Formation of an optically active 2-phenyl[1,2,4]triazolo[1,5-*a*]pyrimidine derivative in the reaction of (+)-3-carene-derived β-chlorovinylketone with benzylidene aminoguanidine

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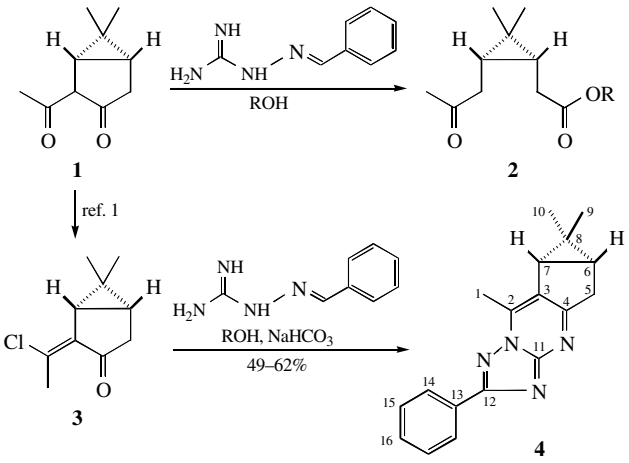
The treatment of a *seco*-carane-type β-chlorovinyl ketone with benzylidene aminoguanidine in boiling methanol in the presence of sodium bicarbonate results in the formation of a substituted 2-phenyl[1,2,4]triazolo[1,5-*a*]pyrimidine.

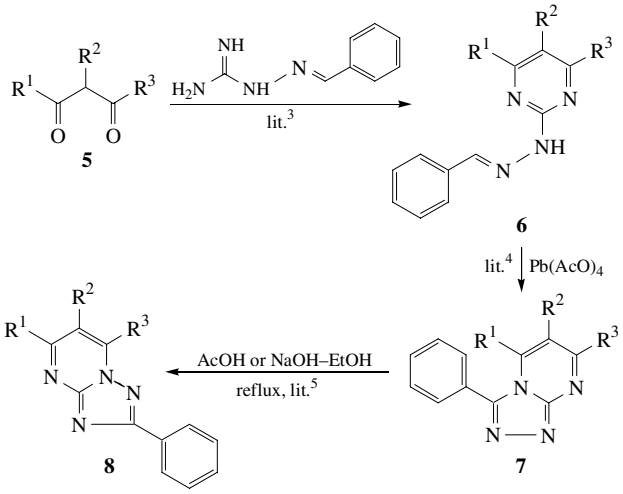
To synthesise optically active polyfunctionalised heterocycles (chiral polydentate ligands), we studied the reaction of benzylidene aminoguanidine with β-diketones and β-chlorovinyl ketones prepared from (+)-3-carene.[1] The main reaction product of the reaction of benzylidene aminoguanidine (and amidines as well[1]) with diketone **1** in methanol or ethanol was found to be *ω*-ketoester **2** formed by retro-condensation. At the same time, the treatment of chlorovinyl ketone **3** with benzylidene aminoguanidine in boiling methanol in the presence of sodium bicarbonate for 5 h resulted in the formation of 2-phenyl[1,2,4]tiazolo[1,5-*a*]pyrimidine derivative **4** in 49% yield (Scheme 1).† The bubbling of air into the reaction mixture (*ca.* 1 dm^3 min^{-1}) resulted in a shortening of the reaction time (from 5 to 2 h) and an increase in the yield of the final product (49 → 62%).

The molecular structure of new compound **4**‡ was solved by X-ray crystallography (Figure 1).§ Within experimental errors, the bond lengths of the 1,2,4-triazolo[1,5-*a*]pyrimidine framework are the same as the values averaged over nine structures with the same fragment extracted from the Cambridge Structural Database.[2]

The formation of compound **4** in the reaction of chlorovinyl ketone **3** is unusual and unpredictable due to the following reasons: the reaction of β-dicarbonyl compounds **5** with benzylidene aminoguanidine is known to lead to the derivatives of benzylidene 2-hydrazinopyrimidine **6**, which are stable[3] and



Scheme 1 The numbering of the carbons shown on the scheme does not coincide with the numbering of the system according to IUPAC and is given for NMR interpretation only.

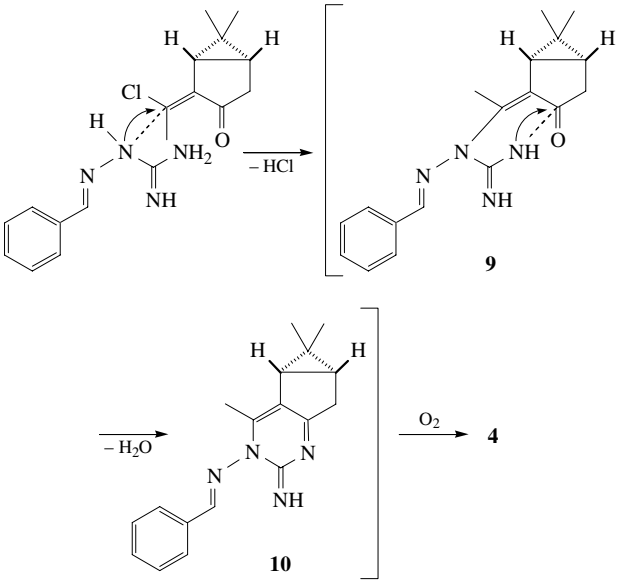


Scheme 2

† Benzylidene aminoguanidine (2.0 g, 1.2 mmol) and $NaHCO_3$ (1.0 g, 1.2 mmol) were added to a solution of chlorovynyl ketone **3** (1.0 g, 5.4 mmol) in MeOH (25 ml), and the reaction mixture was stirred with reflux for 5 h. The solvent was removed in a vacuum, and the residue was treated with water (50 ml) and extracted with $CHCl_3$ (2×30 ml). The combined organic extracts were washed with 1 M H_2SO_4 (30 ml), dried (Na_2SO_4) and concentrated at a reduced pressure to give a crude product, which was chromatographed (SiO_2, EtOAc) and crystallised to give 0.76 g (49%) of compound **4**.

‡ *(1a*S*,7a*R*)-1,1,2-Trimethyl-4-phenyl-1,1a,7,7a-tetrahydro-2a,3,5,6-tetraazacyclopropa[a]-s-indacene* **4**: yellowish crystals, mp 200–202 °C (PrⁱOH), $[\alpha]_{578}^{20}$ –26 (*c* 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) *δ*: 2.78 (s, 3H, H-1), 2.96 (ddd, 0.7 and 0.7 1H, H-5a, *J* 19.4 Hz), 3.28 (dd, 1H, H-5b, *J* 19.4 and 7.3 Hz), 1.75 (ddd, 1H, H-6, *J* 7.3, 6.9 and 0.7 Hz), 2.17 (dd, 1H, H-7, *J* 6.9 and 0.7 Hz), 1.20 (s, 3H, H-9), 0.70 (s, 3H, H-10), 8.30 (m, 2H, H-14, H-18), 7.39–7.46 (m, 3H, H-15,16,17). ^{13}C NMR (125 MHz) *δ*: 14.35 (C-1), 164.33 (C-2), 131.00 (C-3), 173.82 (C-4), 34.13 (C-5), 26.40 (C-6), 30.43 (C-7), 22.78 (C-8), 27.44 (C-9), 14.22 (C-10), 156.61 (C-11 or C-12), 141.12 (C-12 or C-11), 123.77 (1C, aromatic carbon), 127.11 (2C, aromatic carbons), 128.38 (2C, aromatic carbons), 129.84 (1C, aromatic carbon). IR ($CHCl_3$, *ν*/cm^{-1}): 1637, 1543, 1523, 1456, 1444, 1434, 1378, 1366, 1323, 11301, 1284, 1205, 1173, 1136, 1069, 1042, 1025. UV [EtOH, λ_{max}/nm^{-1} (*ε*)]: 251 (30110), 312 (1260). MS, *m/z* (%): 290.15342 (M$^+$, 65%, $C_{18}H_{18}N_4$ requires 290.15314), 275 (100), 260 (3), 248 (16), 157 (6), 104 (6), 91 (4), 77 (9), 65 (2), 51 (2).

§ *Crystallographic data for compound* **4**: $C_{18}H_{18}N_4$, *M* = 290.36, crystal class orthorhombic, space group $P2_12_12_1$, *a* = 5.8715(6), *b* = 14.570(2) and *c* = 18.038(3) Å, *V* = 1543.1(3) Å^3, *Z* = 4, d_{calc} = 1.250 mg cm^{-3}, *μ* = = 0.077 mm^{-1}, *λ* = 0.71073 Å, crystal size of 0.22×0.22×1.35 mm. A Bruker P4 diffractometer with graphite-monochromated MoKα radiation was used to measure the unit cell dimensions and to collect data (*θ*/2*θ* scans, 2*θ* < 50°). Absorption corrections were applied by the integration method (transmission 0.9811–0.9886). The structure was solved by direct methods and refined by a full matrix least-squares anisotropic–isotropic (for H atoms) procedure using the SHELXL97 program. The hydrogen atom positions were obtained geometrically and refined using a riding model. The final indexes are wR_2 = 0.1166, *S* = 1.237 for all 1595 F^2 and R_1 = 0.0429 for 1352 $F_o > 4\sigma$. The absolute structure parameter (Flack parameter) is equal to 7(5). Atomic coordinates, bond lengths, bond angles and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre (CCDC). For details, see 'Notice to Authors', *Mendeleev Commun.*, Issue 1, 2002. Any request to the CCDC for data should quote the full literature citation and the reference number 1135/119.



Scheme 3

can be oxidised to 3-phenyl[1,2,4]triazolo[4,3-*a*]pyrimidines **7** (Scheme 2).[4] The oxidation of 2-hydrazinopyrimidines **6**, prepared from non-symmetric β-diketones, with a strong oxidising agent like $Pb(OAc)_4$ could result in a pair of regioisomeric 3-phenyl-[1,2,4]triazolo[4,3-*a*]pyrimidines **7**. Compounds **7** can undergo the Dimroth-type rearrangement to form 2-phenyl-[1,2,4]triazolo[1,5-*a*]pyrimidines **8**, although severe reaction conditions are required for the rearrangement to take place (boiling acetic acid or alkali alcohol).[5] The Dimroth-type rearrangement seems unlikely under the reaction conditions of the transformation **3** → **4** ($NaHCO_3$, boiling methanol). Thus, we assume that the formation of compound **4** is described by Scheme 3. According to Scheme 3, enaminocarbonyl-type derivative **9** is formed due to the primary attack of the carbon–carbon double bond of the chlorovinyl ketone with the hydrazine nitrogen followed by intramolecular condensation and subsequent oxidation of compound **10** with atmospheric oxygen to afford final compound **4**.

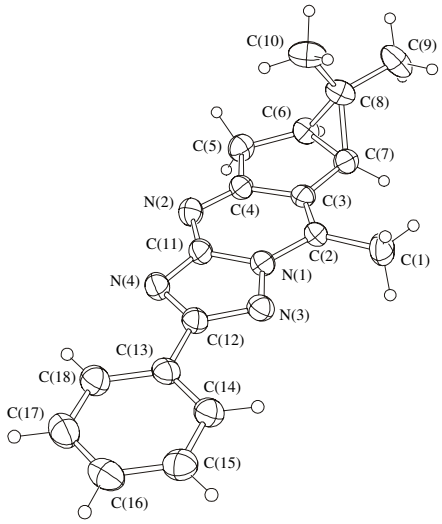


Figure 1 Molecular structure of compound **4** in a crystal. The almost planar tricyclic fragment (mean-square deviation of the atoms from the averaged plane is equal to 0.019 Å) forms a 66.4(2)° angle with cyclopropane plane and 5.4(1)° angle with phenyl plane.

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