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Syntheses and Crystal Structures of Three Electron Poor *N*-Vinyltheophylline Derivatives

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Abstract Protonation of the highly reactive 1:1 intermediates, produced in the reaction between triphenylphosphine and alkyl acetylenecarboxylates (or dialkyl acetylenedicarboxylates) by theophylline leads to vinyltriphenylphosphonium salts, which undergo Michael addition reaction with conjugate base to produce phosphorus ylides. Silica gel was found to catalyze conversion of the phosphorus ylides to electron-poor *N*-vinyl imidazoles in solvent-free conditions under thermal (90 °C, 1 h) conditions. The structures of these compounds were confirmed by IR, ¹H, and ¹³C NMR spectroscopy, and single crystal X-ray structure determination. The structural analysis of the products indicated that the reaction is completely regio- and stereoselective.

Keywords Silica gel · Theophylline · Acetylenic esters · Vinyltriphenylphosphonium salts · Crystal structure · *N*-Vinyl imidazole

Introduction

Imidazole chemistry currently attracts considerable attention, where the imidazole derivatives are widely applied as

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M. Rouhani Young Researchers Club, Zanjan Branch, Islamic Azad University, Zanjan, Iran *N*-ligands coordinating transition metals [1, 2]. The application of imidazoles in medicinal chemistry [3] or chemistry of natural products/alkaloids [4, 5] or of 1, 3-disubstituted imidazole salts as ionic liquids [6, 7] are also well known.

1-Vinylimidazole is employed as a copolymer in the production of cationic polymers for various uses. Alkylimidazoles are used as hardeners for epoxy resins and for polyurethanes [8]. Less important uses for alkyl- and arylimidazoles include photography and dyes.

 β -Additions of nucleophiles to the vinyl group of vinylic phosphonium salts leading to the formation of new alkylidenephosphoranes has attracted much attention as a very convenient and synthetically useful method in organic synthesis [9]. Organophosphorus compounds have been extensively used in organic synthesis as useful reagents as well as ligands of a number of transition metal catalysts [10]. Phosphorus ylides are a class of special type of zwitterions, which bear strongly nucleophilic electron rich carbanions. The electron distribution around the P⁺-C⁻ bond and its consequent chemical implications had been probed and assessed through theoretical, spectroscopic and crystallographic investigations [9]. The nucleophilicity at the ylidic carbon is a factor of essential mechanistic importance in the use of these ylides as Wittig reagents. Phosphorus ylides are important reagents in synthetic organic chemistry, especially in the synthesis of naturally occurring products, compounds with biological and pharmacological activity [11]. These ylides are usually prepared by treatment of a phosphonium salt with a base, and phosphonium salts are usually obtained from a phosphine and an alkyl halide. Phosphonium salts are also prepared by Michael addition of phosphorus nucleophiles to activated olefins and in other ways [12]. The phosphonium salts are most often converted to the ylide by treatment with a strong base, though weaker bases can be used if the salt is acidic enough. In recent years, we have established a one-pot method for the synthesis of stabilized phosphorus ylides [13-22]. In this paper, we wish to describe the preparation of sterically congested electron-poor *N*-vinyl imidazoles from alkyl acetylenecarboxylates (or dialkyl acetylenedicarboxylates) and theophylline in the presence of triphenylphosphine in fairly good yields.

Results and Discussion

The zwitterionic intermediate 7 may result from initial addition of triphenylphosphine 1 to the alkyl acetylenecarboxylate 2 and concomitant protonation of the 1:1 adduct 3, followed by attack of the NH-acid anion on the vinyltriphenylphosphonium cation to form the phosphorane 6 (Scheme 1). That phosphorane 6 undergoes intramolecular proton transfer [23] leading to formation of zwitterionic intermediate 7. TLC indicated formation of zwitterionic

Scheme 1 Proposed mechanism for the formation of electron-poor *N*-vinyl imidazoles 8(a-b) intermediates 7 in CH₂Cl₂. Silica gel powder was found to catalyze conversion of the zwitterionic intermediates 7 to electron-poor imidazoles 8 in solvent-free conditions [24] under thermal (90 °C, 1 h) conditions. In the absence of the SiO₂ powder, the conversion of the zwitterionic intermediate 7 to electron-poor *N*-vinyl imidazoles 8(a-b) was not observed and decomposition of the starting materials was observed (Scheme 1). The reaction proceeds smoothly and cleanly under mild conditions and no side reactions were observed. The mechanism of the reaction has not been established experimentally. However, a possible explanation [24] is proposed in Scheme 1.

We have also used dialkyl acetylenedicarboxylate and ethyl 3-phenyl-2-propynoate **11** (Scheme 2) instead of alkyl acetylenecarboxylate **2** in this reaction. The compound **14** may result from initial addition of triphenylphosphine to the dialkyl acetylenedicarboxylate or ethyl 3-phenyl-2-propynoate and concomitant protonation of the 1:1 adduct **12**, followed by attack of the NH-acid anion [24] on the vinyltriphenylphosphonium cation to form the



8a: R=Me ; 8b: R=Et

Scheme 2 Synthesis of electron-poor *N*-vinyltheophyllines 16(a–b)



phosphorane 14 (Scheme 1). SiO₂ powder was found to catalyze conversion of the compound 14 to electron-poor *N*-vinyl imidazoles 16(a-b) in solvent-free conditions [23] under thermal (90 °C, 1 h) conditions. In the absence of the SiO₂ powder, the reaction time for the conversion of the compound 14a to electron-poor *N*-vinyl imidazole 16a amounted to 48 h at 90 °C. In the absence of the SiO₂ powder, the conversion of the zwitterionic intermediate 14b to electron-poor *N*-vinyl imidazole 16b was not observed and decomposition of the starting materials was

observed in 48 h at 90 °C (Scheme 2). The reaction proceeds smoothly and cleanly under mild conditions and no side reactions were observed. The mechanism of the reaction has not been established experimentally. However, a possible explanation [24] is proposed in Scheme 2. The NMR spectra indicated that solutions of compound **16(a–b)** contain two isomers (*E* and *Z*). The relative percentages of rotamers of **16a–b** in CDCl₃ were determined from the ¹H NMR spectra. The structures **8(a–b)** and **16(a–b)** were deduced from their IR, ¹H and ¹³C NMR spectra.





Fig. 1 Molecular structures of compounds **8a**, *E***-16a** and *Z***-16a** (two crystallographically independent molecules A and B) with the atom numbering schemes and intramolecular C–H···O/N contacts forming S(5) and S(6) motifs, respectively (*dashed lines*). For *Z***-16a** molecule

A with -x, -y, -z atomic coordinates is shown for comparison with molecule **B**. Disorder of one of the methyl groups and the ester moiety in molecule **B** is shown. Displacement ellipsoids represent the 50% probability level

Table 1 Selected interatomic distances (Å) and torsion angles		8a	Z-16a		<i>E</i> -16a
(°) of 8a , Z-16a and E-16a			Molecule A	Molecule B	
	Bond lengths				
	N(7)-C(7)	1.433(2)	1.433(3)	1.436(3)	1.436(2)
	C(7)–C(10)	1.324(2)	1.335(3)	1.340(4)	1.339(2)
	C(7)–C(17)	1.491(2)	1.482(4)	1.495(4)	1.501(2)
	C(10)-C(11)	_	1.467(3)	1.471(4)	1.472(2)
	Torsion angles				
	C(18)-O(4)-C(17)-C(7)	176.34(10)	180.0(2)	172.4(5)	176.58(9)
	C(17)-O(4)-C(18)-C(19)	_	167.2(3)	$-169.5(9)^{a}$	-83.55(13)
	C(5)-N(7)-C(7)-C(10)	113.09(14)	-91.4(3)	85.3(3)	126.66(11)
^a In the disordered region the respective C(17B)–O(4B)–	N(7)-C(7)-C(10)-C(11)	_	0.2(4)	3.0(4)	172.70(10)
	C(10)-C(7)-C(17)-O(3)	170.11(12)	168.0(3)	-174.7(3)	153.93(11)
$C(18C) - C(19C)$ torsion angle is $-115.6(11)^{\circ}$	C(7)-C(10)-C(11)-C(12)	-	-174.6(3)	175.5(3)	133.13(12)

E-16a

Crystal Structures of Compounds 8a, Z-16a and E-16a

The crystals of **8a**, **Z-16a** and **E-16a** are built up from molecules shown in Fig. 1. In all **8a**, **Z-16a** and **E-16a** the carbonyl atom O(3) of the ester group is in *antiperiplanar* conformation in relation to the vinyl atom C(10) [see the O(3)-C(17)-C(7)-C(10) torsion angles in Table 1], as previously found in most of the related compounds

described by us previously and deposited at the Cambridge Structural Database [25]. The molecules **A** and **B** of **Z-16a** adopt Z geometry with respect to the double bond C(7)=C(10), which is reflected in the value of the torsion angle N(7)-C(7)-C(10)-C(11) of $0.2(4)^{\circ}$ and $3.0(4)^{\circ}$ for **A** and **B**, respectively (Table 1). The molecule in *E*-16a is *E* isomer with respect to C(7)=C(10) with the N(7)-C(7)-C(10)-C(11) of $172.7(1)^{\circ}$.

The overall geometries of both crystallographically independent molecules A and B of Z-16a and that of 8a seem to be similar to each other, and additionally similar to that observed in the structurally related compounds [25]. Like previously observed, two planes (with the atoms N(7)) and C(7) being common) may be distinguished in the molecules of 8a and Z-16a: plane 1 including methyl- or ethylacrylate moiety, atom N(7) and phenyl ring in Z-16a, and plane 2 including the phylline part and atom C(7). The dihedral angles between the least-squares planes 1 and 2 in both molecules of Z-16a (87.3(1)° for A and 84.5(1)° for **B**) reveal that the two planes are almost perpendicular to each other, whereas the same angle in **8a** is only $69.6(1)^{\circ}$. The C(11) ~ C(16) phenyl ring in both A and B of Z-16a is only slightly twisted (see C(7)-C(10)-C(11)-C(12) torsion angles in Table 1), which was also previously observed in most of the Z geometrical isomers of similar structures [25]. Some more significant deviation from the planarity is observed in the ester methyl group of **Z-16a**, as seen from C(17)-O(4)-C(18)-C(19) torsion angles of $167.2(3)^{\circ}$ for molecule A and $-169.5(9)^{\circ}$ for molecule **B**. It is to be noted that the unusually high deviation is observed in the disordered region of the molecule **B** denoted in Fig. 1 as C(18C) and C(19C) with s.o.f. = 0.47(2), as seen from C(17B)-O(4B)-C(18C)-C(19C)torsion angle of $-115.6(11)^{\circ}$.

Like previously observed in the structurally related compounds [25], in both **A** and **B** of **Z-16a** the weak intramolecular contacts formed in plane 1: C(10)–H(10)···O(4) and C(16)–H(16)···N(7), give rise to respectively five-membered S(5) and six-membered S(6) motifs (Fig. 1; Table 2). The close C–H···N contacts are accompanied by the intramolecular C(16)–H(16)··· π [*Cg*(1)] interactions of the geometry given in Table 3.

Quite different geometry is observed in the molecule of *E* isomer present in *E*-16a. Here the ethyl 3-phenylacrylate moiety is not planar and both the phenyl and ester groups are twist relative to the plane defined by the atoms C(17), C(7), C(10), C(11) and N(7). That is reflected in the values of the following torsion angles: C(7)–C(10)–C(11)–C(12) (133.1(2)°), C(10)–C(7)–C(17)–O(3) (153.9(1)°) and C(17)–O(4)–C(18)–C(19) ($-83.6(2)^\circ$). Due to such a huge difference in the molecular conformation (shown in Fig. 2), none of described above intramolecular interactions observed in the molecules **A** and **B** of **Z**-16a are possible in the molecule of *E* isomer in *E*-16a.

The crystal packing diagrams of **8a**, **Z-16a** and **E-16a** are dominated by weak C–H···O contacts (Table 2). Important role is also played by the C–H···N interactions (Table 2) and C–H··· π and π ··· π contacts summarized in Table 3. In the crystal lattice, the molecules of **8a** related by the action of 2₁ axis are joined to each other by

C(8)–H(8)····O(6)^{*ii*} and C(10)–H(10A)····O(3)^{*ii*} bonds to form helical chains along the *b*-axis (Fig. 3). The adjacent chains interact with each other via C(10)–H(10B)····N(9)^{*iv*} and C(18)–H(18B)····O(6)^{*v*} contacts, giving rise to layers parallel to $(10\overline{1})$ plane (Fig. 3). Additional stabilization of the layer structure is provided by the weak C(3)– H(3A)···· π [Cg(1)]^{*xv*} contacts, and the inter-layer interactions are realized through stacking π [Cg(2)]··· π [Cg(2)]^{*iii*} interactions (Table 3). These, in combination with weaker C–H···O contacts result in a three-dimensional network of interactions in the crystal of **8a**.

Three different types of C-H···O/N intermolecular interactions are observed in the crystal lattice of Z-16a: between A molecules, between B molecules, and between A and B molecules (Fig. 4). In the $A \cdots A$ contacts the main role is played by the centrosymmetric bifurcated bonds with atom O(6A) acting as acceptors, which are additionally stabilized by the C-H $\cdots\pi$ interactions, as shown in Fig. 4a. The more numerous $\mathbf{B}\cdots\mathbf{B}$ contacts are realized mainly via two different types of the centrosymmetric bonds and additional C(3B)–H(3BC)···O(3B)^{vi} interactions, as shown in Fig. 4b. The respective $\mathbf{A}\cdots\mathbf{A}$ and $\mathbf{B}\cdots\mathbf{B}$ connections are formed in *bc* plane and result in two types of "layers" parallel to (100) plane: at x = 1/2, 3/2,..., and at x = 0, 1,... for "layer" A and "layer" B, respectively. The inter-layer contacts are provided by the $\mathbf{A}\cdots\mathbf{B}$ interactions, which are C(8A)- $H(8A)\cdots N(9B)$, $C(8B)-H(8B)\cdots O(4A)$ and C(1B)- $H(1BC)\cdots O(2A)^{viii}$ bonds, as shown in Fig. 4c, giving rise to a three-dimensional network of interactions in the crystal of Z-16a.

The molecules of **E-16a** in its crystal interact with each other via centrosymmetric $C(8)-H(8)\cdots O(3)^{iii}$ and $C(10)-H(10)\cdots O(2)^{ix}$ bonds (Table 2) and $\pi\cdots\pi$: $Cg(1)\cdots Cg(2)^{ix}$ and $Cg(2)\cdots Cg(2)^{ix}$ stacking interactions (Table 3) to form ribbons running down the *a*-axis, shown in Fig. 5. Weaker C-H···O contacts provide the inter-layer interactions and additional stabilization of a three-dimensional crystal structure of **E-16a**.

Conclusion

In conclusion, we have developed a convenient, one-pot regio- and stereoselective method for preparing electronpoor imidazoles 8(a-b) and 16(a-b) utilising in situ generation of the phosphonium salts. The crystal structures for both Z and E isomers of 16a as well as for 8a have been determined. The influence of the phenyl group and its orientation with respect to the double bond on the molecular geometry has been discussed. Compound

D–H···A

 Table 2 Geometry of proposed
C-H···O/N close contacts for

8a, Z-16a and E-16a	8a	$C(1)-H(1B)\cdots O(2)$	0.99(2)	2.30(2)	2.713(2)	104(2)
		$C(1)-H(1C)\cdots O(3)^{i}$	0.97(2)	2.68(2)	3.607(2)	162(2)
		C(3)–H(3B)····O(2)	0.97(2)	2.35(2)	2.771(2)	105(2)
		C(8)– $H(8)$ ···· $O(6)$ ^{<i>ii</i>}	0.97(2)	2.37(2)	3.278(2)	156(2)
		C(10)–H(10A)····O(2) ⁱⁱⁱ	0.98(2)	2.64(2)	3.173(2)	115(2)
		C(10)–H(10A)····O(3) ⁱⁱ	0.98(2)	2.46(2)	3.264(2)	140(2)
		$C(10)-H(10B)\cdots N(9)^{iv}$	0.97(2)	2.50(2)	3.388(2)	152(2)
		$C(18)-H(18B)\cdots O(6)^{\nu}$	0.92(2)	2.46(2)	3.379(2)	176(2)
	Z-16a	$C(1A)-H(1AB)\cdots O(6A)$	1.00(3)	2.28(3)	2.755(4)	108(2)
		$C(3A)-H(3AA)\cdots O(3A)^{vi}$	0.99(3)	2.35(3)	3.269(4)	154(2)
		$C(3A)-H(3AC)\cdots N(9A)$	0.95(2)	2.56(2)	2.944(4)	104(2)
		C(8A)– $H(8A)$ ···N(9B)	1.02(2)	2.40(2)	3.382(4)	160(2)
		C(10A)-H(10A)···O(4A)	0.98(2)	2.40(2)	2.760(3)	101(2)
		$C(10A)-H(10A)\cdots O(6A)^{iii}$	0.98(2)	2.36(2)	3.320(4)	168(2)
		$C(12A)-H(12A)\cdots O(6A)^{iii}$	1.00(3)	2.63(3)	3.535(4)	151(2)
		C(16A)-H(16A)N(7A)	1.01(2)	2.43(2)	3.062(4)	120(2)
		$C(19A)-H(19B)\cdots O(3A)^{vii}$	1.02(3)	2.65(3)	3.617(4)	159(2)
		$C(1B)-H(1BB)\cdots O(2B)$	1.02(3)	2.26(3)	2.716(4)	106(2)
		$C(1B)-H(1BC)\cdots O(2A)^{viii}$	0.96(3)	2.50(3)	3.122(4)	122(2)
		$C(3B)-H(3BD)\cdots N(9B)$	0.98	2.53	2.934(4)	105
		$C(3B)-H(3BC)\cdots O(3B)^{vi}$	0.98	2.28	3.256(3)	172
		$C(3B)-H(3BA)\cdots O(2B)$	0.98	2.34	2.750(3)	104
		$C(3B)-H(3BF)\cdots N(1B)^{ix}$	0.98	2.50	3.421(3)	157
		$C(8B)-H(8B)\cdots O(4A)$	1.04(2)	2.35(2)	3.339(3)	158(2)
		$C(10B)-H(10B)\cdots O(4B)$	0.97(3)	2.36(2)	2.743(3)	103(2)
		$C(10B)-H(10B)\cdots O(6B)^{x}$	0.97(3)	2.45(3)	3.399(4)	164(2)
		$C(12B)-H(12B)\cdots O(6B)^{x}$	0.94(2)	2.64(2)	3.499(4)	151(2)
		$C(13B)-H(13B)\cdots O(2B)^{xi}$	1.00(3)	2.68(3)	3.625(4)	157(2)
		$C(14B)-H(14B)\cdots N(1B)^{xi}$	1.01(3)	2.70(3)	3.460(4)	133(2)
		$C(15B)-H(15B)\cdots O(2B)^{ix}$	1.01(3)	2.52(3)	3.255(4)	130(2)
Symmetry codes: (i) $-x + 3/2$,		$C(16B)-H(16B)\cdots N(7B)$	0.99(2)	2.42(2)	3.053(4)	121(2)
$y - \frac{1}{2}, -z + \frac{1}{2}; (ii) - x + \frac{3}{2}$		$C(16B)-H(16B)\cdots O(2B)^{tx}$	0.99(2)	2.67(3)	3.314(4)	123(2)
2, $y + 1/2$, $-z + 1/2$; (<i>ui</i>) - $x + 1 - y + 1 - z + 1$; (<i>iv</i>)		$C(19B)-H(19E)\cdots O(3B)^{vu}$	0.98	2.66	3.560(8)	154
x - 1/2, -y + 3/2, z - 1/2;	<i>E</i> -16a	$C(1)-H(1B)\cdots O(6)$	0.96(2)	2.31(2)	2.757(2)	108(2)
(v) -x + 1, -y + 1, -z; (vi) x,		$C(3)-H(3A)\cdots N(9)$	1.00(2)	2.50(2)	2.955(2)	107(1)
$-y + \frac{1}{2}, z + \frac{1}{2}; (vii) x,$		$C(3)-H(3B)\cdots O(2)^{xu}$	0.95(2)	2.66(2)	3.502(2)	147(2)
-y + 1/2, z - 1/2, (viii) x - 1, y, z - 1; (ix) -x, -y + 1,		$C(8)-H(8)\cdots O(3)^m$	0.96(2)	2.38(2)	3.133(2)	135(1)
-z + 1; (x) - x, -y + 1, -z;		$C(10)-H(10)\cdots O(2)^{tx}$	0.99(2)	2.43(2)	3.360(2)	157(1)
(xi) - x, y + 1/2, -z + 1/2;		$C(13)-H(13)\cdots O(3)^{xu}$	0.96(2)	2.66(2)	3.287(2)	124(1)
(xii) -x, -y, -z + 1; (xiii) x, y + 1, z; (xiv) - x + 1		$C(14)-H(14)\cdots O(3)^{xu}$	0.98(2)	2.66(2)	3.297(2)	123(1)
-y + 2, -z		$C(18)-H(18A)\cdots O(4)^{\lambda l \nu}$	0.95(2)	2.65(2)	3.334(2)	129(1)

D-H (Å)

H···A (Å)

D···A (Å)

Experimental

Melting points were measured on an Electrothermal 9100 apparatus and are uncorrected. Elemental analyses were performed using a Heraeus CHN-O-Rapid analyzer. IR spectra were recorded on a Shimadzu IR-460 spectrometer. ¹H and ¹³C NMR spectra were measured with a Bruker Spectrospin spectrometer at 250 and 62.5 MHz, respectively.

Preparation of Alkyl 2-(1,3-dimethyl-2,6-dioxo-1,2,3, 6-tetrahydro-7H-purin-7-yl)acrylate (8(a-b))

To a magnetically stirred solution of triphenylphosphine (0.262 g, 1 mmol) and theophylline (0.18 g, 1 mmol) in dichloromethane (5 mL) was added dropwise a mixture of alkyl acetylenecarboxylates 2 (1 mmol) in dichloromethane (2 mL) at -10 °C over 15 min. The mixture was

 $D-H\cdots A$ (°)

Compound	$C-H\cdots\pi/\pi\cdots\pi$	C-H (Å)	$H\cdots\pi$ (Å)	$\begin{array}{c} \mathbf{C} \cdots \boldsymbol{\pi} \ (\mathbf{\mathring{A}}) \\ \boldsymbol{\pi} \cdots \boldsymbol{\pi} \ (\mathbf{\mathring{A}}) \end{array}$	C–Η····π (°)
8a	$C(3)-H(3A)\cdots Cg(1)^{x\nu}$	0.98(2)	2.70(2)	3.539(2)	144(2)
	$Cg(2)\cdots Cg(2)^{iii}$	-	_	3.557(2)	_
Z-16a	$C(3A)-H(3AB)\cdots Cg(2A)^{xvi}$	0.98(3)	2.85(3)	3.550(4)	130(2)
	$C(16A)-H(16A)\cdots Cg(1A)$	1.01(2)	2.64(2)	3.522(3)	146(2)
	C(18A)– $H(18A)$ ···· $Cg(3A)$ ⁱⁱⁱ	1.00(3)	2.67(3)	3.595(4)	154(2)
	$C(16B)-H(16B)\cdots Cg(1B)$	0.99(2)	2.58(2)	3.452(3)	148(2)
	$C(18C)-H(18E)\cdots Cg(3B)^{x}$	0.99	2.77	3.413(8)	123
<i>E</i> -16a	$C(13)-H(13)\cdots Cg(2)^{xiii}$	0.96(2)	2.80(2)	3.550(2)	136(2)
	$Cg(1)\cdots Cg(2)^{ix}$	-	-	3.560(2)	_
	$Cg(2)\cdots Cg(2)^{ix}$	_	_	3.595(2)	-

Table 3 Geometry of proposed C-H··· π and π ··· π interactions for 8a, Z-16a and E-16a

Symmetry codes: (iii) -x + 1, -y + 1, -z + 1; (ix) -x, -y + 1, -z + 1; (x) -x, -y + 1, -z; (xiii) x, y + 1, z; (xv) -x + 2, -y + 1, -z + 1; (xvi) -x + 1, -y + 1, -z + 2; Cg(1), Cg(2) and Cg(3) are the centroids of C(4) ~ N(9), N(1) ~ C(6) and C(11) ~ C(16) rings, respectively



Fig. 2 Comparison of molecular structures of compounds **8a** (*thin line*), *E***-16a** (*open line*) and **Z-16a** (two crystallographically independent molecules shown with *solid line*) [A least-squares fit using the OFIT instruction in XP program; the common reference points are N(7), C(7) and C(10) atoms.]

allowed to warm up to room temperature. Silica gel powder (1.5 g) was added and the solvent was evaporated. Dry silica gel and the residue were heated for 1 h at 90 °C and then placed over a column of silica gel powder (12 g). The column chromatography was washed using ethyl acetate-light petroleum ether (3:10) as eluent. The solvent was removed under reduced pressure and the products were obtained as colorless crystals.

Selected Data for Methyl 2-(1,3-dimethyl-2,6-dioxo-1,3,3,6-tetrahydro-7H-purin-7-yl)acrylate (**8a**)

Colorless crystals. Yield: 0.238 g (90%). mp 160–163 °C. IR (KBr): v = 2953, 1707, 1669, 1453, 1230 cm⁻¹. ¹H NMR (CDCl₃): $\delta_H = 3.36$, 3.60 (2s, 6H, 2CH₃); 3.86 (1s, 3H, OCH₃); 5.99–6.51 (d of d, 2H, ² $J_{HH} = 1$ Hz, =CH₂);



Fig. 3 Arrangement of the molecules **8a** in the crystal lattice showing two adjacent helical chains along *b*-axis (*solid* and *open lines*) interacting with each other via C–H···O/N contacts (*dashed lines*) to form layers parallel to $(10\overline{1})$ plane. Symmetry codes are given in Table 2

7.63 (1s, 1H, imidazole). ¹³C NMR (CDCl₃): $\delta_C = 28.07$ and 29.66 (2CH₃); 53.23 (OCH₃); 107.94, 133.39 and 148.74 (3C); 123.69 (=CH₂); 140.95 (CH imidazole); 151.60 and 154.47 (2C=O of amide); 162.33(C=O of ester). C₁₁H₁₂N₄O₄ (264.24): calcd. C, 50.00; H, 4.58; N, 21.20; found C, 49.96; H, 4.55; N, 21.17.

Preparation of Single Crystals of Methyl 2-(1,3-dimethyl-2,6-dioxo-1,3,3,6-tetrahydro-7H-purin-7-yl)acrylate (**8a**)

Colorless single crystals of **8a** were obtained from slow evaporation of its dichloromethane/light petroleum ether



Fig. 4 Three types of intermolecular interactions in **Z-16a**: *a* between **A** molecules, *b* between **B** molecules, and *c* between **A** and **B** molecules. C–H···O/N contacts are shown with *dashed lines*, $\pi \cdots \pi$ stacking interactions with *dashed open*. Intramolecular contacts are not shown for clarity. Symmetry codes are given in Table 2

(1:3) solution (20–25 °C). The colorless single crystals were filtered off, washed with a cold mixture of dichloromethane/light petroleum ether (1:3) and dried at room temperature (mp 160–163 °C).

Selected Data for Ethyl 2-(1,3-dimethyl-2,6-dioxo-1,3,3,6-tetrahydro-7H-purin-7-yl)acrylate (**8b**)

Colorless crystals. Yield: 0.236 g (85%); mp143–146 °C IR (KBr): v = 2984, 1715, 1676, 1453, 1230 cm⁻¹. ¹H NMR (CDCl₃): $\delta_H = 1.27$ (1t, 3H, ³ $J_{HH} = 7.25$ Hz, CH₃); 3.38, 3.62 (2s, 6H, 2CH₃); 4.29 (q, 2H, ³ $J_{HH} = 7$ Hz, OCH₂); 5.99–6.52 (d of d, 2H, ² $J_{HH} = 1$ Hz, =CH₂); 7.63 (1s, 1H, imidazole). ¹³C NMR (CDCl₃): $\delta_C = 14.04$, 28.07 and 29.66 (3CH₃); 62.55 (OCH₂); 107.97, 133.62 and 148.73 (3C); 123.42 (=CH₂); 141 (CH imidazole); 151.64



03ⁱⁱⁱ

Fig. 5 Arrangement of the molecules *E***-16a** within the ribbon along *a*-axis formed by the centrosymmetric C–H···O bonds (*dashed lines*) and π ··· π stacking interactions (*dashed open*). Symmetry codes are given in Table 2

C10^D

and 154.46 (2C=O of amide); 161.82 (C=O of ester). $C_{12}H_{14}N_4O_4$ (278.26): calcd C, 51.80; H,5.07; N,20.13; found C,51.77; H,5.03; N,20.11.

Selected Data for Ethyl (Z,E)-2-(1,3-dimethyl-2, 6-dioxo-1,3,3,6-tetrahydro-7H-purin-7-yl)-3-phenyl-2-peropenoate (**16a**)

Colorless crystals. Yield: 0.343 g (97%); mp: 145-148 °C. IR (KBr): v = 2946, 1707, 1661, 1453, 1269 cm⁻¹. ¹H NMR (CDCl₃, % E = 40 and % Z = 60) for Z: $\delta_H = 1.28$ $(1t, 3H, {}^{3}J_{HH} = 7 \text{ Hz}, \text{CH}_{3}); 3.31 \text{ and } 3.58 (2s, 6H, 2CH_{3});$ 4.29 (q, 2H, ${}^{3}J_{HH} = 7$ Hz, OCH₂); 6.93(d, 2H, ${}^{3}J_{HH} = 7.25$ Hz, arom); 7.20–7.29 (m, 3H, arom); 7.40 (1s, 1H, imidazole); 7.89 (1s, 1H, =CH); ¹³C NMR (CDCl₃) for Z: $\delta_C = 14.13$, 27.95 and 29.91 (3CH₃); 62.28 (OCH₂); 129.11, 129.70, 130.90, 138.66 and 141.19 (7CH); 107.39, 123.77, 131.06 and 148.68 (5C); 151.64 and 154.24 (2C=O of amide); 163.10 (C=O of ester). ¹H NMR (CDCl₃, % E = 40 and % Z = 60) for *E*: $\delta_H = 1.59$ (1t, 3H, ${}^{3}J_{HH} = 7.25$ Hz, CH₃); 3.40 and 3.65 (2s, 6H, 2CH₃); 4.25 (q, 2H, ${}^{3}J_{HH} = 7$ Hz, OCH₂); 7.30(1s, 1H, =CH); 7.34– 7.77 (m, 5H, arom); 7.81 (1s, 1H, imidazole); ¹³C NMR (CDCl₃) for E: $\delta_C = 13.55,28.07$ and 29.90 (3CH₃); 62.02 (OCH₂); 128.38, 129.70, 131.98, 132.14 and 141.58 (7CH); 107.96, 125.96, 137.02 and 148.75 (4C); 151.61 and 154.50 (2C=O of amide); 162.75 (C=O of ester). C₁₈H₁₈N₄O₄ (354.13): calcd C, 61.01; H, 5.12; N, 15.81; found C, 60.07; H, 5.08; N, 15.78.

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Preparation of Single Crysta	als Of Ethyl (Z,E)-2-
(1,3-dimethyl-2,6-dioxo-1,3	,3,6-tetrahydro-7H-purin-
7-yl)-3-phenyl-2-peropenoat	te (16a)

Colorless single crystals of **16a** were obtained from slow evaporation of its dichloromethane/light petroleum ether (1:2) solution (20–25 °C). The colorless single crystals were filtered off, washed with a cold mixture of dichloromethane/light petroleum ether (1:2) and dried at room temperature (mp 145–148 °C).

Selected Data for Dimethyl (Z,E)-2-(1,3-dimethyl-2, 6-dioxo-1,2,3,6-tetrahydro-7H-purin-7-yl)butenedioate

Viscous yellow oil, Yield: 0.258 g 80% IR (Neat): v = 3115, 2953, 1715, 1669, 1230 and 1276. ¹H NMR (CDCl₃, %*E* = 21 and %*Z* = 79) for *Z*: $\delta_H = 3.32$ and 3.60 (2s, 6H, 2CH₃), 3.69 and 3.83 (2s, 6H, 2OCH₃), 7.67 (1s, 1H, =CH), 7.11 (1s, 1H, imidazole). ¹³C NMR (CDCl₃) for *Z* δ_C : 28.03 and 30.03 (2CH₃), 52.67 and 53.88 (2OCH₃), 102.84, 134.19 and 148.47 (3C), 125.43 (=CH),

Table 4 Experimental data for 8a, Z-16a and E-16a

	8a	Z-16a	<i>E</i> -16a
Empirical formula	$C_{11}H_{12}N_4O_4$	$C_{18}H_{18}N_4O_4$	C ₁₈ H ₁₈ N ₄ O ₄
Formula weight (g mol ⁻¹)	264.25	354.36	354.36
Crystal system	Monoclinic	Monoclinic	Triclinic
Space group	$P2_1/n$	$P2_1/c$	$P\overline{1}$
a (Å)	8.679(2)	16.372(3)	9.531(3)
b (Å)	10.799(3)	17.305(3)	9.593(2)
c (Å)	12.356(3)	13.147(3)	10.776(3)
α (°)			67.93(3)
β (°)	94.10(3)	111.67(3)	68.93(3)
γ (°)			86.48(3)
$V(\text{\AA}^3)$	1155.1(5)	3461.5(12)	848.9(4)
Ζ	4	8	2
$D_{\rm calc} \ ({\rm g \ cm}^{-3})$	1.519	1.360	1.386
$\mu (\mathrm{mm}^{-1})$	0.12	0.10	0.10
<i>F</i> (000)	552	1488	372
Crystal size (mm)	$0.32 \times 0.13 \times 0.10$	$0.25 \times 0.22 \times 0.11$	$0.60 \times 0.33 \times 0.14$
Crystal colour	Colourless	Colourless	Colourless
Crystal form	Needle	Block	Plate
Radiation type, λ (Å)	Μο Κα, 0.71073	Μο Κα, 0.71073	Μο Κα, 0.71073
<i>T</i> (K)	100(2)	100(2)	100(2)
θ Range (°)	2.78-36.87	2.88-27.00	3.39-37.49
h, k, l range	$-14 \le h \le 14$	$-16 \le h \le 20$	$-15 \le h \le 13$
	$-15 \le k \le 18$	$-22 \le k \le 21$	$-15 \le k \le 16$
	$-20 \le l \le 20$	$-16 \le l \le 16$	$-18 \le l \le 17$
Measured reflections	20051	24094	12510
Independent reflections	5372	7549	6793
Observed reflections $(I > 2\sigma(I))$	3098	3961	4039
R _{int}	0.047	0.067	0.029
Refinement on	F^2	F^2	F^2
Data/restraints/parameters	5372/0/220	7549/9/598	6793/0/307
$R_1; wR_2 (F_o^2 > 2\sigma(F_o^2))$	0.044; 0.106	0.069; 0.100	0.045; 0.101
R_1 ; wR_2 (all data)	0.098; 0.140	0.159; 0.116	0.081; 0.108
GooF = S	1.034	1.022	1.009
Weighting parameter a; b	0.0699; 0.0695	0.0374; 0.0	0.0480; 0.0
$\Delta \rho_{\rm max}; \ \Delta \rho_{\rm min} \left({\rm e} {\rm \AA}^{-3} \right)$	0.51; -0.28	0.20; -0.24	0.44; -0.30

 $R_{1} = \sum_{c} ||F_{o}| - |F_{c}|| / \sum_{c} |F_{o}|; \quad wR_{2} = \sqrt{\sum_{c} [w(F_{o}^{2} - F_{c}^{2})^{2}] / \sum_{c} [w(F_{o}^{2})^{2}]}; \quad \text{weighting scheme:} \quad w = 1 / [\sigma^{2}(F_{o}^{2}) + (aP)^{2} + bP], \quad \text{where } P = (F_{o}^{2} + 2F_{c}^{2}) / 3$

142.44 (CH imidazole), 151.57 and 154.55 (2C=O of amid), 162.14 and 162.80 (2C=O of ester). ¹H NMR (CDCl₃, %*E* = 21 and %*Z* = 79) for *E*: δ_H = 3.35 and 3.58 (2s, 6H, 2CH₃), 3.78 and 3.83 (2s, 6H, 2OCH₃), 6.64 (1s, 1H, =CH), 7.72 (1s, 1H, imidazole). ¹³C NMR (CDCl₃) for *E* δ_C = 28.26 and 30.03 (2CH₃), 52.72 and 53.64 (2OCH₃), 104.02, 134.19 and 148.47 (3C), 123.03 (=CH), 141.11 imidazole), 151.57 and 154.55 (2C=O of amid), 162.14 and 162.80 (2C=O of ester). C₁₃H₁₄N₄O₆ (322.27): C, 48.45; H, 4.38; N, 17.38; O, 29.79; found: C, 48.40; H, 4.33; N, 17.35; O, 29.75.

X-Ray Crystallography

The crystallographic measurements of 8a, Z-16a and **E-16a** were performed on a κ -geometry KUMA KM4CCD automated four-circle diffractometer with graphite-monochromatized MoK α radiation (λ , 0.71073 Å). The data for the crystals were collected at 100(2) K by using the Oxford-Cryosystems cooler. The data were corrected for Lorentz and polarization effects. Data collection, cell refinement, and data reduction and analysis were carried out with the KUMA KM4CCD software (Oxford Diffraction Ltd.): CrysAlis CCD and CrysAlis RED, respectively [26]. The structures were solved by direct methods with the SHELXS-97 program [27], and refined by a full-matrix least-squares technique with SHELXL-97 [27] and anisotropic thermal parameters for non-H atoms. The ester ethyl group in the molecule **B** of **Z-16a** is disordered over two sites with s.o.f. = 0.53(2) for C(18B), C(19B) and 0.47(2)for C(18C), C(19C). Geometrical restraints (SAME instructions) were applied to the disordered region, and the two positions of atom O(4) in **B** [O(4B) and O(4C)] were constrained (using EXYZ and EADP) to have the same positional and displacement parameters. All H atoms were found in difference Fourier maps, which showed that the methyl H atoms on atom C(3B) in Z-16a were disordered equally over two sites, therefore this methyl group was refined with AFIX 127 instruction. H atoms in the disordered regions of molecule B in Z-16a were treated as riding atoms, with C-H distances of 0.98-0.99 Å, and with $U_{iso}(H)$ values of $1.2U_{iso}(C)$ for CH₂ groups and $1.5U_{iso}(C)$ for CH₃ groups. The remaining H atoms in 8a, Z-16a and E-16a were refined isotropically. Figures were made with the XP program [28]. A summary of the conditions for the data collection and the structure refinement parameters are given in Table 4. Further details on the crystal structures investigations may be obtained from The Cambridge

Crystallographic Data Centre via www.ccdc.cam.ac.uk/ data_request/cif by quoting the deposition numbers CCDC-809464 (for 8a), CCDC-809465 (for Z-16a) and CCDC-809466 (for *E*-16a).

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