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Synthesis of cyclic nitrone and 1,2-oxazine from 1,2,4-triaryl-but-2-ene-1,4-dione and hydroxylamine

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Abstract. The reaction of hydroxylamine hydrochloride with differently substituted phenyldibenzoylethylene has been investigated. Both cyclic nitrone and 1,2-oxazine have been isolated and characterized by one- and two-dimensional NMR data and also by single crystal X-ray analysis.

Keywords. 1,2,-Oxazines; cyclic nitrones; 1,4-diketones; regioselectivity; two-dimensional NMR.

1. Introduction

Cyclic nitrones have drawn special attention due to their successful application as building blocks in the synthesis of various natural and biologically active compounds.[1] They are commonly used as precursors[2] in the synthesis of a variety of heterocycles, as spin-trapping reagents in the identification of transient radicals[3] and as therapeutic agents.[4] Nitrones possess one of the largest dipole moments known for any functional group type (3.37-3.47 D) making them potentially useful for NLO applications and control of molecular orientation. They offer a simple route to stable radicals *via* one-electron electrochemical reduction.[5] Annealation of imidazolidinyl-based nitronyl nitroxides leads to stable planar spin delocalized radicals, the benzonitronyl nitroxides, which exhibit strong magnetic exchange through efficient π-π stacking interactions in the solid state.[6]

1,2-Oxazines have gained interest in organic synthesis as useful intermediates[7] in the synthesis of natural products[8] and unnatural cyclic amino acids.[9] 1,2-Oxazines exhibit a broad spectrum of biological activities.[10]

We are interested in the reactions of different nucleophiles with diketones in the process of generating new heterocycles.[11] In this connection, it has been planned to investigate the reaction of phenyldibenzoylethylene with hydroxylamine hydrochloride. A few references[12] are available in which the reaction of unsubstituted phenyldibenzoylethylene with hydroxylamine hydrochloride has been mentioned, but a systematic study has now been carried out in order to (i) analyse the structure of the products unambiguously, (ii) look upon the regioselectivity, if any, in the case of substituted phenyldibenzoylethylene and (iii) ascertain the mechanism of the reaction.

2. Experimental

2.1 *General*

Nuclear Magnetic Resonance (^{1}H and ^{13}C NMR) spectra were recorded on a Bruker 300 MHz spectrometer in $CDCl_3$ using TMS as an internal standard. Chemical shifts are reported in parts per million (δ), coupling constants (J values) are reported in Hertz (Hz). ^{13}C NMR spectra were routinely run with broadband decoupling. Infrared spectra were recorded on a Shimatzu FT-IR instrument (in KBr pellet). Band positions are reported in reciprocal centimeters (cm^{-1}). Melting points were determined on a melting point apparatus (Inlab Pvt Ltd, India) equipped with a thermometer and were uncorrected. Column chromatography was carried out in silica gel (60-120 mesh) using petroleum ether-ethyl acetate as eluent. Elemental analyses were performed on a Perkin Elmer 2400 series II Elemental CHNS analyzer.

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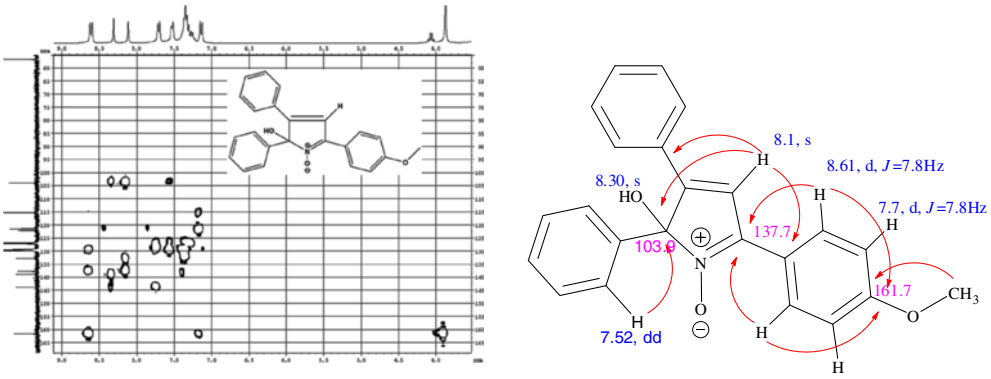


Figure 1. HMBC-NMR spectra of **7e** and some selected correlation diagram.

2.2 *General procedure*

A mixture of 1,2-diphenyl-4-arylbut-2-ene-1,4-dione (**2**) (3.61 mmol), hydroxylamine hydrochloride (7.22 mmol) and sodium acetate (7.22 mmol) in ethanol was heated under reflux for 2 h. After completion of the reaction, the reaction mixture was poured into crushed ice and filtered. The crude product was purified by column chromatography using petroleum ether-ethyl acetate mixture as eluent to yield **7** and **4/8**.

2.2a *4-(5-Bromothiophen-2-yl)-4-(hydroxyimino)-1,2-diphenylbut-2-en-1-one (**4f**)*: Yellow colour solid; m.p. 156–158°C; IR (KBr) 3625, 1654, 1632, 1210 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.10$ (d, $J = 4.2$ Hz, 1H), 7.25–7.29 (m, 3H), 7.39–7.43 (m, 3H), 7.46 (s, 1H), 7.57 (d, $J = 4.2$ Hz, 1H), 7.58–7.66 (m, 4H), 8.44 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 120.5$, 123.0, 126.4, 127.2, 128.5, 129.2, 129.6, 130.6, 131.3, 131.9, 133.7, 135.2, 147.2, 149.0, 156.9, 179.3; Anal. Calcd. for $C_{20}H_{14}BrNO_2S$ (%): C, 58.26; H, 3.42; N, 3.40; S, 7.78. Found (%): C, 58.02; H, 3.26; N, 3.24; S, 7.62.

2.2b *2-Hydroxy-2,4,5-triphenyl-2H-pyrrole-1-oxide (**7a**)*: Yellow colour solid; m.p. 179–181°C (lit. m.p. 179°C);[12a] IR (KBr) 3088, 3061, 2850, 1674, 1593, 1523, 1485, 1371, 1205 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 6.75$ (s, 1H), 7.24–7.63 (m, 13H), 8.09 (dd, $J = 7.8$ Hz, 1.2 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 103.9$, 117.6, 125.7, 126.5, 127.2,* 127.9, 128.3, 128.5, 128.6, 128.9, 129.2, 130.9, 136.7, 140.5, 146.9; Anal. Calcd. for $C_{22}H_{17}NO_2$ (%): C, 80.71; H, 5.23; N, 4.28. Found (%): C, 80.59; H, 5.12; N, 4.09. * two carbons are merged together.

2.2c *5-(4-Chlorophenyl)-2-hydroxy-2,4-diphenyl-2H-pyrrole-1-oxide (**7b**)*: Yellow colour solid; m.p. 152–154°C; IR (KBr): 3095, 2939, 2840, 1665, 1598, 1531, 1438, 1213, 780 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 6.81$ (s, 1H), 7.25–7.55 (m, 13H) 8.12 (d, $J = 7.2$ Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 103.1$, 117.2, 126.0, 126.5, 127.2, 127.9 128.0, 128.3, 128.7, 128.9, 129.0, 129.6, 131.2, 136.9, 140.4, 144.5; Anal. Calcd. for $C_{22}H_{16}ClNO_2$ (%): C, 73.03; H, 4.46; N, 3.87. Found (%): C, 72.92; H, 4.35; N, 3.76.

2.2d *5-(4-Bromophenyl)-2-hydroxy-2,3-diphenyl-2H-pyrrole-1-oxide (**7c**)*: Yellow colour solid; m.p. 171–173°C; IR (KBr) 3075, 3028, 2846, 1671, 1591, 1524, 1438, 1213, 688 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): $\delta = 7.11$–7.24 (m, 6H), 7.38–7.41 (m, 2H), 7.54 (d, $J = 7.5$ Hz, 2H), 7.64 (d, $J = 8.7$ Hz, 2H), 8.02 (s, 1H), 8.32 (s, 1H), 8.42 (d, $J = 8.7$ Hz, 2H); ^{13}C NMR (75 MHz, DMSO-d_6): $\delta = 104.7$, 121.0, 124.3, 126.8, 127.2, 128.4, 129.4, 129.6, 129.7, 129.8, 130.0, 132.6, 132.9, 137.4, 138.5, 143.8; Anal. Calcd. for $C_{22}H_{16}BrNO_2$ (%): C, 65.04; H, 3.97; N, 3.45. Found (%): C, 64.92; H, 3.84; N, 3.29.

2.2e *2-Hydroxy-2,3-diphenyl-5-p-tolyl-2H-pyrrole-1-oxide (**7d**)*: Yellow colour solid; m.p. 151–153°C; IR (KBr) 3067, 2938, 2825, 1662, 1596, 1529, 1438 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): $\delta = 2.39$ (s, 3H), 7.24–7.53 (m, 10H), 7.66 (d, $J = 7.2$ Hz, 2H), 7.90 (s, 1H), 8.30 (s, 1H), 8.44 (d, $J = 7.2$ Hz, 2H); ^{13}C NMR (75 MHz, DMSO-d_6): $\delta = 19.5$, 101.4, 118.0, 123.6, 123.8, 124.3, 125.1, 126.3, 126.4, 126.6, 126.8, 127.4, 129.7, 135.4, 135.7, 138.3, 141.3; Anal. Calcd. for $C_{23}H_{19}NO_2$ (%): C, 80.92; H, 5.61; N, 4.10. Found (%): C, 80.79; H, 5.54; N, 3.96.

2.2f *2-Hydroxy-5-(4-methoxyphenyl)-2,3-diphenyl-2H-pyrrole-1-oxide (**7e**)*: Yellow colour solid; m.p. 163–165°C; IR (KBr): 3088, 3022, 2927, 2816, 1657,

1589, 1531, 1438 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ = 3.48 (s, 3H), 7.13 (d, J = 8.7 Hz, 2H), 7.23–7.37 (m, 6H), 7.51–7.53 (m, 2H), 7.70 (d, J = 7.5 Hz, 2H), 8.11 (s, 1H), 8.30 (s, 1H), 8.61 (d, J = 8.7 Hz, 2H); ^{13}C NMR (75 MHz, DMSO-d_6): δ = 56.6, 103.9, 115.3, 121.5, 122.1, 126.9, 127.1, 129.2, 129.5, 129.7, 129.8, 130.9, 132.7, 137.7, 138.9, 143.9, 161.7; Anal. Calcd. for $C_{23}H_{19}NO_3$ (%): C, 77.29; H, 5.36; N, 3.92. Found (%): C, 77.18; H, 5.28; N, 3.80.

2.2g *5-(5-Bromothiophen-2-yl)-2-hydroxy-2,3-diphenyl-2H-pyrrole 1-oxide (**7f**)*: Yellow colour solid; m.p. 144–146°C; IR (KBr): 3068, 2929, 2847, 1669, 1592 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 6.77 (s, 1H), 7.05 (d, J = 4.2 Hz, 1H), 7.10 (d, J = 4.2 Hz, 1H). 7.25–7.35 (m, 6H), 7.59–7.62 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 102.7, 114.8, 119.2, 125.8, 126.9, 128.6, 128.7, 129.4,* 129.5,* 130.2, 130.6, 136.2, 137.9, 148.6; Anal. Calcd. for $C_{20}H_{14}BrNO_2S$ (%): C, 58.26; H, 3.42; N, 3.40; S, 7.78. Found (%): C, 58.08; H, 3.34; N, 3.31; S, 7.65. * two carbons are merged together.

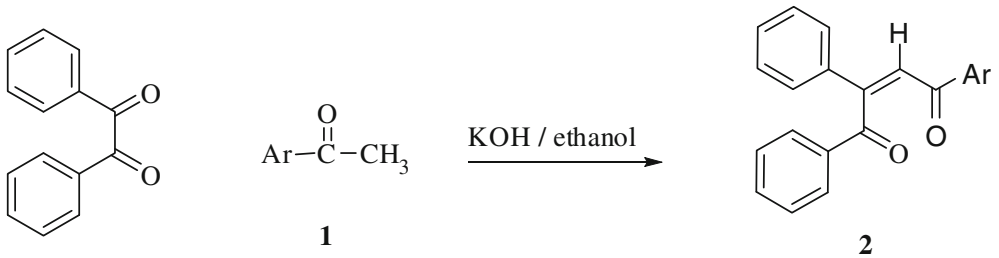
2.2h *3,5,6-Triphenyl-6H-1,2-oxazin-6-ol (**8a**)*: Yellow colour solid; m.p. 159–160°C; IR (KBr): 3198, 1624, 1491, 1209, 1008, 692 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 3.99 (bs, 1H), 6.75 (s, 1H), 7.15–7.55 (m, 13H), 7.80 (dd, J = 7.8 Hz, 1.2 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 97.4, 113.0, 126.2, 127.3, 127.8,* 128.1, 128.2, 128.6, 128.8, 129.9, 133.8, 135.6, 139.7, 143.2, 153.3; Anal. Calcd. for $C_{22}H_{17}NO_2$ (%): C, 80.71; H, 5.23; N, 4.28. Found (%): C, 80.58; H, 5.17; N, 4.23. * two carbons are merged together.

2.2i *3-(4-Chlorophenyl)-5,6-diphenyl-6H-1,2-oxazin-6-ol (**8b**)*: Yellow colour solid; m.p. 163–165°C; IR (KBr): 3192, 1632, 1497, 1212, 1012, 725 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ = 4.01 (bs, 1H), 6.75 (s, 1H), 7.15–7.55 (m, 12H), 7.80 (d, J = 7.2 Hz, 2H); ^{13}C NMR (75 MHz, DMSO-d_6): δ = 97.6, 112.9, 126.4, 127.5, 127.8, 127.9, 128.2, 128.5, 128.7, 128.9, 130.0, 133.2, 135.4, 139.5, 143.5, 152.1; Anal. Calcd. for $C_{22}H_{16}ClNO_2$ (%): C, 73.03; H, 4.46; N, 3.87. Found (%): C, 72.92; H, 4.35; N, 3.75.

2.2j *3-(4-Bromophenyl)-5,6-diphenyl-6H-1,2-oxazin-6-ol (**8c**)*: Yellow colour solid; m.p. 172–174°C; IR (KBr): 3201, 1629, 1496, 1205, 1002, 682 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ = 6.95 (s, 1H), 7.11–7.16 (m, 6H), 7.34–7.41 (m, 4H), 7.61 (d, J = 8.1 Hz, 2H), 7.79 (d, J = 8.1 Hz, 2H), 8.06 (s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6): δ = 96.2, 111.6, 122.7, 126.8, 127.0, 127.4, 127.8, 127.9, 128.4, 131.2, 131.7, 132.6, 135.1, 140.5, 141.2, 151.1; Anal. Calcd. for $C_{22}H_{16}BrNO_2$ (%): C, 65.04; H, 3.97; N, 3.45. Found (%): C, 64.91; H, 4.02; N, 3.34.

2.2k *5,6-Diphenyl-3-p-tolyl-6H-1,2-oxazin-6-ol (**8d**)*: Yellow colour solid; m.p. 146–148°C; IR (KBr): 3192, 1641, 1497, 1222, 1011, 656 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 2.39 (s, 3H), 4.10 (s, 1H), 6.71 (s, 1H), 7.19–7.51 (m, 12H), 7.68 (d, J = 7.5 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.3, 97.2, 113.0, 126.0, 127.3, 127.7, 128.0, 128.1, 128.5, 128.7, 129.4, 130.9, 135.6, 139.7, 140.1, 143.2, 153.2; Anal. Calcd. for $C_{23}H_{19}NO_2$ (%): C, 80.92; H, 5.61; N, 4.10. Found (%): C, 80.85; H, 5.57; N, 4.04.

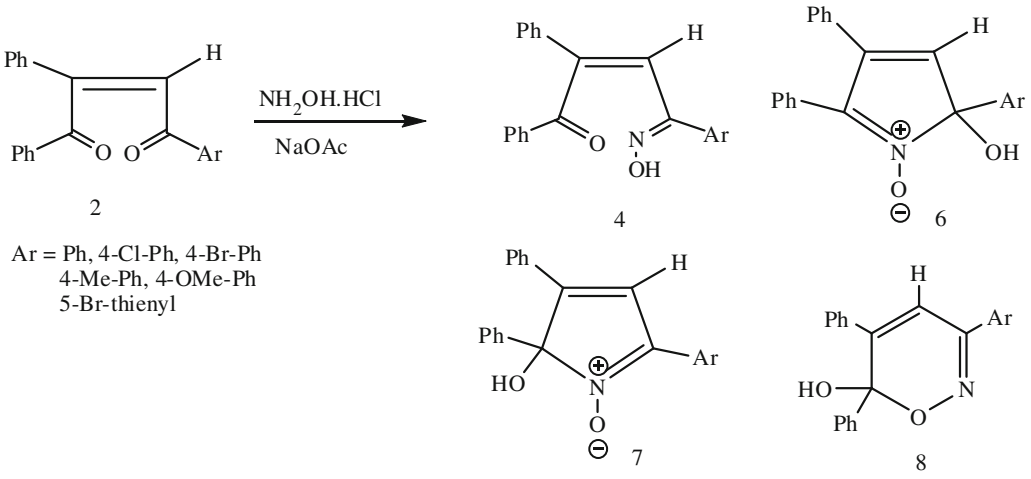
2.2l *3-(4-Methoxyphenyl)-5,6-diphenyl-6H-1,2-oxazin-6-ol (**8e**)*: Yellow colour solid; m.p.179–181°C; IR (KBr): 3209, 1632, 1498, 1213, 1012, 662 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ = 3.42 (s, 3H), 7.13 (d, J = 7.5 Hz, 2H), 7.23–7.37 (m, 4H), 7.52 (m, 2H), 7.68 (d, J = 7.5 Hz, 2H), 7.70 (d, J = 7.2 Hz, 2H), 8.02 (s, 1H), 8.30 (s, 1H), 8.61 (d, J = 8.1 Hz, 2H);



1 **2**

a) Ar = Phenyl; b) Ar = 4-Chlorophenyl;
c) Ar = 4-Bromophenyl; d) Ar = 4-Methylphenyl;
e) Ar = 4-Methoxyphenyl; f) Ar = 5-Bromo-2-thienyl

Scheme 1. Preparation of differently substituted phenyldibenzoylethylene.



Scheme 2. The reactions of hydroxylamine hydrochloride with differently substituted phenyldibenzoylethylene.

^{13}C NMR could not be recorded due to poor solubility; Anal. Calcd. for $C_{23}H_{19}NO_3$ (%): C, 77.29; H, 5.36; N, 3.92. Found (%): C, 77.08; H, 5.28; N, 3.88.

The reaction has led to two products in all the case (scheme 2). While **2a** to **2e** have yielded **7** and **8**, **2f** has led to **4f** and **7f** (table 1).

3. Results and discussion

The 1,2,4-Triaryl-but-2-ene-1,4-diones (**2**) can be prepared by the condensation of benzil and the derivatives of acetophenone/heteroaryl ketone[13] (scheme 1). To the best of our knowledge, the ketone **2f** is not reported in the literature.

1,2,4-Triaryl-but-2-ene-1,4-diones **2** were allowed to react with hydroxylamine hydrochloride and sodium acetate taken in 1:3:3 ratio. Excess hydroxylamine was used to ascertain complete hydroxylation in order to establish whether both the carbonyl groups are reactive towards the nucleophile or not. The course of the reaction was monitored by TLC. After 2 h, the diketone vanished (TLC) and the products obtained were separated and analysed for their structures. The reaction has been conducted in different protic solvents and it was found that ethanol produced the best results.

Table 1. Isolated yields of the products **4**, **7** and **8**.

Entry	Aryl	Yield of **4**	Yield of **7**	Yield of **8**
a	Phenyl	–	55	26
b	4-Chlorophenyl	–	58	21
c	4-Bromophenyl	–	48	23
d	4-Methylphenyl	–	49	22
e	4-Methoxyphenyl	–	61	20
f	5-Bromo-2-thienyl	11	68	–

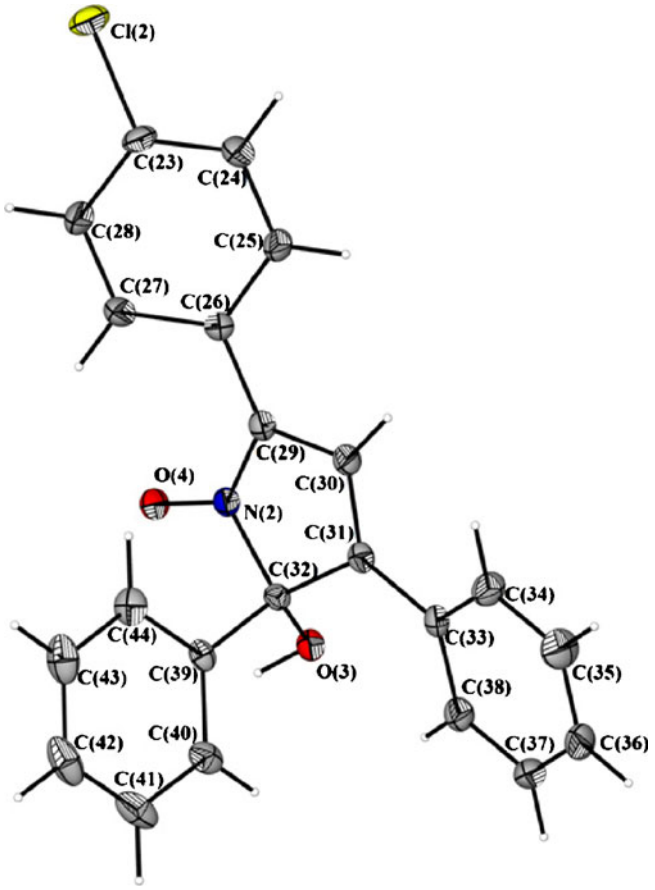


Figure 2. ORTEP diagram of **7b**.

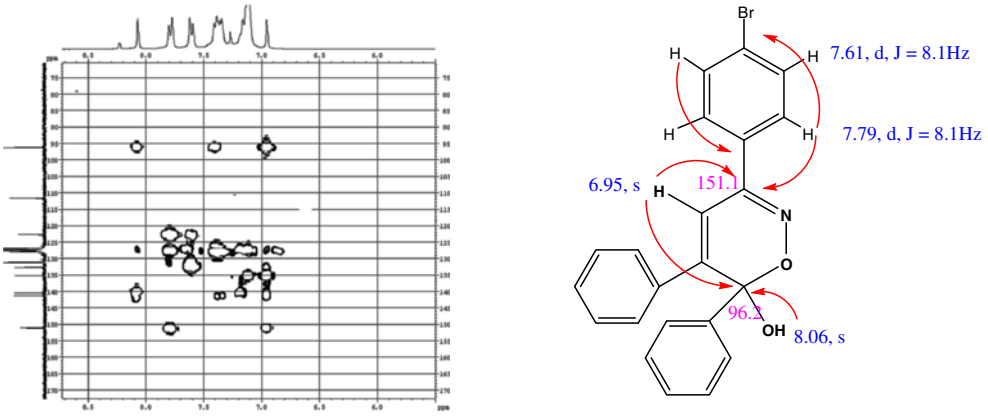


Figure 3. HMBC-NMR spectra of **8C** and some selected correlation diagram.

The structure of nitrone **7** was established by ^{1}H, ^{13}C and 2D NMR spectral data, ruling out the possibility of the regioisomer **6**, as illustrated for a representative example **7e** (figure 1). HMBC spectrum of **7e** has contours connecting deshielded doublet at 8.61 ppm with the carbons at 129.8 ppm, 137.7 ppm and 161.7 ppm. Thus, it is clear that these hydrogens are *meta* to methoxy group and this doublet is not giving any contour with the saturated quaternary carbon at 103.9 ppm.

But the doublet of doublet at 7.52 ppm due to two hydrogen has HMBC connection with the carbon at 103.9 ppm. These informations helped to unambiguously assign the regiochemistry of the product **7**. Thus the *p*-anisyl group is attached to azomethine carbon, while the aryl is attached to the saturated quaternary carbon. The structure of the cyclic nitrone **7b** was confirmed by single crystal X-ray analysis also (figure 2).[14]

Similarly the structure of 1,2-oxazine **8** has been established by ^{1}H, ^{13}C and 2D NMR spectral data as illustrated for a representative example **8c** (figure 3). Here, it is noticed that the downfield two hydrogen signal at 7.79 ppm is not a doublet of doublet, but a perfect doublet, which gives HMBC contour with the carbon at 151.1 ppm. Hence, the *p*-bromophenyl group is attached to the azomethine carbon. The olefinic singlet hydrogen at 6.95 ppm has HMBC contour with the carbons at 96.2, 135.1, 140.5 and 151.1 ppm. The alcoholic proton appears at 8.06 singlet giving an HMBC contour with the carbon 96.2 ppm revealing two bond connectivity, clearly establishing the structure of the molecule. The structure of **8c** has been confirmed by single crystal X-ray analysis (figure 4).[15]

It can be noticed that in all the cases, the regioisomer **7**, is formed exclusively and not **6**. As hydroxylamine prefers to attack the less hindered carbonyl group, the intermediate **3** would have been formed from

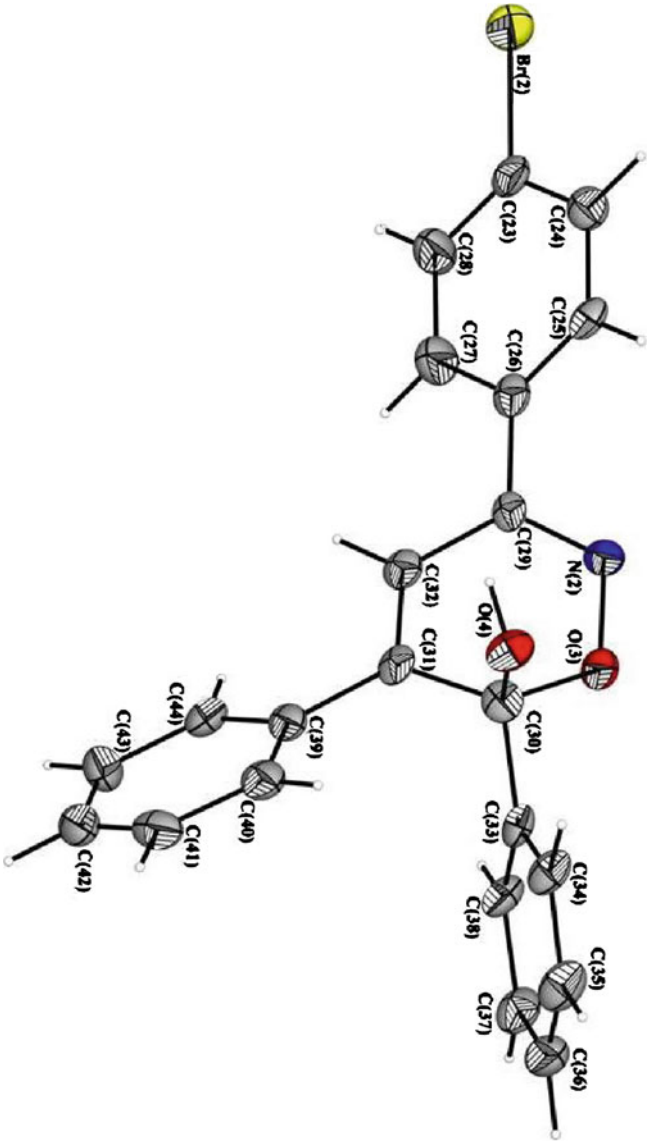
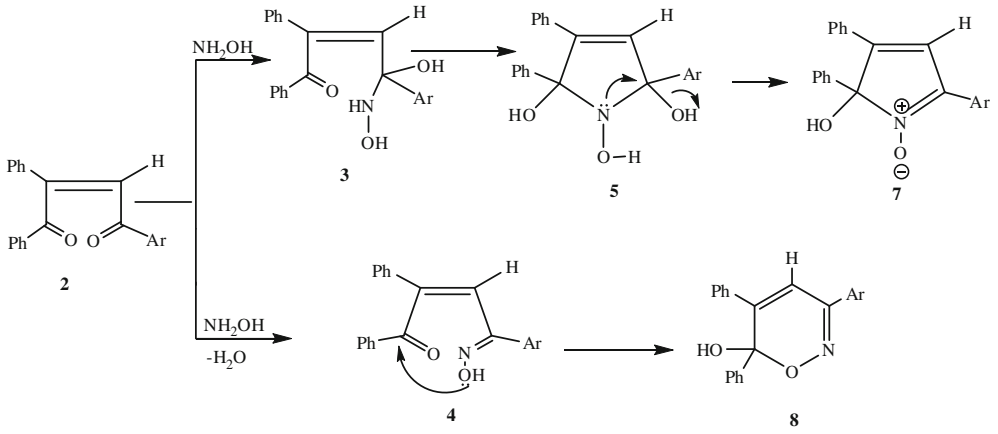


Figure 4. ORTEP diagram of **8c**.



Scheme 3. Proposed mechanism.

2 (scheme 3) easily. This can undergo water elimination to give monooxime **4**. But, the -NHOH group prefers to attack the other free carbonyl and forms the intermediate **5**. Intermediate **5** can lose water molecule to form cyclic nitrone **7**. The oxygen of the oxime **4** can attack the free carbonyl carbon to form **8**. But in **4f**, the oxime has not undergone the subsequent cyclisation. The above described steps are depicted in scheme 3.

4. Conclusion

Reaction between differently substituted 1,4-diketones with hydroxylamine hydrochloride has been investigated. Cyclic nitrone, and 1,2-oxazine have been isolated and characterized adequately by NMR and single crystal X-ray analysis. Possible mechanism for the formation of these products has been suggested accounting for the observed regioselectivity.

Supporting information

The electronic supporting information can be seen in www.ias.ac.in/chemsci.

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References

1. Breuer E, Aurich H G and Nielsen A 1989 *Nitrones, nitronates and nitroxides* (New Jersey: John Wiley and Sons); (b) Torsell K B G 1988 *Nitrile oxides, nitrones and nitronates in organic synthesis* (New York: VCH Publishers)
2. Sridharan V, Muthusubramanian S, Sivasubramanian S and Polborn K 2004 *Tetrahedron* **60** 8881; (b) Jayapradha S R, Sridharan V, Muthusubramanian S and Polborn K 2007 *J. Heterocycl. Chem.* **44** 1105; (c) Sridharan V, Saravanakumar S P and Muthusubramanian S 2005 *J. Heterocycl. Chem.* **42** 515; (d) Dondas H A, Cummins J E, Grigg R and Thornton-Pett M 2001 *Tetrahedron* **57** 7951; (e) Alibes R, Blanco P, de March P, Figueredo M, Font J, Alvarez-Larena A and Piniella J F 2003 *Tetrahedron Lett.* **44** 523; (f) Gothelf K V and Jorgensen K A 2000 *Chem. Commun.* 1449; (g) Pineiro M and Pinhoe Melo T M V D 2009 *Eur. J. Org. Chem.* 5287; (h) Andrade M M, Barros M T and Pinto R C 2008 *Tetrahedron* **64** 10521; (i) Blanarikova I, Dugovic D, Fisera L, Hametner C and Pronayova N 2001 *Arkivoc* **2** 109
3. Villamena F A and Zweier J L 2004 *Antioxid. Redox Signaling.* **6** 619
4. Floyd R A and Hensley K 2000 *Ann. N. Y. Acad. Sci.* **899** 222; (b) Arya P, Stephens J C, Griller D, Pou S, Ramos C L, Pou W S and Rosen G M 1992 *J. Org. Chem.* **57** 2297; (c) Fevig T L, Bowen S M, Janowick D A, Jones B K, Munson H R, Ohlweiler D F and Thomas C E 1996 *J. Med. Chem.* **39** 4988; (d) Wang P- F, Gao P and Xu P-F 2006 *Synlett* 1095
5. McIntire G L, Blount H N and Janzen E G 1980 *J. Phys. Chem.* **84** 916; (b) Reznikov V A, Gutorov I A and Rybalova T V 1996 *Russ. Chem. Bull.* **45** 384; (c) O'Neil I A, Potter A J and Barkley J V 1998 *Chem. Commun.* 2511
6. Gough T E and Puzic R 1976 *J. Magn. Reson.* **23** 31; (b) Zakrassov A, Shteiman V, Sheynin Y, Tumanskii B, Botoshansky M, Kapon M, Keren A, Kaftory M, Vos T E and Miller J S 2004 *J. Mater. Chem.* **14** 1827
7. Reviews dealing with 1,2-oxazines in organic synthesis: (a) Gilchrist T L 1983 *Chem. Soc. Rev.* **12** 53; (b) Lyapkalo I M and Ioffe S L 1998 *Russ. Chem. Rev.* **67** 467; (c) Tsoungas P G 2002 *Heterocycles* **57** 915; (d) Tsoungas P G 2002 *Heterocycles* **57** 1149; (e) Santos J, Ignacio R, Aparicio D, Palacios F and Ezpeleta J M 2009 *J. Org. Chem.* **74** 3444; (f) Winter C and Krause N 2009 *Angew. Chem.* **121** 6457; (g) Tabolin A A, Lesiv A V,

Khomutova Y A, Nelyubina Y V and Ioffe S L 2009 *Tetrahedron* **65** 4578; (h) Lalonde, R L, Wang Z J, Mba M, Lackner A D and Toste F D 2010 *Angew. Chem.* **122** 608

8. Terano H, Takase S, Hosoda J and Kohsaka M 1989 *J. Antibiotics* **42** 145; (b) Lin Y, Shao Z, Jiang G, Zhou S, Cai J, Vrijmoed L P and Jones E B 2000 *Tetrahedron* **56** 9607
9. Lee V J and Woodward R B 1979 *J. Org. Chem.* **44** 2487
10. Uchida I, Takase S, Kayakiri H, Kiyoto S, Hashimoto M, Tada T, Koda S and Morimoto Y 1987 *J. Am. Chem. Soc.* **109** 4108; (b) Iwami M, Kiyoto S, Terano H, Kohsaka M, Aoki H and Imanaka H 1987 *J. Antibiotics* **40** 589; (c) Kiyoto S, Shibata T, Yamashita M, Komori T, Okuhara M, Terano H, Kohsaka M, Aoki H and Imanaka H 1987 *J. Antibiotics* **40** 594; (d) Shimomura K, Hirai O, Mizota T, Matsumoto S, Mori J, Shibayama F and Kikuchi H 1987 *J. Antibiotics* **40** 600
11. Nagaraj M, Boominathan M, Muthusubramanian S and Bhuvanesh N 2011 *Org. Biomol. Chem.* **9** 4642
12. Blatt A H 1934 *J. Am. Chem. Soc.* **56** 2774; (b) Blatt A H 1936 *J. Am. Chem. Soc.* **58** 590; (c) Blatt A H 1938 *J. Org. Chem.* **3** 91; (d) Blatt A H 1950 *J. Org. Chem.* **15** 869
13. Demirdji S H, Haddadin M J and Issidorides C H 1985 *J. Heterocycl. Chem.* **22** 495
14. CCDC No. 851421
15. CCDC No. 851422