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Synthesis of 1-(2,4-Dinitrophenyl)-3,5-diphenyl-1*H*-pyrazol-4-ol via *trans*-1,3-Diphenyl-2,3-epoxy-1-propanone

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Abstract

The *trans*-1,3-diphenyl-2,3-epoxy-1-propanone was synthesized from benzaldehyde and 2-bromoacetophenone in 20 min which is more economical. The presence of ethanol and Br in 2-bromoacetophenone facilitated the reaction. The vicinal diaxial coupling constant of *trans*-1,3-diphenyl-2,3-epoxy-1-propanone was zero, an indication of *trans* configuration for a rigid 3-membered ring at ~90^{o} dihedral angle. 1-(2,4-Dinitrophenyl)-3,5-diphenyl-1*H*-pyrazol-4-ol was synthesized from *trans*-1,3-diphenyl-2,3-epoxy-1-propanone and 2,4-dinitro phenylhydrazine in glacial CH_3COOH to give 85.5% yield and characterized using FTIR, ^{1}H, ^{13}C NMR, DEPT 135 and MS spectra. The 1-(2,4-dinitrophenyl)-3,5-diphenyl-1*H*-pyrazol-4-ol can be exploited for unique biological activities and in the synthesis of synthetic fibers.

Keywords: 1-(2,4-dinitrophenyl)-3,5-diphenyl-1*H*-pyrazol-4-ol, *trans*-1,3-diphenyl-2,3-epoxy-1-propanone, synthesis, 2,4-dinitro phenylhydrazine.

Introduction

Chalcone epoxides are produced through Darzens reaction of *α*-halo carbonyl with aldehydes in a basic condition such as sodium hydroxide, lithium hydroxide, lithium carbonate, potassium carbonate, potassium hydroxide, sodium ethoxide, sodium amide, sodium *tert*-butoxide (Tanaka and Shiraishi 2001, Li and Li 2014, Preveena et al. 2015, Mphahlele et al. 2019). They are useful synthons in the synthesis of organic compounds through ring opening to produce C–C bond. Chalcone epoxides act as electrophiles due to their inherent polarity caused by the oxygen atom and strain in the three-membered epoxide ring responsible for the facile formation and higher reactivity toward nucleophiles. They react easily with various nucleophiles such as hydrazines, thiols, alcohols, amines or imines, hydroxylamines under nucleophilic substitution reactions to produce pyrazolines, furans, oxazolidines, pyrimidines, isoxazoles, quinolinones (Huo et al. 2013, Roman 2016, Mphahlele et al. 2019).

Pyrazoles resemble cyclic hydrazines with endocyclic double bonds. The pyrazoles are formed from the reactions of hydrazines with 1,3-diketones (Komendantova et al. 2020), *α, β*-unsaturated aldehydes and ketones (Ding et al. 2016, Zhu et al. 2020), enol-ethers (Tarabová et al. 2014) acetals (Lukicheva et al. 2018, Khatab et al. 2019), enamines (Duan et al. 2019), alkynes (Meng et al. 2019) under acidic conditions (Jiang et al. 2013, Akbari 2017), basic conditions (Girish et al. 2014) or neutral conditions (Wang et al. 2018) with a mixture or a regioisomer. Pyrazoles are synthesized from chalcone epoxides through chalcone oxidation, cyclization and aromatization (Bhat et al. 2005, Roman 2016, Bakthadoss and Surendar 2020, Farooq and Ngaini 2020). Pyrazoles are found to have

profound biological and pharmacological activities such as anti-microbial, anti-cancer, antileishmanial, anti-inflammatory, analgesic, anti-tubercular activities (Karrouchi et al. 2018, Costa et al. 2021).

The reactivity of chalcone epoxides towards nucleophiles as well as their facile transformation to heterocyclic compounds geared the synthesis of 1-(2,4-dinitrophenyl)-3,5-diphenyl-1*H*-pyrazol-4-ol which can be a novel compound with unique biological activities and also exploited in the synthesis of synthetic fibers.

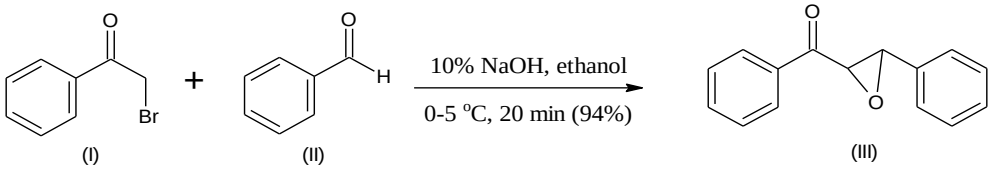
Materials and Methods

Analytical grade reagents were used. Melting points were determined uncorrected on Stuart SMP-10. Infrared spectra (ATR, IR) of the neat sample were recorded in transmittance on a CARY 630. IR spectra data were reported in frequency of absorption in cm^{-1} and were assigned as s, for strong; m, for medium; as, for asymmetry; and sy, for symmetry. NMR spectra data for ^{1}H, ^{13}C and the nature of C, CH, and CH_2 were determined by DEPT 135, and were recorded in HDO and $CDCl_3$ on a Bruker Avance DPX-500 spectrometer. The NMR signals were labelled as s (singlet), d (doublet), t (triplet), q (quartet), and m (multiplet). The molecular ion was determined using gas chromatography-mass spectrometry (GC-MS) of Multi-User Science Research Laboratory ABUZ.

Methods

Synthesis of *trans*-1,3-diphenyl-2,3-epoxy-1-propanone

To a mixture of NaOH (0.40 g, 0.01 mol), water (10 mL), ethanol (5 mL) in a conical flask, 2-bromoacetophenone (I) (1.99 g, 0.01 mol) was added and then benzaldehyde (II) (1.06 g, 0.01 mol) stirred 0-5 °C for 20 min. The solid formed was filtered and washed with distilled water and air-dried. The crude product was recrystallized from ethanol to give a pure trans-1,3-diphenyl-2,3-epoxy-1-propanone (**III**) (2.11 g, 94 %) (Ovonramwen et al. 2021) (Scheme 1).

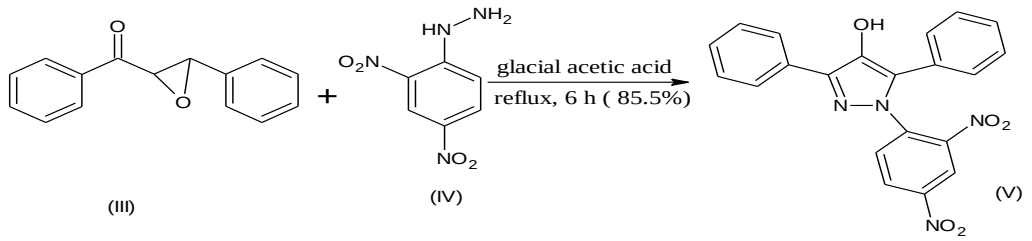


Scheme 1: Synthesis of *trans*-1,3-diphenyl-2,3-epoxy-1-propanone.

$C_{15}H_{12}O_2$: yield 94%; white crystals; m.p. 88-90 °C (lit 82-85 °C, Tanaka and Shiraishi 2001; 86-89 °C, Sigma-Aldrich 2021); R_f 0.75 ($CHCl_3$: Pet 3:7). FT-IR (ATR), *V*/cm^{-1}: 3019 (Aromatic C-H, str), 1685 (C=O, str), 1595, 1495 (C=C, str), 1409 (C=C, str), 1234 (C–H as *trans*-epoxide, str), 1111 (C–O–C, m), 1074, 1033, 939, 891 (C–H sy, *trans*-epoxide, str), 831 (epoxide), 753, 668, 693; ^{1}H NMR (500 MHz, $CDCl_3$), δ: 4.09 (d, H, CH*α*, *J* = 0 Hz), 4.33 (d, H, CH*β*, *J* = 0 Hz), 7.39-7.42 (m, 5 H, C_6H_5), 7.47-7.51 (t, 2 H, *m*-CO-C_6H_5, J_1 = 10 Hz, J_2 = 10 Hz), 7.61-7.63 (t, H, *p*-CO-C_6H_5, J_1 = 10 Hz, J_2 = 10 Hz), 8.01-8.03 (d, 2 H, *o*-CO-C_6H_5, *J* = 10 Hz). ^{13}C NMR (120 MHz $CDCl_3$), δ: 59.43 (C-*β*, CH-epoxy), 61.02 (C-*α*, CH-epoxy), 125.86 (*o*-2C, epoxy phenyl), 128.38 (*p*-C epoxy phenyl), 128.82 (*m*-2C, epoxy phenyl), 128.93 (*m*-2C, CO-phenyl), 129.11 (*o*-2C, CO-phenyl, 134.05 (C, *p*-CO phenyl), 135.48 (C, CO-phenyl), 135.53 (C, epoxy phenyl), 193.08 C=O.

Synthesis of 1-(2,4-dinitrophenyl)-3,5-diphenyl-1*H*-pyrazol-4-ol

An equimolar of the *trans*-1,3-diphenyl-2,3-epoxy-1-propanone (**III**) (2.24 g, 0.01 mol) and 2,4-dinitrophenylhydrazine (**IV**) (1.68 g, 0.01 mol) was dissolved in 30 mL glacial CH_3COOH in a flat bottom flask. The solution was refluxed for 6 h, cooled, and poured into crushed ice. The solid (3.30 g) obtained was recrystallized from *iso*-amyl acetate to give orange crystals 85.5% (Scheme 2).

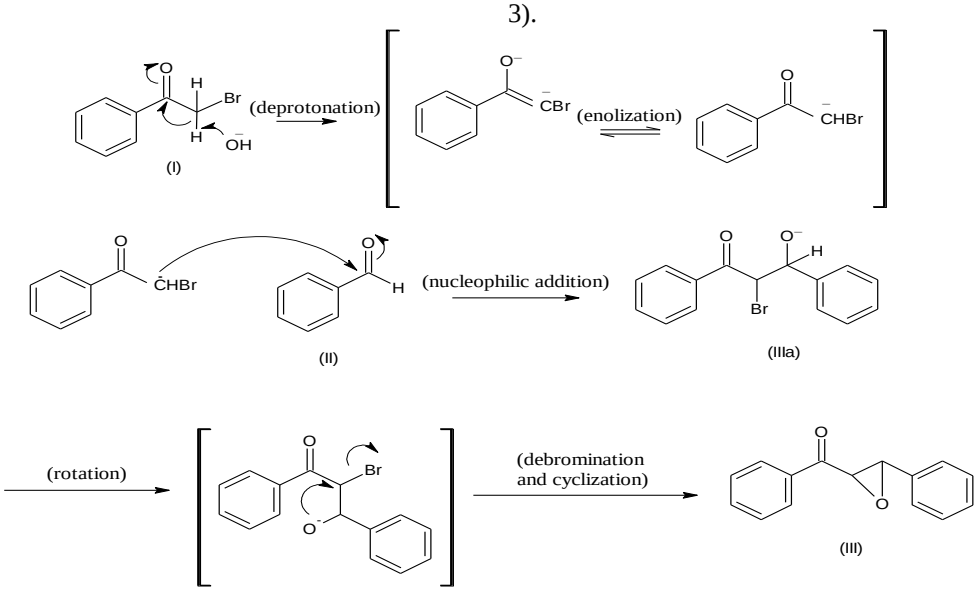


Scheme 2: Synthesis of 1-(2,4-dinitrophenyl)-3,5-diphenyl-1*H*-pyrazol-4-ol.

$C_{21}H_{14}N_4O_5$: orange crystals; m.p. 243-245 ^oC; R_f 0.53 ($CHCl_3$: Hex 1:1). FT-IR (ATR), V/cm^{-1}: 3276 (OH, str), 3068 (Aromatic C–H, str), 1618 (C=N, str), 1584 (C=C str), 1502 (NO_2 as, str), 1416 (C=C, str), 1312 (NO_2 sy, str), 1260, 1215 (C–N bend, str), 924, 890 (C–H bend). ^1H NMR (500 MHz, $CDCl_3$), δ: 7.49-7.51 (m, 6 H), 7.80–7.82 (m, 4 H), 8.13–8.17 (m, H, *o*- NO_2-phenyl), 8.38-8.41 (dd, H, *m*-NO_2-phenyl, J_1 = 5 Hz, J_2 = 5 Hz,), 9.18–9.19 (d, H, *m*-NO_2-phenyl, J = 5 Hz), 11.35 (OH). ^{13}C NMR ($CDCl_3$), δ: 116.80, 123.52, 127.66, 129.04, 129.42, 130.05, 131.05, 133.12, 138.29, 144.85, 147.87; MS: m/e, calcd 402.00, found 402.3.

Results and Discussion

The compound *trans*-1,3-diphenyl-2,3-epoxy-1-propanone (**III**) was prepared from benzaldehyde (**II**) and 2-bromoacetophenone (**I**) at 0–5 °C in ethanolic NaOH in 20 min to give 94% yield which is more economical compared to 2 h reported by Tanaka and Shiraishi (2001). The presence of ethanol and Br in compound **I** facilitated the reaction. Deprotonation of compound **I** with NaOH led to an enolate formation which was reacted with compound **II** to produce an oxyanion tetrahedral intermediate (**IIIa**). This was followed by rotation, debromination, and subsequent cyclization to give *trans*-1,3-diphenyl-2,3-epoxy-1-propanone (**III**) (Scheme 3).



Scheme 3: Possible mechanism of *trans*-1,3-diphenyl-2,3-epoxy-1-propanone.

The structure of the compound was determined using spectroscopic analyses (FTIR, ^{1}H, ^{13}C NMR, and DEPT 135). The IR spectrum of *trans*-1,3-diphenyl-2,3-epoxy-1-propanone showed vibrations for the C=O (1685 cm^{-1}), asymmetry and symmetry *trans*-epoxide (1234 and 891 cm^{-1}, respectively) (Pretsch et al. 2009). ^{1}H-NMR spectrum for CH-*α* and CH-*β* appeared as doublets at 4.09 and 4.33 ppm, respectively. This correlated with the reported data (Li et al. 2009, Roman 2016, Mphahlele et al. 2019). A small coupling constant was reported for chalcone epoxide to produce *trans*-isomers (Roman 2016, Mphahlele et al. 2019). The vicinal diaxial coupling constant was zero, an indication of *trans* configuration for a rigid 3-membered ring at ~90° dihedral angle (Simpson 2012, Mphahlele et al. 2019). The 10 aromatic protons were in the range of 7.39–8.03 ppm (Roman 2016, Mphahlele et al. 2019). The ^{13}C NMR confirmed the compound where CH-*β* and CH-*α* shifts are at δ 59.43 and δ 61.02 ppm, respectively as expected for *trans* chalcone epoxide and C=O at 193.08 ppm (Roman 2016, Mphahlele et al. 2019, Gunstone et al. 2021) (Figures 1-3).

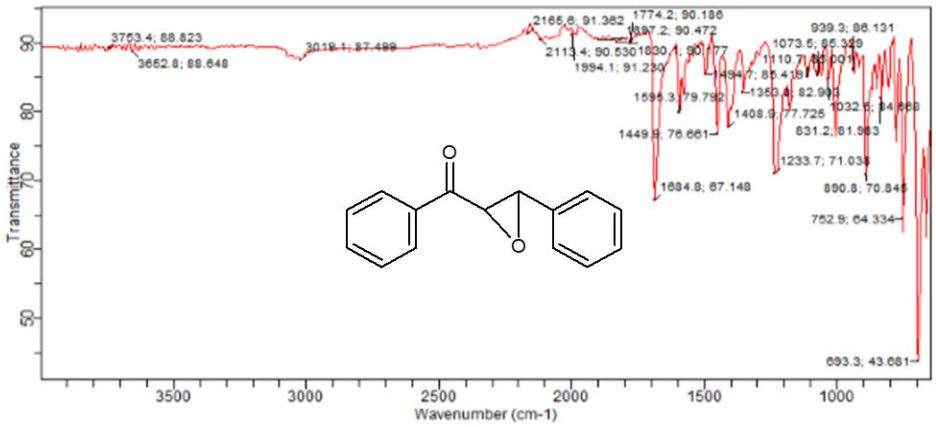


Figure 1: FTIR of *trans*-1,3-diphenyl-2,3-epoxy-1-propanone.

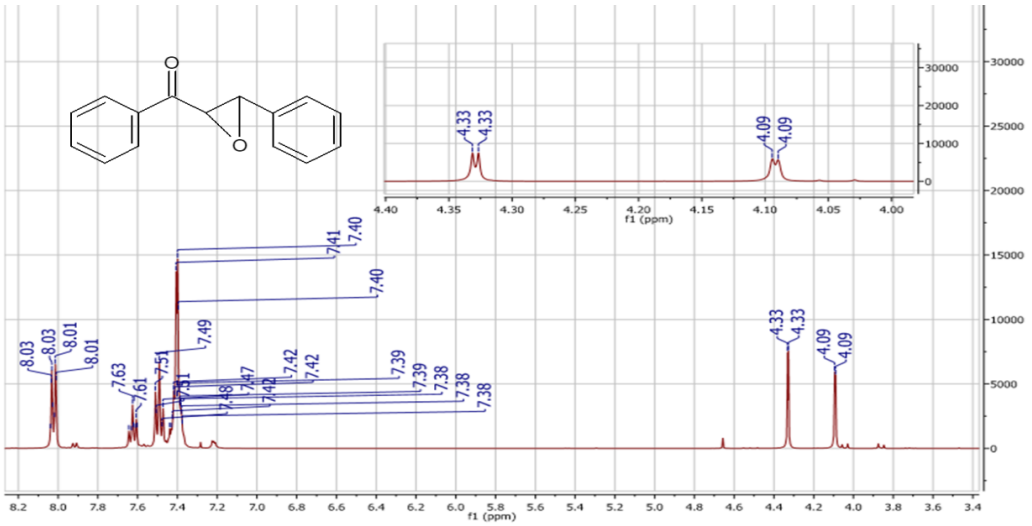


Figure 2: ^{1}H spectrum of *trans*-1,3-diphenyl-2,3-epoxy-1-propanone in $CDCl_3$.

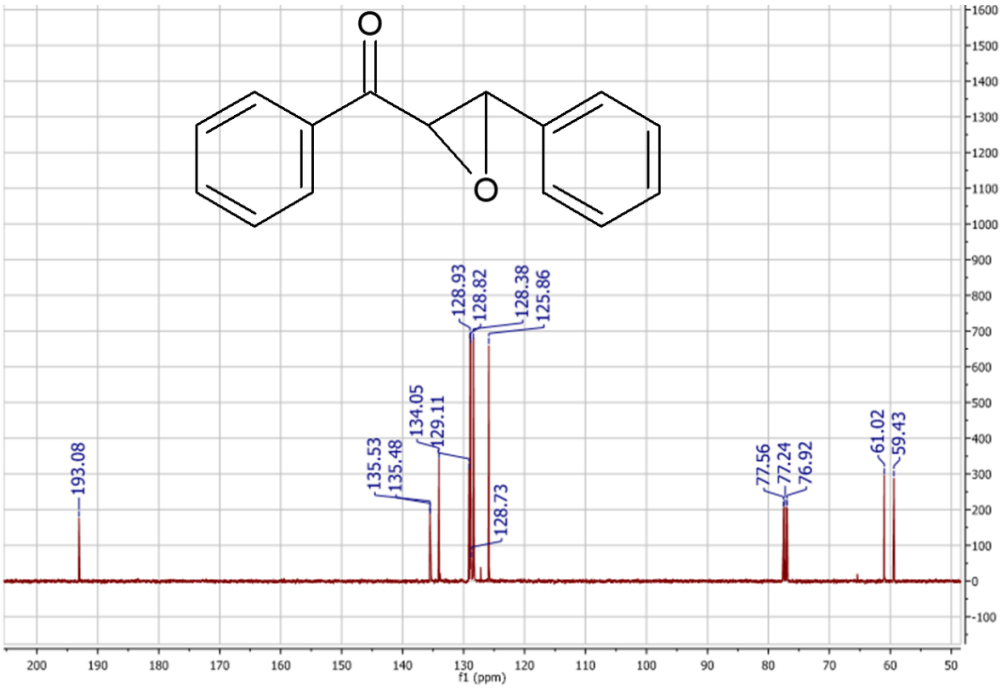


Figure 3: ^{13}C spectrum of *trans*-1,3-diphenyl-2,3-epoxy-1-propanone in $CDCl_3$.

The compound 1-(2,4-dinitrophenyl)-3,5-diphenyl-1*H*-pyrazol-4-ol was synthesized from *trans*-1,3-diphenyl-2,3-epoxy-1-propanone and 2,4-dinitro phenylhydrazine in glacial acetic acid to give 85.5% yield.

The IR spectrum showed the absence of C=O absorption band of *trans*-1,3-diphenyl-2,3-epoxy-1-propanone at 1685 cm^{-1} and the appearance of OH, C=N, NO_2 (as) and NO_2 (sy) in 1-(2,4-dinitrophenyl)-3,5-diphenyl-1*H*-pyrazol-4-ol at 3276, 1618, 1502, and 1312 cm^{-1} absorption bands, respectively (Pretsch et al. 2009). The ^{1}H-NMR spectrum of 1-(2,4-dinitrophenyl)-3,5-diphenyl-1*H*-pyrazol-4-ol showed the presence of OH signal at 11.35 ppm and the completely disappearance of CH-*α* and CH-*β* in the *trans*-1,3-diphenyl-2,3-epoxy-1-propanone. There was an increase in aromatic protons which shifted downfield from 7.39–8.03 of *trans*-1,3-diphenyl-2,3-epoxy-1-propanone to 7.49-9.19 ppm of 1-(2,4-dinitrophenyl)-3,5-diphenyl-1*H*-pyrazol-4-ol due to the mesomeric deshielding effect of electronegative nitrogen atoms in the compound. The ^{1}H-NMR spectrum was within reported data (Akbari and Mirjalili 2016). The ^{13}C NMR confirmed the formation of the compound with the absence of CH-*β* and CH-*α* at 59.43 and 61.02 ppm, respectively and C=O at 193.08 ppm. The molecular ion (402) M^+ of 1-(2,4-dinitrophenyl)-3,5-diphenyl-1*H*-pyrazol-4-ol also supported the formation (Figures 4-7).

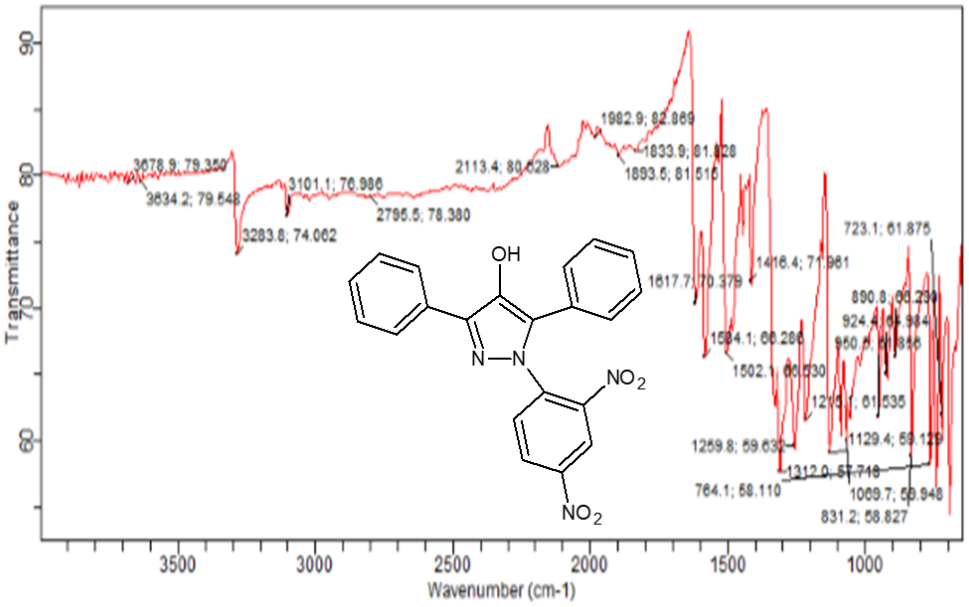


Figure 4: FTIR of 1-(2,4-dinitrophenyl)-3,5-diphenyl-1*H*-pyrazol-4-ol.

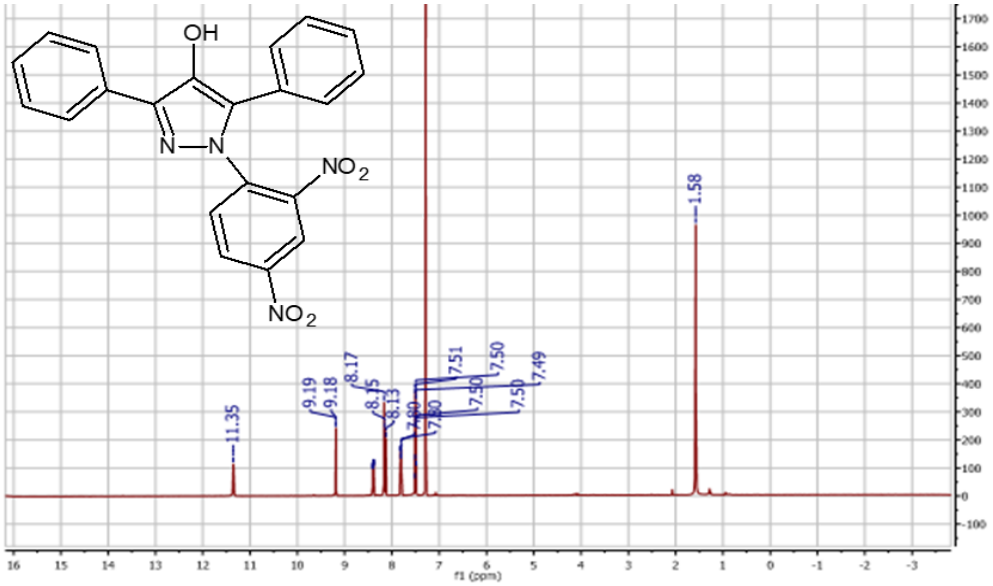


Figure 5: ^{1}H spectrum of 1-(2,4-dinitrophenyl)-3,5-diphenyl-1*H*-pyrazol-4-ol in $CDCl_3$.

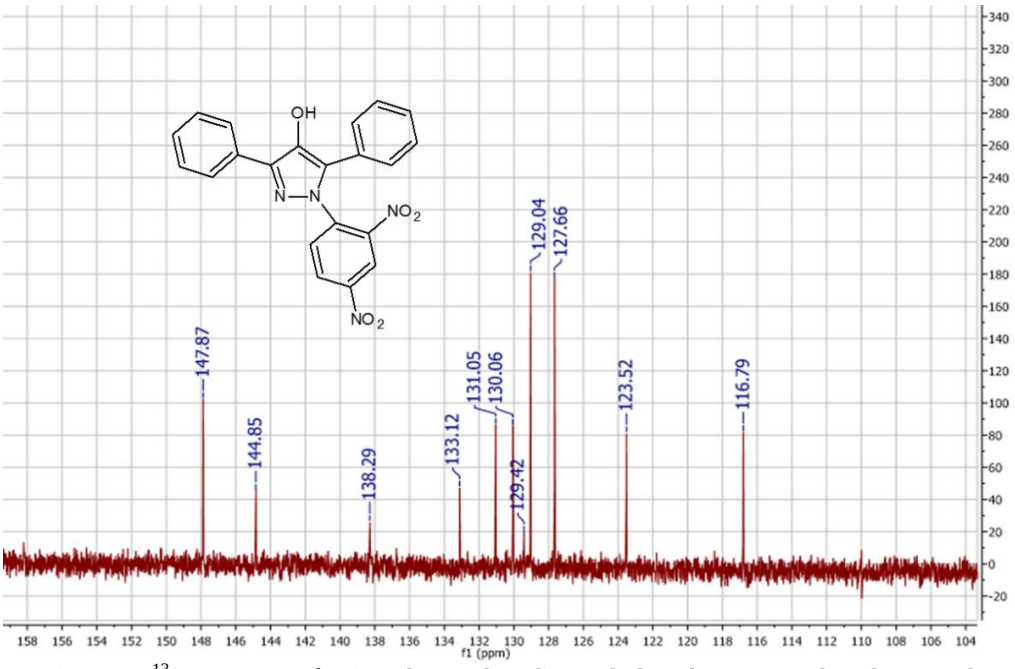


Figure 6: ^{13}C spectrum of 1-(2,4-dinitrophenyl)-3,5-diphenyl-1*H*-pyrazol-4-ol in $CDCl_3$.

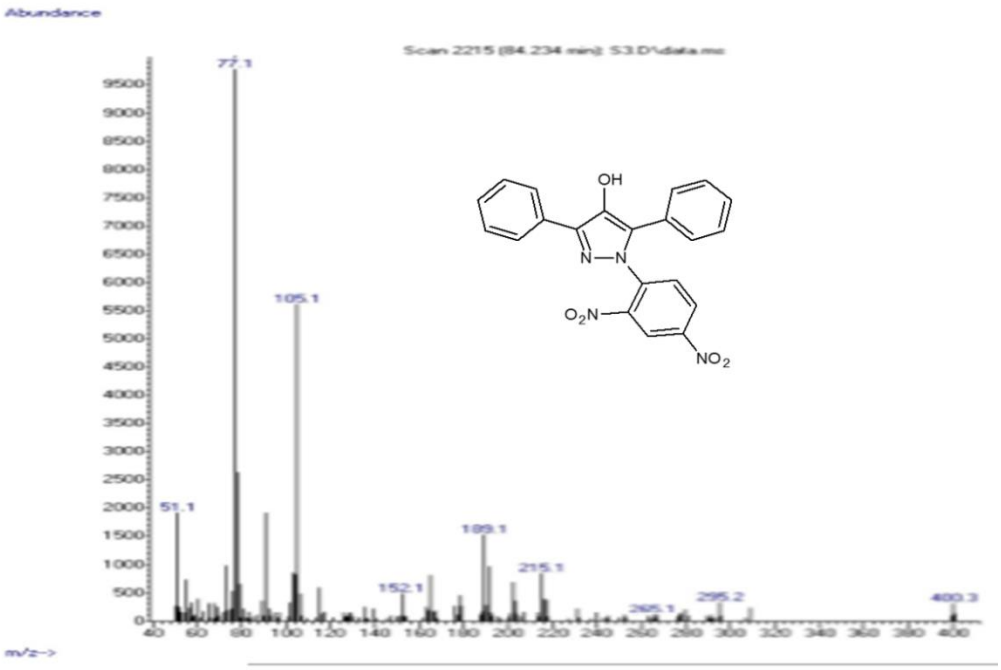


Figure 7: MS spectrum of 1-(2,4-dinitrophenyl)-3,5-diphenyl-1*H*-pyrazol-4-ol in $CDCl_3$.

Conclusions

The compound *trans*-1,3-diphenyl-2,3-epoxy-1-propanone was synthesized to give 94% yield in 20 min which is more economical. The presence of ethanol and Br in 2-bromoacetophenone facilitated the reaction. The vicinal diaxial coupling constant of the *α*- and *β*-hydrogens in *trans*-1,3-diphenyl-2,3-epoxy-1-propanone was zero, an indication of *trans* configuration for a rigid 3-membered ring at ~90° dihedral angle. The desired compound 1-(2,4-dinitrophenyl)-3,5-diphenyl-1*H*-pyrazol-4-ol was synthesized via *trans*-1,3-diphenyl-2,3-epoxy-1-propanone and the spectra data (FTIR, ^{1}H, ^{13}C NMR, DEPT 135 and MS spectra) corresponded with available data in the literature.

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