Celal Bayar University Journal of Science
Volume 16, Issue 2, 2020, p 129-134
Doi: 10.18466/cbayarfbe.457856

Celal Bayar University Journal of Science

An experimental and theoretical approach to synthesis of novel indolizine type heterocycles

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Received: 06 September 2018
Accepted: 15 June 2020
DOI: 10.18466/cbayarfbe.457856

Abstract

Indolizine derivatives are interesting due to their anti-inflammatory and antioxidant properties as well as their known fluorescent properties. Theoretical studies supported by the experimental evidences can shed light on the fundamental understanding of the versatility of the synthetic approaches. Herein, 1,3-dipolar cycloaddition reactions of three pyridinium ylides with seven dipolarophiles was studied theoretically at FMO level (PM3-RHF calculations) for the first time. The theoretical studies suggested a more probable reaction of pyridinium ylides with the dipolarophiles such as vinyl acetate and vinylene carbonate. However, the ylides have reacted only with dimethyl acetylenedicarboxylate and diethyl acetylene dicarboxylate, indicative of the effect of other reaction parameters (e.g. solvent, temperature etc.). Experimentally, only six indolizine heterocycles, two of which are not reported previously (18 and 19), were synthesized and theoretical predictions were further compared with experimental findings. The structural analysis of synthesized indolizine compounds was performed by ^{1}H NMR, FTIR, GC-MS and elemental analysis.

Keywords: 1,3-Dipolar cycloaddition reactions, indolizine, FMO level.

1. Introduction

In addition to the use of indolizine derivatives in the field of pharmacology due to their anti-inflammatory and antioxidant properties [1-3], they also show fluorescence properties due to their electron rich structure [4-6]. The light emitting properties of indolizines have paved the way of using these structures and their hybrids as sensors [7-9].

Thus the synthesis of indolizine ring systems which are found in natural products attracted special attention in the past years due to their multifold practical utilities and their wide range of biological and chemical activity [10, 11]. The methods for the preparation of indolizines have been reviewed [12] and some new procedures have been reported recently [1, 13, 14]. Intermolecular 1,3-dipolar cyclization is very important for the preparation of five-membered heterocycles [15]. Pyridinium ylides undergo [3+2] dipolar cycloaddition reactions with various activated carbon-carbon double and triple bonds to yield indolizine type heterocycles [16].

Synthetic indolizine derivatives, including mainly pyridine heterocycle, have also been recently studied because of their fluorescent properties and indeed some of them already found have practical applications as dyes and pigments [17, 18].

As a continuation of our research to find useful derivatives of indolizine as potential candidates in both medicinal and dye chemistry, some new indolizines were designed as target products for synthesis.

Herein, 1,3-dipolar cycloaddition reaction of six different dipolarophiles with pyridinium ylides was studied both theoretically and experimentally. Among the dipolarophiles, only two of them which are relatively electron-deficient acetylenes showed reactivity towards the ylides employed. The reason why the other dipolarophiles were not reactive was discussed

comparing the FMO energies. To the best of our knowledge, there is limited report dealing with the 1,3-dipolar [3+2] cycloaddition reactions between pyridinium ylides (5b and 6b) and the electron-deficient acetylenic dipolarophiles (7a and 7b) and the evaluation of the reactivity by theoretical calculations.

2. Materials and Methods

2.1. General

^{1}H NMR spectra were recorded with BRUKER 400 MHz NMR spectrophotometers with tetramethylsilane as an internal standard. Chemical shift (δ) values are reported in ppm and coupling constants (J) are in Hz. The Mass spectra were recorded using Thermo Scientific DSQ II Single Quadrupole GC/MS. Programming of the column oven temperature was done at 80 ºC for 0.5 min, then increased to 200 ºC at 4 ºC/min, to 300 ºC at 8 ºC/min, and held at 300 ºC for 3min. Elemental analysis was done using Thermo-Finnigan Flash EA 1112 Organic Elemental Analyzer. FT-IR spectra were recorded using a JASCO 430 instrument. Melting points were determined with Electrothermal apparatus and uncorrected. Compounds were purified using preparative t.l.c and column chromatography techniques until they were observed as single spots on t.l.c. (Kieselgel PF 254; Chloroform, Ethyl acetate, Hexane as eluent). The solvents, that were mainly used, were dried before using. The purity of compounds was controlled by a gas chromatography apparatus.

2.1 Experimental

General procedure for the preparation of 12-15 and 18-19. In a typical procedure**,** triethylamine (0.39 mL, 0.03 mol) was added to pyridinium salt 1 (0.73 g, 3.2 mmol) dissolved in 10 mL $CHCl_3$. Then, 2.8 mmol of dipolarophile 7a-b was added dropwise to the above solution, under vigorous stirring at room temperature. Then, the solvent was evaporated. After solvent removal, the reaction product was obtained by eluting from chloroform on t.l.c or hexane-ethyl acetate on column chromatography.

2.1.1 Preparation of pyridinium bromide salts

Pyridinium bromide salt 1 was prepared following the literature method[19] and the procedure was further adapted to the synthesis of 2[20] and 3[21]. For the pyridinium bromide salt 1, ethyl 2-bromoacetate **(**0.02 mol, 2.30 mL) was added to pyridine (0.02 mol, 1.67 mL) and the mixture was kept at 20 °C for 2 h. The precipitated salt was washed with diethylether. Yield 95%, mp 101-103 ^{o}C. IR (Nujol, cm^{-1}): 1737 (C=O, ester), 1637 (C=N), 1577 (C=C). ^{1}H NMR (δ_H, 400MHz, $CDCl_3$): 9.52 (d, 2H$_a$, J_{ab}=6.06), 6.34 (s, H$_d$), 4.29 (q, 2H$_e$, J_{ef}=7.14), 8.58 (t, 2H$_b$, J_{ba}=7.81, J_{bc}=7.80), 8.13 (t, H$_c$), 1.32 (t, H$_f$, J_{fe}=7.05). ^{13}C NMR (δ_C, 400MHz, $CDCl_3$): 165.8 (C$_g$), 146.7 (C$_c$), 146.1 (C$_a$), 127.7 (C$_b$), 63.4 (C$_d$), 61.1 (C$_e$), 14.1 (C$_f$).

2.1.2 3-ethyl-1,2-dimethyl-1,2,3,8a-tetrahydro indolizine-1,2,3-tricarboxylate (12)[22]

The product was eluted with chloroform and recrystallized from diethylether and yellow crystals were obtained. Yield 75%, mp 115.5-116.5 ^{o}C, R_f 0.47 ($CHCl_3$). IR (Nujol, cm^{-1}): 1740 and 1708 (C=O, ester), 1600 (C=C, aromatic stretching). ^{1}H NMR (δ_H, 400MHz, $CDCl_3$): 9.47 (d, H$_d$, J_{dc}=7.17), 8.26 (d, H$_a$, J_{ab}=9.05), 7.31 (t, H$_b$, J_{bd}=1.30, J_{bc}=6.89), 6.97 (t, H$_c$, J_{cb}=6.99, J_{cd}=6.99, J_{ca}=1.30), 4.30 (q, 2H$_f$, J_{fg}=7.24), 3.92 (s, 3H$_e$), 3.82 (s, 3H$_{e'}$), 1.32 (t, 3H$_g$). GC-MS RT: 27.24 min. *m/z (%)*: 305 (M$^+$, 100), 274 (28), 233 (34), 214 (52), 202 (85), 170 (58). Found: C, 58.96; H, 5.18; N, 4.45; O, 31.41. $C_{15}H_{15}NO_6$ requires C, 59.01; H, 4.95; N, 4.59; O, 31.45%.

2.1.3 triethyl-1,2,3,8a-tetrahydroindolizine-1,2,3-tricarboxylate (13) [22]

The product was eluted with chloroform and recrystallized from diethylether and yellow crystals were obtained. Yield 70%, mp 101-103 ^{o}C, R_f 0.47 ($CHCl_3$). IR (Nujol, cm^{-1}): 1732(C=O, ester), 1688 (C=C, vinyl stretching). ^{1}H NMR (δ_H, 400MHz, $CDCl_3$):9.48 (d, H$_d$, J_{dc}=7.15), 8.29 (d, H$_a$, J_{ab}=9.01), 7.30 (t, H$_b$, J_{bd}=1.28, J_{bc}=6.85), 6.96 (t, H$_c$, J_{cb}=6.97, J_{cd}=6.99, J_{ca}=1.29), 4.38 (q, 2H$_f$, J_{fg}=7.26), 4.30 (q, 4H$_{e,e'}$), 1.33 (t, 9H$_{g,n,n'}$). GC-MS RT: 28.32 min. *m/z (%)*: 333 (M$^+$, 100), 288 (34), 214 (59), 188 (41), 170 (61), 143 (31). Found: C, 61.36; H, 5.88; N, 4.16; O, 28.60. $C_{17}H_{19}NO_6$ requires C, 61.25; H, 5.75; N, 4,20; O, 28.80%.

2.1.4 3-ethyl-1,2-dimethyl-7-cyanoindolizine-1,2,3-tricarboxylate (14) [23, 24]

The product was eluted with hexane-ethyl acetate (2:1 v/v) and recrystallized from chloroform-hexane and white powder was obtained. Yield 75%, mp 184-186 ^{o}C, R_f 0.51 ($CHCl_3$). IR (Nujol, cm^{-1}): 2232 (C≡N), 1741,1714 (C=O, ester), 1687 (C=C, vinyl stretching). ^{1}H NMR (δ_H, 400MHz, $CDCl_3$):9.63 (d, H$_d$, J_{dc}=7.31), 8.74 (s, H$_a$), 7.14 (d, H$_c$, J_{cd}=7.26, J_{ca}=1.58), 4.42 (q, 2H$_f$), 4.02 (s, 3H$_e$), 3.98 (s, 3H$_{e'}$), 1.43 (t, 3H$_g$). GC-MS RT: 28.92 min. *m/z (%)*: 330 (M$^+$, 100), 299 (18), 258 (22), 227 (51), 195 (26), 168 (18). Found: C, 58.25; H, 4.22; N, 8.44; O, 29.09. $C_{16}H_{14}N_2O_6$ requires C, 58.18; H, 4.27; N, 8.48; O, 29.06%.

2.1.5 triethyl-7-cyanoindolizine-1,2,3-tricarboxylate (15) [**24**, **25**]

The product was eluted with hexane-ethyl acetate (2:1) and recrystallized from chloroform-hexane and white

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powder was obtained. Yield 71%, mp 184-186 ^{o}C, R_f 0.51 ($CHCl_3$). IR (Nujol, cm^{-1}): 2230 (C≡N), 1737, 1715 (C=O, ester), 1698 (C=C, vinyl stretching). ^{1}H NMR (δ_H, 400MHz, $CDCl_3$):9.60 (d, H_d, J_{dc}=7.34), 8.76 (s, H_a), 7.11 (d, H_c, J_{cd}=7.24, J_{ca}=1.61), 4.44 (q, $6H_{f,e,e'}$), 1.42 (t, $9H_{g,n,n'}$). GC-MS RT: 29.94 min. *m/z (%)*: 358 (M^+, 100), 313 (28), 286 (18), 239 (89), 213 (54), 195 (75), 168 (43). Found: C, 60.29; H, 5.09; N, 7.87; O, 26.75. $C_{18}H_{18}N_2O_6$ requires C, 60.33; H, 5.06; N, 7.82; O, 26.79%.

2.1.6 3-ethyl-1,2-dimethyl-6-cyanoindolizine-1,2,3-tricarboxylate (18)

The product was eluted with hexane-ethyl acetate(2:1) and recrystallized from chloroform and yellow powder was obtained. Yield 30%, mp 125.5-127 ^{o}C, R_f 0.52 ($CHCl_3$). IR (Nujol, cm^{-1}): 2238 (C≡N), 1741 (C=O, ester), 1695 (C=C, vinyl stretching). ^{1}H NMR (δ_H, 400MHz, $CDCl_3$):10.0 (s, H_d), 8.43 (d, H_a, J_{ab}=9.46), 7.42 (d, H_b, J_{ba}=9.24, J_{bd}=1.28), 4.42 (q, $2H_f$), 4.00 (s, $3H_e$), 3.92 (s, $3H_{e'}$), 1.39 (t, $3H_g$). GC-MS RT: 29.89 min. *m/z (%)*: 330 (M^+, 100), 299 (21), 258 (32), 239 (55), 227 (75), 195 (41), 168 (24). Found: C, 58.29; H, 4.22; N, 8.37; O, 29.12. $C_{16}H_{14}N_2O_6$ requires C, 58.18; H, 4.27; N, 8.48; O, 29.06%.

2.1.7 triethyl-6-cyanoindolizine-1,2,3-tricarboxylate (19)

The product was eluted with hexane-ethyl acetate(2:1 v/v) and recrystallized from chloroform and yellow powder was obtained. Yield 30%, mp 125.5-127 ^{o}C, R_f 0.52 ($CHCl_3$). IR (Nujol, cm^{-1}): 2233 (C≡N), 1750,1700 (C=O, ester), 1695 (C=C, vinyl stretching). ^{1}H NMR (δ_H, 400MHz, $CDCl_3$):9.94 (s, H_d), 8.38 (d, H_a, J_{ab}=9.47), 7.35 (d, H_b, J_{ba}=9.25, J_{bd}=1.26), 4.30 (q, $6H_{f,e,e'}$), 1.35 (t, $9H_{g,n,n'}$). GC-MS RT: 28.83 min. *m/z (%)*: 358 (M^+, 100), 313 (36), 286 (16), 239 (91), 213 (53), 195 (68), 168 (33). Found: C, 60.29; H, 5.09; N, 7.87; O, 26.75. $C_{18}H_{18}N_2O_6$ requires C, 60.27; H, 4,95; N, 7.89; O, 26.89%.

3. Results and Discussion

The aim of the present study can be classified under five subsections; (*i*) investigation of the effect of electron deficiency of the pyridinium ylide on the cycloaddition (5b and 6b are electron deficient systems), (*ii*) comparison of the reactivity of alkyne (7a-7d) and alkene (7e and 7f) containing dipolarophiles towards the 1,3-dipoles, (*iii*) investigation of the effect of electron deficiency in the 1,3-dipolar cycloaddition reaction by choosing an electron deficient (7a and 7b) and rich (7c and 7d) acetylenic dipolarophiles, (*iv*) to study regio-chemistry of the cycloaddition reactions by using antisymmetric (7c and 7e) dipolarophiles and (*v*) the experimental verification of theoretical predictions.

The first part of the paper presents a theoretical study concerning the interaction between the ylides and dipolarophiles and also the regio-chemistry of the cycloaddition reactions between the pyridinium ylides 4b-6b and 7a-7f (Figure 1). Ylide 6b possesses two different reaction sites which are named as 6b(4,7) and 6b(2,7) (the numbers in parenthesis show the termini undergoing 1-3 dipolar cycloaddition reactions).

In the present study, the general theory of perturbation of the frontier molecular orbital has been used. The coefficients of the atomic orbitals and corresponding molecular orbital energies have been calculated by using semi empirical PM3 (RHF) method [26, 27]. The interaction energies and the regio-chemistry of the reactions have been studied by the application of the Klopman-Salem equation [28].

Klopman-Salem equation is composed of three terms, the charge interaction of the atomic sites, the charge interaction of the molecules and the molecular orbital interactions. Since all of our systems possess zero total charge, the second term is neglected and the simplified form of the Klopman-Salem equation has been considered. First, all the structures were geometry optimized with PM3 (RHF) method (All the molecular orbital calculations were performed using Hyperchem 7.5 package program [29]). The molecular orbital energies (eV) of the present systems and the coefficients of the atomic orbitals of the reaction sites have been tabulated in Table 1.

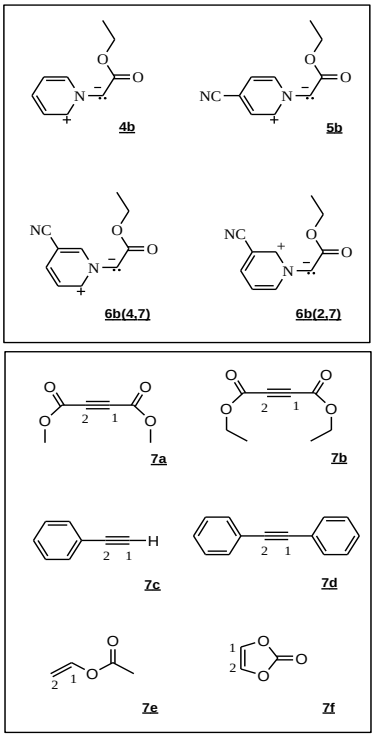

Figure 1. The structures of the ylides (4b-6b) dipolarophiles (7a-7f) under present study.

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Figure 2 shows the frontier molecular orbital energies of the present systems on a diagram for comparison of Y_HD_L and Y_LD_H interaction (Y_HD_L represents the interaction of the ylide's HOMO with the dipolarophile's LUMO) (Figure 2). Figure 2 implies that as a first approximation, the cycloaddition reactions of the present systems are $HOMO_{ylide}$-$LUMO_{dipolarophile}$ controlled, with some exceptions (in the case of 5b and 6b with 7c and 7d are $HOMO_{dipolarophile}$-$LUMO_{ylide}$ controlled).

Table 2 shows the interaction energies of the ylides and dipolarophiles. In each case the first row represents the contribution of the atomic charges to the interaction energy, and the second row shows the interaction energy by the orbital term. As can be seen from Table 2, both the charge and molecular orbital the interaction energies of the ylide 4b with the electron deficient dipolarophiles are greater than the other ylides. Generally, electron deficient ylides have greater probability to react with electron rich dipolarophiles. This is confirmed also in the case of 7e (an electron rich dipolarophile) when the MO interaction is considered, the interaction energies are greater for the 5b, 6b(4,7), 6b(2,7) ylides cases.

The acetylenic dipolarophiles have been expected to react more preferably than the alkene type dipolarophiles as states in the introduction part. Although the theoretical studies suggest a more probable reaction of 4b-6b with 7e and 7f (see Table 2), according to the experimental observations, the ylides 4b-6b have reacted only with 7a and 7b**,** but not with the others. This anti-parallelism may not be very surprising, since the experiments involve the effect of many other factors (solvent, temperature, etc.) than charge and molecular orbital interactions, in vacuum conditions.
Table 3 shows the contribution of orbital interaction terms, Y_HD_L and Y_LD_H to the total interaction energy. As can be seen from the corresponding table the orbital interaction is Y_HD_L controlled with only a few exceptions. The regio-chemistry of the reactions can also be drawn from Table 3 (the 7c and 7e cases). In the case of 7c the orbital interaction is expected to occur through the 4,7 of betaine with 1,2 termini of the dipolarophile, however, 7e is expected to react through 2,1 position with betaine's 4,7 sites.

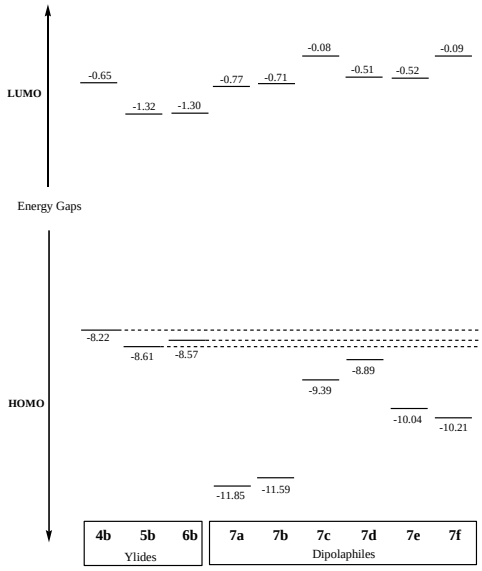

Figure 2. Frontier molecular orbital energy diagrams of the systems under present consideration.

Table 1. HOMO, LUMO energies, and corresponding atomic orbital coefficients of the reaction sites (Next HOMO (NHOMO) is used when the orbital coefficient of the reaction site is zero).

Compound	Orbital	Energy, eV	Atom No	Coefficient	Atom No	Coefficient
4b	HOMO LUMO	-8.21714 -0.64683	4	0.37813 0.12793	7	-0.68589 0.34661
5b	HOMO LUMO	-8.61156 -1.32030	4	0.38153 -0.16560	7	-0.65062 -0.38251
6b (4,7)	HOMO LUMO	-8.57764 -1.29933	4	0.37938 0.47174	7	-0.67752 0.12523
6b (2,7)	HOMO LUMO	-8.57640 -1.29933	2	0.39274 -0.35098	7	-0.67752 0.12523
7a	NHOMO LUMO	-11.85122 -0.77023	1	0.11420 0.47061	2	0.11420 -0.47061
7b	HOMO LUMO	-11.59469 -0.70875	1	0.00011 0.47167	2	-0.00020 -0.47167
7c	HOMO LUMO	-9.39603 -0.08115	1	0.23507 -0.20517	2	0.38856 0.35370
7d	HOMO LUMO	-8.89524 -0.51231	1	0.34222 -0.31921	2	0.34222 0.31921
7e	HOMO LUMO	-10.03528 0.52062	1	-0.66882 -0.51414	2	-0.53511 0.47967
7f	HOMO LUMO	-10.21338 0.089946	1	0.56262 0.68393	2	0.56262 -0.68393

Table 2. Interaction energies of the ylides (4b-6b) and the dipolarophiles (7a-7f) (in each case the first row represent the contribution of the charge interactions and the second row shows the interaction energy through frontier molecular orbitals).

	4b	**5b**	**6b (4,7)**	**6b (2,7)**
7a	-1.3420 -0.0184	-1.3070 -0.0163	-1.3110 -0.0174	-1.2930 -0.0176
7b	-1.3440 -0.0182	-1.3090 -0.0160	-1.3130 -0.0170	-1.2950 -0.0173
7c	-1.4430 -0.0102	-1.1080 -0.0103	-1.4120 -0.0092	-1.3940 -0.0086
7d	-1.5220 -0.0100	-1.4870 -0.0098	-1.4910 -0.0113	-1.4730 -0.0099
7e	-1.3600 -0.0125	-1.3250 -0.0210	-1.3290 -0.0297	-1.3110 -0.0250
7f	-1.2760 -0.0390	-1.2410 -0.0370	-1.2450 -0.0417	-1.2270 -0.0387

Table 3. The contribution of the frontier molecular orbitals of ylide and dipolarophile to the interaction energy (Y_HD_L represents the interaction of the ylide's HOMO with the dipolarophile's LUMO and R_1 indicates the regioisomer when the ylides' 4 position react with 1 position of the dipolarophiles).

	4b		**5b**		**6b**		**6b-2**	
	Y_HD_L	Y_LD_H	Y_HD_L	Y_LD_H	Y_HD_L	Y_LD_H	Y_HD_L	Y_LD_H
7a	-0.0182	-0.00016	-0.0161	-0.00023	-0.0171	-0.0003	-0.0174	-0.0020
7b	-0.0182	0	-0.0160	0	-0.0170	0	-0.0173	0
7c (R_1)	-0.0081	-0.0022	-0.0074	-0.0029	-0.0075	-0.0021	-0.0075	-0.0011
7c (R_2)	-0.0025	-0.0010	-0.0042	-0.0015	-0.0044	-0.0040	-0.0045	-0.0024
7d	-0.0081	-0.0019	-0.0071	-0.0027	-0.0076	-0.0037	-0.0077	-0.0021
7e (R_1)	-0.0017	-0.0044	-0.0149	-0.0061	-0.0178	-0.0119	-0.0182	-0.0068
7e (R_2)	-0.052	-0.0062	-0.0159	-0.0084	-0.0191	-0.0081	-0.0194	-0.0048
7f	-0.0345	-0.0045	-0.0306	-0.0064	-0.033	-0.0085	-0.0338	-0.0049

The second part of the paper describes the course of the reaction between pyridinium ylides 4b-6b with dimethyl acetylene-dicarboxylate (DMAD), diethyl acetylene-dicarboxylate (DEAD), phenylacetylene (PA), diphenylacetylene (DPA), vinyl acetate (VA) and vinylene carbonate (VC) (7a-7f). Pyridinium salts 1-3, were synthesized by reaction of pyridine, 4-cyanopyridine and 3-cyanopyridine with reactive ethyl-2-bromoacetate [19]. Ylides 4b-6b were obtained in situ by the reaction between pyridinium salts 1-3 and triethylamine in $CHCl_3$ (Figure 3).

Pyridinium ylides 4b-6b reacted with DMAD (7a) and DEAD (7b) to give cycloadducts (8-11, 16 and 17) (Figure 4). However, the expected cycloadducts could not be isolated. Instead, isolable cyclic products 12-15, 18 and 19 were obtained suggesting an *in-situ* stabilization via a dehydrogenation process.

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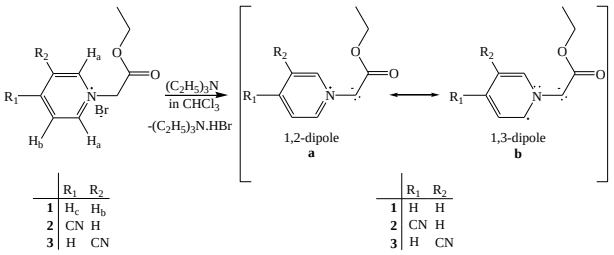

Figure 3. Zwitterionic structure of pyridinium ylides.

In the case of reactions between pyridinium ylide 6b and dipolarophiles 7a and 7b, theoretically, there could be two reaction pathways (I and II) with the formation of two regioisomers. (A and B in Figure 4) However, only one regioisomer was isolated as a result of each cycloaddition reaction between ylide 6b and dipolarophiles 7a and 7b. The ^{1}H NMR analysis showed that the regioisomer A of the cycloadducts 18 and 19 was the sole product (Figure 5). The representative ^{1}H NMR spectrum of the cycloadduct 19 is given in Figure 5a.

The structure of 12-15, 18 and 19 compounds were further studied by GC-MS. Figure 5b shows the representative GC-MS data of the cycloadduct 19. The molecular ion of the corresponding cycloadduct is clearly observed as the major signal. This result can be attributed to the aromaticity of the indolizine structures that stabilize the molecular ion.

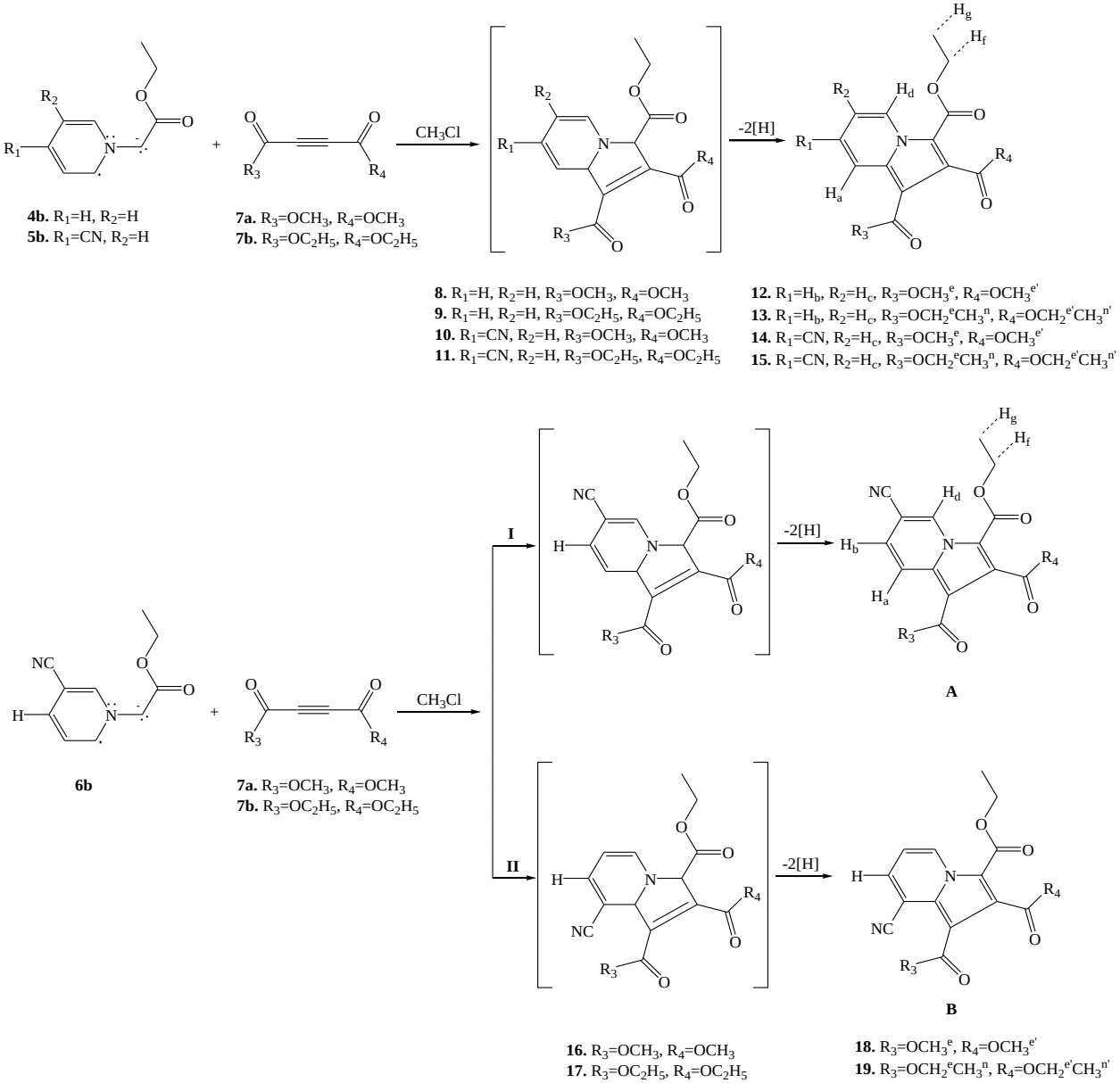

Figure 4. Reactions of pyridinium ylides 4b-6b with dipolarophiles 7a and 7b.

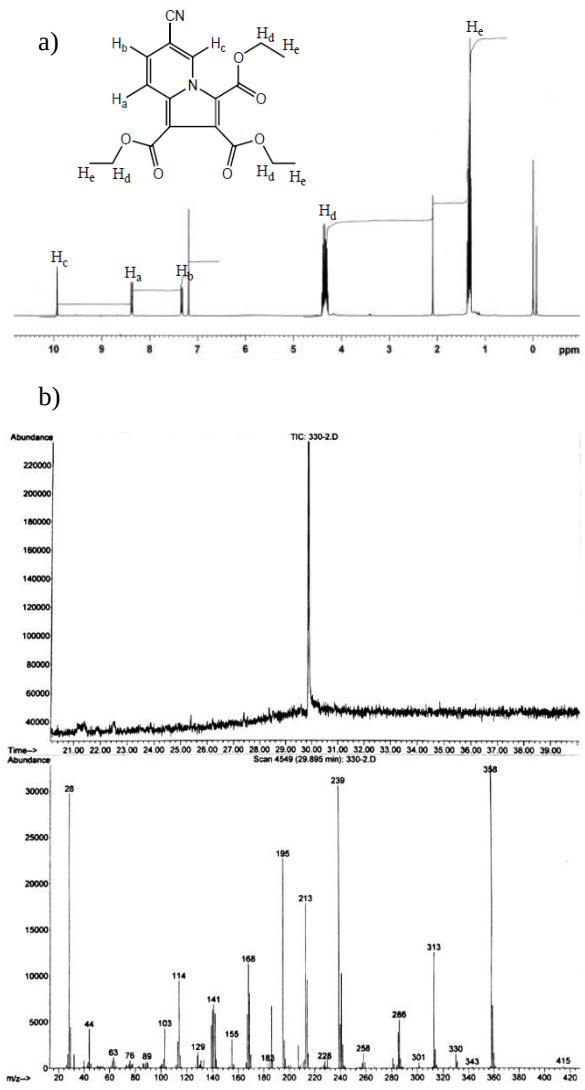

Figure 5 a) ^{1}H NMR spectrum of the cycloadduct 19 and b) Gas chromatogram and mass spectrum of the cycloadduct 19.

4. Conclusion

Six indolizines, two of which are novel (18 and 19), were synthesized by the 1,3-dipolar cycloaddition reaction of pyridinium ylides 4b-6b with electron-deficient DMAD and DEAD. Complementary theoretical studies were mostly in accord with the experimental findings. Calculations revealed that both the charge and the molecular orbital interaction energies of the ylide 4b with the electron deficient dipolarophiles is greater than the other ylides. However, relatively electron rich PA, DPA, VA and VC showed no reactivity towards pyridinium ylides, although the theoretical studies suggested a more probable reaction of 4b-6b with 7e and 7f, indicative of the effect of other reaction parameters (e.g. solvent, temperature etc.). This is actually consistent with the 1,3-dipolar cycloadditions of heteroaromatic *N*-ylides with alkenes and electron-rich acetylenes which yields unstable tetrahydroindolizines, which are reversibly transformed into its components or ring-opened betaines[30].

Acknowledgement

This work has been supported by Abant Izzet Baysal University (Scientific Research Fund, BAP 2002 02.03.03.110).

Author's Contributions

Mustafa Kemal Bayazıt: Performed all experiments, collected all experimental data and performed all data analysis, wrote the manuscript and submitted.

Nihat Çelebi: Supervised the whole study and edited the manuscript.

Selçuk Gümüş: Performed the theoretical study, interpreted the data and drafted the theoretical section.

Lemi Türker: Supervised the theoretical study and edited the manuscript.

Ethics

There are no ethical issues after the publication of this manuscript.

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