SYNTHESIS AND SPECTROSCOPIC STUDY OF ACETYL ACETONE MONO OXIME AND ITS CORRESPONDING BENZOYL ESTER

Ramadan Ali Bawa* and Mohammed Ali Sawalem
Department of Chemistry, Faculty of Science, Misurata University, Misurata, Libya
*Email: ram_bawa@hotmail.com

ABSTRACT

*The mono oxime of the acetyl acetone **4** was synthesized through a solvent-free procedure yielding only 27% of E/Z isomeric mixture in a ratio of (9:1). The benzoyl ester of this oxime was also obtained in 49% yield and formed in two isomeric conformations Z/E in a ratio of (9:1). The MM2 molecular mechanics method showed, as expected, that the E-isomer of the mono oxime **4 I** was the favored to be formed as it has the lower total energy than the Z-isomer **4 II**. However, the MM2 method predicted unexpectedly that the Z-isomer of the benzoyl ester **6 IV** has a lower total energy than its counterpart E-isomer **6 III**.*

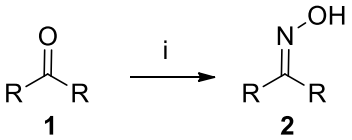
KEYWORDS

Mono oxime, synthesized, solvent-free, isomeric mixture, MM2.

1. INTRODUCTION

Oximes have been reported to be useful molecules for protecting and purifying carbonyl compounds in organic synthesis [1]. These molecules have also been found to possess antimicrobial [2], antioxidant [3,4], antitumor [5], antiviral agents and anticonvulsant properties [6]. Cyclic ketones, such as cyclopentanone, cyclohexanone, 4-^{t}-butylcyclohexanone, and cycloheptanone were converted to the corresponding oximes by simple grinding at room temperature, in presence of hydroxylamine hydrochloride and sodium hydroxide without any catalyst or solvent. The

reaction does not require heating or to be exposed to microwave irradiation. Oximes of very high purity were isolated in excellent yields (85–100%) **(Scheme 1)** [1].



Where R is Alkyl or Aryl or H

Reagents & reaction conditions: (i) $NH_2OH.HCl$, NaOH

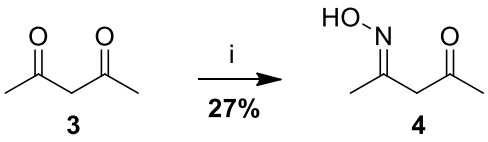
Scheme 1: Typical oximation reaction

Phenolic oximes and other oximes have many industrial uses mainly as extractants for copper ions and also in the synthesis of some industrially important compounds such as anti-corrosives, which are used as protective coatings [5,7]. Herein, acetyl acetone mono oxime and its corresponding benzoyl ester have been synthesized and their spectroscopic data has been studied.

2. RESULTS AND DISCUSSION

2.1. Synthesis of (*E*)-4-(Hydroxyimino)pentan-2-one 4:

Acetylacetone mono-oxime **4**, (*E*)-4-(hydroxyimino)pentan-2-one, was prepared through a solvent-free reaction between the acetyl acetone **3** and hydroxylamine hydrochloride in the ratio of (1:1 mol/mol) in the presence of anhydrous sodium sulphate and potassium carbonate. These materials were ground for 45 min giving only 27% yield of the desired mono oxime **4 (Scheme 2)**.



Reagents & reaction conditions: (i) $NH_2OH.HCl$, K_2CO_3, Na_2SO_4, rt, 30 - 45 min

Scheme 2: The formation of the acetylacetone mono oxime 4

The formation of this compound was confirmed by the use of spectroscopic methods such as IR, NMR and mass spectrometer. The appearance of the vibrational bands at 3403 cm^{-1} to 3193 cm^{-1} belongs to the hydroxyl group *OH*, whereas the vibrational band that is seen at 1601 cm^{-1} is due to the presence of the imino group *C=N*. The appearance of an absorption band at 1710 cm^{-1} is referred to the carbonyl group *C=O*. These IR findings gave a good sign of the formation of the (*E*)-4-(hydroxyimino)pentan-2-one **4**. The mass spectroscopic data showed the molecular ion peak at 115 m/z along with a convincing fragmentation pattern. The mass spec analysis provided another piece of information about the confirmation of the structural formula of the (*E*)-4-(hydroxyimino)pentan-2-one **4**. The HNMR analysis was carried out on the product as a further piece of information to prove the structural formula of the (*E*)-4-(hydroxyimino)pentan-2-one **4**. The chemical shifts in the HNMR indicated that the (*E*)-4-(hydroxyimino)pentan-2-one **4** was formed. It is worthwhile mentioning that this monoketoxime **4** was obtained in two isomeric forms **I** and **II (***E* and *Z***)** in ratio of (9:1) respectively. This was clearly observed in the HNMR spectrum of the crude product. These two *E* and *Z* isomers were formed in total yield of

27% and the 3D structures with lowest energies of both geometric isomers were obtained **(Figure 1)**.

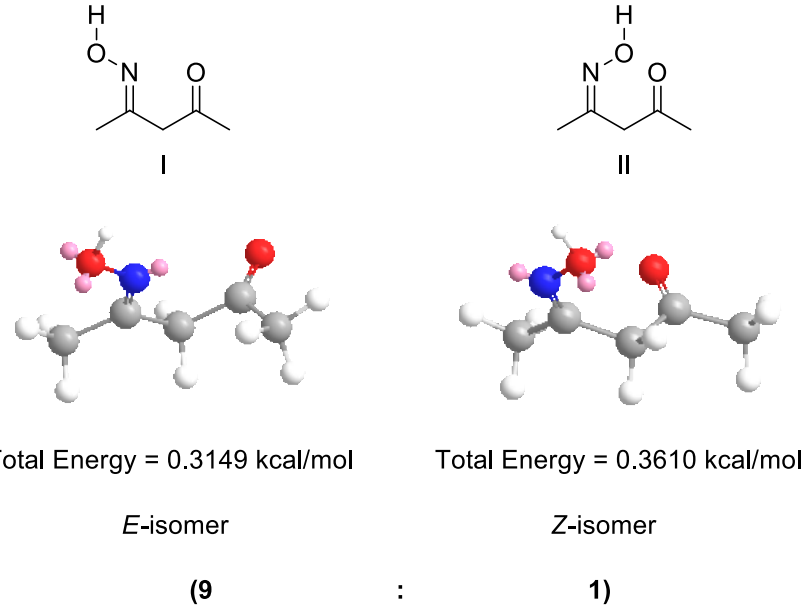
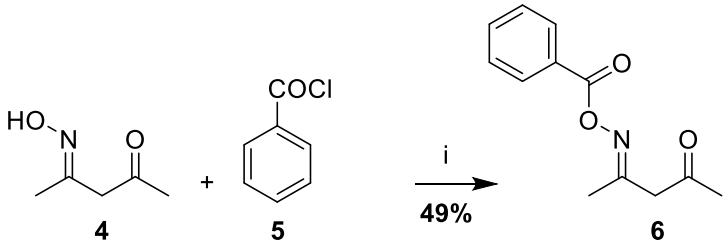


Figure 1: The energies predicted using MM2 for E and Z-isomers of compound 4

2.2. Synthesis of (*E*)-4-(Benzoyloxyimino)pentan-2-one 6:

This compound was obtained in moderate yield, 49%, through a reaction between the the mono oxime (*E*)-4-(hydroxyimino)pentan-2-one **4** and the benzoyl chloride **5** in (1:1) molar ratio in the presence of triethylamine as a mild base at room temperature **(Scheme 3)**.



Reagents & reaction conditions: (i) Et_3N, $CHCl_3$, 0 - 5 °C, 30 min, then rt, 2 hrs

Scheme 3: The formation of benzoyl oxime ester 6

The structural formula of the (*E*)-4-(benzoyloxyimino)pentan-2-one **6** was confirmed using a number of spectroscopic techniques such as IR, MS and NMR spectroscopy. The IR data showed two vibrational bands at 1784 cm^{-1} and 1717 cm^{-1} for the ester carbonyl group and the ketone carbonyl group respectively. In addition, a vibrational band appeared at 1598 cm^{-1} belongs to the imine group *C=N*. The absence of the stretching band of the hydroxyl group initially indicates the synthesis of the title compound, (*E*)-4-(benzoyloxyimino)pentan-2-one **6**, was successful. The mass spectrometer gave more clarity about the formation of the (*E*)-4-(benzoyloxyimino)pentan-2-one **6**, which the molecular ion peak was observed in the mass spectrum, as expected, at 219 m/z with a relative intensity of 52% along with a good fragmentation pattern in which the base peak was seen at 105 m/z with a relative intensity of 100% matching the molecular weight of the benzoyl fragment (C_6H_5CO; Mwt 105). The ^{1}HNMR of the (*E*)-4-(benzoyloxyimino)pentan-2-one **6** was obtained in which all the expected chemical shifts were observed in the ^{1}HNMR spectrum. However, the methylene group CH_2 has an unexpected chemical shift, which appeared in far further down field on the spectrum

than it was expected (appeared at 8.25 ppm). This could be rationalized to the great withdrawing effect of the benzoate group in which this methylene group. The ^{1}HNMR data of the crude product also showed the formation of two conformational isomers **III** and **IV** in ratio of (9:1). These two isomers could be predicted to be the (*E*)-4-(benzoyloxyimino)pentan-2-one **III** and the (*Z*)-4-(benzoyloxyimino)pentan-2-one **IV (Figure 2)**.

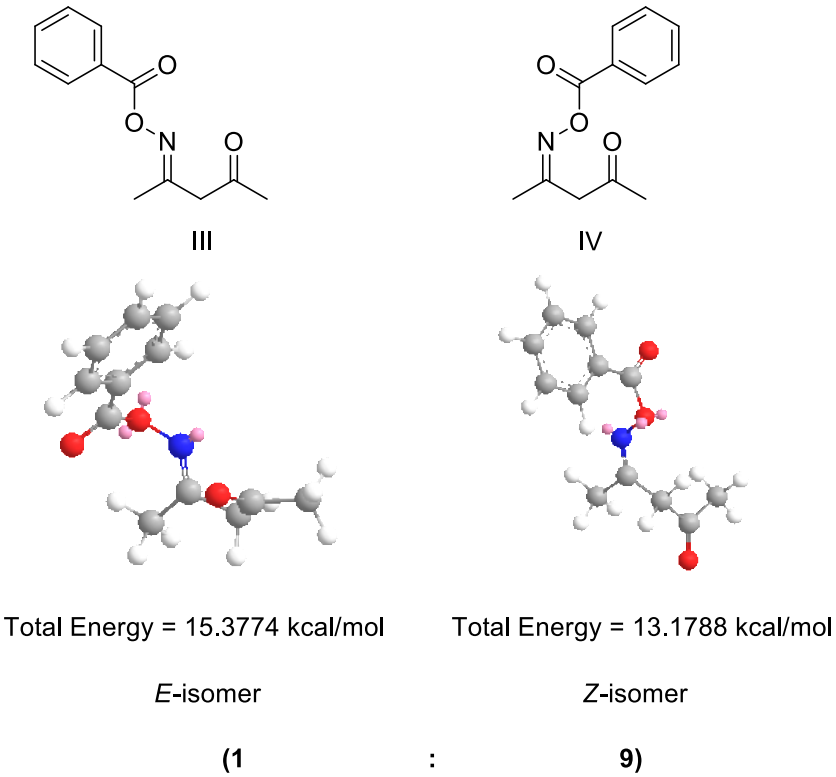


Figure 2: The energies predicted using MM2 for E and Z-isomers of compound 6

3. EXPERIMENTAL

3.1. Materials

The chemicals that were required for this research are as follows: Acetyl Acetone, hydroxylamine hydrochloride, benzoyl chloride, potassium carbonate, anhydrous sodium sulphate, triethylamine and chloroform were purchased from S Park. All chemicals were used without further purification.

3.2. Instrumentation

^{1}HNMR spectrum was recorded on a Bruker Avance 300 spectrometer. Residual proton signal from the deuteriated solvent was used as reference [DMSO (^{1}H, 2.50 ppm)]. Coupling constants were measured in Hz. Infrared spectrum was recorded on Jasco FT/IR-4100 Fourier transform infrared spectrometer. Mass spectrum was recorded on a Micromass Autospec M spectrometer.

3.3. Synthesis of (*E*)-4-(Hydroxyimino)pentan-2-one 4

An adapted synthetic procedure [1] was followed towards the synthesis of oxime **4**. Hydroxylamine hydrochloride (6.94 g, 100 mmol), acetyl acetone (10 g, 100 mmol) and potassium carbonate (13.80 g, 100 mmol) in the presence of anhydrous sodium sulphate (14.20 g, 100 mmol) were placed in a mortar and ground at room temperature for 30 min. Chloroform (20 cm^3) was then added to the resulting paste, filtered and the solvent was evaporated *in vacuo*. The desired monoketoxime **4** was obtained, as two isomeric forms **I** and **II** in ratio of (9:1), in low yield (3.10 g, 26.95 mmol, 27%) as yellow oil. The analysis was carried out on

the crude material in order to observe the possible isomerism. IR ν_{max} (cm^{-1}) 3298 (OH), 2987 (C-H), 2922 (C-H), 1710 (C=O), 1601 (C=N). ^{1}HNMR (DMSO-d6, 400 MHz) **Major isomer (I, formation ratio of 89.2%):** δ 8.181 (1H, s, O*H*), 1.87 (3H, s, CH_3), 1.74 (2H, s, CH_2), 1.45 (3H, s, CH_3); **Minor isomer (II, formation ratio of 10.8%):** δ 5.98 (1H, s, O*H*), 2.81 (3H, s, CH_3), 2.63 (2H, s, CH_2), 2.69 (3H, s, CH_3). Mass spec m/z ($C_5H_9NO_2$, MWt 115.13) 115 (59%), 98 (72%), 82 (100%), 73 (79%), 59 (82%).

3.3. Synthesis of (*E*)-4-(Benzoyloxyimino)pentan-2-one 6

An adapted literature procedure [8] was followed towards the synthesis of the oxime ester **6**. Mono oxime (*E*)-4-(hydroxyimino)pentan-2-one **4** (3.45 g, 30.0 mmol) in chloroform (40 cm^3) in the presence of triethylamine (4.04 g, 40.0 mmol) were placed in a round-bottomed flask and stirred at 0 – 7 °C. A solution of benzoyl chloride (4.49 g, 32.0 mmol) in chloroform (50 cm^3) was then added dropwise over 30 min. The reaction mixture was left stirring at room temperature for 2 hours, after which distilled water (30 cm^3) was added to the mixture and stirred for further 10 min. The organic layer was extracted, dried over anhydrous Na_2SO_4 and filtered. The solvent was evaporated *in vacuo* to obtain the desired oxime ester **6** in moderate yield (3.20 g, 14.61 mmol, 49%) as dark oil. The analysis was carried out on the crude material in order to observe the possible isomerism. IR ν_{max} (cm^{-1}) 3065 (C-H), 2980 (C-H), 1784 (C=O), 1717 (C=O), 1598 (C=N). ^{1}HNMR (DMSO-d6, 400 MHz) **Major isomer (IV, formation ratio of 91.0%):** δ 8.25 (2H, s, CH_2), 7.99 – 7.96 (2H, m, 2 × Ar-*H*), 7.56 – 7.47 (3H, m, 3 × Ar-*H*), 2.21 (3H, s, CH_3), 2.09 (3H, s,

CH_3); **Minor isomer (III, formation ratio of 9.0%):** δ 8.60 (2H, s, CH_2), 8.10 – 8.00 (2H, m, 2 × Ar-*H*), 7.70 – 7.50 (3H, m, 3 × Ar-*H*), 3.65 (3H, s, CH_3), 3.48 (3H, s, CH_3). Mass spec m/z ($C_{12}H_{13}NO_3$, MWt 219.24) 219 (52%), 202 (88%), 159 (65%), 122 (60%), 105 (100%).

4. CONCLUSIONS

The mono oxime of the acetyl acetone was obtained in two isomeric forms in ratio of (9:1) and total yield of 27%. The benzoyl ester of this oxime was also formed in two isomeric conformations in a ratio of (9:1). The MM2 molecular mechanics method showed, as expected, that the *E*-isomer of the mono oxime **4 I** was the favored to be formed as it has the lower total energy than the *Z*-isomer **4 II**. Whereas, the MM2 method predicted unexpectedly that the *Z*-isomer of the benzoyl ester **6 IV** has a lower total energy than its counterpart *E*-isomer **6 III**.

5. ACKNOWLEDGMENTS

Authors would like to thank the department of chemistry, faculty of science, Misurata University for their unstoppable support to this project.

6. REFERENCES

1. Damljanovic´, I.; Vukic´evic´, M. and Vukic´evic, R., *A simple synthesis of oximes*, *Monatshefte fur Chemie*, 2006,**137**, p: 301 – 305.
2. Ramanjaneyulu, K.; Rao, P.; Rambabu1, T., Jayarao1, K., Devi1, C.; Rao, B., *Cupper supported silica promoted one-pot synthesis of aromatic oxime derivatives*, *Der Pharma Chemica*, 2012, **4**, p: 473 – 478.
3. Vessally E.; Saeidian, H.; Hosseinian, A.; Edjlali, L. and Bekhradnia, A., *A review on synthetic applications of oxime esters*, *Current Organic Chemistry*, 2017, **21**, p: 249 – 271.

4. Smith, A.; Tasker, P. and White, D., *The structures of phenolic oximes and their complexes*, *Coordination Chemistry Reviews*, 2003, **241**, p: 61 – 85.
5. Thorpe, J.; Beddoes, R.; Collison, D.; Garner, C.; Helliwell, M.; Holmes, J. and Tasker, P., *Surface coordination chemistry: corrosion inhibition by tetranuclear cluster formation of iron with salicylaldoxime*, *Angew. Chem. Int. Ed*, 1999, **38**, p: 1119 – 1121.
6. Alcalde, E. ; Mesquida, N.; Alvarez-Rúa, C.; Cuberes, R.; Frigola, J. and García-Granda, S., *1,2-Diaryl(3-pyridyl)ethanone oximes. intermolecular hydrogen bonding networks revealed by x-ray diffraction*, *Molecules*, 2008, **13**, p: 301 – 318.
7. Bolotin, D.; Bokach, N.; Demakova, M. and Kukushkin, V., *Metal-involving synthesis and reactions of oximes*, *Chem. Rev.*, 2017, **117**, p: 13039 – 13122.
8. Gao, Y.; Song, J.; Shang, S.; Wang, D. and Li, J., *Synthesis and antibacterial activity of oxime esters from dihydrocumic acid*, *BioResources*, 2012, **7**, p: 4150 – 4160.