm): 6.97 (s, 1 H, 4-H), 4.2 (s, 1 H, NH). ^{13}C-NMR ($CDCl_3$ δ, ppm): 103.8 (C4), 145.6 (C3,C5). IR (KBr): (ν_{cm-1}) 578 (m), 734 (m), 782 (m), 870 (m), 912 (m), 1002 (m), 1123 (s), 1309 (m), 1393 (s), 1450 (m), 1470 (m), 1540 (m), 1566 (s), 1590 (m), 3740 (m).

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