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Synthesis and crystal structure of (E)-3-(2-methyl-1H-indol-3-yl)-1-(4-methylphenyl)propenone

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(*E*)-3-(2-Methyl-1*H*-indol-3-yl)-1-(4-methylphenyl)propenone has been prepared, and its crystal structure ($C_{19}H_{17}NO$, Mr = 275.34) has been determined by single-crystal X-ray diffraction analysis. The title compound crystallized in the triclinic system with space group P_1 and unit cell parameters: a = 9.4014 (5) Å, b = 9.8347 (4) Å, c = 10.0318 (5) Å, α = 62.821 (3)°, β = 85.539 (3)°, γ = 65.262 (3)° and Z = 2. The final reliability index is 0.053 for the 2807 observed reflections. The title compound is linked through N–H···O hydrogen bonds.

1. Introduction

The indole scaffold is a prominent and privileged structural motif found in numerous natural products and various synthetic compounds. Recently, a number of indole-containing compounds have revealed remarkable pharmacological activity and their utility as therapeutic agents has attracted considerable attention from chemists[1,2]. Libraries based on the indole scaffold have been developed to address the need for novel drugs with increased potency[3,4]. Subsequently, the development of efficient methods that allow rapid access to functionalized indoles with different substitution patterns (at C–2, C–3, N–atom, and aromatic ring) constitutes an emerging area[5].

Prompted by the above we recently reported an environment friendly $KHSO_4$-assisted Michael addition–elimination reactions of indole with 3-dimethylamino-1-phenylprop-2-en-1-ones in water that leads to the formation of 3-indolylchalcones. In this study we envisaged cyclisation of the indolylchalcones to give carbazole under the reaction conditions but unfortunately no trace of this product was formed. Confronted by this difficulty, we decided to study the details of the structure of **3** which held it back from cyclisation to give the envisaged carbazole **4** shown in **Scheme 1**.

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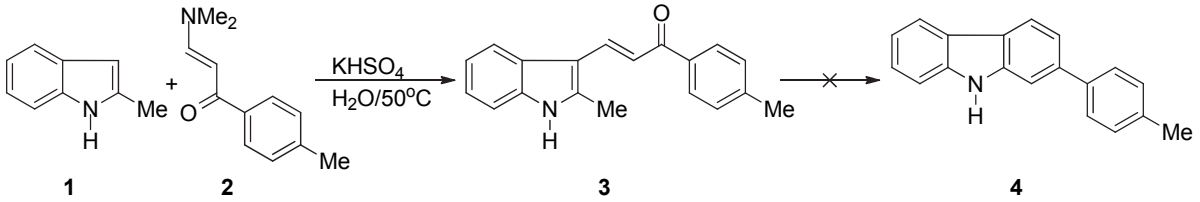

Scheme 1 Schematic diagram for synthesis of 3-(2-methyl-1H-indol-3-yl)-1-(4-methylphenyl)propenone

2. Results and Discussion

Crystal structure of **3** shows *E* configuration around the C10–C11 double bond (**Figure 1**). Also, the indole ring and the phenyl ring lies at different planes. Intermolecular hydrogen bonding is seen between N–H of indole ring and carbonyl O (**Figure 2**).The D—H···A angle is 140.7° while H···A distance is 2.007 Å (**Table 2**). The packing diagram (**Figure 3**) shows two chains connected via hydrogen bonding running anti-parallel in a ladder-like structure due to the alignment of the phenyl ring on the same side. Crystal data are given in **Table 1**.

Table. 1. Crystallographic data [CCDC 936083]

Crystal data	
Chemical formula	$C_{19}H_{17}NO$
M_r	275.34
Crystal system, space group	Triclinic, *P*1
Temperature (K)	296
a, *b*, *c* (Å)	9.4014 (5), 9.8347 (4), 10.0318 (5)
α, β, γ (°)	62.821 (3), 85.539 (3), 65.262 (3)
V (Å^3)	741.99 (6)
Z	2
Radiation type	Mo *K*a
μ (mm^{-1})	0.08
Data collection	
Diffractometer	CCD area dectector diffractometer
No. of measured, independent and	12402, 3374, 1743
R_{int}	0.033
Refinement	
$R[F^2 > 2s(F^2)]$, $wR(F^2)$, *S*	0.056, 0.206, 0.85
No. of reflections	3374
No. of parameters	202
No. of restraints	0
H-atom treatment	H atoms treated by a mixture of independent and
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.22, -0.20

Table. 2. Hydrogen Bonding Geometry (Å, °)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N1—HN1A···O1	0.890	2.007	2.879	140.7

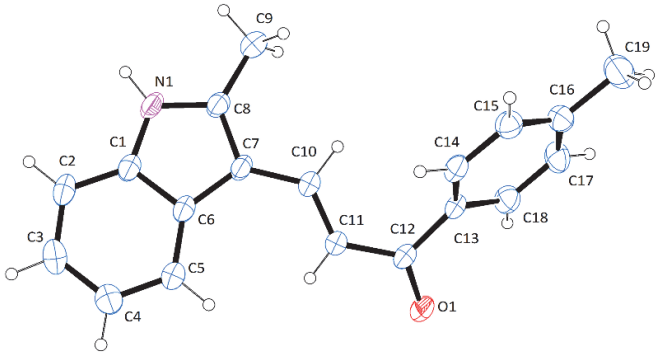

Fig. 1. ORTEP diagram of **3** drawn with 30 % ellipsoid probability with atom numbering scheme

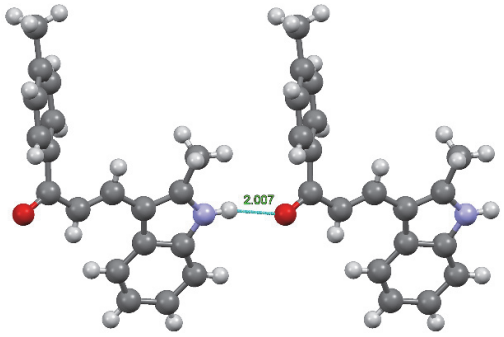

Fig. 2. Molecular structure of **3** showing intermolecular hydrogen bonding

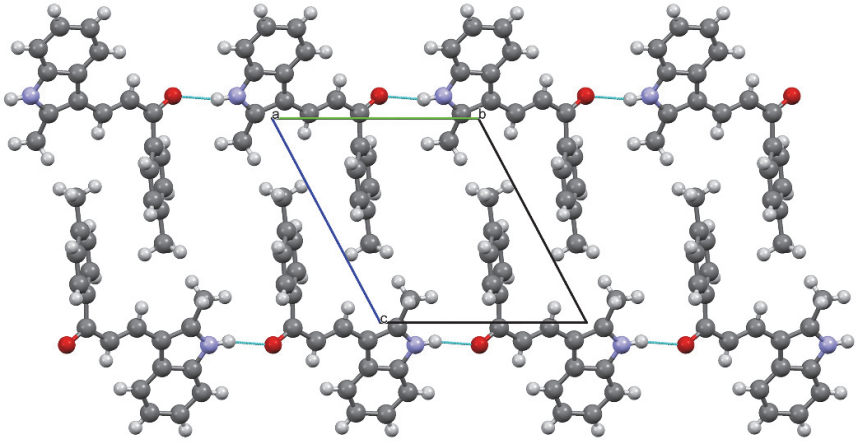

Fig. 3. Packing molecular structure of **3** along the *a* axis

3. Conclusions

X-ray studies of the product shows the existence of the chalcone in *E*-form with intermolecular hydrogen bonding between N-H of one unit and O of the other unit. Failure of cyclisation of the chalcone (**3**) to give the expected carbazole could be attributed to its unfavourable geometry.

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4. Experimental

4.1. Materials and Methods

Indole, 1-(*p*-tolyl)ethanone and DMF-DMA were purchased from ACROS Organics (99 %), Lancaster (97 %) and Spectrochem (99 %) respectively. $KHSO_4$ was bought from S. D. Fine-Chem Ltd (99 %). Ethyl acetate used for recrystallization was obtained from Merck (99 %). The reagents and chemicals procured were used without further purification.

Melting points were recorded by open capillary method and are uncorrected. The IR spectra were recorded on a Perkin–Elmer 983 spectrometer (Perkin–Elmer). ^{1}H and ^{13}C NMR spectra were recorded on Bruker ACF-300 spectrometer taking Me_4Si as the internal standard in $CDCl_3$. Data collection were carried out using Bruker SMART CCD area detector diffractometer with graphite monochromated Mo Kα radiation at 296 K. The structures were solved by direct methods (*SHELXS97*)[6] and refined by a full-matrix least-squares procedures based on F2(*SHELLXL97*)[6]. All calculations were carried out using *WinGX* system Ver-1.80.05. All non-hydrogen atoms were refined anisotropically; hydrogen atoms were located at calculated positions. The Structures were drawn using *ORTEP* and Mercury.

4.2. General procedure

Preparation of 3-(2-methyl-1*H*-indol-3-yl)-1-(4-methylphenyl)propenone
3-(2-Methyl-1*H*-indol-3-yl)-1-(4-methylphenyl)propenone was prepared using our previously reported method[7]. To a mixture of 1 mmol each of 2-methylindole and 3-(dimethylamino)-1-(*p*-tolyl)prop-2-ene-1-one suspended in 4 mL of water, 2 mmol of $KHSO_4$ was added and the resulting mixture was heated with stirring for 5 hr. On completion of the reaction (monitored by TLC), the oily product formed was extracted with CH_2Cl_2 (3 x 2 mL), the combined extract washed with water (3 x 2 mL), dried (Na_2SO_4) and the solvent distilled off to give a viscous mass which on trituration with hexane gave practically pure 3-(2-methyl-1*H*-indol-3-yl)-1-(4-methylphenyl)propenone. In order to obtain crystals of the product it was dissolved in a minimum quantity of ethyl acetate, filtered and the filtrate was allowed to cool slowly overnight when colourless crystals were obtained which were carefully collected by filtration followed by washing with ethyl acetate.

4.3 Physical and Spectral Data

M.p. 210 °C; IR (KBr): 3258, 1638, 1607, 1558 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.47 (s, 3H, CH_3), 2.61 (s, 3H, CH_3), 7.31 (m, 5H, 3H–indole and 2H–phenyl), 7.61 (d, 1H, J = 15Hz, H_α), 8.01 (m, 3H, H–indole and 2H–phenyl), 8.20 (d, 1H, J = 15 Hz, H_β), 8.69 (br s,1H, NH); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 12.5 (CH_3), 21.7 (CH_3), 110.7 (Cq), 111.1 (CH–indole),116.5 (CH-α), 120.3 (CH–indole), 121.6 (CH–indole), 122.7 (CH–indole), 126.4 (Cq),128.4 (2 CH–phenyl), 129.2 (2 CH–phenyl), 135.9 (Cq), 136.6 (Cq), 137.8 (CH-β), 141.4(Cq), 142.9 (Cq), 190.4 (CO); MS: m/z 276 (MH^+).

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