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Study on Reduction of β-Aromatic Amino Substituted Triazolyl Ketene Compounds

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Abstract: A series of β-aromatic amino substituted triazolyl ketenes were reduced at different conditions to enols and saturated alcohols, respectively. The preliminary biological tests showed that some of them exhibit good fungicidal activities.

Keywords: 1, 2, 4-Triazole, reduction, fungicidal activity.

During these years, a great variety of 1, 2, 4-triazolyl ketene compounds have been synthesized due to their broad spectrum biological activities, such as fungicidal, insecticidal, herbicidal and plant-growth regulative activities[1-3]. Usually the biological activities are increased markedly for this kind of compounds when carbonyl group is reduced to hydroxyl group. For example, the fungicidal and plant-growth regulative activities of triadimenol exceed those of triademefon[4], and diniconazole shows better biological activities than the ketene derivatives[5]. In this paper, a series of β-aromatic amino substituted triazolyl ketene compounds were reduced at different conditions to enol form and saturated alcohol form compounds, respectively. All of them are new compounds and their structures have been confirmed by IR, ^{1}HNMR and elemental analysis. Stability of enol form compounds was studied. The preliminary biological tests showed that some of them exhibit good fungicidal activities.

Experimental

The reduction products **4a~e** and **5a~c** were prepared as described in **Scheme 1**, the key intermediates **3a~e** were prepared according to literature[6].

General procedure for preparation of compounds **4a~e**: **3a~e** (1 mmol) was dissolved in methanol (10 mL), then sodium hydroxide (30 mg) was added. The mixture was stirred at room temperature for 30 minutes, then $NaBH_4$ (0.057 g, 1.5 mmol) was added slowly. The reaction mixture was stirred till the spot **3a~e** disappeared on silica gel TLC, then the reaction was quenched with hydrochloric acid (5%, v/v), and extracted

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Scheme 1

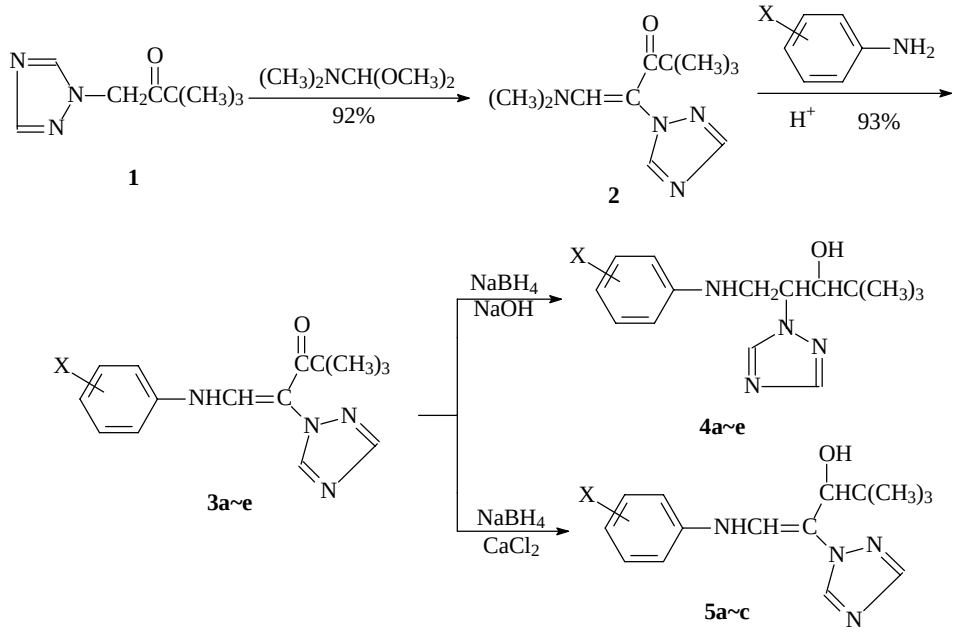


Table 1 Physical data of the compounds **4a~e** and **5a~c**

Compd.	X	Yield (%)	m.p.(℃)	Elemental analysis (%, Calcd.)		
				C	H	N
4a	2-Cl	93.6	99～100	58.37 (58.34)	6.77 (6.85)	18.39 (18.14)
4b	2-CH_3	90.1	124～125	66.50 (66.64)	8.57 (8.39)	19.54 (19.43)
4c	2,3-2Cl	92.1	158～160	52.42 (52.49)	5.68 (5.87)	16.40 (16.32)
4d	4-Cl	93.5	111～112	58.42 (58.34)	6.77 (6.85)	18.40 (18.14)
4e	3,4-2Cl	90.7	129～131	52.52 (52.49)	5.65 (5.87)	16.49 (16.32)
5a	2-Cl	63.3	116~117	58.66 (58.73)	6.37 (6.24)	18.39 (18.26)
5b	2-CH_3	50.7	136~138	67.15 (67.11)	7.78 (7.74)	19.46 (19.56)
5c	2,3-2Cl	60.1	96 (decompose)	52.74 (52.80)	5.59 (5.32)	16.37 (16.42)

with ether (15 mL×2). The combined extract was dried over anhydrous $MgSO_4$, filtered and then concentrated to give a crude product. Recrystallization from ether-petroleum ether gave the desired product **4a~e**.

General procedure for preparation of compounds **5a~c**: A solution of **3a~c** (1 mmol) and anhydrous $CaCl_2$ (0.44 g, 4 mmol) in 30 mL methanol was stirred at room temperature for 30 minutes. The mixture was cooled in an ice-water bath, then $NaBH_4$ (0.057 g, 1.5 mmol) was added slowly. The reaction mixture was stirred for 2 hours, then the reaction was quenched with saturated aqueous NaCl (10 mL), and extracted with

ether (15 mL×2). The combined extract was dried over anhydrous $MgSO_4$, filtered and then concentrated to give the crude product. The product was purified by column chromatography (ethyl acetate/petroleum ether 1/4, v/v) to get the pure product **5a~c**.

Table 2 ^{1}HNMR data of compounds **4a~e** and **5a~c**

Compd.	^{1}HNMR (200MHz, TMS), δ (ppm), J (Hz)	Solvent
4a	8.24,8.39(2s,2H,Tr-H),6.82~7.40(m,4H,Ph-H), 4.96(1s,1H,TrCH), 4.06(s,2H,NH&OH),3.86(d,2H,CH_2), 3.72(s,1H,CH-O),0.72(s,9H,C(CH_3)$_3$)	$CDCl_3$
4b	7.96,8.10(2s,2H, Tr-H),6.66~7.24(m,4H, Ph-H), 4.79(1s,1H,TrCH),4.50(s,2H,NH&OH),3.79(d,2H,CH_2), 3.64(s,1H,CH-O), 1.98(s,3H,Ph-CH_3),0.70(s,9H,C(CH_3)$_3$)	$CDCl_3$
4c	8.10,8.25(2s,2H, Tr-H),6.72~7.29(m,3H, Ph-H), 4.88(1s,1H,TrCH),4.04(s,2H,NH&OH),3.80(d,2H,CH_2), 3.68(s,1H,CH-O),0.72(s,9H,C(CH_3)$_3$)	$CDCl_3$
4d	8.04,8.33(2s,2H, Tr-H),6.51~7.20(m,4H, Ph-H), 4.81(1s,1H,TrCH),4.02(s,2H,NH&OH),3.77(d,2H,CH_2), 3.63(s,1H,CH-O),0.70(s,9H,C(CH_3)$_3$)	$CDCl_3$
4e	8.31,8.58(2s,2H, Tr-H),6.83~7.53(m,3H, Ph-H), 4.93(1s,3H,TrCH&NH&OH),3.86(d,2H,CH_2), 3.70(s,1H,CH-O), 0.74(s,9H,C(CH_3)$_3$)	$CDCl_3$
5a	8.42(d,1H,NH,J=11.2Hz), 8.27,8.84(2s,2H, Tr-H), 6.83~7.38(m,4H, Ph-H),7.04(d,1H,CH=C,J=11.2Hz), 5.45(s,1H,OH),4.21(s,1H,CH-O),0.72(s,9H,C(CH_3)$_3$)	DMSO-d_6
5b	8.09(d,1H,NH,J=11.2Hz), 8.06,8.46(2s,2H, Tr-H), 6.86~7.44(m,5H, Ph-H &CH=C),6.21(s,1H,CH-O), 2.46(s,1H,OH),2.08(s,3H,Ph-CH_3), 1.08,1.03(2s,9H,C(CH_3)$_3$)	$CDCl_3$
5c	8.35(d,1H,NH,J=11.2Hz), 8.36,8.90(2s,2H, Tr-H), 6.95~7.55(m,4H, Ph-H &CH=C),5.28(s,1H,OH), 4.29(s,1H,CH-O),0.88(s,9H,C(CH_3)$_3$)	DMSO-d_6

* Tr = triazole

Results and Discussion

Effect of acidity and handling

Reduction of the intermediates **3a~e** in faintly alkaline medium by $NaBH_4$ could afforded saturated alcohol form compounds **4** with high yields, which were purified easily by recrystallization. However, the content of enol form compounds **5** were increased when the intermediates were reduced in neutral or faintly acid medium. Because the enol form compounds were sensitive to acid, it would bring lots of by-product having used acid to handle. By-product was aromatic amine traced by silica gel TLC, so it was inferred that C-N bond of the enamine is broken.

Selective reduction

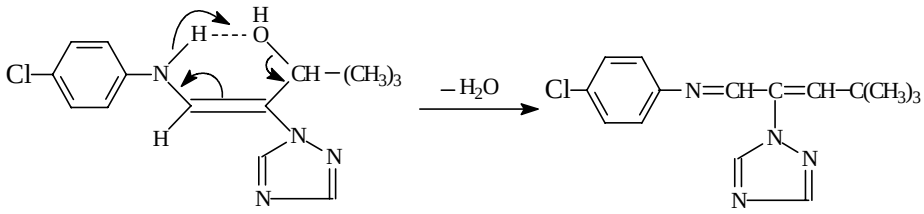
In order to get pure enol form compounds, the reduction was performed in the presence of $CaCl_2$ and by-product could be avoided by changing the way of handling: the reaction

mixture was quenched with saturated aqueous NaCl instead of HCl[7], then we got satisfactory result. But substantial amounts of saturated alcohols have been always found, for the reason that the π-π conjugation of intermediate systems is not extended to an aromatic ring[8].

Stability of enol form compounds

It was found that many enol form compounds were unstable, which decomposed at room temperature. The product was relatively stable only when there was substituting group on adjacent position of arylamine. It was speculated that this reaction could be occurred intramolecular dehydration as showed in **Scheme 2**. The structure of the dehydration product have been confirmed by MS and elemental analysis.

Scheme 2



Biological tests

The preliminary biological tests showed that the fungicidal activities of compounds **4** was higher than that of **5**. For example, the inhibitory rate of compound **4a** to *cercospora arachidicola* (*in vitro*) was 96.4% at 6.25 mg/L, while that of **5a** was 41.2% at 25 mg/L.

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