Chemistry of Heterocyclic Compounds, Vol.35, No. 3, 1999

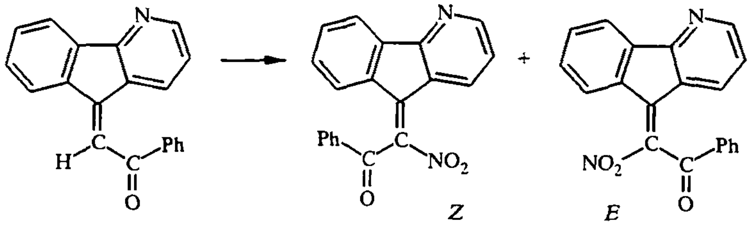
SYNTHESIS AND REDUCTION OF 9-(α-NITROPHENACYLIDENE)-4-AZAFLUORENE

A. V. Varlamov, S. V. Gozun, N. M. Mikhailova, and A. I. Chernyshev

Reaction of 9-phenacylidene-4-azafluorene with acetyl nitrate produces a mixture of geometric isomers of 9-(α-nitrophenacylidene)-4-azafluorene. The nitro group splits off upon reduction of the product in the system zinc–ammonia and zinc–acetic acid and on Raney nickel. Proceeding of the Henry retro-reaction has been pointed out.

Fulvenes possessing functional groups at the exocyclic double bond are of theoretical and practical interest primarily for elucidating the mutual influence of the substituents and the fulvene system on the reactivity. Little is known about nitro-substituted fulvenes. The synthesis of 9-nitromethylenefluorene from iminofluorene and nitromethane was reported [1]. The synthesis of 9-(α-nitrobenzylidene)-4-azafluorene by nitration of 9-benzylidene-4-azafluorene with acetyl nitrate is also known [2].

In order to determine the synthetic potential of the latter reaction and the influence of the substituents on the reactivity of the exocyclic double bond, we have studied nitration of 9-phenacylidene-4-azafluorene (I) [3]. In contrast to 9-benzylidene-4-azafluorene, where nitration by acetyl nitrate begins at temperatures above 50°C, I as a mixture of the Z- and E-isomers is nitrated at room temperature. A mixture of the geometric Z- and E-isomers of 9-(α-nitrophenacylidene)-4-azafluorene in a 1:1.5 ratio is formed in ~85% yield.



I II

The high reactivity of the exocyclic double bond in I is apparently due to the electron-accepting effect of the benzoyl group, which increases the electron density on the $C_{(10)}$ atom. The structures of the geometric isomers of II are based on the positions of the PMR signals for the protons 1-H and 8-H (Table 1). These protons should be the most sensitive to anisotropic effects of substituents on the exocyclic double bond. These protons in the geometric isomers of 9-(α-nitrobenzylidene)-4-azafluorene are located in the position *cis* to the nitro group and undergo a significant weak-field shift owing to its anisotropic effect [2]. The structures of the geometric isomers of II-*E* and II-*Z* were established by comparing their ^{1}H NMR spectra with those for the *Z*- and *E*-isomers, respectively, of the starting material I, in which the benzoyl group is oriented analogously relative to

---

Russian Peoples' Friendship University, Moscow 117918, Russia; e-mail: avarlamov@sci.pfu.edu.ru. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 3, pp. 342-347, March, 1999. Original article submitted January 16, 1998.

the protons 1-H and 8-H. The structures of I-*E* and I-*Z* isomers were established previously from the PMR spectra [3].* Considering the influence of magnetic anisotropy of the benzoyl group on the chemical shifts of the *cis*-positioned protons 1-H and 8-H, the *Z*-configuration should be assigned to the isomer with the 1-H signal at weaker field (by 0.73 ppm). The isomer with the 8-H signal at weaker field (by 0.43 ppm) should be the one with the *E*-configuration.

A simple comparison of the chemical shifts of the easily identified protons 1-H, 2-H and 3-H on the pyridine moieties in isomers of α-nitrophenacylidene-substituted II with the shifts of the analogous protons in the isomers of I and 9-α-nitrobenzylidene-4-azafluorene enables the *E*-configuration (*cis* 1-H and benzoyl group) to be assigned to the isomer with the 1-H signal at weaker field and the *Z*-configuration, to the isomer with the 8-H signal (*cis* 8-H and benzoyl group) at weaker field. We used an empirical approach to confirm this supposition. The approach consisted of incremental changes that enabled the effect of substituents on the chemical shifts of the protons to be revealed. Thus, the chemical shifts of the protons 1-H on going from I-*E* to II-*Z* and from I-*Z* to II-*E* (see the formulas of the compounds in the diagram) can be represented by the expressions:

$$\begin{gathered}\delta_{II\text{-}Z} = \delta_{I\text{-}E} + \Delta(\mathrm{NO_2}\text{-}cis),\\ \delta_{II\text{-}E} = \delta_{I\text{-}E} + \Delta(\mathrm{COPh}\text{-}cis) + \Delta(\mathrm{NO_2}\text{-}trans),\\ \delta_{I\text{-}Z} = \delta_{I\text{-}E} + \Delta(\mathrm{COPh}\text{-}cis)\end{gathered} \tag{1}$$

where δ are the chemical shifts of the protons 1-H in I-*E*, I-*Z*, II-*E* and II-*Z* and Δ_i are the increments of the *i*th groups *cis* and *trans* to the proton 1-H. We are forced to neglect the effect of the *trans* benzoyl group because the more general case has not been solved.

Simultaneous solution of Eqs. (1) gives the following values for the increments:

$$\Delta(\mathrm{NO_2}\text{-}cis) = -0{,}62,\quad \Delta(\mathrm{NO_2}\text{-}trans) = -0{,}75,\quad \Delta(\mathrm{COPh}\text{-}cis) = 0{,}73 \text{ ppm}$$

It means that nitro group located in the *cis* or *trans* positions to the proton 1-H in the isomers of II produces substantial shifts of similar magnitude to strong field for this proton. Let us analyze an alternate version for the structures of II-*E* and II-*Z*. For this, the chemical shifts of 1-H for II-*Z* and II-*E* must be switched when solving Eqs. (1). Now the increments are

$$\Delta(\mathrm{NO_2}\text{-}cis) = -0{,}02,\quad \Delta(\mathrm{NO_2}\text{-}trans) = -1{,}35,\quad \Delta(\mathrm{COPh}\text{-}cis) = 0{,}73 \text{ ppm}$$

In this instance the unusually large difference in the influence of the *cis* and *trans* nitro groups on the position of the 1-H signals in the spectra of II isomers is difficult to explain. This confirms that the proposed configurations for II-*E* and II-*Z* are correct.

The substituent increments for the chemical shifts of the protons 8-H can be compared in the same way. On going from I-*E* to II-*Z*, II-*E* and I-*Z*, the chemical shifts of the protons can be expressed by:

$$\begin{gathered}\delta_{II\text{-}Z} = \delta_{I\text{-}E} + \Delta(\mathrm{NO_2}\text{-}trans),\\ \delta_{II\text{-}E} = \delta_{I\text{-}E} - \Delta(\mathrm{COPh}\text{-}trans) + \Delta(\mathrm{NO_2}\text{-}cis),\\ \delta_{I\text{-}Z} = \delta_{I\text{-}E} - \Delta(\mathrm{COPh}\text{-}cis)\end{gathered} \tag{2}$$

---

* The spectrum of a mixture of *Z*- and *E*-isomers of I was recorded in C_6D_6. In the present work the chemical shifts of I and II were compared only for spectra in $CDCl_3$.

Solving these equations using the chemical shifts of the protons 8-H gives the following values of increments:

$$\Delta(NO_2\text{-}cis) = -0{,}70,\quad \Delta(NO_2\text{-}trans) = -0{,}61,\quad \Delta(COPh\text{-}cis) = 0{,}45\ \text{ppm}$$

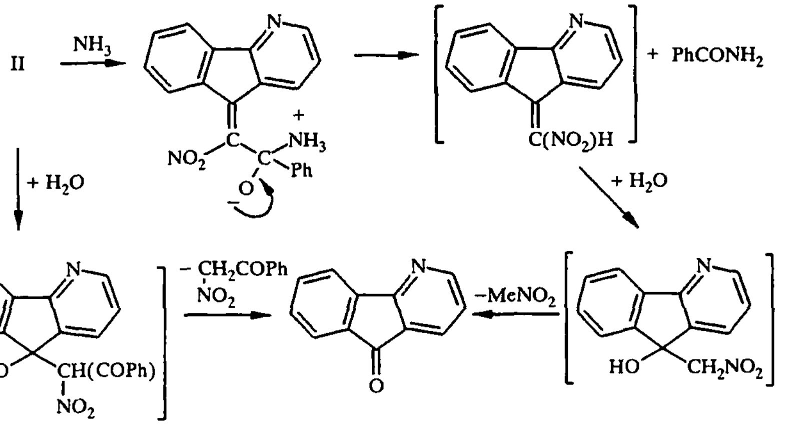
The values for $\Delta(NO_2)$ indicate that introduction of nitro group in the *cis* or *trans* position to the proton 8-H, like for the proton 1-H, shifts the signal to strong field by similar amounts.

For alternative configurations of the geometric isomers of the compound II, the increments would be: $\Delta(NO_2\text{-}cis) = -0.16$ and $\Delta(NO_2\text{-}trans) = -1.15$ ppm. Like for the proton 1-H, it is difficult to explain such a large shift (-1.15 ppm) of the signal of the proton 8-H to strong field by nitro group in the *trans* position and the large difference in the effect of the nitro group in the *cis* and *trans* positions.

We note that the influence of the benzoyl group in the position *trans* to the protons 1-H and 8-H on the chemical shifts of these protons was not considered owing to mathematical limitations of the simple scheme of increments. The presence of two bulky polarized substituents in the 10-position of II-*E* and II-*Z*, owing to their steric and electrostatic interactions, changes their orientation relative to the exocyclic double bond and the benzoyl and pyridine moieties. This also changes the electronic and magnetic-anisotropic influence on the chemical shifts of the protons 1-H and 8-H in comparison with multiply substituted analogs. It is impossible to separate each of these contributions in a simplified scheme of increments. However, on the basis of calculated values of $\Delta(NO_2)$ from the chemical shifts of the protons 1-H and 8-H for the alternate structures the structures of the isomers of II can be considered to be sufficiently convincingly established.

Considering the possibility of synthesizing α-aminoketones, we studied the reduction of the nitro derivative II under various conditions. We used zinc in alcohol–ammonia medium in the presence of ammonium acetate, an acetic acid–acetic anhydride mixture, and hydrogen at atmospheric pressure on Raney nickel as reductants. In none of the experiments the products with a reduced nitro group were found. In all instances the nitro group was split off. The reduction of 9-(α-nitrobenzylidene)-4-azafluorene with zinc dust in alcohol–ammonia solution proceeds readily, giving 9-(α-aminobenzylidene)-4-azafluorene in 74% yield [2]. Reduction of nitro compound II under the same conditions gives 4-azafluorenone (45%) and benzamide (10%) instead of the expected 9-(α-aminophenacylidene)-4-azafluorene or its condensation products.

Benzamide is probably formed by cleavage of the ammonia addition product to the carbonyl group of the benzoyl radical. 9-Nitromethylene-4-azafluorene formed adds water in Henry retro-reaction [4, 5] and reverts to 4-azafluroeneone. The high yield of the latter suggests proceeding of Henry retro-reaction for II.



Reduction of II by zinc dust in a boiling mixture of acetic anhydride and glacial aceitc acid [6] produces a complicated mixture of reaction products, among which 4-azafluorenone is not observed. 9-Phenacyl-4-azafluorene (III) was chromatographically isolated from the mixture in 12% yield.

TABLE 1. ^{1}H NMR Spectral Characteristics of I-III in $CDCl_3$

Compound		Chemical shift, δ, ppm (multiplicity)										
		1-H*^{2}	2-H*^{2}	3-H*^{2}	5-H	6-H	7-H	8-H	9-H	10-H	C_6H_5		
											ortho	*meta*	*para*
I*	*Z*	8,72 (dd)	7,16 (dd)	8,54 (dd)	8,00 (m)	7,4...7,7 (m)		7,84 (m)	—	7,77 (s)	8,10 (m)	7,4...7,7 (m)	
	E	7,99 (dd)	7,20 (dd)	8,59 (dd)	7,98 (dd)*^{3}	7,48 (dd)*^{3}	7,33 (dd)*^{3}	8,29 (dd)*^{3}	—	7,55 (s)	8,10 (m)	7,4...7,7 (m)	
II*	*Z*	7,37 (dd)	6,92 (dd)	8,49 (dd)	7,95 (m)	7,4...7,7 (m)		7,68 (m)	—		8,13 (m)	7,1...7,7 (m)	
	E	7,97 (dd)	7,21 (dd)	8,61 (dd)	7,95 (m)	7,4...7,7 (m)		7,14 (m)	—	—	8,13 (m)	7,1...7.7 (m)	
III		7,82 (dd)	7,14 (dd)	8,58 (dd)	8,10 (m)	7,35...7,65 (m)			4,77 (dd)*^{4}	3,59 (A) (dd)*^{4} 3,35 (B) (dd)*^{4}	7,99 (m)	7,35...7,65 (m)	

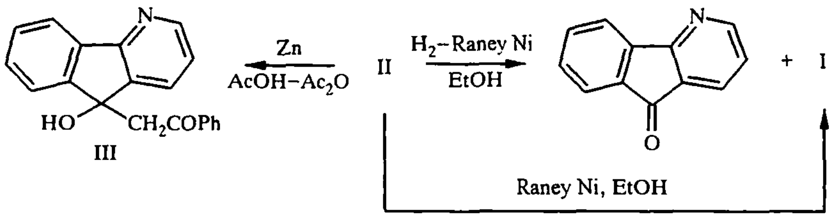
---

*Measured on mixtures of isomers in ratios I-*E* – I-*Z* from 3:1 to 5:1; II-*E* – II-*Z* from 1:1 to 3:1.

*^{2}J_{12} = 7.9 Hz, J_{13} = 1.5 Hz, J_{23} = 4.9 Hz.

*^{3}$J_{56} = J_{67} = J_{78}$ = 7.6 Hz; $J_{57} = J_{68}$ = 1.2 Hz.

*^{4}$J_{9,10A}$ = 5.8 Hz; $J_{9,10B}$ = 8.2 Hz, $J_{10A,10B}$ = 18.0 Hz.



Reduction of II in the presence of Raney nickel at atmospheric pressure and 40°C produces 4-azafluroenone (42%) and a mixture of 9-phenacylidene-4-azafluorene isomers (I, 29%). Apparently 4-azafluorenone is formed through Henry retro-reaction since II under the conditions mentioned above at 20°C in absolute ethanol does not react. It was demonstrated by experiment that the carbonyl group of 4-azafluorenone is not reduced on Raney nickel at atmospheric pressure. Moreover, under these conditions 4-azafluoren-9-ol is converted to 4-azafluorenone. We note that II loses the nitro group on Raney nickel in 95% alcohol in the absence of hydrogen. In this instance, the yield of I is 71%.

Thus, the benzoyl group in benzopyridofulvene II causes the nitro group in the α-position to be highly labile upon reduction. The presence of two electron-acceptor groups at the exocyclic double bond in II makes it sensitive to nucleophilic attack and causes Henry retro-reaction to occur.

EXPERIMENTAL

IR spectra were recorded on a UR-20 spectrometer in KBr pellets. Mass spectra were recorded on a Varian MAT-112 instrument in a direct probe at 70 eV ionizing potential. ^{1}H NMR spectra were taken from 1-2% solutions in $CDCl_3$ at 30°C on a Bruker WP-200 spectrometer. Chemical shifts were measured relative to TMS as internal standard. Assignment of signals to actual protons in I-III was confirmed by double-resonance spectra. For column chromatography Brockman II activated aluminum oxide and L 100/140 silica gel were used. The course of the reaction and the purity of the products were monitored by TLC on Alufol and Silufol UV-254 plates. Iodine vapors were used for visualization.

9-(α-Nitrophenacylidene)-4-azafluorene (II). Solution of mixture of 9-phenacylidene-4-azafluorene isomers (0.5 g, 1.77 mmol) in glacial acetic acid (15 ml) at 20°C was treated with fuming nitric acid ($d = 1.5$ g/cm^3, 1.5 ml). The mixture was stirred for 16 h at 20°C, poured into water (100 ml), and adjusted to pH 9-10 with saturated sodium carbonate solution. The products were extracted with $CHCl_3$. The extract was dried over $MgSO_4$. Yield 0.49 g (84%) of a mixture of II-*Z* and II-*E*, yellow crystals, R_f 0.52 (Silufol, hexane–ethyl acetate, 2:1); mp 118-121°C (heptane–ethyl acetate, 2:1). IR spectrum: 1670 (CO), 1532 and 1352 cm^{-1} (NO_2). Mass spectrum, m/z (I_{rel}, %): 328 (M$^+$, 77), 282 (4), 254 (29), 251 (8), 207 (96), 177 (5), 151 (10), 105 (100), 77 (75). Found, %: C 73.1; H 3.8; N 8.8. $C_{20}H_{12}N_2O_3$. Calculated, %: C 73.2; H 3.7; N 8.5.

9-Phenacyl-4-azafluorene (III). Zinc dust (1.8 g, 28.2 mmol) was added to boiling mixture of II isomers (0.5 g, 1.52 mmol), acetic anhydride (0.16 g, 1.52 mmol) and acetic acid (30 ml) over 30 min under stirring. The mixture was boiled for 2.5 h. Water was added. The reaction mixture was neutralized with sodium carbonate. The products were extracted with ether and dried over $MgSO_4$. Yield 0.05 g (12%) of III, white crystals; mp 105-108°C (hexane–ethyl acetate, 1:1), R_f 0.54 (Silufol, hexane–ethyl acetate, 1:1). IR spectrum: 1675 cm^{-1} (CO). Mass spectrum, *m/z* (I_{rel}, %): 285 (M$^+$, 23), 180 (50), 166 (22), 153 (10), 105 (100), 77 (10). Found, %: C 84.2; H 5.0; N 5.1. $C_{20}H_{15}NO$. Calculated, %: C 84.2; H 5.3; N 4.9.

Reduction of II with Zinc Dust in Alcohol–Ammonia Medium. Mixture of II (0.6 g, 1.83 mmol), zinc dust (0.24 g, 3.66 mmol), ammonium acetate (0.3 g, 3.66 mmol), 25% aqueous ammonia (50 ml), and ethanol (50 ml) was held at 20°C for one day. Alcohol was distilled off. The aqueous layer was extracted with $CHCl_3$ and dried with $MgSO_4$. Chloroform was distilled off and the residue was chromatographed on aluminum oxide column (1.5×30 cm), eluent ethyl acetate–hexane 1:5. Yield 0.05 g (15%) of 4-azafluorenone, yellow crystals; mp 137-140°C, R_f 0.46 (Silufol, ethyl acetate–hexane, 1:1). Literature data [7]: mp 139-143°C. Found: M$^+$ 181. $C_{12}H_7NO$. Calculated: M 181. Subsequently benzamide was isolated; yield 0.021 g (9%), colorless crystals. The depression of melting point for a mixture with a standard sample is not observed.

The work was supported by GKRF and NTP (Fine Organic Synthesis), grant FT-15.

REFERENCES

1. G. Charles, *Bull. soc. chim. France*, No. 2, 234 (1962).
2. A. V. Varlamov, A. N. Levov, A. A. Fomichev, A. E. Aliev, S. Dush Santush, A. A. Ustenko, I. L. Pashentseva, and N. S. Prostakov, *Khim. Geterotsikl. Soedin.*, No. 2, 212 (1991).
3. N. S. Prostakov, Mikhalis Makuli, N. M. Mikhailova, and N. D. Sergeeva, *Khim. Geterotsikl. Soedin.*, No. 4, 510 (1984).
4. O. Convert and J. Armand, *C. R. Acad. Sci.*, **162**, 1013 (1966).
5. G. A. Bonetti, C. B. De Savigny, C. Michaleski, and R. Rosental, *J. Org. Chem.*, **33**, 237 (1968).
6. V. M. Lyubchanskaya and V. G. Granik, *Khim. Geterotsikl. Soedin.*, No. 5, 597 (1990).
7. O. Kruber and L. Rappen, *Chem. Ber.*, **81**, 483 (1948).