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SYNTHESIS OF 2-(4′-R-BENZYLIDENE)-4-AZA-1,3-INDANEDIONES AND INVESTIGATION OF ISOMERIZATION AROUND THE EXOCYCLIC DOUBLE BOND

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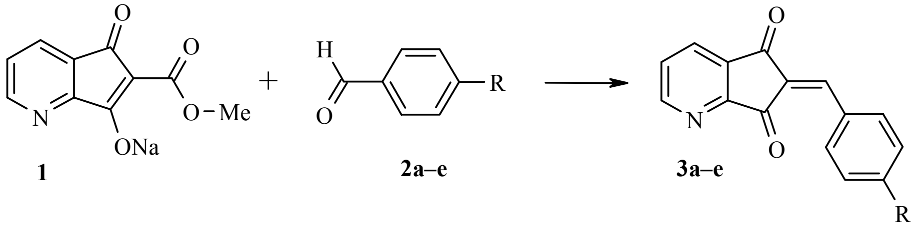
2-Benzylidene-4-aza-1,3-indanediones have been synthesized and their structures have been investigated by NMR spectroscopy and quantum chemistry in the AM1 approximation. It was established that rotation about the exocyclic C(2)=C(10) formal double bond occurs in chloroform solutions of these compounds. The energy characteristics of this process have been determined experimentally and estimated theoretically.

Keywords: 2-(4′-R-benzylidene)-4-aza-1,3-indanediones, internal rotation, *E,Z*-isomerism, AM1 method, NMR spectroscopy.

Many derivatives of 1,3-indanediones, in which there is a conjugated π-electron system, are of interest as starting reactants in the synthesis of new materials, used in molecular electronics, and nonlinear optics [1-4]. Continuing the systematic search for new compounds, potential polar molecular crystals with nonlinear optical properties, we have synthesized a series of 2-benzylidene-4-aza-1,3-indanediones. Their structure and kinetic behavior in deuterochloroform solution were investigated by ^{1}H and ^{13}C NMR spectroscopy (Table 1) and quantum chemistry.



2, 3 a R = NO_2, **b** R = CN, **c** R = Me, **d** R = OMe, **e** R = NMe_2

We discovered that the ^{1}H and ^{13}C NMR spectra of compounds **3**, taken directly after dissolving them in chloroform, comprise one set of resonance signals, however on expiry of a certain interval of time new signals begin to be displayed in the spectra, belonging to the other isomer. Analysis of ^{1}H, ^{13}C NMR, and two-dimensional heteronuclear ^{1}H-^{13}C-HSQC and ^{1}H-^{13}C-HMBC correlation spectra showed that both isomers differ

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TABLE 1. ^{1}H and ^{13}C NMR Spectral Characteristics of the Compounds **3a-e**

Com-pound	Chemical shifts, δ, ppm*													
	C-1	C-2	C-3	C-5	C-6	C-7	C-8	C-9	C-10	C-1'	C-2'	C-3'	C-4'	R
Z-**3a***^{2}	186.9	131.2	186.3	157.1 (9.16)	128.9 7.75	132.0 (8.38)	138.2	158.3	144.3 (8.01)	138.0	134.6 (8.59)	123.9 (8.37)	148.8	–
E-**3a**	186.3	131.2	187.1	157.1 (9.17)	128.9 7.75	132.0 (8.39)	137.6	159.3	144.9 (8.03)	138.0	134.6 (8.55)	123.8 (8.35)	149.8	–
Z-**3b**	187.3	130.9	187.0	157.6 (9.15)	128.9 (7.74)	131.9 (8.37)	138.1	157.6	145.6 (7.98)	136.3	134.0 (8.49)	134.4 (7.80)	116.1	118.1
E-**3b***^{2}	186.4	130.9	188.4	157.6 (9.16)	128.4 (7.74)	132.0 (8.36)	135.4	159.3	148.0 (7.96)	136.3	134.0 (8.53)	132.5 (7.82)	116.1	118.1
Z-**3c***^{2}	188.5	127.3	187.5	156.8 (9.09)	128.3 (7.67)	131.5 (8.30)	134.9	159.3	148.8 (8.01)	130.5	134.9 (8.43)	129.9 (7.35)	145.8	22.1 (2.45)
E-**3c**	187.0	127.3	189.6	156.7 (9.08)	128.4 (7.68)	131.4 (8.34)	137.8	157.5	149.5 (7.98)	130.4	134.9 (8.39)	129.8 (7.34)	145.7	22.0 (2.45)
Z-**3d**	188.8	126.5	187.8	156.7 (9.05)	128.3 (7.64)	131.5 (8.27)	135.0	159.6	148.6 (7.98)	125.9	138.0 (8.59)	114.9 (7.04)	165.0	55.9 (3.96)
E-**3d***^{2}	187.3	126.6	189.9	156.8 (9.06)	128.4 (7.65)	131.4 (8.29)	137.8	157.8	149.3 (7.94)	125.9	138.0 (8.54)	114.8 (7.02)	165.1	55.9 (3.92)
Z-**3e***^{2}	189.7	122.0	187.9	155.5 (8.98)	127.4 (7.56)	130.6 (8.18)	134.5	159.4	148.7 (7.91)	121.9	138.7 (8.57)	111.6 (6.75)	154.6	40.2 (3.16)
E-**3e**	187.7	122.0	190.6	155.3 (8.97)	127.45 (7.57)	130.5 (8.20)	137.2	157.8	149.4 (7.88)	121.9	138.7 (8.52)	111.6 (6.73)	154.6	40.2 (3.16)

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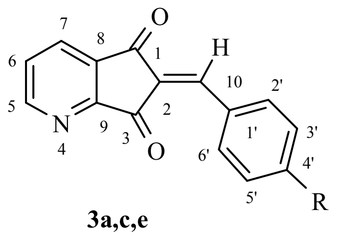
* Chemical shifts of protons at the corresponding carbon atoms are given in parentheses.

*^{2} Predominant initial isomer.

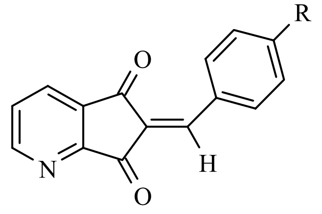
in the orientation of the 4′-R-benzylidene fragment relative to the nitrogen atom in the indanedione portion of the molecule. The *cis* and *trans* $^3J_{C,H}$ constants of proton H-10 with the C(1) and C(3) carbonyl atoms differed 2.5-fold and were equal to 3 and 8 Hz, respectively, for both isomers. Assignment of the carbonyl carbon atoms was further carried out by drawing on the analysis of the H(7)–C(1) interaction. For the *E*-isomer such an interaction is observed with the carbonyl having the larger $^3J(^{13}CO\text{-}H(10))$ coupling constant. However it was absent for the carbonyl with the lower $^3J(^{13}CO\text{–}H(10))$ constant. For the *Z*- isomer similar interactions have the reverse direction. The H(7)–C(1) interaction is observed with the carbonyl carbon atom having the lower $^3J(^{13}CO\text{–}H(10))$ coupling constant, and is absent for the carbonyl with the larger $^3J(^{13}CO\text{–}H(10))$ coupling constant. *E-Z-i*somerization or hindered rotation about the exocyclic C(2)=C(10) formal double bond therefore occurs in the compound **3** molecules. This process is fairly slow in the NMR time scale and after 10-12 h a 1:1 equilibrium of both isomers is established in solutions of compounds **3** (Table 1).

The hindered rotation of substituents around the formal double bonds (*E*- or *Z*-isomerization) is known for a large number of compounds of different classes, of which the most studied up to the present time are the push-pull derivatives of ethylene and certain enamines [5-7]. Various mechanisms facilitating the process of internal rotation have been considered by Nogrady [8]. In our case this process may be caused by a scheme comprising the intermediate tautomeric conversion of the compound into an ylide containing a single exocyclic bond, rotation around which is essentially facilitated.



3a,c,e

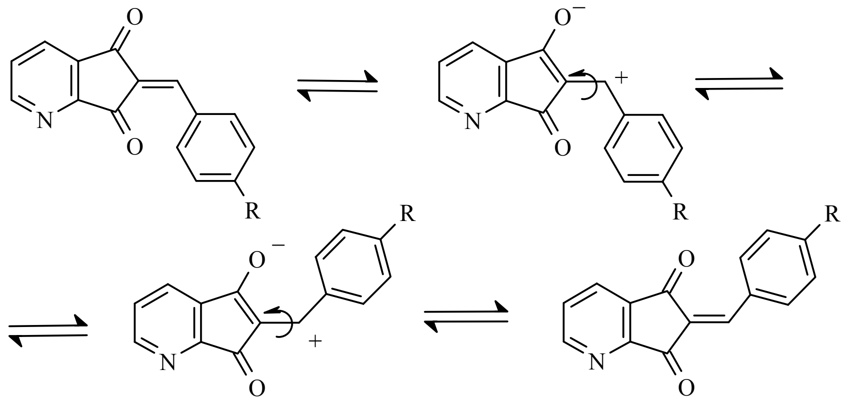
Z-Isomer



3b,d

E-Isomer

It is interesting to note that the initial isomer of compounds **3a,c,e** corresponds to the *Z*-form and of compounds **3b,d** to the *E*-form. What caused such a difference of forms in the process of crystallization is as yet unclear.



Since the exchange processes were relatively slow in the time scale of NMR, we determined the kinetic characteristics of this process by simple analysis of the spectral intensities. The time dependence of the change of integral intensities (I_{int}) in the case of both individual isomers (Fig. 1) is typical of zero order reactions and is described by the following equation.

$$\ln[C] = \ln[C_0] - 2kt \qquad (1)$$

The rate constants for the dynamic process in compounds **3** were calculated according to equation (1) (Table 2). Barriers for the rotation around the exocyclic C(2)=C(10) double bond were determined as Gibbs free energies of activation $\Delta G^{\#}_{298}$ from equation (2) [9].

$$\Delta G^{\#}_{298} = 4.575T(10.319 + \log T/k) \qquad (2)$$

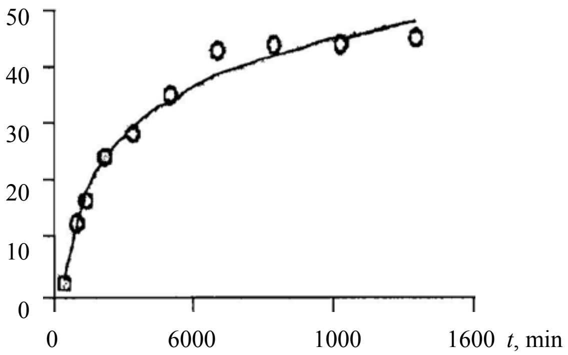
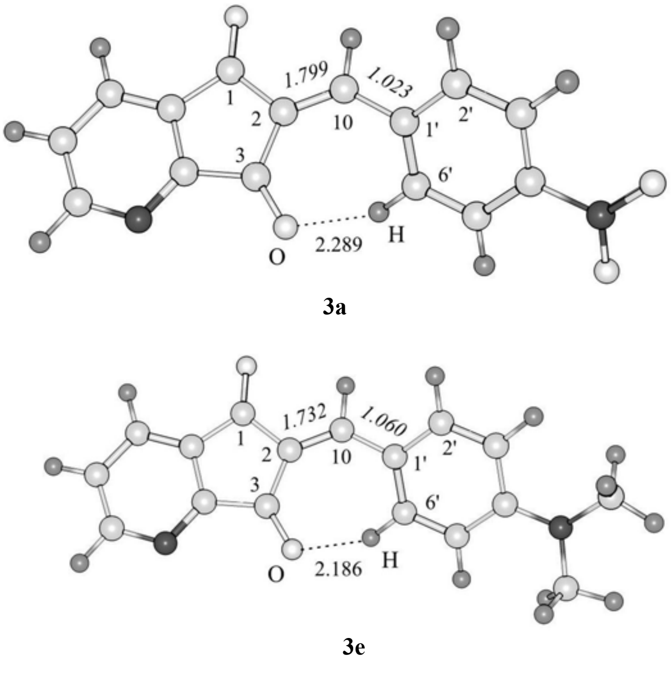


Fig. 1. Dependence of the integral intensity (I_{int}) of the H-10 proton signal of the minor isomer of compound **3b** on time (t).

It is therefore possible to note the insignificant growth of $\Delta G^{\#}_{298}$ values in the following sequence of *para* substituents in the benzene ring, CN < NO_2 < OMe < NMe_2 < Me.

Previously we determined the barriers of rotation around the exocyclic double bond in a series of 2-aminomethylenedimedones by a dynamic NMR method [10] The relatively small values of $\Delta G^{\#}_{298}$ = 19.71 and 17.94 kcal/mol were explained by the reduction in the order of the C(2)=C(10) exocyclic double bond due to the increase in contribution of resonance dipolar structure caused by p-π-conjugation of the unshared electron pair of the nitrogen atom with the carbonyl groups. According to the data of Table 3 the order of the C(2)=C(10) bond was even lower in compounds **3** than in the dimedone derivatives.



3a

3e

Fig. 2. Most stable conformations of compounds **3a** and **3e**, calculated by the AM1 method (bond lengths are given in Å, bond orders are given in italics).

TABLE 2. Kinetic and Thermodynamic Characteristics for *E*-*Z*-Isomerization around the C(2)=C(10) Formal Double Bond in Compounds **3a-e**

Compound	k, sec^{-1}	Error, sec^{-1}	Correlation coefficient	$\Delta G^{\#}_{298}$, kcal/mol
3c	6.1	0.5	0.96	16.39
3e	7.5	0.5	0.96	16.24
3d	10.9	0.8	0.98	16.03
3a	11.5	1.4	0.93	16.01
3b	12.0	0.6	0.99	15.98

To assess the optimum geometry of compounds **3a-e**, and also the possibility of a theoretical description of the process of rotation around the C(2)=C(10) exocyclic double bond, we carried out semiempirical quantum chemical calculations in the AM1 approximation. Proceeding from the geometry of the optimized ground state, we scanned the potential energy surface in the reaction coordinates mode with a 30° step for rotation around the C(2)=C(10) bond. The barrier to rotation (ΔE) was determined as the difference in energy of the transition and ground states of the compound.

The results (Fig. 2 and Table 3) disclosed a tendency towards reduction of the barriers with the fall of C(2)=C(10) bond order on going from withdrawing to donor substituents as a result of the increase in delocalization of the intramolecular charge distribution. However this tendency was very insignificant which corresponds to the experimental data (Table 2).

The calculated values of the heats of formation (ΔH_f) show the energy equivalence of both *Z*- and *E*-isomers and are in agreement with NMR experimental data.

The other notable feature of compounds **3a-e** is the significant low field displacement (of the order of 1 ppm) of the H-2′,6′ aromatic protons in comparison with *para*-substituted styrenes [11].

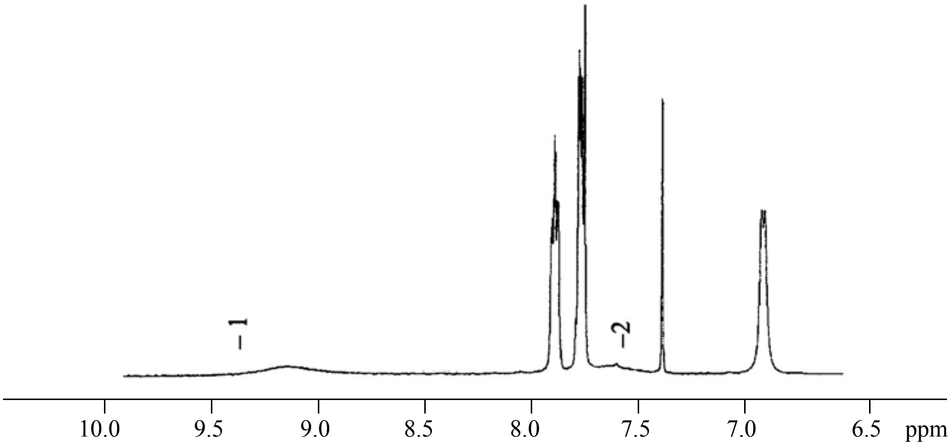


Fig. 3. Aromatic region of the ^{1}H NMR spectrum of 2-(4′-N,N-dimethylaminobenzyliden)-1,3-indanedione at -65°C.

The effect noted may be caused by the formation of a C–H···O= type hydrogen bond between the *ortho* protons and a carbonyl group of the indanedione fragment. Short interactions of the C–H···O type play an important role in biology and have been observed previously [12]. It was established [13] that the H-2',6' aryl protons, located spatially close to the carbonyl group may undergo a low field displacement and even become nonequivalent on slow hindered rotation of the phenyl group at low temperatures. Our investigations of the

TABLE 3. Characteristics of the *Z*- and *E*-Isomers of Compounds **3a-e** Calculated by the AM1 Method.

Compound	ΔH_f, kcal/mol	ΔE, kcal/mol	*l*, C=O···H–C, Å	θ, grad.*	*N**2 C(2)=C(10)	*N**2 C(10)–C(1')
Z-**3a**	34.43	28.49	2.289	1.2	1.799	1.023
E-**3a**	34.48		2.289	-178.9	1.799	1.023
Z-**3b**	61.75	28.19	2.266	1.6	1.785	1.029
E-**3b**	61.78		2.264	-179.2	1.786	1.029
Z-**3c**	21.56	27.66	2.235	2.3	1.763	1.039
E-**3c**	21.60		2.233	-179.8	1.763	1.039
Z-**3d**	-8.99	27.39	2.212	2.8	1.754	1.047
E-**3d**	-8.97		2.208	179.9	1.754	1.047
Z-**3e**	36.87	27.04	2.186	3.2	1.732	1.060
E-**3e**	36.96		2.180	-179.4	1.733	1.060

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* Torsion angle C(3)–C(2)–C(10)–C(1')

*2 *N* is bond order.

^{1}H NMR spectra of 2-(4′-N,N-dimethylaminobenzylidene)-1,3-indanedione in $CDCl_3$ at -65°C showed that the difference in chemical shifts of the protons in positions 2′ and 6′ of the aryl ring reached 1.9 ppm (Fig. 3).

Geometric characteristics are frequently used when describing the strength of C–H···O type hydrogen bonds. In our case the calculated O···H–C distances (Table 3) were in agreement with the data of ^{1}H NMR spectra. According to the AM1 calculation the O···H–C distance is reduced but the order of the C(10)–C(1′) bond is increased on going from compound **3a** to compound **3e** (Table 3). The shortest O(3)···H (6′) distance (2.19 Å) and the highest C(10)–C(1′) bond order (1.06) were observed in compound **3e**. In this case the resonance signals of the H-2′,6′ protons in the ^{1}H NMR spectrum were broadened, but the same protons remain magnetically nonequivalent even at room temperature (Fig. 4).

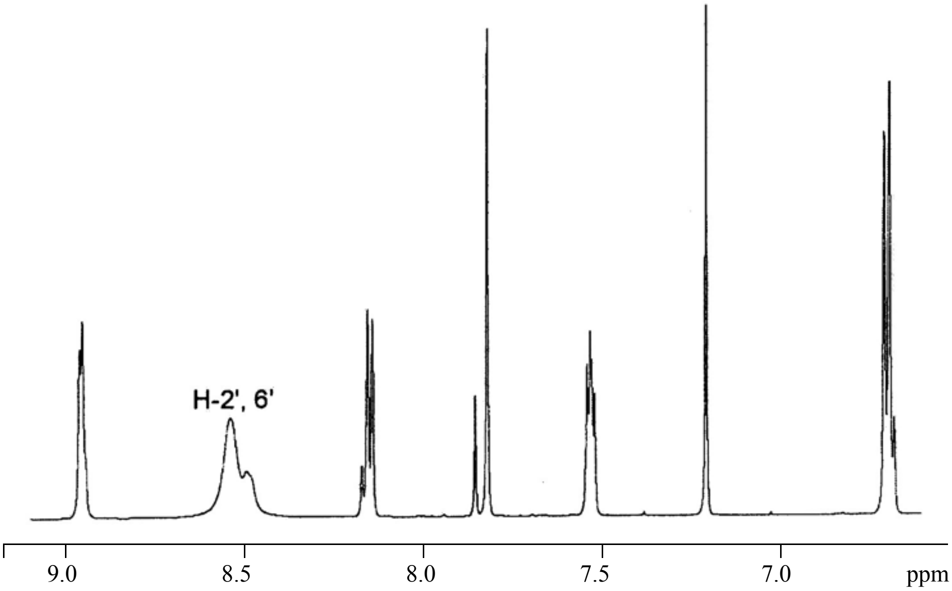

Fig. 4. Aromatic region of the ^{1}H NMR spectrum of compound **3e** at 25°C.

This observation confirms the limitation of rotation around the C(10)–C(1′) bond of the aromatic ring caused by the formation of an intramolecular hydrogen bond of the C=O···H–C type, even at 25°C.

EXPERIMENTAL

The ^1H and ^{13}C NMR spectra were obtained on a Varian UNITY INOVA instrument (600 and 150 MHz respectively), fitted with a cryoadapter, in $CDCl_3$ at 25°C. The low temperature measurements were carried out on a Varian Mercury 400 instrument (400 and 100 MHz respectively) fitted with a low temperature attachment. The temperature of the sample was controlled with a precision of 0.01°C and was measured with the aid of a calibrated sample of methanol.

Chemical shifts are given relative to the residual signal of the solvent (^1H 7.24, ^{13}C 77 ppm).

The ^1H-^{13}C-HMBC spectra were recorded using gradient technics with time of evolution of an interaction for the generation of long range correlations of 62.5 msec. A data matrix of size 4098×1024 was used for recording all the two-dimensional spectra, which provided $\tau_{2max} = 250$ msec for ^1H when recording along the *F*2 axis and $\tau_{1max} = 100$ msec for ^1H or $\tau_{1max} = 50$ msec for ^{13}C when recording along the *F*1 axis. To improve the signal–noise ratio the data matrix was supplemented before the Fourier conversion with zeros twice and augmented by a cosine function.

Calculations were carried out using the MOPAC 6.0 set of programs [14]. All the structures were completely optimized by the AM1 method [15]. The optimization of the geometric parameters of all the structures was carried out using keywords of the EF and PRECISE programs. The character of the stationary points of the potential energy surface was checked by analysis of the vibrational frequencies of the system. Computer design of the investigated structures was carried out with the aid of the ChemCraft and Jmol programs [16, 17].

2-(4′-R-Benzylidene)-4-aza-1,3-indanediones 3a-e. 4-Aza-1,3-indanedione-2-carboxylic acid methyl ester (0.45 g, 2 mmol) and 4-R-benzaldehyde (2 mmol) in glacial acetic acid (5 ml) were heated to 70-75°C and maintained at the same temperature for 1 h. The reaction mixture was left at room temperature for 24 h and filtered. The filtrate was evaporated in vacuum to an oily residue, which was crystallized from isopropyl alcohol. Yield of compounds was 40-60%. **Compound 3a**. Mp ~220°C (decomp.). Found, %: C 64.35; H 2.68; N 9.98. $C_{15}H_8N_2O_4$. Calculated, %: C 64.29; H 2.88; N 10.00. **Compound 3b.** Mp ~240°C (decomp.). Found, %: C 73.95; H 2.97; N 10.82. $C_{16}H_8N_2O_2$. Calculated, %: C 73.84; H 3.10; N 10.76. **Compound 3c.** Mp ~214°C (decomp.). Found, %: C 76.72; H 4.31; N 5.66. $C_{16}H_{11}NO_2$. Calculated, %: C 77.10; H 4.45; N 5.62. **Compound 3d.** Mp ~245°C (decomp.). Found, %: C 72.26; H 4.02; N 5.31. $C_{16}H_{11}NO_3$. Calculated, %: C 72.45; H 4.18; N 5.28. **Compound 3e.** Mp ~235°C (decomp.). Found, %: C 73.42; H 5.02; N 10.01. $C_{17}H_{14}N_2O_2$. Calculated, %: C 73.37; H 5.07; N 10.07.

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