Asian Journal of Chemistry; Vol. 25, No. 15 (2013), 8600-8602

ASIAN JOURNAL OF CHEMISTRY

http://dx.doi.org/10.14233/ajchem.2013.14862

Structure-Activity Relationship of Diacylhydrazine Derivatives Fluoride-Containing Pyrazolyl Moiety

HUI-MIN BI[1,*], PENG-TAO XIE[1], SHU-XIAN LI[1], YONG-LI LI[1] and CHUN-HUA DONG[1,2]

[1]Handan Key Laboratory of Organic Small Molecule Materials, Handan College, Hebei Handan 056002, P.R. China
[2]Institute of Chemistry, Chinese Academy of Sciences, Beijing 100190, P.R. China

*Corresponding author: E-mail: binbi99@163.com

(*Received*: 23 November 2012; *Accepted*: 26 August 2013) AJC-14005

Diacylhydrazine derivatives fluoride-containing pyrazolyl moiety compounds were studied by Gaussian03. They have good herbicidal activity. The optimized geometries were calculated and the information of their electron density of these compounds and energy levels, main composition and proportion of the frontier orbitals were obtained by the HF method. The structure-activity relationship was discussed and the possible mechanism was suggested. It could provide guidance for configuration of these compounds to improve the biological activity.

Key Words: Fluoride pyrazole, Diacylhydrazine, Biological activity, Structure-activity relationship.

INTRODUCTION

In search of novel bioactive compounds, 19 compounds were designed and synthesized by introducing the fluoro-pyrazolyl pharmacophore into the diacylhydrazine scaffold by Zhang *et al.*[1] and others[2-5]. The herbicidal activities of these compounds were evaluated. The bioassay results showed that most of them exhibited higher herbicidal activities against dicotyledonous weeds (*Abutilon theophrasti*, *Amaranthus ascedense* and *Amaranthus retroflexus*) than monocotyledonous weeds.

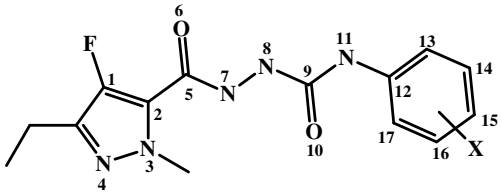
The quantum study of diacylhydrazine derivatives fluoride-containing pyrazolyl moiety was calculated by Gaussian 03 program. The study found the correlation between the herbicidal activity of these compounds and structural parameters and filter the main factors to affect the biological activity and the influence to biological activity from the changes in the molecular structure was explained, the mechanism and sites of action of compound was also discussed[6,7].

EXPERIMENTAL

The geometries of all compounds were optimized using the *ab initio* HF with the 6-31G* basis set. Harmonic vibrational frequencies calculated at the same level were used for characterization of stationary points as a minimum. All quantum calculations were performed with the Gaussian 03 program.

RESULTS AND DISCUSSION

Stability configurations and natural charge: The structure of compounds as follows:



I: X = (**3a**)16-C; (**3c**)16-H; (**3g**)13-C; (**3h**)15-C; (**3k**)15-C, 17-C; (**3l**) 14-C, 15-C; (**3n**)13-C, 17-C; (**3o**)14-C, 17-C; (**3p**)14-C, 16-C, II: X= (**3b**)15-Cl; (**3i**)13-Cl; (**3j**)14-Cl, III: X = (**3m**)13-F, 15-F; (**3q**)16-F, 17-F; (**3r**)13-F, 16-F; (**3s**)13-F, 17-F, IV: X = (**3d**)13-NO_2; (**3e**)15-NO_2; (**3f**)14- NO_2

Fig. 1. Structure of compounds

Energy of the frontier molecules orbital: According to the theory of molecular orbital (MO), the highest occupied molecular orbital (HOMO) and the lowest unoccupied molecular orbital (LUMO) have the greatest influence on the activity of compounds. The reaction between active molecule and receptor macromolecular operated on the frontier molecules orbital. E_{HOMO} is the energy of HOMO, which relate to the ability of electron donor. E_{LUMO} is the energy of LUMO, which relate to the ability of acceptance of electronic. For pesticide molecules, too low-E_{LUMO} or too high-E_{HOMO} means that the molecule itself activity is too strong, it is easy to be metabolized in organism, The effect of pesticide is difficult to control, so the E_{LUMO} or E_{HOMO} of the pesticide molecule should be suitable to estimate expected value[8-10].

From Table-1, the data of herbicidal activity is the best of compound **3h**, **3k** and **3l**, the E_{HOMO} of **3h**, **3k** and **3l** is the higher, so it has strong ability to provide electron and the data

TABLE-1
ENERGY OF THE FRONTIER MOLECULES ORBITALS

Compound	E_{HOMO}	E_{LUMO}	ΔE	Compound	E_{HOMO}	E_{LUMO}	ΔE
3a	-8.2051	2.7680	10.9731	**3i**	-8.6122	2.7688	11.3810
3c	-8.3134	2.7530	11.0664	**3j**	-8.6326	2.6433	11.2759
3g	-8.2914	2.7574	11.0487	**3m**	-9.2574	2.7261	11.9834
3h	-8.0789	2.7756	10.8544	**3q**	-9.3213	2.7070	12.0283
3k	-8.0797	2.7810	10.8607	**3r**	-9.0789	2.7103	11.7892
3l	-7.9904	2.7876	10.7780	**3s**	-9.3113	2.8218	12.1331
3n	-8.6900	2.8191	11.5091	**3d**	-9.0715	1.5655	10.6370
3o	-8.1814	2.7704	10.9519	**3e**	-8.6670	2.4140	11.0810
3p	-8.1532	2.7813	10.9336	**3f**	-8.9380	1.6710	10.609
3b	-8.4478	2.6373	11.0852	–	–	–	–

of herbicidal activity is not good for compound **3m**, **3q** and **3s**, the E_{HOMO} of **3m**, **3q** and **3s** is low, so it has low ability to provide electron. It is concluded that the higher E_{HOMO} of compound, relatively better herbicidal activity of the compound. And the conclusion is consistent with the experimental values. This may be the reason of these compounds to served as herbicidals. Therefore, the mechanism is that herbicidal molecule provide electronic to receptor possibly.

Main composition and proportion of the frontier molecules orbital: From Table-2, the main composition and proportion of E_{HOMO} of compounds **I**, **II** and **IV** in the N(8), O(10), N(11) and the C of benzene ring. The main composition and proportion of E_{HOMO} of them in the pyrazole ring and diacylhydrazine. The main composition and proportion of E_{HOMO} of compounds **III** in the N(11) and the C of benzene ring and the composition is low of N(8) and O(10), this is one of the reasons for the difference of the herbicidal activity.

Natural charge: The atom natural charge of compounds is given in Table-3. These data show that, the negative charge is mainly concentrated in the N(8), O(10) and N(11) of

TABLE-2
MAIN COMPOSITION AND PROPORTION OF FRONTIER MOLECULES ORBITAL

Compound		HOMO	LUMO
I	**3a**	N(8)1.42; O(10)2.62; N(11)19.62; C(12)20.02; C(13)7.02; C(14)2.07; C(15)25.19; C(16)14.07; C(17)4.94	C(1)11.69; C(2)11.06; N(3)12.28; N(4)11.34; C(5)19.41; O(6)15.18; N(7)5.63; N(8)2.63
	3c	N(8)1.50; O(10)2.98; N(11)21.39; C(12)20.94; C(13)9.83; C(14)3.69; C(15)24.09; C(16)4.61; C(17)9.25	C(1)11.70; C(2)11.04; N(3)15.18; N(4)11.33; C(5)19.44; O(6)12.31; N(7)5.62; N(8) 2.63
	3g	N(8)1.20; O(10)2.75; N(11)19.40; C(12)22.98; C(13)12.10; C(14)2.42; C(15)22.73; C(16)6.23; C(17)6.37	C(1)11.64; C(2)11.17; N(3)15.25; N(4)11.27; C(5)19.19; O(6)12.17; N(7)5.61; N(8)2.43
	3h	N(8)1.31; O(10)2.65; N(11)18.90; C(12)20.75; C(13)8.25; C(14)4.85; C(15)23.14; C(16)5.62; C(17)8.39	C(1)11.68; C(2)11.08; N(3)15.19; N(4)11.34; C(5)19.39; O(6)12.28; N(7)5.63; N(8)2.60
	3k	N(8)1.05; O(10)2.43; N(11)17.08; C(12)23.03; C(13)5.96; C(14)6.94; C(15)22.03; C(16)3.86; C(17)9.95	C(1)11.68; C(2)11.26; N(3)15.34; N(4)11.34; C(5)19.20; O(6)5.64; N(7)12.16; N(8)2.39
	3l	N(8)1.28; O(10)2.40; N(11)17.73; C(12)19.92; C(13)4.84; C(14)7.33; C(15)24.05; C(16)3.43; C(17)11.71	C(1)11.68; C(2)11.09; N(3)15.20; N(4)11.35; C(5)19.36; O(6)12.25; N(7)5.64; N(8)2.61
	3n	C(13)21.87; C(14)26.10; C(16)23.97; C(17)19.42	C(1)11.55; C(2)11.41; N(3)15.39; N(4)11.33; C(5)18.88; O(6)11.94; N(7)5.60; N(8)2.57
	3o	N(8)0.99; O(10)2.39; N(11)16.35; C(12)19.84; C(13)17.30; C(14)10.43; C(15)23.15; C(17)2.18	C(1)11.68; C(2)11.22; N(3)15.31; N(4)11.32; C(5)19.25; O(6)12.20; N(7)5.63; N(8)2.45
	3p	N(8)1.38; O(10)2.66; N(11)19.29; C(12)19.56; C(13)11.29; C(14)3.40; C(15)26.99; C(16)5.04; C(17)6.82	C(1)11.69; C(2)11.07; N(3)15.19; N(4)11.35; C(5)19.38; O(6)12.26; N(7)5.64; N(8)2.63
II	**3b**	N(8)1.24; O(10)2.34; N(11)17.54; C(12)17.58; C(13)7.52; C(14)4.47; C(15)21.09; C(16)3.86; C(17)7.61; Cl(X)15.32	C(1)11.71; C(2)10.85; N(3)15.05; N(4)11.20; C(5)19.61; O(6)12.42; N(7)5.57; N(8)2.71
	3i	N(8)1.53; O(10)2.83; N(11)21.05; C(12)19.26; C(13)12.82; C(14)2.48; C(15)20.87; C(16)4.97; C(17)6.25; Cl(X)6.25	C(1)11.62; C(2)10.97; N(3)15.15; N(4)11.37; C(5)19.32; O(6)12.21; N(7)5.60; N(8)2.76
	3j	N(8)1.36; O(10)2.81; N(11)19.88; C(12)17.44; C(13)4.79; C(14)6.78; C(15)24.00; C(17)14.00; Cl(X)5.72	C(1)11.72; C(2)10.84; N(3)15.04; N(4)11.20; C(5)19.62; O(6)12.42; N(7)5.57; N(8)2.71
III	**3m**	N(11)7.76; C(12)27.16; C(13)12.99; C(15)16.87; C(16)18.69; $F(X_1)$4.52; $F(X_2)$6.23	C(1)11.68; C(2)11.43; N(3)15.38; N(4)11.22; C(5)19.05; O(6)12.16; N(7)5.61; N(8)2.45
	3q	N(11)3.17; C(12)6.99; C(13)8.62; C(14)24.16; C(15)3.25; C(16)11.13; C(17)27.45; $F(X_1)$9.52; $F(X_2)$3.69	C(1)11.63; (2)11.39; N(3)15.33; N(4)11.15; C(5)19.03; O(6)5.60; N(7)12.17; N(8)2.40
	3r	N(11)5.81; C(12)14.07; C(13)22.83; C(14)3.73; C(15)13.25; C(16)20.11; C(17)2.60; $F(X_1)$7.81; $F(X_2)$7.09	C(1)11.55; C(2)11.20; N(3)15.13; N(4)11.02; C(5)19.01; O(6)12.12; N(7)5.54; N(8)2.39
	3s	N(11)14.43; C(12)26.15; C(13)13.81; C(15)17.18; C(16)14.04; $F(X_1)$4.83	C(1)11.47; C(2)11.08; N(3)15.16; N(4)11.28; C(5)19.12; O(6)12.11; N(7)5.60; N(8)2.39;
IV	**3d**	N(8)1.83; O(10)2.61; N(11)23.35; C(12)15.78; C(13)6.52; C(14)9.44; C(15)22.34; C(16)1.52; C(17)14.12	C(12)11.12; C(13)10.11; C(14)10.27; C(16)15.32; C(17)2.07; N(X)20.24; O(X1)12.23; O(X2)13.19
	3e	N(8)1.71; O(10)2.13; N(11)23.33; C(12)16.56; C(13)11.09; C(14)1.84; C(15)24.74; C(16)2.15; C(17)9.76; $O(X_1)$2.20; $O(X_2)$2.89	C(9)2.62; N(11)1.84; C(12)20.43; C(14)11.86; C(15)13.78; C(16)11.01; N(X)19.70; O(X1)13.31
	3f	O(10)3.18; N(11)24.34; C(12)19.60; C(13)12.70; C(14)3.50; C(15)20.64; C(16)3.96; C(17)7.33	C(13)11.93; C(14)14.41; C(15)9.08; C(16)2.41; C(17)16.08; N(X)18.53; O(X1)12.91; O(X2)12.53

TABLE-3
ATOM NATURAL CHARGE OF COMPOUNDS

Compound		C(1)	C(5)	O(6)	N(7)	N(8)	C(9)	O(10)	N(11)
I	**3a**	0.41496	0.82737	-0.68694	-0.55891	-0.55823	1.01201	-0.74829	-0.72018
	3c	0.41489	0.82732	-0.68644	-0.55903	-0.5581	1.01196	-0.74868	-0.7209
	3g	0.41349	0.8274	-0.68767	-0.55795	-0.55874	1.01207	-0.7475	-0.73183
	3h	0.4147	0.82732	-0.68696	-0.55871	-0.55822	1.01144	-0.75001	-0.72059
	3k	0.4136	0.82748	-0.68862	-0.55754	-0.55885	1.0116	-0.74875	-0.73228
	3l	0.41484	0.82738	-0.68743	-0.55866	-0.55833	1.01154	-0.74951	-0.71962
	3n	0.41344	0.8268	-0.69055	-0.55418	-0.55848	1.00856	-0.74859	-0.75503
	3o	0.41352	0.82743	-0.68777	-0.55785	-0.55885	1.01231	-0.74776	-0.73092
	3p	0.41506	0.82741	-0.68726	-0.55876	-0.55834	1.01221	-0.74851	-0.71976
II	**3b**	0.41465	0.82705	-0.68384	-0.56022	-0.55728	1.01272	-0.74752	-0.72085
	3i	0.41617	0.82831	-0.6852	-0.55807	-0.55587	1.01521	-0.74866	-0.72786
	3j	0.41472	0.82708	-0.68386	-0.56029	-0.55726	1.01272	-0.74446	-0.72084
III	**3m**	0.40994	0.8265	-0.68603	-0.55616	-0.55897	1.01313	-0.73943	-0.75006
	3q	0.40886	0.82602	-0.68469	-0.55571	-0.55868	1.01277	-0.7336	-0.74951
	3r	0.40923	0.82608	-0.68458	-0.55581	-0.55862	1.01309	-0.73364	-0.74878
	3s	0.41431	0.82657	-0.68778	-0.55419	-0.55723	1.01448	-0.73518	-0.74441
IV	**3d**	0.41554	0.82963	-0.6827	-0.55419	-0.55365	1.01562	-0.74554	-0.73869
	3e	0.41474	0.82665	-0.67979	-0.56203	-0.55622	1.0146	-0.73991	-0.72088
	3f	0.41479	0.8267	-0.67982	-0.56117	-0.5561	1.01361	-0.74767	-0.72199

acylhydrazine, these atoms make the electronegative area and they could combine with positive area of receptor. the positive charge is mainly concentrated in the C(1) of carbon-fluorine bond and C(5), C(9) of carbonyl, These atoms make the positive area, they could combine with negative area of receptor.

The groups (-Cl, -F, $-NO_2$) of **II**, **III** and **IV** are electron-withdrawing groups, they conjugate with benzene ring and reduces the density of electron of benzene ring. The group ($-CH_3$) of **I** is electron-donating group, it conjugate with benzene ring, it increases the density of electron of benzene ring. The **I** provide electronic to receptor easier than **II**, **III** and **IV**, this is one of the reasons for the difference of the herbicidal activity. For example, the herbicidal activity of **3k** and **3l** is better than **3d**, **3j** and **3s**.

Conclusion

The characteristics of HOMO and LUMO are the main factors to influence antibacterial activities of these kinds of compounds. The mechanism is that diacylhydrazine derivatives fluoride-containing pyrazolyl moiety provide electronic to the receptor. The results indicate that acylhydrazine might be an important active site, of which the potency of electric charge translocation has a great influence on the herbicidal activity of this kind of compounds.

ACKNOWLEDGEMENTS

This project was supported by the Science and Technology Projects of Hebei Province (Contract No. 10273939) and Handan Key Laboratory of Organic Small Molecule Materials, Handan College.

REFERENCES

1. X.Y. Zhang, Y.S. Li, J.Q. Weng and C.X. Tan, *Chin. J. Org. Chem*., **31**, 1295 (2011)
2. S.L. Labhade and V.B. Gaikwad, *Asian J. Chem*., **21**, 7117 (2009).
3. J.J. Heller, H. Mattioda, E. Klein and A. Sagenmuller, Brighton Crop Protection Conference Pests and Diseases, Brighton, 1, 59 (2000).
4. X.H. Liu, Y.X. Shi, Y. Ma, C.Y. Zhang, W.L. Dong, P. Li, B.L. Wang, B.J. Li and Z.M. Li, *Eur. J. Med. Chem*., **44**, 2782 (2009).
5. X.H. Liu, Y.X. Shi, Y. Ma, G.R. He, W.L. Dong, C.Y. Zhang, B.L. Wang, S.H. Wang, B.J. Li and Z.M. Li, *Chem. Biol. Drug Des*., **73**, 320 (2009).
6. G.C.L. Ee, S.H. Teo, R. Go, C.K. Lim, Y.M. Lim and C.F.J. Bong, *Asian J. Chem*., **24**, 231 (2012).
7. B.K. Sharma, Yashwant and B. Srivastava, *Asian J. Chem*., **22**, 8231 (2010).
8. T.B. Wei, Y.L. Leng, Y.C. Wang, J.H. Zhang and Y.M. You, *Chin. J. Org. Chem*., **29**, 216 (2009).
9. G.F. Yang, H.Y. Liu, Z.H. Yang and X.F. Yang, *Acta Chim. Sin*., **56**, 729 (1998).
10. D.B. Zhang, Y.H. Ren, D.W. Fu, B. Yan, J.R. Song and X.Q. Lv, *Acta Chim. Sin*., **66**, 2409 (2008).