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Synthesis and Herbicidal Activity of 2-(1-anilinobutylidene)-5,5-dimethyl-3-hydroxy-2-cyclohexen-1-ones

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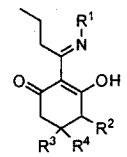
Abstract : Fourteen 2-(1-anilinobutylidene)-5,5-dimethyl-3-hydroxy-2-cyclohexen-1-ones were prepared by condensation of 2-butanoyl-5,5-dimethyl-3-hydroxy-2-cyclohexen-1-one with various substituted anilines in good yield. These were tested for herbicidal activity against six different submerged paddy weed species. Most compounds showed significant activity against *Echinochloa crus-galli* and *Sagittaria pygmaea* with excellent tolerance to rice (Received August 12, 1994; accepted November 14, 1994).

Introduction

Many cyclohexanedione derivatives represented by compounds **1-3** are synthesized and tested as herbicides.[1] Especially alloxydim sodium (**1**) was commercialized in 1978.[2] The target enzyme for biological activity of cyclohexanediones were known to be a key enzyme in the fatty acid biosynthetic pathway, acetyl-CoA carboxylase (E.C.4.6.1.2.).[3] Most of the 2-butyl-cyclohexane-1,3-diones exist as enols, and the correct nomenclatures are 2-butyryl-3-hydroxy-2-cyclohexen-1-ones.[4] On the way to develop a new agrochemicals in our laboratory,[5] the present research concerns introduction of anilino moiety as imine to 2-butyryl-3-hydroxy-2-cyclohexen-1-one for the preparation of 2-(1-anilinobutylidene)-5,5-dimethyl-3-hydroxy-2-cyclohexen-1-one (**4**).



1 $R^1 = OCH_2CHCH_2$, $R^2 = CO_2^-$, $R^3 = R^4 = CH_3$

2 $R^1 = OCH_2CH_3$, $R^2 = H$, $R^3 = H$, $R^4 = CH_2CH(CH_3)SCH_2CH_3$

3 $R^1 = OCH_2CHCHCl$, $R^2 = H$, $R^3 = H$, $R^4 = CH_2CH(CH_3)SCH_2CH_3$

4 $R^1 = Ar$, $R^2 = H$, $R^3 = R^4 = CH_3$

Materials and Methods

Analyses

^{1}H-NMR spectra were recorded with either a Varian EM60 (60 MHz) or a Jeol JNM-PMX 60-S1 (60 MHz) spectrometer. Chemical shifts were given in ppm using TMS as an internal standard. IR spectra were recorded with an FX-6160 KTIR spectrophotometer. Mass spectra were obtained on a Hewlett Packard Model 5985B spectrometer. Microanalyses were done with a Perkin-Elmer 240 DS elemental analyzer.

Synthesis

The titled compounds, 2-(1-anilinobutylidene)-5,5-dimethyl-3-hydroxy-2-cyclohexen-1-ones were synthesized from 2-butanoyl-5,5-dimethyl-3-hydroxy-2-cyclohexen-1-one[6] with the corrpesonding substituted anilines. To a stirred solution of 2-butanoyl-5,5-dimethyl-3-hydroxy-2-cyclohexen-1-one (5 mmol) in benzene was added aniline (5 mmol). The reaction mixture was stirred under reflux for 20 hrs with the removal of water *via* Dean-Stark trap equipped at the reaction unit. Addition of one mole equivalent BF_3OEt_2 as a Lewis acid makes the reaction faster.[7] After the reaction was completed showing

Key words : 2-(1-Anilinobutylidene)-5,5-dimethyl-3-hydroxy-2-cyclohexen-1-one, Herbicidal acitivity
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Table 1. Characteristics[a] and physical properties of 2-(1-anilinobutylidene)-5,5-dimethyl-3-hydroxy-2-cyclohexen-1-ones, **4**

Comp	Ar	Yield(%)	m.p.(℃)	IR(μ cm^{-1})	PMR (TMS, $CHCl_3$-d, ppm)
4a	H	91%	113-115	1640, 1575, 1269	0.87 (t, J=7, 3H); 1.04 (s, 6H); 1.32-1.93 (m, 2H); 2.40 (s, 4H); 2.87 (t, J=8, 2H); 6.43-7.42 (m, 5H); 12.4 (s, 1H)
4b	2-CH_3	79%	106-108	1662, 1556, 1274	0.83 (t, J=7, 3H); 1.06 (s, 6H); 1.42 (six, J=7, 2H); 2.19 (s, 3H); 2.38 (s, 2H); 2.46 (s, 2H); 2.85 (t, J=7, 2H); 7.10-7.41 (m, 5H); 11.9 (s, 1H)
4c	4-CH_3	92%	117-119	1630, 1576, 1269	0.87 (t, J=7, 3H); 1.08 (s, 6H); 1.52 (six, J=7, 2H); 2.38 (s, 3H); 2.40 (s, 2H); 2.48 (s, 2H); 2.88 (t, J=7, 2H); 7.05 (d, J=8, 2H); 7.23 (d, J=8, 2H); 12.8 (s, 1H)
4d	2,3-$(CH_3)_2$	84%	131-133	1643, 1583, 1255	0.84 (t, J=7, 3H); 1.04 (s, 6H); 1.25-1.73 (m, 2H); 2.08 (s, 3H); 2.31 (s, 3H); 2.42 (s, 4H); 2.82 (t, J=7, 2H); 6.86-7.33 (m, 3H); 13.3 (s, 1H)
4e	2,5-$(CH_3)_2$	69%	63-66	1642, 1586, 1255	0.89 (t, J=7, 3H); 1.05 (s, 6H); 1.18-1.67 (m, 2H); 2.17 (s, 3H); 2.34 (s, 3H); 2.42 (s, 4H); 2.82 (t, J=7, 2H); 6.41-7.30 (m, 3H); 12.8 (s, 1H)
4f	2-Et	90%		1647, 1553, 1251	0.83 (t, J=7, 3H); 1.03 (s, 6H); 1.18 (t, J=6, 3H); 1.18-1.67 (m, 2H); 2.42 (s, 4H); 2.65 (q, J=6, 2H); 2.83 (t, J=7, 2H); 6.50-7.28 (m, 4H); 12.5 (s, 1H)
4g	4-Et	75%	67-69	1639, 1585, 1253	0.86 (t, J=7, 3H); 1.06 (s, 6H); 1.27 (t, J=7, 3H); 1.29-1.71 (m, 2H); 2.43 (s, 4H); 2.70 (q, J=7, 2H); 2.93 (t, J=7, 2H); 7.12 (d, J=8, 2H); 7.33 (d, J=8, 2H); 12.9 (s, 1H)
4h	2-OCH_3	78%	78-80	1642, 1584, 1257	0.84 (t, J=7, 3H); 1.06 (s, 6H); 1.27-1.83 (m, 2H); 2.36 (s, 2H); 2.39 (s, 2H); 2.87 (t, J=7, 2H); 3.81 (s, 3H); 6.72-7.46 (m, 4H); 13.4 (s, 1H)
4i	3-OCH_3	69%	63-65	1652, 1562, 1283	0.90 (t, J=7, 3H); 1.05 (s, 6H); 1.23-1.81 (m, 2H); 2.43 (s, 4H); 2.93 (t, J=7, 2H); 3.76 (s, 3H); 6.67-7.46 (m, 4H); 12.7 (s, 1H)
4j	4-OCH_3	82%	93-95	1638, 1584, 1244	0.87 (t, J=7, 3H); 1.03 (s, 6H); 1.23-1.86 (m, 2H); 2.41 (s, 4H); 2.92 (t, J=7, 2H); 3.83 (s, 3H); 6.67-7.34 (m, 4H); 13.1 (s, 1H)
4k	2-Cl	74%	95-98	1646, 1588, 1267	0.84 (t, J=7, 3H); 1.06 (s, 6H); 1.23-1.84 (m, 2H); 2.42 (s, 2H); 2.50 (s, 2H); 2.83 (t, J=7, 2H); 7.23-7.65 (m, 4H); 12.7 (s, 1H)
4l	4-Cl	85%	112-115	1648, 1550, 1247	0.87 (t, J=7, 3H); 1.07 (s, 6H); 1.27-1.81 (m, 2H); 2.43 (s, 4H); 2.89 (t, J=7, 2H); 7.12 (d, J=9, 2H); 7.44 (d, J=9, 2H); 12.5 (s, 1H)
4m	2-F	70%	109-111	1643, 1557, 1267	0.83 (t, J=7, 3H); 1.06 (s, 6H); 1.50 (six, J=7, 2H); 2.41 (s, 2H); 2.47 (s, 2H); 2.83 (t, J=7, 2H); 7.11-7.43 (m, 4H); 12.4 (s, 1H)
4n	4-F	71%	122-123	1643, 1558, 1257	0.86 (t, J=7, 3H); 1.03 (s, 6H); 1.51 (six, J=7, 2H); 2.42 (s, 4H); 2.85 (t, J=7, 2H); 7.16 (d, J=6, 4H); 12.6 (s, 1H)

[a]Satisfactory microanalyses were obtained within a tolerance of +/−0.4% for C, H and N except **4f**.

in TLC, solvent was removed under reduced pressure. The reaction product was dissolved in $CHCl_3$. The organic layer was washed successively with water and brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure to give a crude product. The crude product was purified by recrystallization from n-hexane or by flash column chromatography.

Biological testing

All of the compounds reported in Table 1 were tested for herbicidal activity against submerged paddy weed species of *Oryza sativa* (Rice), *Echinochloa crus-galli* (Barnyard grass). *Scirpus juncoides* (Bulrush), *Monochoria vaginalis* (monochoria), *Cyperus serotinos* (Flat-sedge), and *Sagittaria pygmaea* (Arrow Head).

The herbicidal activity of foliar treatment was assessed using the paddy pot of 60 cm^2 at which tested species were planted and submerged with 2 cm depth for one day. The sample solution was applied onto the plants in the rate of 4 kg/ha. After the tested plants were grown in the green house for two weeks the level of herbicidal activity was assessed by comparison with control. Activity was expressed on the scale: ++ (51~100%) inhibition of growth; + (20~50%) inhibition of growth; − no effect.

Results and Discussion

Condensation reaction between 2-butanoyl-5,5-dimethyl-3-hydroxy-2-cyclohexen-1-one[7] and the corresponding aniline was quite successful by conventional method. Addition of one mole equivalent BF_3OEt_2 as a Lewis acid makes the reaction faster.[7] Table 1 shows characteristics and physical properties of 2-(1-anilinobutylidene)-5,5-dimethyl-3-hydroxy-2-cyclohexen-1-one. ^{1}H-NMR spectra gave one noteworthy observation. Compounds derived from anilines bearing substituent at ortho-position exhibit two different singlets of each two protons on C-4 and C-6 of cyclohexane ring, while others has just one singlet for four protons except **1c**.

Table 2. Postemergent herbicidal activity[a] of 2-(1-anilinobutylidene)-5,5-dimethyl-3-hydroxy-2-cyclohexen-1-one (**4**) under submerged paddy condition[b]

Compound	Orysa1	Orysa2	Echor	Scpju	Moova	Cypse	Sagpy
4a	−	−	++	−	−	−	+
4b	−	−	−	−	−	−	+
4c	−	−	+	−	−	−	+
4d	−	−	−	−	−	−	+
4e	−	−	−	−	−	−	+
4f	−	−	+	−	++	−	+
4g	−	−	+	−	−	−	+
4h	−	−	++	−	−	−	−
4i	−	−	++	−	−	−	−
4j	−	−	+	−	−	−	+
4k	−	−	++	−	−	+	+
4l	−	−	+	−	−	−	+
4m	−	−	+	−	−	−	−
4n	−	−	+	−	−	+	−

[a] Activity was expressed on the scale: ++ (51~100%); + (20~50 %) inhibition of growth; − no effect.

[b] Orysa1: *Oryza sativa* (3 leaf), Orysa2: *Oryza sativa* (seed), Echor: *Echinochloa crus-galli*, Scpju: *Scirpus juncoides*, Mooma: *Monochoria vaginalis*, Cypse: *Cyperus serotinos*, Sagpy: *Sagittaria pygmaea*.

The results of the biological testing are given in Table 2. Most compounds showed moderate activity against grassy weeds with excellent tolerance to rice. Significant activity against *Echinochloa crus-galli* and *Sagittaria pygmaea* was observed from the most of compounds tested. However, tested compounds were generally not effective toward *Scirpus juncoides*, *Monochoria vaginalis* and *Cyperus serotinos* while compound **4f** showed good activity against *Monochoria vaginalis*. Compounds **4d** and **4e** which have dimethylanilino moiety showed no activity while the others were active at least against *Echinochloa crus-galli*. Compounds of **4h** and **4i** derived from anisidines have good activity against *Echinochloa crus-galli* with no significant activity against others. When aniline moiety was substitued by halogen of chlorine or fluorine (**4k** and **4n**) additional activity against *Cyperus serotinos* was observed.

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2-(1-Anilinobutylidene)-5,5-dimethyl-3-hydroxy-2-cyclohexen-1-ones의 합성과 제초활성

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초록 : 2-Butanoyl-5,5-dimethyl-3-hydroxy-2-cyclohexen-1-one과 여러 가지의 치환 아닐린의 축합반응으로 14가지의 2-(1-anilinobutylidene)-5,5-dimethyl-3-hydroxy-2-cyclohexen-1-ones들을 좋은 수율로 합성하였다. 이들 화합물들을 여섯 가지의 다른 담수조건 잡초들에 대하여 제초활성을 검색하였다. 대부분의 화합물들은 벼의 생육에 지장을 주지 않는 우수한 선택성을 가지면서 피(*Echinochloa crus-galli*)와 올미(*Sagittaria pygmaea*)에 대하여 우수한 제초활성을 보였다.