SHORT PAPER

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The crystal structure of 1-phenyl-3-methyl-5-[2′-(4′′-phenylmethoxylphenyl) ethoxyl]pyrazole, a potential insect juevnile hormone mimic†

Sun Dianqing, Li Zhong and Qian Xuhong*

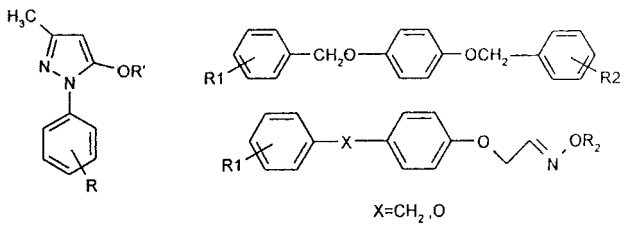
Institute of Pesticides and Pharmaceuticals, East China University of Science and Technology, Shanghai, 200237, China

The crystal structure of 1-phenyl-3-methyl-5-[2′-(4′′-phenylmethoxylphenyl)ethoxyl] pyrazole, a potential JH mimic, has been established; the crystal belongs to the triclinic system with z = 2, and the distance between C(25) and H(14) (19.64Å), an important steric factor, which is very near the optimum value (21Å) for JH activity expression, may yield an explanation to the potential bioactivity of the new pyrazole compound.

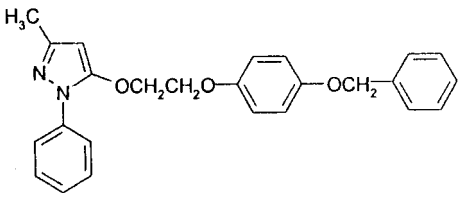
Analogues of insect juevnile hormones (JH), JH mimics have been candidate as insect control agents, and there have been extensive searches for such compounds with high activity, high field stability and safety.

In general, structure similarity always results in mimic activity, so designing a similar molecule that mimics the structural essentials of bioactivity unit is a shortcut to developing a lead compound with potential activity. In the study of potential insect JH mimics, we assembled the bioactivity unit of the pyrazole derivatives **1** and JH mimics **2** to design and synthesize the title compound **3** and its derivatives in order to find a lead compound with high bioactivity as an JH mimic and inhibitor of DNA and protein synthesis.[1–3]

In recent years, in order to find the true conformation and explore key factor of activity structure, many researchers have investigated JHs and a related 2,4-dodecadienone series of compounds to analyse their JH activity against *Aedes aegypti* (yellow fever mosquito) and *Tenebrio molitor* (yellow mealworm). Nakayama *et al*.[4] found that the steric dimensions and hydrophobicity are important factors related to JH activity.



1 **2**



3

Further study on their quantitative structure – activity relationship (QSAR) implied that the length of the whole molecule, constructed by molecular modelling, is a very important factor, and relating to the optimum for JH activity, the length was estimated as ca 21Å, which also implies that the diameter of JH receptor is common to all these insects.[4]

The title compound was prepared by reaction of 3-methyl-1-phenyl-2-pyrazolin-5-one with 1-(2-bromoethoxyl)-4-(phenylmethoxyl)-benzene in DMF. It was recrystallized from ethanol to give crystals with mp 96°C.

The bioscreen of title compound shows IGR activity, and to some extent it looks like JH activity. For developing the series of title compounds to find novel JH mimics, we therefore investigated and studied the crystal structure of compound **3** by X-ray diffraction to obtain more information about the structural character and true conformation (Fig. 1).

From the crystal data, the distance between C (25) and H (14) is 19.64Å, which is a very important steric parameter as mentioned above, and is very near the optimum value (21Å). As well known, this parameter stands for the total length and the steric property of the bioactivity molecule. The crystal data obtained will be very valuable in estimating the space factor in the QSAR of the lead compound and the 19.64Å steric parameter may yield an explanation for the compound's potential JH activity.

Experimental

Crystal data for compound 3: $C_{25}H_{24}O_3N_2$, *Mr* = 400.48 (*F*(000) = 424.00, colourless crystal, prismatic system, *a* = 12.624(3), *b* = 12.678(2), *c* = 6.838(3)Å, U=1071.8(6)Å^3, α = 95.74(3)°. β = 98.09(4)°, γ = 95.34(2)°, space group, P1, *Z* = 2, *D*c = 1.241g cm^{-1}, μ(Mo – Kα) = 0.82 cm^{-1}.

The intensity data were collected on Riguka AFC7R diffractometer with MoKα radiation (λ = 0.71968Å) and ω-2θ scan technique [*T* = 293(1)K; $0 \le h \le 13$, $-14 \le k \le 14$, $-8 \le l \le 7$; $2\theta_{max}$ = 50.0°].

The structure was solved by direct methods (SHELXS 86)[5] and expanded using Fourier techniques[6]. The non-hydrogen atoms were refined anisotropically. Hydrogen atoms were included but not

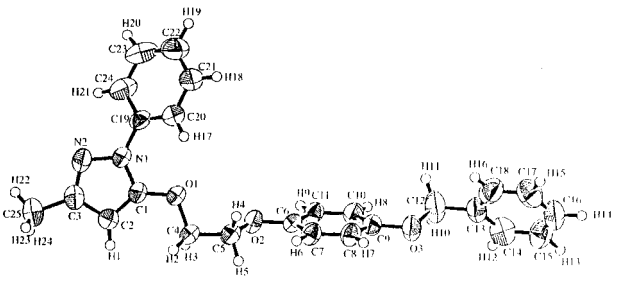


Fig. 1 X-Ray crystal structure of compound **3**

* To receive any correspondence.

† This is a Short Crystallographic Paper, there is therefore no corresponding material in *J Chem. Research (M).*

Table 1. Atomic coordinates and B_{iso}/B_{eq}

Atom	*x*	*y*	*z*	B_{eq}
O(1)	0.6770(1)	0.3402(1)	0.3775(2)	4.71(4)
O(2)	0.6422(1)	0.5139(1)	0.1300(2)	4.71(4)
O(3)	0.7319(1)	0.7846(1)	–0.4245(2)	5.67(4)
N(1)	0.7420(1)	0.2598(1)	0.6549(3)	4.35(5)
N(2)	0.7069(2)	0.1926(2)	0.7846(3)	5.07(5)
C(1)	0.6582(2)	0.2758(2)	0.5165(3)	4.16(5)
C(2)	0.5683(2)	0.2199(2)	0.5552(4)	4.82(6)
C(3)	0.6029(2)	0.1686(2)	0.7220(4)	5.17(7)
C(4)	0.5839(2)	0.3479(2)	0.2340(4)	5.09(6)
C(5)	0.6183(2)	0.4026(2)	0.0677(3)	4.69(6)
C(6)	0.6659(2)	0.5781(2)	–0.0129(3)	3.91(5)
C(7)	0.6740(2)	0.5410(2)	–0.2063(3)	4.48(6)
C(8)	0.6975(2)	0.6121(2)	–0.3385(3)	4.64(6)
C(9)	0.7124(2)	0.7201(2)	–0.2796(3)	4.36(6)
C(10)	0.7053(2)	0.7570(2)	–0.0854(3)	4.62(6)
C(11)	0.6820(2)	0.6859(2)	–0.0473(3)	4.30(5)
C(12)	0.7827(3)	0.8884(2)	–0.3616(4)	8.09(9)
C(13)	0.8098(2)	0.9383(2)	–0.5405(3)	5.28(7)
C(14)	0.7546(2)	1.0185(2)	–0.6095(4)	6.49(8)
C(15)	0.7807(3)	1.0672(2)	–0.7676(5)	7.11(9)
C(16)	0.8602(3)	1.0384(3)	–0.8607(4)	6.97(9)
C(17)	0.9177(2)	0.9589(3)	–0.7989(5)	7.32(9)
C(18)	0.8929(3)	0.9090(2)	–0.6389(4)	6.70(8)
C(19)	0.8521(2)	0.3030(2)	0.6796(4)	4.55(6)
C(20)	0.9005(2)	0.3267(2)	0.5206(4)	5.91(7)
C(21)	1.0069(2)	0.3701(3)	0.5481(5)	7.14(9)
C(22)	1.0642(2)	0.3882(3)	0.7335(6)	7.80(10)
C(23)	1.0179(3)	0.3626(3)	0.8917(5)	8.2(1)
C(24)	0.9103(2)	0.3190(2)	0.8681(4)	6.66(8)
C(25)	0.5363(2)	0.0932(2)	0.8236(4)	7.41(9)
H(1)	0.4991	0.2178	0.4935	5.3715
H(2)	0.5475	0.2744	0.1870	6.1031
H(3)	0.5348	0.3880	0.3054	6.3684
H(4)	0.6851	0.3766	0.0251	5.3865
H(5)	0.5586	0.3933	–0.0426	5.4731
H(6)	0.6635	0.4673	–0.2475	4.8905
H(7)	0.7013	0.5873	–0.4712	4.7645
H(8)	0.7158	0.8286	–0.0424	4.7736
H(9)	0.6751	0.7107	0.1831	4.9387
H(10)	0,7267	0.9280	–0.3035	20.4290
H(11)	0.8553	0.8708	–0.2805	12.7836
H(12)	0.6951	1.0378	–0.5423	8.2413
H(13)	0.7391	1.1252	–0.8220	12.2920
H(14)	0.8826	1.0725	–0.9771	8.8194
H(15)	0.9729	0.9371	–0.8729	12.2339
H(16)	0.9266	0.8633	–0.5888	5.8878
H(17)	0.8624	0.3090	0.3882	7.4493
H(18)	1.0421	0.3877	0.4239	8.8703
H(19)	1.1409	0.4194	0.,7475	9.3701
H(20)	1.0467	0.3694	1.0237	10.3039
H(21)	0.8740	0.3004	0.9823	6.5513
H(22)	0.5757	0.0741	0.9409	10.7767
H(23)	0.5084	0.277	0.7365	13.2517
H(24)	0.4727	0.1151	0.8483	11.1756

$B_{eq} = {}^{8}/_{3}\ \pi^2\ (U_{11}(aa^*)^2 + U_{22}\ (bb^*)^2 + U_{33}(cc^*)^2 + 2U_{12}aa^*bb^*\ cos\ \gamma + 2U_{13}aa^*cc^*\ cos\ \beta + 2U_{33}bb^*\ cc^*\ cos\ \alpha)$

refined. The final cycle of full-matrix least squares refinement was based on 2240 observed reflections [$I > 3.00\sigma(I)$] and 272 variable parameters and converged (largest parameter was 0.01 times its esd) to $R = 0.041$ and $R_w = 0.050$. The weighing scheme, $w = 1/[\sigma 2(F_o)]$ was found to give a satisfactory analysis of variance. The estimated standard deviation for the geometrical parameters involving non-hydrogen atoms lies within the following ranges: bond lengths, 0.002 – 0.004 Å; bond angles 0.2 – 0.3°.

Neutral atom scattering factors were taken from Cromer and Waber[7]. Anomalous dispersion effects were included in F_{calc}[8], the value for $\Delta f'$ and $\Delta f''$ were those of Creagh and McAuley[9]. The values for the mass attenuation coefficients are those of Creagh and Hubbel[10]. All calculations were performed using the teXsan[11] crystallographic software package of the Molecular Structure Corporation.

Table 2 Anisotropic displacement parameters

Atom	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
O(1)	0.0529(10)	0.0600(10)	0.0660(10)	0.0047(8)	–0.0040(8)	0.264(8)
O(2)	0.076(1)	0.0549(10)	0.0492(9)	0.0087(8)	0.0068(8)	0.0157(9)
O(3)	0.099(1)	0.062(1)	0.0498(9)	–0.0144(9)	0.0064(9)	0.0133(8)
N(1)	0.057(1)	0.053(1)	0.056(1)	0.0086(9)	0.0018(10)	0.0186(9)
N(2)	0.076(2)	0.059(1)	0.061(1)	0.009(1)	0.011(1)	0.023(1)
C(1)	0.057(1)	0.046(1)	0.056(1)	0.009(1)	0.005(1)	0.015(1)
C(2)	0.056(1)	0.060(1)	0.068(2)	0.005(1)	0.006(1)	0.018(1)
C(3)	0.073(2)	0.059(2)	0.068(2)	0.006(1)	0.018(1)	0.018(1)
C(4)	0.057(1)	0.069(2)	0.065(2)	0.003(1)	–0.009(1)	0.027(1)
C(5)	0.061(2)	0.056(1)	0.059(1)	0.004(1)	–0.002(1)	0.015(1)
C(6)	0.048(1)	0.055(1)	0.046(1)	0.008(1)	0.002(1)	0.015(1)
C(7)	0.070(2)	0.049(1)	0.051(1)	0.010(1)	0.006(1)	0.006(1)
C(8)	0.072(2)	0.061(2)	0.044(1)	0.007(1)	0.011(1)	0.007(1)
C(9)	0.060(1)	0.058(1)	0.047(1)	0.000(1)	0.005(1)	0.011(1)
C(10)	0.070(2)	0.050(1)	0.052(1)	0.000(1)	0.003(1)	0.005(1)
C(11)	0.063(1)	0.058(1)	0.042(1)	0.007(1)	0.004(1)	0.006(1)
C(12)	0.157(3)	0.076(2)	0.064(2)	–0.039(2)	0.010(2)	0.014(2)
C(13)	0.088(2)	0.060(2)	0.049(1)	–0.016(1)	0.012(1)	0.004(1)
C(14)	0.094(2)	0.072(2)	0.084(2)	0.011(2)	0.028(2)	0.001(2)
C(15)	0.127(3)	0.064(2)	0.079(2)	0.014(2)	0.010(2)	0.015(2)
C(16)	0.123(3)	0.069(2)	0.072(2)	–0.013(2)	0.022(2)	0.015(2)
C(17)	0.089(2)	0.102(2)	0.092(2)	–0.002(2)	0.039(2)	0.010(2)
C(18)	0.097(2)	0.070(2)	0.085(2)	0.012(2)	–0.004(2)	0.019(2)
C(19)	0.053(1)	0.053(1)	0.066(2)	0.014(1)	–0.004(1)	0.015(1)
C(20)	0.059(2)	0.086(2)	0.079(2)	0.003(1)	–0.001(1)	0.029(2)
C(21)	0.060(2)	0.101(2)	0.113(2)	0.007(2)	0.001(2)	0.044(2)
C(22)	0.061(2)	0.102(2)	0.129(3)	0.007(2)	–0.009(2)	0.029(2)
C(23)	0.078(2)	0.130(3)	0.091(2)	0.019(2)	–0.028(2)	0.006(2)
C(24)	0.072(2)	0.105(2)	0.073(2)	0.020(2)	–0.007(2)	0.011(2)
C(25)	0.098(2)	0.096(2)	0.093(2)	–0.006(2)	0.026(2)	0.040(2)

The general temperature factor expression:

$\exp(-2\pi^2(a^{*2}\ U_{11}\ h^2 + b^{*2}\ U_{22}\ k^2 + c^{*2}\ U_{33}\ l^2 + 2a^*\ b^*\ U_{12}\ hk + 2a^*c^*\ U_{13}\ hl + 2b^*c^*\ U_{23}\ kl))$

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