JOURNAL OF AGRICULTURAL AND FOOD CHEMISTRY

Synthesis and Fungicidal Activity of Novel 4,4′-Bis(2″-aryl-5″-methyl/unsubstituted-4″-oxo-thiazolidin-3″-yl) Bibenzyl

IBADUR R. SIDDIQUI, PRAVIN K. SINGH,* JAYA SINGH, AND JAGDAMBA SINGH

Laboratory of Synthetic Organic Chemistry, Department of Chemistry, University of Allahabad, Allahabad 211002, India

Reduction followed by nitration of benzil **I** yielded 4,4′-dinitrobibenzyl (**III**) which by reduction furnished quantitatively and analytically pure 4,4′-diaminobibenzyl (**IV**) which on condensation with different carbonyl compounds gave 4,4′-bis (benzylideneamino) bibenzyls (**Va**−**f**). Compounds (**Va**−**f**) on cycloaddition with mercaptoacetic acid/2-mercaptopropionic acid yielded the corresponding 4-oxo-thiazolidin-3-yl bibenzyls (**VIa**−**l**). The compounds **VIg**−**l** have two chiral centers in each thiazolidinone moiety so two diastereomers are possible, but on crystallization and repeated chromatography, one diastereomer was obtained. The absolute configuration of the diastereomer was tentatively assigned on the basis of ^{1}H NMR spectra. ^{1}H NMR spectra of the product showed a distinct doublet at δ 1.22 for C_5-CH_3 of thiazolidinone ring (22, 23) and a distinct quartet at δ 4.20 for the C_5-H proton. Similarly, the C_2 proton showed an independent singlet at δ 5.95, so the diastereomers obtained were assigned trans configuration. Compounds **Va**−**f** and **VIa**−**l** were evaluated in vitro for their fungitoxicities against *Fusarium oxysporium* and *Penicillium citrinum.* All the compounds were found to be antifungal active. Some of the compounds displayed activities comparable with that of the commercial fungicide Dithane M-45. Structure−activity relationships for the screened compounds are discussed.

KEYWORDS: Fungicide; oxothiazolidinyl; bibenzyl

INTRODUCTION

The application of thiazolidinones as toxic agents into cells of pathogenic microorganisms have evoked considerable attention during the past 20 years (*1*−*3*). 4-Thiazolidinones are well-known for their hypnotic (*4*) and anticonvulsant (*5*,*6*) properties. The presence of the N−C−S linkage in heterocycles has been reported to have antitubercular (*7*), antifungal (*8*), and antianalgesic (*9*) activity. 4-Thiazolidinones have also been shown to have anti HIV (*10*) activity.

A literature survey (*11*−*13*) have revealed that bryophytes are not damaged by fungi although they contain nutritious material like fatty acids, sterols, triglycerides, etc. (*11*). The reported reason is the presence in these bryophyte of structural variants of bibenzyl and bisbibenzyl (*13*). It has been found that both natural and synthetic bibenzyl show antifungal activity against spore germination of *Alternaria brassicola*, *Botrytis cinerea*, *Uromyces fabal* (*13*).

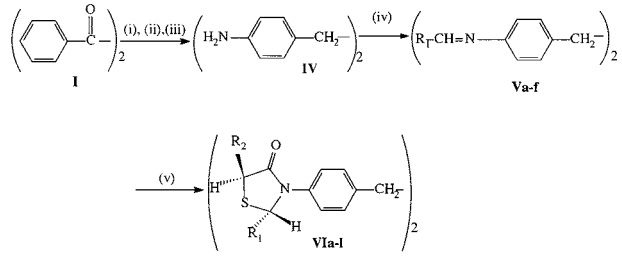
The above facts coupled with our desire to develop efficacious agricultural fungicides prompted us to devise a convenient synthesis of 4-thiazolidinone derivatives incorporating bibenzyl moiety hitherto unknown title compounds, 4,4′-bis-(2″-aryl-5″-methyl/unsubstituted-4″-oxothiazolidin-3″-yl) bibenzyl **VIa**−**l**. Compounds **Va**−**f** are also new ones. The reaction sequence leading to the formation of **Va**−**d** and **VIa**−**h** is outlined in **Scheme 1**. The starting compound benzil **I** was reduced to bibenzyl **II**, which on nitration gave 4,4′-dinitrobibenzyl **III**. Reduction of 4,4′-dinitrobibenzyl **III** by Pd−C and HCOOH yielded quantitatively and analytically pure 4,4′-diaminobibenzyl **IV.** Compound **IV** on condensation with various carbonyl compounds gave 4,4′-bis (benzylideneamino) bibenzyls **Va**−**f**, which on cycloaddition with mercaptoacetic acid/ mercaptopropionic acid afforded corresponding 4,4′-bis (2“-aryl-5”-methyl/ unsubsituted-4″-oxothiazolidin-3″-yl) bibenzyl **VIa**−**l**.

The structural assignments of the synthesized products were based on elemental analysis (C, H, N, S, and Cl) and ^{1}H NMR spectra (**Tables 1** and **2**). ^{1}H NMR spectral studies have shown that the synthesis is highly diastereoselective because only one diastereomer could be obtained. The reduction of dinitro compound **III** in good yield (90−95%) into corresponding diamino compounds **IV** at room temperature was done by HCOOH in the presence of 10% palladised charcoal (*16*). The catalyst was recovered and reused after washing with water and ethanol. The results indicated that there is no loss of catalytic activity. Of the tested compounds **Va**−**f** and **VIa**−**l**, compounds **Vc**, **VIc**, **VIf**, **Vig**, **VIh**, **VIk**, and **VIl** displayed in vitro fungitoxicity comparable to that of the commercial fungicide Dithane M-45 (a mixed Mn^{2+} and zinc salt of *N*, *N*′-ethylenebis (dithiocarbamic acid)) at 1000 ppm concentration against *Fusarium oxysporium* and *Penicillium citrinum* (**Table 3**).

* To whom correspondence should be addressed. E-mail: irspksjs@rediffmail.com.

10.1021/jf0342324 CCC: $25.00
Published on Web 10/22/2003

Scheme 1



Scheme conditions:

(i). Zn-Hg/HCl
(ii). HNO_3-H_2SO_4 in AcOH
(iii). Zn-HCOOH / Pd-C as catalyst
(iv). R_1—CH=O
(v). HS—CH(R$_2$)—COOH

Compd.	R 1
Va.	C_6H_5
Vb.	4-CH_3O. C_6H_4
Vc.	4-ClC_6H_4
Vd.	3,4-$(CH_3O)_2$-C_6H_3
Ve.	2-HO.C_6H_4
Vf.	4-OH.(3-OCH_3).C_6H_3

Compd.	R 1	R2
VIa.	C_6H_5	H
VIb.	4-CH_3O. C_6H_4	H
VIc.	4-ClC_6H_4	H
VId.	3,4-$(CH_3O)_2$-C_6H_3	H
VIe.	2-HO.C_6H_4	H
VIf.	4-OH.(3-OCH_3).C_6H_3	H
VIg.	C_6H_5	CH_3
VIh.	4-CH_3O. C_6H_4	CH_3
VIi.	4-ClC_6H_4	CH_3
VIj.	3,4-$(CH_3O)_2$-C_6H_3	CH_3
VIk.	2-HO.C_6H_4	CH_3
VIl.	4-OH.(3-OCH_3).C_6H_3	CH_3

Table 1. Analytical Data of Compounds Va–f and VIa–l

cpd	yield %	mp (deg C)	mol formula[a]
V a	67	168	$C_{28}H_{24}N_2$
b	70	181	$C_{30}H_{28}N_2O_2$
c	63	187	$C_{28}H_{22}N_2Cl_2$
d	58	204	$C_{32}H_{32}N_2O_4$
e	54	201	$C_{28}H_{24}N_2O_2$
f	61	194	$C_{30}H_{28}N_2O_4$
VIa	85	191	$C_{32}H_{28}N_2O_2S_2$
b	73	197	$C_{34}H_{32}N_2O_4S_2$
c	71	205	$C_{32}H_{26}N_2O_2S_2Cl_2$
d	90	201	$C_{36}H_{36}N_2O_6S_2$
e	82	203	$C_{34}H_{32}N_2O_2S_2$
f	74	234	$C_{36}H_{36}N_2O_4S_2$
g	76	227	$C_{34}H_{30}N_2O_2S_2Cl_2$
h	87	213	$C_{38}H_{40}N_2O_6S_2$
i	78	202	$C_{32}H_{28}N_2O_4S_2$
j	73	207	$C_{34}H_{32}N_2O_6S_2$
k	61	209	$C_{34}H_{32}N_2O_4S_4$
l	65	213	$C_{36}H_{36}N_2O_6S_2$

[a] Satisfactory elemental microanalyses obtained C ± 0.30, H ± 0.18, N ± 0.24, S ± 0.16, and Cl ± 0.2.

EXPERIMENTAL PROCEDURE

Melting points were determined on to an open glass capillary method and are uncorrected. Completion of the reaction was monitored by TLC (silica gel, benzene: ethyl acetate, 8:2). The final products were purified by column chromatography using silica gel (100 mesh) with increasing percentage of MeOH in benzene. ^{1}H NMR spectra were recorded on a Varian FT-20 spectrometer in $CDCl_3$, using TMS as an internal reference; chemical shifts are expressed in δ values.

Bibenzyl (II). Following the standard reduction procedure (*15*) **I** was treated with Zn−Hg and HCl to yield **II**.

4,4′-Dinitrobibenzyl (III). It was prepared by nitration of bibenzyl **II** following a reported procedure (*14*). **III** agreed well with the analytical data already reported in the literature (*14*).

4,4′-Diaminobibenzyl (IV). Dinitro compound **III** was reduced by formic acid in the presence of 10% palladium on carbon following the standard procedure (*16*) to **IV** in 95% yield. **IV** agreed well with the mp already reported (*17*).

4,4′-bis (Benzylideneamino) Bibenzyl (Va−f): To a solution of **IV** (0.0058 mole, 1.231 g) in dry ethanol (20 mL) was added benzaldehyde (0.01 mole, 1.061 g) and traces of fused $ZnCl_2$. The reaction mixture was refluxed on water-bath for 30 min and cooled to RT. Excess of ethanol was distilled-off under reduced pressure. The resultant residue was taken in 20 mL of chloroform and filtered. The filtrate was evaporated to give crude **Va**, which was recrystalized from an ethanol: water mixture (50 mL, 1:1, v/v). Compounds **Vb−f** were synthesized in similar way by using anisaldehyde, veratraldehyde, *p*-chlorobenzaldehyde, salicylaldehyde, and vanilline in place of benzaldehyde, respectively.

Table 2. Spectral Data of Compounds Va–d and VIa–h

cpd	^{1}H NMR ($CDCl_3$)δ (J, Hz)
Va	2.85 (4H, s, acyclic CH_2CH_2), 7.21–7.53 (18H, m, ArH), 8.31 (2H, s, CH═N)
Vb	2.86 (4H, s, acyclic CH_2CH_2), 3.95 (6H, s, OCH_3), 7.20–7.72 (16H, m, ArH), 8.31 (2H,s,CH═N)
Vc	2.86 (4H, s, acyclic CH_2CH_2), 7.24–7.94 (16H, m, ArH), 8.31 (2H, s, CH═N)
Vd	2.87 (4H, s, acyclic CH_2CH_2), 3.93 (6H, s, OCH_3), 3.95 (6H, s, OCH_3), 7.23–8.10, (14H, m, ArH), 8.31 (2H, s, CH═N)
Ve	2.85 (4H, s, acyclic CH_2CH_2), 7.21–7.53 (16H, m, ArH), 8.31 (2H, s, CH═N), 12.1 (2H, s, ArOH)
Vf	2.85 (4H, s, acyclic CH_2CH_2), 3.93 (6H, s, OCH_3), 7.21–7.53 (14H, m, ArH), 8.31 (2H, s, CH═N), (2.1 (2H, s, ArOH)
VIa	2.85 (4H, s, acyclic CH_2CH_2), 4.29 (4H, q, cyclic CO–CH_2–S), 5.95 (2H, s, cyclic S–CH–N), 7.21–7.53 (18H, m, ArH)
VIb	2.86 (4H, s, acyclic CH_2CH_2), 3.95 (6H, s, OCH_3), 4.29 (4H, q, cyclic CO–CH_2–S), 5.95 (2H, s, cyclic S–CH–N), 7.20–7.72 (16H, m, ArH)
VIc	2.86 (4H, s, acyclic CH_2CH_2), 4.30 (4H, q, cyclic CO–CH_2–S), 5.95 (2H, s, cyclic S–CH–N), 7.24–7.95 (16H, m, ArH)
VId	2.87 (4H, s, acyclic CH_2CH_2), 3.93 (6H, s, OCH_3), 3.95 (6H, s, OCH_3), 4.30 (4H, q, cyclic CO–CH_2–S), 5.95 (2H, s, cyclic N–CH–S), 7.20–8.14 (14H, m, ArH).
VIe	1.22 (6H, d, J = 8, CH_3), 2.85 (4H, s, acyclic CH_2CH_2), 4.20 (2H, q, J = 8, cyclic $CHCH_3$), 5.95 (2H, s, cyclic S–CH–N), 7.21–7.53 (18H, m, ArH)
VIf	1.22 (6H, d, J = 8, CH_3), 2.86 (4H, s, acyclic CH_2CH_2), 3.95 (6H, s, OCH_3), 4.20 (2H, q, J = 8, cyclic $CHCH_3$), 5.95 (2H, s, cyclic S–CH–N), 7.20–7.72 (16H, m, ArH)
VIg	1.22 (6H, d, J = 8, CH_3), 2.86 (4H, s, acyclic CH_2CH_2), 4.21 (2H, q, J = 8, cyclic $CHCH_3$), 5.95 (2H, s, cyclic S–CH–N), 7.24–7.91 (16H, m, ArH)
VIh	1.22 (6H, d, J = 8, CH_3), 2.87 (4H, s, acyclic CH_2CH_2), 3.93 (6H, s, OCH_3), 3.95 (6H, s, OCH_3), 4.20 (2H, q, J = 8, cyclic $CHCH_3$), 5.95 (2H, s, cyclic S–CH–N), 7.20–8.14 (14H, m, ArH)
VIi	2.85 (4H, s, acyclic CH_2CH_2), 4.29 (4H, q, cyclic CO–CH_2–S), 5.95 (2H, s, cyclic S–CH–N), 7.21–7.53 (16H, m, ArH), 12.1 (2H, s, ArOH)
VIj	2.85 (4H, s, acyclic CH_2CH_2), 3.93 (6H, s, OCH_3), 4.29 (4H, q, cyclic CO–CH_2–S), 5.95 (2H, s, cyclic S–CH–N), 7.21–7.53 (14H, m, ArH), 12.1 (2H, s, ArOH)
VIk	1.22 (6H, d, J = 8, CH_3), 2.85 (4H, s, acyclic CH_2CH_2), 4.20 (2H, q, J = 8, cyclic $CHCH_3$), 5.95 (2H, s, cyclic S–CH–N), 7.21–7.53 (16H, m, ArH), 12.1 (2H, s, ArOH)
VIl	1.22 (6H, d, J = 8, CH_3), 2.85 (4H, s, acyclic CH_2CH_2), 3.93 (6H, s, OCH_3), 4.20 (2H, q, J = 8, cyclic $CHCH_3$), 5.95 (2H, s, cyclic S–CH–N), 7.21–7.53 (14H, m, ArH), 12.1 (2H, s, ArOH)

4,4′-bis (2″-Aryl-5″-methyl/unsubstituted-4″-oxo-thiazolidin-3″-yl) Bibenzyl (VIa−l). A mixture of **Va−f** (0.005 mole) and mercaptoacetic acid/ 2-mercaptopropionic acid (0.01 mole) in dry benzene was refluxed on a steam bath for 3−4 h. The excess of benzene was then distilled-off under reduced pressure. The reaction mixture was poured over crushed ice and centrifuged.

Table 3. Antifungal Screening Results of Compounds Va–f and VIa–l

	Av % inhibition after 96 h against					
	F. oxysporium			P. citrinum		
cpd	1000 ppm	100 ppm	10 ppm	1000 ppm	100 ppm	10 ppm
V a	50	24	9	56	20	13
b	46	36	29	58	44	21
c	83	47	20	88	30	15
d	55	43	31	42	27	19
e	62	53	25	50	33	23
f	51	47	48	57	45	37
VIa	55	30	12	51	20	10
b	61	50	24	46	32	17
c	82	43	15	87	33	8
d	38	26	24	67	50	26
e	61	50	39	67	40	25
f	78	65	40	73	56	38
g	100	81	59	100	79	53
h	85	62	41	88	69	45
i	75	65	40	68	42	30
j	71	58	51	63	55	46
k	88	71	30	78	65	37
l	91	85	76	87	58	45
Dithane M-45	100	91	86	100	95	89

The resulting solid was washed with ice-cold saturated aqueous solution of sodium bicarbonate, dried and recrystalized from methanol to give yellow colored crystals of **VIa**−**l**.

Yields, melting points, molecular formula, and elemental analysis of compounds **Va**−**f** and **VIa**−**l** are recorded in **Table 1** and spectral data in **Table 2**.

Antifungal Screening. In vitro antifungal activity of compounds **Va**−**f** and **VIa**−**l** was evaluated against *Fusarium oxysporium* and *Penicillium citrinum* by the poisoned food technique (*18*) (1000, 100, and 10 ppm) using Czapek's agar as medium as previously described (*19*, *20*). The number of replicate assays in each were three, and six replicate controls were used. Commercial fungicide, Dithane M-45 was used as standard. No remarkable morphological change was observed in the developing fungi. The antifungal screening results are summarized in **Table 3**.

For the most active compounds **Vc**, **VIc**, **Vig**, **VIh**, **VIk**, and **VIl**, it was ascertained whether they are fungistatic or fungicidal. Thus, following the procedure of Garber and Houston (*21*), compounds **Vc**, **VIc**, **VIg**, **VIh**, **VIk**, and **VIl** were added separately to Czapek's agar medium in different Petri dishes to maintain the final concentrations at their lethal dose (800, 900, and 1000 ppm, respectively). The test fungi were inoculated in the center of these Petri dishes and incubated at 28 ± 1 °C for 96 h, after which time, the percent inhibition of mycelial growth compared with that in control dishes was recorded. Then, the fungal disks were taken from the treated and control dishes, washed with sterilized double-distilled water, and reinoculated in fresh Petridishes containing Czapek's agar medium only. The plates were incubated for 96 h at 28 ± 1 °C and the percent inhibition was recorded. The number of replicate assays in each case was three, and six replicate controls were used.

The plates were incubated for 96 h at 28 ± 1 °C and the percent inhibition was recorded. The number of replicate assays in each case was three, and six replicate controls were used. It was found that compounds **Vc**, **VIc**, **VIg**, **VIh**, **VIk**, and **VIl** caused complete inhibition of mycelial growth of the test fungi in treated as well as reinoculated dishes and hence were fungicidal.

RESULTS AND DISCUSSION

Most of the screened compounds have significant fungitoxicity at (1000 ppm) (**Table 3**) against both tested fungi, but their toxicity considerably decreased on dilution (100 and 10 ppm). Of the tested compounds, the most active benzylideneamino bibenzyl **Vc** and oxothiozolidinyl bibenzyl **VIc**, **VIg**, **VIh**, **VIk**, and **VIl** displayed fungicidal action comparable with that of Dithane M-45 at 1000 ppm and inhibited 15−59% mycelial growth of both fungal species even at the lowest concentration. Compounds **Va**−**f,** which have no oxothiazolidine nucleus are less fungitoxic than **VIa**, **VIb**, **VIf**, **VIg**, **VIh**, and **VIi** which have 5-methyl oxothiazolidine nucleus. This demonstrates that the presence 5-methyl oxothiazolidine nucleus with the bibenzyl nucleus resulted in appreciable enhancement of fungitoxicity of these compounds.

The present study indicates that the 4,4′-bis(oxo-thiazolidinyl) bibenzyl framework reported herein might be useful for developing efficacious fungicides by suitable structural variation in the bibenzyl nucleus and heterocylic ring.

ACKNOWLEDGMENT

We sincerely thank Dr. L. D. S. Yadav, Reader, Department of Chemistry, University of Allahabad, Allahabad, India 211002 for many helpful discussions pertaining to the material in this article. We are thankful to Dr. Rashmi Sanghi, FEAT, Labs, IIT, Kanpur, India for spectral studies and elemental analysis of synthesized compounds.

LITERATURE CITED

(1) Jadhav, K. P.; Ingle, D. B. Synthesis of potential fungicidal compounds. *J. Indian Chem. Soc.* **1978**, 55, 424−426.

(2) Sharma, R. C.; Kumar, D. Synthesis of some new thiazolidin-4-ones as possible antimicrobial agents. *J. Indian Chem. Soc.* **2000**, *77*, 492−493.

(3) Srivastava, S. K.; Srivastava, S. L.; Srivastava, S. D. Synthesis of 5-arylidene-2-aryl-3- (2- chlorophenothiazinoyacetamidyl)-1,3-thiazolidin-4-ones as antifugal and anticonvulsant agents. *J. Indian Chem. Soc.* **2000**, *77*, 104−105.

(4) Doran, W. J.; Shonle, H. A. Dialkyl Thiazolidiones. *J. Org. Chem.* **1939**, *3*, 193−197.

(5) Mishra, S.; Srivastava, S. K.; Srivastava, S. D. Synthesis of 5-arylidene-2-aryl-3-(phenothiazino/ benzotriazoloacetamidyl)-1,3-thiazolidine-4-ones as antiinflammatory, anticonvulsant, analgesic, and anti-microbial agents. *Indian J. Chem.* **1997**, *36B*, 826−830.

(6) Troutman, H. D.; Long, L. M. The Synthesis of 2,3-Disubstituted-4-thiazolidones. *J. Am. Chem. Soc.* **1948**, *70*(10), 3436−3439.

(7) Oza, H.; Joshi, D.; Parekh, H. Synthesis and antitubercular activity of novel thiazolidinone derivatives. *Indian J. Chem.* **1998,** *37B*, 822−824.

(8) Singh, S. R. 4-Thiazolidinones: Synthesis and fungicidal activity of 5-methyl-3-aryl-2-arylimino-4-thiazolidinones and their Acetoxymercuric derivative. *J. Indian Chem. Soc.* **1976**, *53*, 593−597.

(9) Srivastava, S. K.; Srivastava, S.; Srivastava, S. D. Synthesis of 2-aryl-3-(N^9-carbazolylacetamidyl)-4-oxothiazolidines and their 5-arylidines as antifungal and analgesic agents. *J. Indian Chem. Soc.* **2001**, *78*, 320−322.

(10) Joshi, H. D.; Upadhyay, P. S.; Baxi, A. J. Studies on 4-thiazolidinones: Synthesis and pharmacological activity of 1,4-bis [2′-methyl/ethyl-2′-substituted styryl-5′−H/methyl/carboxymethyl-4′-thiazolidinon-3′-ylamino] phthalazines. *Indian J. Chem.* **2000**, *39B*, 967−970.

(11) Pavletic, Z.; Stilionic, B. Untersuchungen über die antibiotische wirkung von moosextrakten aut enige Bakterien. *Acta Bot. Croatica* **1963**, *22*, 133.

(12) Gorham, J. Lunularic acid and related compounds in liverworts, algae, and hydrangea. *Phytochemistry* **1977**, *16*, 249−253.

(13) Pryce, R. J. Metabolism of lunularic acid to new plant stilbene by *Lunularia cruciata*. *Phytochem.* **1972**, *11*, 1355−1364.

(14) Rinkenbach, W. H.; Aaronson, H. A. The nitration of symdiphenylethane. *J. Am. Chem. Soc.* **1930**, *52*, 5040−5045.

(15) Martin, E. L.; Adams, R. Organic Reaction, 4th reprint; John Wiley: London, 1947; I, p 181.
(16) Gowda, D. C.; Gowda, S. Formic acid with 10% palladium on carbon: A reagent for selective reduction of aromatic nitro compounds. *Indian J. Chem.* **2000**, *39B*, 709−711.
(17) Fuson, C. R.; House, H. O. Heterocycles containing *p*-phenylene units. I. Ethers. *J. Am. Chem. Soc.* **1953**, *75*, 1325−1327.
(18) Horsfall, J. G. Quantitative bioassay of fungicides in the laboratory. *Bot. Rev.* **1945**, *11*, 357−397.
(19) Yadav, L. D. S.; Misra, A. R.; Singh, H. Synthesis of new 7H-1,3,4-thiadiazolo [3,2-a] [1, 3, 5] triazine-7-thiones as potential fungicides. *Pestic Sci.* **1989**, *25*, 219−225.
(20) Yadav, L. D. S.; Tripathi, R. L.; Dwivedi, R.; Singh, H. Synthesis of new 1,3,4-oxadiazolo [3,2-d] thiadiazines with fungicidal action. *J. Agric. Food Chem.* **1991**, *39*, 1863−1865.
(21) Garber, R. H.; Houston, B. R. An inhibitor of *Verticillium alboatrum* in cotton seed. *Phytophthology* **1959**, *49*, 449−450.
(22) Dikshit, D. K.; Munshi, R.; Kapil, R. S.; Anand, N.; Van Der Veen, J. M.; Fujiwara, H. Synthesis of Diastereomers of 4,5-Dihydro-3,4,5-triphenylfuran-2(3*H*)-one. *Indian J. Chem.* **1977**, *15B*, 977−980.
(23) Rajanarendar, E.; Afazal, M.; Ramu, K. Synthesis of isoxazolyl oxadiazolines and thiazolidinones. *Indian J. Chem.* **2003**, *42B*, 927−930.

Received for review March 10, 2003. Revised manuscript received September 3, 2003. Accepted September 15, 2003.

JF0342324