Synthesis of 1,2,4-oxadiazolidine derivatives from 1,3-cycloaddition reaction of nitrones onto Schiff bases

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The 1st Scientific Annual Conference for College of Basic Education (23-24/May/2007)

Abstract:

A series of new heterocyclic compounds of 1,2,4-oxadiazolidines (3a-l) were synthesized by 1,3-dipolar cycloaddition reaction of different nitrones (1a,b) with different Schiff bases (2a-f) under reflux condition in good yields.

The structures of all synthesized compounds were confirmed by physical and spectral data.

تصنيف مشتقات الاوكساديا زوليدين من تفاعل النيوترونات التدويري الاضافي على قواعد شيف

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ملخص البحث :

يتضمن البحث تحضير سلسلة من المركبات الحلقية غير المتجانسة 1،2،4- اوكسادايازولدين (3a-l) من تفاعل الاضافة الحلقية (3،1) الثنائية القطب لنيترونات مختلفة (1a,b) الى عدد من قواعد شيف (2a-f) وبنسبة ناتج جيدة.

تم التاكد من صحة تراكيب جميع المركبات المحضرة من خلال المعلومات الفيزيائية والطيفية.

Introduction :

Nitrones[1] are quite versatile intermediate in organic synthesis and are employed for instance in stereoselective formation of synthetically useful of new heterocyclic compounds have oxygen and nitrogen heteroatoms like isoxazolidine[2] and oxadiazolidine[3] by their 1,3-dipolar cycloaddition with alkenes[4] or other double bond compounds like imines[5].

For the preparation of nitrones, the most popular method is the condensation of aldehydes or ketones with N-monosubstituted hydroxyl amines[6] or by direct oxidation of secondary amines[7].

The nitrones play an important rules in the preparation of variety biologically active compounds[8,9] oxadiazoline compounds could be prepared from reaction of substituted hydroxyl amine with isocyanate[10] or as by Helmat found[11] that the N,N-disubstituted hydroxyl guanidine react with ethyl chloroformate to give 1,2,4-oxadiazolin-5-one.

In our recent work the nitrones prepared by the reaction of 4-picoline and 4-methyl quinoline with p-nitroso-N,N-dimethyl aniline[12]. Oxadiazolidine derivatives are vastly applications in the biological fields as antihyperglycemic agent[13] and antidepressant agents[14].

Other oxadiazolidines were used as pesticides[15]. Antifungi and herbicides[16].

Experimental

All chemicals were purchased from Flucka and BDH Chemical Ltd. The melting points were measured on an Electrothermal 9300 Engineering LTD and were uncorrected. IR spectra were recorded on Infrared Spectrophotometer Model Tensor 27, Bruker Co., Germany, using KBr discs.

Nitrone compounds (1a,b) were prepared according to the published literature[17].

1a: m.p. 176-178 °C (Lit. 176-177 °C), 63%

2a: m.p. 215-217 °C (Lit. 216-218 °C), 70%

Synthesis of arylidene amino acid (2a-f)

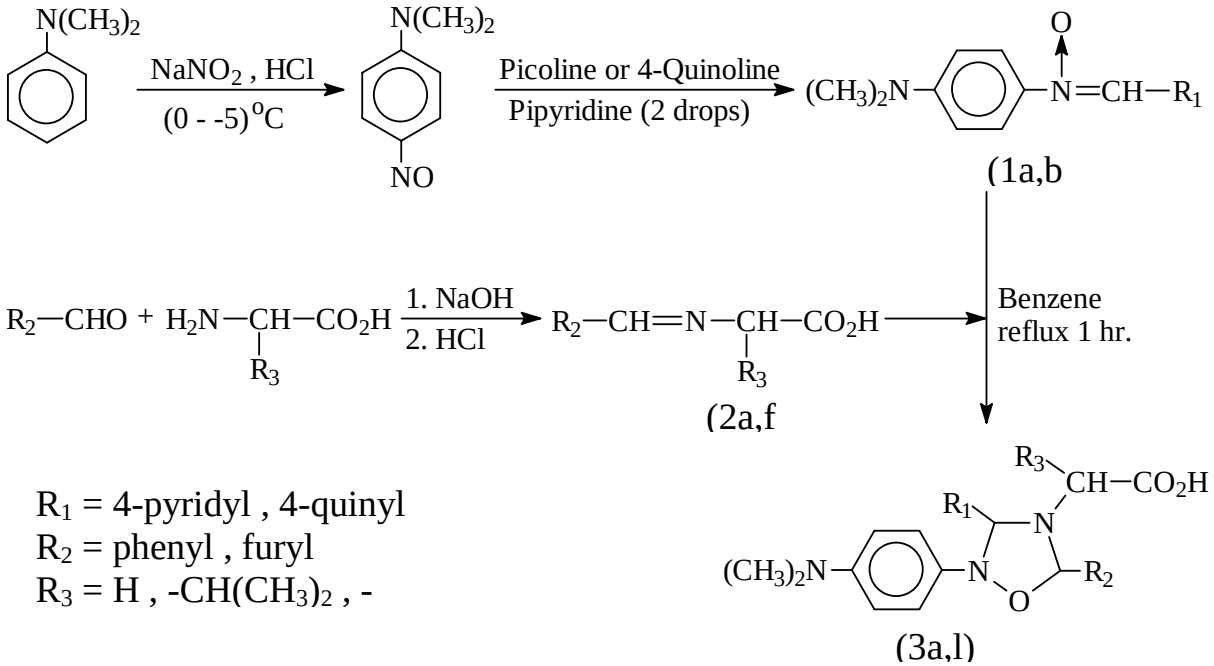
A mixture of (0.01 mole) amino acid, (0.01 mole) benzaldehyde or furfural and (0.01 mole, 0.4 gm) sodium hydroxide, was heated in a water bath at (60 °C) for (2 hrs.). The mixture was cooled and acidified with hydrochloric acid and allowed to stand overnight. The solid was filtered off, washed with cold water and recrystalized from ethanol-water (1:1) (Table 1).

Synthesis of 1,2,4-oxadiazolidine (3a-l)

A mixture of equimolar of nitrone compounds (1a,b) and Schiff bases (2a-f) in dry benzene was refluxed for 1 hr. The solvent was then evaporated under reduced pressure. The solid was collected and recrystallized from absolute ethanol (Table 2).

Results and Discussion

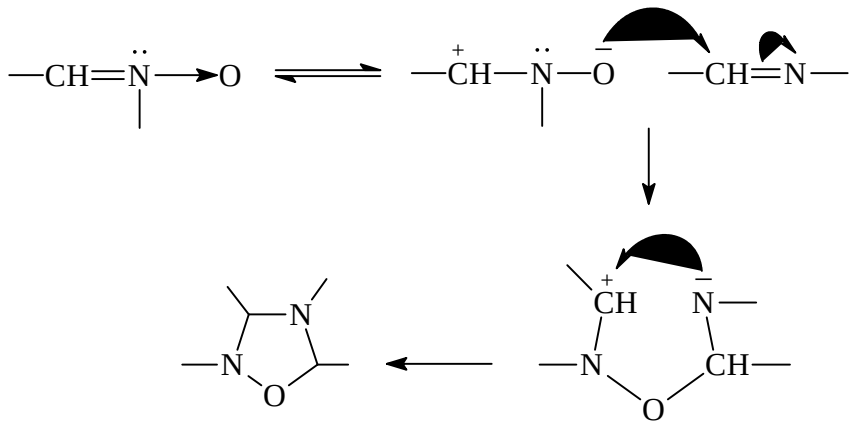
The oxadiazolidine compounds (3a-l) could be prepared by the reaction of equimolar of nitrones with imines prepared from amino acids (Scheme 1).



R_1 = 4-pyridyl , 4-quinyl
R_2 = phenyl , furyl
R_3 = H , -$CH(CH_3)_2$, -

Scheme (1)

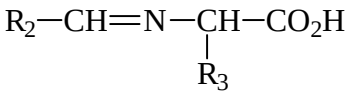
The reaction was carried out through a nucleophilic addition from the oxygen of nitrone at the carbon atom of the imines, the reaction proceed through 1,3-dipolar cycloaddition reaction of 1,3-dipole (nitrone) with dipolarophile (imine) involves the 4π electrons of the dipole and the 2π electrons of the dipolarophile.



All bonds created simultaneously but not necessarily to the same extent at a certain time. On the other hand, the reaction proceed via two steps mechanism.

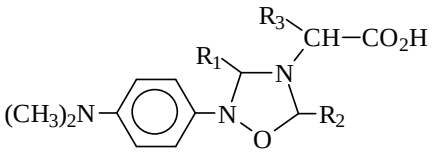
The I.R spectral data of these compounds showed an absorption bands at (1134-1171 cm^{-1}), (1260-1329 cm^{-1}), (1700-1752 cm^{-1}) and (3423-3484 cm^{-1}) related to the stretching vibration of C-O, N-O, C=O and O-H. the other stretching bands are listed in Table (2).

Table (1): Physical and I.R. data of compounds (2a-f)



Comp. No.	R_2	R_3	Yield %	m.p. °C	I.R. (KBr disk) cm^{-1}				
					O-H	C=O	C=N	C=C	C-O
2a	Ph	H	81	218-220	3456	1725	1674	1598	1162
2b	Ph	$-CH(CH_3)_2$	56	257-259	3442	1742	1681	1623	1160
2c	Ph	$-CH_2CH_2SCH_3$	70	200 d.	3482	1727	1676	1594	1159
2d	Furyl	H	69	47-50	3426	1734	1673	1601	1154
2e	Furyl	$-CH(CH_3)_2$	77	219-221	3472	1722	1684	1613	1163
2f	Furyl	$-CH_2CH_2SCH_3$	74	227-229	3428	1728	1672	1604	1167

Table (2): Physical and I.R. data of compounds (3a-f)



Comp. No.	R_1	R_2	R_3	Yield %	m.p. °C	I.R. (KBr disk) cm^{-1}					
						O-H	C=O	C=N	C=C	N-O	C-O
3a	4-pyridyl	Ph	H	85	162-164	3442	1732	1670	1599	1269	1160
3b	4-quinyl	Ph	H	91	Oily	3484	1716	1653	1600	1317	1161
3c	4-pyridyl	Furyl	H	57	240-243	3482	1726	1684	1601	1307	1159
3d	4-quinyl	Furyl	H	73	208-210	3445	1752	1641	1696	1261	1163
3e	4-pyridyl	Ph	$-CH(CH_3)_2$	77	195-197	3473	1722	1671	1600	1260	1161
3f	4-quinyl	Ph	$-CH(CH_3)_2$	82	177-179	3444	1718	1633	1599	1314	1160
3g	4-pyridyl	Furyl	$-CH(CH_3)_2$	51	213-215	3423	1720	1631	1595	1329	1134
3h	4-quinyl	Furyl	$-CH(CH_3)_2$	74	220-222	3457	1733	1644	1601	1329	1160
3i	4-pyridyl	Ph	$-CH_2CH_2SCH_3$	67	186-188	3445	1725	1604	1510	1275	1156
3j	4-quinyl	Ph	$-CH_2CH_2SCH_3$	80	191-193	3446	1716	1630	1599	1301	1171
3k	4-pyridyl	Furyl	$-CH_2CH_2SCH_3$	73	208-210	3447	1710	1602	1600	1300	1160
3l	4-quinyl	Furyl	$-CH_2CH_2SCH_3$	64	223-225	3447	1700	1610	1599	1289	1158

References:

1. Hamer J. and A. Macaluso, Chemical Rev., 64, 473, (1964).
2. B.S. Black, Molecules, 5, 135, (2000).
3. D.C. Black, R.F. Crozier and V.C. Davis, Synthesis, 205, (1975).
4. De Shony P. and dicken C.M., J. org. Chem., 2047, (1982).
5. Huisgen R., J. Org. Chem., 41, 403, (1976).
6. Khallow K.I., Ezzat S.S. and Al-Omari N.A., Bull. Chim. Farm., 141, 447, (2002).
7. Cicchi S. and Corsi M., J. Org. Chem., 64, 7243, (1999).
8. Helmat G. and Gerwalt Z., Chem. Ber., 105 (5), 1709, (1972).
9. Kametani T., Nagahara T. and Honda T., J. Org. Chem., 50, 2327, (1985).
10. Al-Ajely M.S., Basheer H.A. and Ezzat N.S., Raf. J. Sci., 16, 3, (2005).
11. Shimizn M., Gama Y. and Shibuya I., Heterocycles, 48, 1935, (1998).
12. Lown J.W. and Akhtar M.H., J. Chem. Soc. Perkin Trans., 1, 1459, (1972).
13. Malamas A. and Sready M.S., J. Med. Chem., 36, 1, (2001).
14. Srivatava P.C. and Robins R.K., J. Med. Chem., 24(10), 1172, (1981); Chem. Abstr., 95, 125911r.
15. Kimura I., Ishii Y. and Takita K., Tpn. Kokai, 7540, 738, (1975); Chem. Abstr., 83, 177502j.
16. Zabik M.J., Leav R.A. and Su G.C.C., Annal Rev. Entom., 21, 61, (1974).