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무수조건하에서 헤테로 옥심의 합성을 위한 간단하고 효율적인 맷돌화학 고체상태의 반응과정

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A Simple and Efficient Grindstone Chemistry Solid-state Reaction Procedure for the Synthesis of Heterocyclic Oximes in Dry Media

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요 약. 무수조건하에서 막자와 막자사발을 이용하여 활성화된 비산회 촉매로 3-alkyl-2,6-diarylpiperidins, tetrahydrothiopyrans 과 tetrahydropyran-4-ones의 다양한 다른 헤테로 옥심을 합성하였고, 녹는점, 원소 분석, MS, FT-IR 그리고 ^{1}H NMR 데이터로 구조 분석하였다.

주제어: Oximation, 활성화된 비산회, 맷돌 화학, 녹색 화학

ABSTRACT. Various diverse heterocyclic oximes of 3-alkyl-2,6-diarylpiperidins, tetrahydrothiopyrans, and tetrahydropyran-4-ones are synthesized using a mortar and pestle in dry media catalyzed by activated fly ash in excellent yields and are characterized by melting point, elemental analysis, MS, FT-IR, and ^{1}H NMR spectroscopic data.

Keywords: Oximation, Activated Fly Ash, Grindstone Chemistry, Green Chemistry

INTRODUCTION

Solvent-free synthesis of organic compounds involving easily separable solid catalysts has attracted notable interest and offers a clean, economical and environmentally-safe protocol. Nowadays, bioactive heterocyclic ring systems having 2,6-diarylpiperidin-4-one moiety and their analogous thiopyran and pyran nuclei have aroused great interest due to their wide variety of biological properties such as antiviral, antitumour,[1,2] central nervous system,[3] local anesthetic,[4] anticancer,[5] and antimicrobial activity,[6] and also act as neurokinin receptor antagonists,[7] analgesic and anti-hypertensive agents.[8] Oximes of various substituted piperidones were also reported to exhibit antimicrobial, analgesic, local anesthetic and antifungal activities.[9]

Oximation has attracted intensive attention for several decades as an efficient method for characterization and purification of carbonyl compounds. Due to the nucleophilic character of oximes, they have been widely used for the preparation of a variety of nitrogen containing compounds such as amides,[10] hydroximinoyl chlorides,[11] nitrones[12] and nitriles.[13] Oximes are usually prepared by the reaction of carbonyl compounds and hydroxylamine hydrochloride with adjustment of pH using a basic aqueous medium. Recently, some new techniques such as microwave irradiation[14] and solvent-free heating[15] were applied to this reaction. Oxidation of

amines was another usual method of the synthesis of oximes.[16]

It has been about 70 years to research and use fly ash. With its application, the action mechanism of fly ash had been recognized. During the initial stage, only its pozzolanic activity is paid attention.[17,18] Many researchers were devoted to the research of the potential activity of fly ash and the hydration process of fly ash cement.[19] Recently, microwave-assisted activated fly ash has been reported to catalyze Knoevenagel condensation, synthesis of amides, Schiff Bases formation, and Biginelli and Hantzsch reactions.[20]

In continuation of our interest in synthesizing pharmacologically important compounds in '*dry media*',[21-24] we wish to report activated fly ash as an efficient catalyst for the synthesis of 3-alkyl-2,6-diarylpiperidin-4-one oximes, 2,6-diaryltetrahydrothiopyran-4-one oximes, and 2,6-diaryltetrahydropyran-4-one oximes using a mortar and pestle in dry media.

RESULTS AND DISCUSSION

Chemistry

The oximes of aldehyde and ketone are served as protecting,[25] selective activating groups[26] and intermediates for many reactions such as Beckmann rearrangement for the preparation of amides. Further, oximes are used for the purification of carbonyl compounds. The oximes can be prepared by the addition of hydroxylamine to aldehydes and ketones. The formation of oximes is usually catalyzed by acids.[27] The preparations of oximes from aldehydes or ketones using hydroxylamine as reactant and sulphuric acid as catalyst[27] have many disadvantages. This procedure is not applicable for acid-sensitive compounds, the yields of the oximes are pH dependent[28] and it requires costly solvent like pure ethanol. Cyclohexanone oximes are synthesized by liquid-phase ammoximation of cyclohexanone using ammonia, hydrogen peroxide as the oxidizing agent and titanium silicate as a catalyst. The ammoximation reaction is suitable for the synthesis of several oximes[29] but use of H_2O_2 and titanium silicate increased the cost of production. To avoid liquid phase oximation reactions, we use activated fly ash as a solid catalyst for the oximation reaction.

The fly ash collected from Neyveli Lignite Corporation, Neyveli, Tamil Nadu, India was utilized for catalyzing the reactions. Specific gravity and specific surface area of the fly ash were 1.9 and 127 m^2/g, respectively. The chemical compositions (%) of insoluble residues of the fly ash after ignition were SiO_2, Fe_2O_3, Al_2O_3, CaO, MgO, in the ratio of 64.03, 6.50, 15.50, 4.62, 3.00, 4.35, and 2.00, respectively.

Target molecules, 2,6-diarylpiperidin/tetrahydrothiopyran/tetrahydropyran-4-one oximes **14-28** are synthesized as a result of single-step solid-state synthetic strategy. In a typical experiment, corresponding 3-alkyl-2, 6-diaryl-piperidin/tetrahydrothiopyran/tetrahydropyran-4-ones **1-14** were mixed with hydroxylamine hydrochloride and activated fly ash in a mortar and pestle. The mixture was grinded briskly for 5 to 10 min to yield the title compounds in high yields. The reaction in dry media provides advantages over the classical method,[21] which requires a longer reaction time using ethanol as solvent medium and the use of column chromatographic technique to purify the products. The most acceptable ratio in terms of efficiency were 50 mg of activated fly ash to 0.001 moles of substrates. Introduction of bulky dimethyl moiety at position 3 of the piperidone ring did not affect the oximation reaction. Also, there is no need of any purification technique to purify the formed oximes since the reaction mixture was shaken well with dichloromethane and the catalyst was removed by simple filtration. Concentration of dichloromethane layer by distilled off under reduced pressure yield the

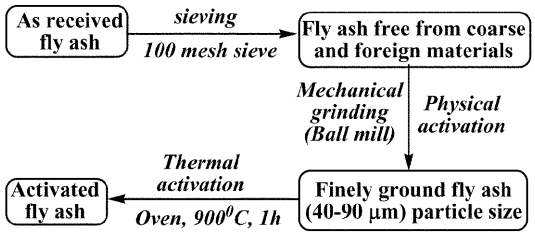
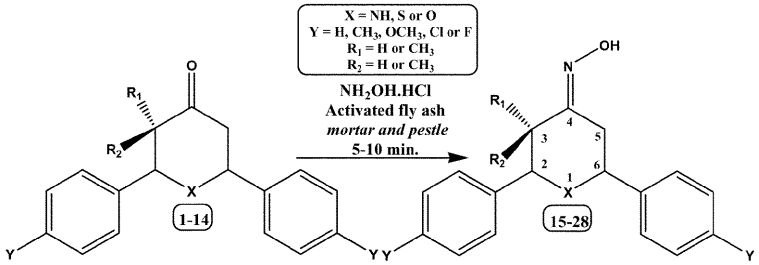


Fig. 1. Flow charr for the preparation of activated fly ash.



Scheme 1. Synthesis of biolabile oximes under dry media reaction conditions.

Table 1. Physical and analytical data of compounds **15-28**

Compounds	X	Y	R_1	R_2	Yield (%)	m.p ºC	Elemental analysis (%) C Found (calculated)	H Found (calculated)	N Found (calculated)	m/z ($M^{+\cdot}$) Molecular formula
15	NH	H	H	H	90	169-171	76.62 (76.66)	6.79 (6.81)	10.47 (10.52)	267 $C_{17}H_{18}N_2O$
16	NH	CH_3	H	H	85	148-150	77.49 (77.52)	7.49 (7.53)	9.47 (9.52)	295 $C_{19}H_{22}N_2O$
17	NH	Cl	H	H	88	161-163	60.88 (60.91)	4.78 (4.81)	8.32 (8.36)	336 $C_{17}H_{16}Cl_2N_2O$
18	NH	H	CH_3	CH_3	90	156-58	73.49 (73.52)	7.11 (7.14)	9.01 (9.03)	(311) $C_{19}H_{22}N_2O_2$
19	NH	CH_3	CH_3	CH_3	95	160-02	74.49 (74.52)	7.71 (7.74)	8.25 (8.28)	(339) $C_{21}H_{26}N_2O_2$
20	NH	OCH_3	CH_3	CH_3	92	146-48	68.05 (68.09)	7.03 (7.07)	7.53 (7.56)	(371) $C_{21}H_{26}N_2O_4$
21	NH	Cl	CH_3	CH_3	95	171-72	60.15 (60.17)	5.30 (5.32)	7.35 (7.39)	(380) $C_{19}H_{20}Cl_2N_2O_2$
22	NH	F	CH_3	CH_3	90	174-76	65.84 (65.88)	5.79 (5.82)	8.05 (8.09)	(347) $C_{19}H_{20}F_2N_2O_2$
23	S	H	H	H	92	186-188	72.01 (72.05)	6.01 (6.05)	4.92 (4.94)	284 $C_{17}H_{17}NOS$
24	S	CH_3	H	H	90	194-196	73.25 (73.27)	6.75 (6.80)	4.47 (4.50)	312 $C_{19}H_{21}NOS$
25	S	Cl	H	H	85	182-184	57.91 (57.96)	4.25 (4.29)	3.93 (3.98)	353 $C_{17}H_{15}Cl_2NOS$
26	O	H	H	H	90	149-150	76.33 (76.38)	6.37 (6.41)	5.21 (5.24)	268 $C_{17}H_{17}NO_2$
27	O	CH_3	H	H	83	161-163	77.23 (77.26)	7.15 (7.17)	4.70 (4.74)	296 $C_{19}H_{21}NO_2$
28	O	Cl	H	H	80	144-146	60.70 (60.73)	4.47 (4.50)	4.13 (4.17)	337 $C_{17}H_{15}Cl_2NO_2$

respective oximes.

The schematic representation and the analytical data of compounds **15-28** are given in *Scheme* 1 and *Table* 1, respectively. The structures of the newly synthesized compounds **15-28** were confirmed by their melting points, elemental analyses, MS, FT-IR, and ^{1}H NMR spectroscopic data. This new synthetic method is applicable to synthesize simple ketoximes and aldoxime from cyclohexanone, cyclopentanone, acetone, butan-2-one, and

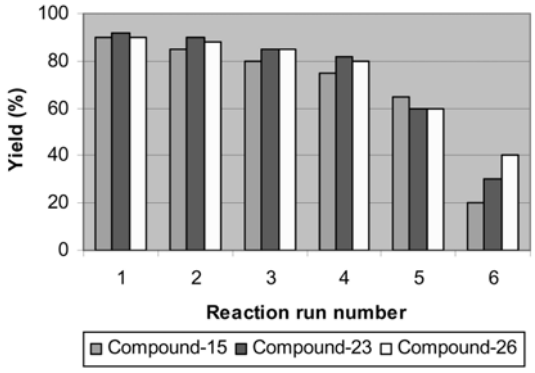


Fig. 2. Reuse of Activated fly ash catalyst for oximation.

benzaldehyde, in good to excellent yields.

The reusability of activated fly ash catalyst was studied using compounds **15**, **23** and **26** with hydroxylamine hydrochloride. After filtering, washing with dichloromethane, drying at 120ºC for 1h, the fly ash was reused for the next round of the reactions to provide excellent reproducibility, as shown in *Fig*. 2. It is evident that the system retains high catalytic efficacies after repeating the reuse procedure up to 4 times since recycling led to loss of efficiency of the catalyst owing to absorption of organics. Organics on the solid surface result in the reduction of the number of active centres. Organic species could be removed at higher temperature, reactivating the catalyst.

CONCLUSION

The present work describes the synthesis of heterocyclic oximes namely 3-alkyl-2,6-diarylpiperidin-4-one oximes **15-22**, 2,6-diphenylthiopyran-4-one oximes **13-15**, and 2,6-diphenylpyran-4-one oximes **16-18** in dry media under solvent-free conditions catalyzed by activated fly ash using grindstone chemistry. Using this protocol, various structurally diverse oximes were synthesized with excellent yields.

EXPERIMENTAL

General

The reactions and the purity of the products were monitored and estimated by TLC. The melting points were measured in open capillaries and are reported uncorrected. IR spectra were recorded in KBr (pellet forms) on a Nicolet-Avatar–330 FT-IR spectrophotometer and noteworthy absorption values are listed in cm^{-1}. ^1H and ^{13}C NMR spectra were recorded at 400 MHz and 100 MHz, respectively, on Bruker AMX 400 NMR spectrometer using $CDCl_3$ as solvent. The positive ESI MS spectra were recorded on a Bruker Daltonics LC-MS spectrometer. Microanalysis was obtained on Carlo Erba 1106 CHN analyzer.

By adopting the literature precedent, 2,6-diarylpiperidin-4-ones[30] **1-8**, 2,6-diaryltetrahydrothiopyran-4-ones[31] **9-11** and 2,6-diaryltetrahydropyran-4-ones[32] **12-14** are prepared.

General synthetic procedure for the synthesis of 2,6-diarylpiperidin-4-one oximes in dry media 15-17

Appropriate 2,6-diarylpiperidin-4-ones **1-3** (0.001 mol) and hydroxylamine hydrochloride (0.001 mol) were mixed thoroughly with activated fly ash (50 mg) in a mortar and pestle. The mixture was grinded briskly for 5-10 min. (monitored by TLC) and the reaction mixture was shaken well with dichloromethane (15 mL). The catalyst was removed by simple filtration. The dichloromethane layer was dried over anhydrous sodium sulphate and distilled off under reduced pressure to yield the respective 2,6-diarylpiperidin-4-one oximes **15-17**.

2,6-diphenylpiperidin-4-one oxime 15 Reaction time: 9 min. IR (KBr) (cm^{-1}): 3250, 3031, 2917, 2801, 1674, 1600, 754, 700; ^1H NMR (δ, ppm): 2.00 (s, 1H, H_1), 3.94 (dd, 1H, H_{2a}, $J_{2a,3a}$=11.4 Hz), 3.88 (dd, 1H, H_{6a}, $J_{6a,5a}$=11.6 Hz), 3.54 (t, 1H, H_{5e}, $J_{6a,5e}$=2.98Hz), 2.56 (t, 1H, H_{3e}, $J_{2a,3e}$=2.92Hz), 2.38 (m, 1H, H_{3a}), 2.01 (m, 1H, H_{5a}), 7.48-7.18 (m, 10H, H_{arom}), 8.00 (s, 1H, N-OH).

2,6-bis(4-methylphenyl)piperidine-4-one oxime 16 Reaction time: 5 min. IR (KBr) (cm^{-1}): 3248, 3028, 2914, 2841, 2804, 1671, 1604, 748, 696; ^1H NMR (δ, ppm): 1.98 (s, 1H, H_1), 3.92 (dd, 1H, H_{2a}, $J_{2a,3a}$=11.30 Hz), 3.86 (dd, 1H, H_{6a}, $J_{6a,5a}$=11.41 Hz), 3.51 (t, 1H, H_{5e}, $J_{6a,5e}$=2.95 Hz), 2.54 (t, 1H, H_{3e}, $J_{2a,3e}$=2.90 Hz), 2.32 (s, 3H, CH_3 at phenyl ring);

2.36 (m, 1H, H_{3a}), 2.04 (m, 1H, H_{5a}), 7.52-7.09 (m, 8H, H_{arom}), 8.03 (s, 1H, N-OH).

2,6-bis(4-chlorophenyl)piperidine-4-one oxime 17 Reaction time: 10 min. IR (KBr) (cm^{-1}): 3253, 3035, 2921, 1677, 1598, 762, 705; ^{1}H NMR (δ, ppm): 2.02 (s, 1H, H_l), 3.96 (dd, 1H, H_{2a}, $J_{2a,3a}$=11.7 Hz), 3.89 (dd, 1H, H_{6a}, $J_{6a,5a}$=11.8 Hz), 3.56 (t, 1H, H_{5e}, $J_{6a,5e}$=2.94 Hz), 2.58 (t, 1H, H_{3e}, $J_{2a,3e}$=2.92 Hz), 2.40 (m, 1H, H_{3a}), 2.08 (m, 1H, H_{5a}), 7.52-7.24 (m, 8H, H_{arom}), 8.06 (s, 1H, N-OH).

General synthetic procedure for the synthesis of 3,3-dimethyl-2,6-diarylpiperidin-4-one oximes in dry media 18-22

Appropriate 3,3-dimethyl-2,6-diarylpiperidin-4-ones **4-8** (0.001 mol) and hydroxylamine hydrochloride (0.001 mol) were mixed thoroughly with activated fly ash (50mg) in a mortar and pestle. The mixture was grinded briskly for 5-10 min. (monitored by TLC) and the reaction mixture was shaken well with dichloromethane (15 mL). The catalyst was removed by simple filtration. The dichloromethane layer was dried over anhydrous sodium sulphate and distilled off under reduced pressure to yield the respective 3,3-dimethyl-2,6-diarylpiperidin-4-one oximes **18-22**.

3,3-dimethyl-2,6-diphenylpiperidin-4-one oxime 18 Reaction time: 5 min. IR (KBr) (cm^{-1}): 3260, 3030, 2980, 2924, 2851, 2819, 1493, 742, 702; ^{1}H NMR (δ, ppm): 0.98 (s, 3H, CH_3 at C-3), 1.24 (s, 3H, CH_3 at C-3), 2.42 (t, 1H, H_{5a}); 3.62 (dd, 1H, H_{5e}, $J_{5e,5a}$=14.95; $J_{5e,6a}$=3.86 Hz), 3.70 (d, 1H, H_{2a}), 3.79 (dd, 1H, H_{6a}, $J_{5a,6a}$ =12.85 Hz), 2.10 (s, 1H, H_l), 7.25-7.71 (m, 10H, H_{arom}), 8.93 (s, 1H, C=N-OH)

3,3-dimethyl-2,6-bis(p-methylphenyl)piperidin-4-one oxime 19: Reaction time: 7 min. IR (KBr) (cm^{-1}): 3254, 3028, 2977, 2922, 2855, 1513, 816; ^{1}H NMR (δ, ppm): 0.97 (s, 3H, CH_3 at C-3), 1.22 (s, 3H, CH_3 at C-3), 2.12 (s, 1H, H_l), 2.34 (t, 1H, H_{5a}); 2.35 (s, 6H, CH_3 at phenyl rings), 3.58 (dd, 1H, H_{5e} $J_{5e,5a}$=14.92; $J_{5e,6a}$=3.93 Hz), 3.63 (d, 1H, H_{2a}), 3.73 (dd, 1H, H_{6a} $J_{5a,6a}$ =12.82 Hz), 7.15-7.41 (m, 8H, H_{arom}), 8.21 (s, 1H, C=N-OH)

3,3-dimethyl-2,6-bis(p-methoxyphenyl)piperidin-4-one oxime 20: Reaction time: 8 min. IR (KBr) (cm^{-1}): 3287, 3026, 2931, 2836, 1513, 831; ^{1}H NMR (δ, ppm): 0.95 (s, 3H, CH_3 at C-3), 1.25 (s, 3H, CH_3 at C-3), 2.10 (s, 1H, H_l), 2.49 (t, 1H, H_{5a}); 3.61 (dd, 1H, H_{5e}, $J_{5e,5a}$=14.85; $J_{5e,6a}$=3.85 Hz), 3.80 (s, 6H, OCH_3 at phenyl rings), 3.74 (d, 1H, H_{2a}), 3.81 (dd, 1H, H_{6a}, $J_{5a,6a}$=12.81 Hz), 6.92-7.71 (m, 8H, H_{arom}), 8.34 (s, 1H, C=N-OH).

3,3-dimethyl-2,6-bis(p-chlorophenyl)piperidin-4-one oxime 21: Reaction time: 8 min. IR (KBr) (cm^{-1}): 3492, 3027, 2981, 2836, 1513, 831; ^{1}H NMR (δ, ppm): 0.98 (s, 3H, CH_3 at C-3), 1.20 (s, 3H, CH_3 at C-3), 2.16 (s, 1H, H_l), 2.33 (t, 1H, H_{5a}); 3.58 (dd, 1H, $H_{5e,}$ $J_{5e,5a}$=14.94; $J_{5e,6a}$=3.88 Hz), 3.67 (d, 1H, H_{2a}), 3.74 (dd, 1H, H_{6a}, $J_{5a,6a}$=12.96 Hz), 7.26-7.58 (m, 8H, H_{arom}), 8.23 (s, 1H, C=N-OH).

3,3-dimethyl-2,6-bis(p-fluorophenyl)piperidin-4-one oxime 22: Reaction time: 7 min. IR (KBr) (cm^{-1}): 3491, 3027, 2980, 2924, 2851, 1496, 1089, 836; ^{1}H NMR (δ, ppm): 0.97 (s, 3H, CH_3 at C-3), 1.18 (s, 3H, CH_3 at C-3), 2.18 (s, 1H, H_l), 2.31 (t, 1H, H_{5a}); 3.55 (dd, 1H, $H_{5e,}$ $J_{5e,5a}$=14.91; $J_{5e,6a}$=3.85 Hz), 3.65 (d, 1H, H_{2a}), 3.72 (dd, 1H, H_{6a}, $J_{5a,6a}$ =12.94 Hz), 7.24-7.55 (m, 8H, H_{arom}), 8.20 (s, 1H, C=N-OH).

General synthetic procedure for the synthesis of 2,6-diaryltetrahydrothiopyran-4-one oximes in dry media 23-25

Appropriate 2,6-diaryltetrahydrothiopyran-4-ones **9-11** (0.001 mol) and hydroxylamine hydrochloride (0.001 mol) were mixed thoroughly with activated fly ash (50mg) in a mortar and pestle. The mixture was grinded briskly for 7-10 min. (monitored by TLC) and the reaction mixture was shaken well with dichloromethane (15 mL). The catalyst was removed by simple filtration. The dichloromethane layer was dried over anhydrous sodium sulphate and distilled off under reduced pressure to yield the respective 2,6-diaryltetrahydrothiopyran-4-one oximes **23-25**.

2,6-diphenyltetrahydrothiopyran-4-one oxime 23 Reaction time: 10 min. IR (KBr) (cm^{-1}): 3172, 3060, 2900, 1649, 748, 696; ^{1}H NMR (δ, ppm): 4.20 (dd, 1H, H_{2a}, $J_{2a,3a}$=12.16 Hz), 4.14 (dd, 1H, H_{6a}, $J_{6a,5a}$=12.4 Hz), 3.96 (dd, 1H, H_{5e}, $J_{6a,5e}$=2.44 Hz), 2.93 (dd, 1H, H_{3e}, $J_{2a,3e}$=2.72 Hz), 2.77 (dd, 1H, H_{3a}, $J_{3a,3e}$=13.52 Hz), 2.37 (dd, 1H, H_{5a}, $J_{5a,5e}$=13.62

Hz), 7.40-7.29 (m, 10H, H_{arom}), 7.55 (s, 1H, N-OH).

2,6-bis(4-methylphenyl)tetrahydrothiopyran-4-one oxime 24 Reaction time: 8 min. IR (KBr) (cm^{-1}): 3170, 3057, 2896, 1647, 744, 693; ^{1}H NMR (δ, ppm): 4.17 (dd, 1H, H_{2a}, $J_{2a,3a}$=12.16 Hz), 4.12 (dd, 1H, H_{6a}, $J_{6a,5a}$=12.30 Hz), 3.94 (dd, 1H, H_{5e}, $J_{6a,5e}$=2.43 Hz), 2.91 (dd, 1H, H_{3e}, $J_{2a,3e}$=2.70 Hz), 2.75 (dd, 1H, H_{3a}, $J_{3a,3e}$=13.54 Hz), 2.30 (s, 3H, CH_3 at phenyl ring); 2.35 (dd, 1H, H_{5a}, $J_{5a,5e}$=13.60 Hz), 7.37-7.26 (m, 8H, H_{arom}), 7.51 (s, 1H, N-OH).

2,6-bis(4-chlorophenyl)tetrahydrothiopyran-4-one oxime 25 Reaction time: 7 min. IR (KBr) (cm^{-1}): 3175, 3066, 2905, 1652, 756, 690; ^{1}H NMR (δ, ppm): 4.22 (dd, 1H, H_{2a}, $J_{2a,3a}$=12.18 Hz), 4.16 (dd, 1H, H_{6a}, $J_{6a,5a}$=12.41 Hz), 3.97 (dd, 1H, H_{5e}, $J_{6a,5e}$=2.40 Hz), 2.95 (dd, 1H, H_{3e}, $J_{2a,3e}$=2.71 Hz), 2.78 (dd, 1H, H_{3a}, $J_{3a,3e}$=13.55 Hz), 2.39 (dd, 1H, H_{5a}, $J_{5a,5e}$=13.64 Hz), 7.45-7.31 (m, 8H, H_{arom}), 7.58 (s, 1H, N-OH).

General synthetic procedure for the synthesis of 2,6-diaryltetrahydropyran-4-one oximes in dry media 26-28

Appropriate 2,6-diaryltetrahydropyran-4-ones **12-14** (0.001 mol) and hydroxylamine hydrochloride (0.001 mol) were mixed thoroughly with activated fly ash (50 mg) in a mortar and pestle. The mixture was grinded briskly for 7-10 min. (monitored by TLC) and the reaction mixture was shaken well with dichloromethane (15 mL). The catalyst was removed by simple filtration. The dichloromethane layer was dried over anhydrous sodium sulphate and distilled off under reduced pressure to yield the respective 2,6-diaryltetrahydropyran-4-one oximes **26-28**.

2,6-diphenyltetrahydropyran-4-one oxime 26 Reaction time: 7 min. IR (KBr) (cm^{-1}): 3226, 3030, 2896, 1661, 736, 690; ^{1}H NMR (δ, ppm): 4.78 (dd, 1H, H_{2a}, $J_{2a,3a}$=10.30 Hz), 5.13 (dd, 1H, H_{6a}, $J_{6a,5a}$=12.53 Hz), 3.34 (m, 1H, H_{5e}), 2.70 (m, 2H, H_3), 2.84 (m, 1H, H_{5a}), 7.62-7.14 (m, 10H, H_{arom}), 7.90 (s, 1H, N-OH).

2,6-bis(4-methylphenyl)tetrahydropyran-4-one oxime 27 Reaction time: 6 min. IR (KBr) (cm^{-1}): 3223, 3027, 2891, 1658, 733, 688; ^{1}H NMR (δ, ppm): 4.77 (dd, 1H, H_{2a}, $J_{2a,3a}$=10.29 Hz), 5.10 (dd, 1H, H_{6a}, $J_{6a,5a}$=12.54 Hz), 3.32 (m, 1H, H_{5e}), 2.28 (s, 3H, CH_3 at phenyl ring); 2.67 (m, 2H, H_3), 2.81 (m, 1H, H_{5a}), 7.58-7.11 (m, 8H, H_{arom}), 7.87 (s, 1H, N-OH).

2,6-bis(4-chlorophenyl)tetrahydropyran-4-one oxime 28 Reaction time: 8 min. IR (KBr) (cm^{-1}): 3229, 3035, 2899, 1665, 739, 696; ^{1}H NMR (δ, ppm): 4.79 (dd, 1H, H_{2a}, $J_{2a,3a}$=10.29 Hz), 5.15 (dd, 1H, H_{6a}, $J_{6a,5a}$=12.55 Hz), 3.37 (m, 1H, H_{5e}), 2.73 (m, 2H, H_3), 2.88 (m, 1H, H_{5a}), 7.68-7.19 (m, 8H, H_{arom}), 7.92 (s, 1H, N-OH).

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REFERENCES

1. El-Subbagh, H. I.; Abu-Zaid, S. M.; Mahran, M. A.; Badria, F. A.; Alofaid, A. M. *J. Med. Chem.* **2000**, *43,* 2915.
2. Watson, A. A.; Fleet, G. W. J.; Asano, N.; Molyneux, R. J.; Nugh, R. J. *Phytochemistry,* **2001**, *56*, 265.
3. Ganellin, C. R.; Spickett, R. G. *J. Med. Chem*. **1965**, *8*, 619.
4. Hagenbach, R.E.; Gysin, H. *Experimentia,* **1952**, *8*, 184.
5. Ileana, B.; Dobre, V.; Nicluescu-Duvaz, I. *J. Prakt. Chem.* **1985,** *27,* 667.
6. Mokio, I. G.; Soldatenkov, A. T.; Federov, V. O.; Ageev, E. A.; Sergeeva, N. D.; Lin, S.; Stashenku, E. E.; Prostakov, N. S.; Andreeva, E. L.; *Khim. Farm. Zh.* **1989,** *23*, 421.
7. Dimmock, J. R.; Kumar, P. *Curr. Med. Chem*. **1997**, *4,* 1.
8. Kubota, H.; Kakefuda, A.; Okamoto, Y.; Fujii, M.; Yamamoto, O.; Yamgiwa, Y.; Orita, M.; Ikeda, K.; Takenchi, M.; Shibanuma, T.; Fsomura, Y. *Chem. Pharm. Bull.* **1998,** *46,* 1538.
9. Rameshkumar, N.; Veena, A.; Ilavarasu, R.; Adiraj, M.; Shanmugapandian, P.; Sridhar, S. K. *Biol. Pharm. Bull.* **2003**, *26*, 188.
10. Park, S.; Choi, Y.; Han, H.; Yang, S.; Chang, S. *Chem. Commun.* **2003**, 1936.
11. Liu, K.; Shelton, B.; How, R. K. A. *J. Org. Chem.* **1980**, *45*, 3916.
12. Schoenewaldt, E. F.; Kinnel, R. B.; Davis, P. *J. Org.*

Chem. **1968**, *33*, 4270.
13. Sarvari, M. H.; *Synthesis*. **2005**, 787.
14. Hajipour, A. R.; Mallakpour, S. E.; Imanzadeh, G. A. *J. Chem. Res. (S)*, **1999**, 228.
15. Sharghi, H.; Hosseini, M. *Synthesis.* **2002**, 1057.
16. Yamada, Y. M. A.; Tabata, H.; Takahashi, H.; Ikegami, S. *Synlett*, **2002**, 2031.
17. Watt, J. D.; Throne, D. J. *J. Appl. Chem*. **1965**, *15*, 595.
18. Throne, D. J.; Watt, J. D. *J. Appl. Chem.* **1966**, *16*, 33.
19. Saraswathy, V.; Muralidharan, S.; Thangavel, K.; Srinivasan, S. *Cement Concr. Res.* **2003**, *25*, 673.
20. Gopalakrishnan, M.; Sureshkumar, P.; Kanagarajan, V.; Thanusu, J.; Govindaraju, R. *Arkivoc.* **2006**, *13*, 1.
21. Gopalakrishnan, M.; Sureshkumar, P.; Thanusu, J.; Kanagarajan. V.; Govindaraju, R.; Jayasri, G. *J. Enz. Inhib. Med. Chem*. **2007**, *22,* 709.
22. Gopalakrishnan, M.; Sureshkumar, P.; Thanusu, J.; Prabhu, C.; Kanagarajan, V. *J. Chem. Res.* **2007**, *2,* 80.
23. Gopalakrishnan, M.; Sureshkumar, P.; Thanusu, J.; Kanagarajan, V. *J. Enz. Inhib. Med. Chem.* **2008**, *23*, 87.
24. Gopalakrishnan, M.; Sureshkumar, P.; Kanagarajan, V.; Thanusu, J. *J. Sulf. Chem.* **2007**, *28*, 383.
25. Greene, T. W.; Wuts, P. G. M. *Protective Group in Organic synthesis*, 2nd Ed.; John Wiley and Sons, New York, U. S. A., 1991; p 175.
26. Whitesell, J. K.; Whitesell, M. A. *Synthesis.* **1983**, 517.
27. Weissermer, K.; Arpe, H. J. *Industrial Organic Chemistry, Springer Verlag,* New York, U. S. A., 1978; p 222.
28. Jencks. *J. Amer. Chem. Soc*. **1959**, *81,* 475.
29. Tvaruzkova, Z.; Habersberger, K.; Zilkovo, N.; Jiru. *Appl. Catal. A* **1991**, *79*, 105.
30. Noller, C. R.; Baliah, V. *J. Amer. Chem. Soc*. **1948**, *70*, 3853.
31. Arndt, F.; Nachtway, P.; Pusch, J. *Chem. Ber*. **1925**, *58*, 1637.
32. Petrenko-Kritschenko; Plotnikoff. *Chem. Ber*. **1877**, *30,* 2802.