The Preparation and the Nucleophilic Reaction of 3,3-Di(1-azolyl)-2-alken-1-ones, Precursor of Acetylketene Derivatives

Choji Kashima*, Tadakuni Tajima, and Yoshimori Omote

Department of Chemistry, University of Tsukuba,
Sakura-mura, Niihari-gun, Ibaraki 305, Japan

Received July 5, 1983

2-Alken-1-ones, 3,3-di-(1-azolyl)-2-alken-1-ones and related compounds were prepared by two methods. These compounds were found to be the useful precursors for acylketene derivatives such as ketene dithioacetals and diaminals by treatment with various nucleophiles.

J. Heterocyclic Chem., **21**, 133 (1984).

As the vinylogues of *N*-acylimidazoles, we have studied the preparation and the properties of 3-(1-azolyl)-2-alken-1-ones and related compounds. By the action of azoles, 3-chloro-2-alken-1-ones and 2-alkyn-1-ones gave 3-(1-azolyl)-2-alken-1-ones in good yield [1]. Also 3-(1-azolyl)-2-alken-1-ones were obtained from 2,3-dibromoalkan-1-ones, which were easily prepared by the addition of bromine to 2-alken-1-ones [2]. Especially 3-aryl-2-alken-1-ones gave conveniently 3-aryl-3-(1-azolyl)-2-alken-1-ones by this procedure [3].

Since azoles belong to the class of heteroaromatic compounds, the further introduction of an azolyl group on the C-3 carbon of 3-(1-azolyl)-2-alken-1-ones is expected after bromination followed by the treatment with azoles. The expected 3,3-di(1-azolyl)-2-alken-1-ones are of interest as a new type of compound having many reaction sites.

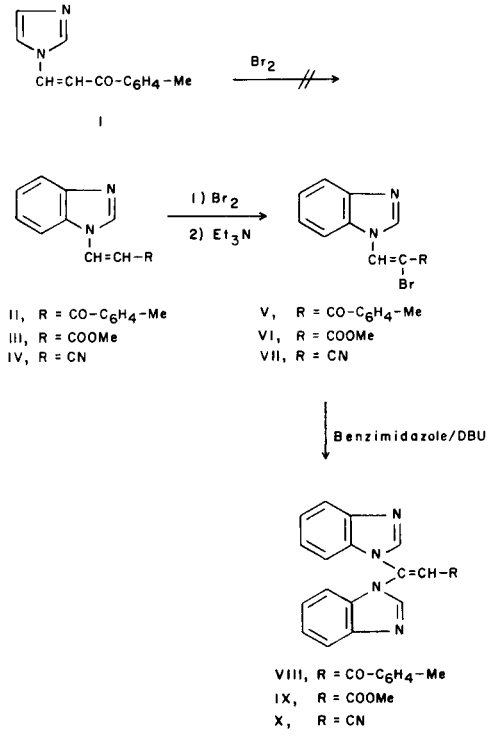
Meanwhile, the reaction of 3-(1-azolyl)-2-alken-1-ones with nucleophiles such as alcohols, thiols, amines [4,5,6], organometallic compounds and sodium borohydride [7] was carried out. In the cases of alcohols, thiols and amines, 3-hetero-substituted 2-alken-1-ones were obtained in good yield by the replacement of the azole group with nucleophiles at the C-3 carbon. This nucleophilic replacement reaction was accelerated by the use of the corresponding methiodide salts of 3-(1-azolyl)-2-alken-1-ones. Considering these replacement properties in the reaction with nucleophiles, 3,3-di(1-azolyl)-2-alken-1-ones should be the useful precursor of ketene acetals and the related compounds. This paper will describe the preparation and the nucleophilic reactions of 3,3-di(1-azolyl)-2-alken-1-ones.

Results and Discussion.

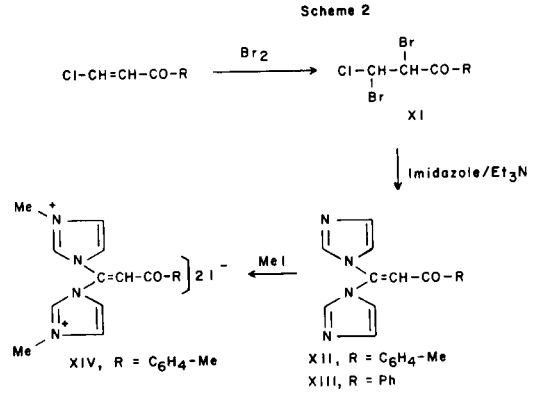
Preparation.

Since 3-(1-imidazolyl)-2-alken-1-ones were prepared in good yield with various conveniences and showed better chemical behaviour [3,4], at first, we attempted the reaction of 1-(4-methylphenyl)-3-(1-imidazolyl)-2-propen-1-one (I) with bromine. However, the reaction was contaminated owing to the rapid side-reaction between the imidazolyl group and bromine, and the product could not be isolated. On the other hand, benzimidazole was inert to bromine and the imidazole derivatives were reactive with bromine.

Scheme 1



Scheme 2



Therefore, 1-(4-methylphenyl)-3-(1-benzimidazolyl)-2-propen-1-one (II) was treated with bromine under ordinary conditions. After treatment with triethylamine, 1-(4-methylphenyl)-3-(1-benzimidazolyl)-2-bromo-2-propen-1-one (V) was obtained in good yield. This bromoenone was treated with benzimidazole in the presence of diazabicycloundecane (DBU). As the result, 1-(4-methylphenyl)-3,3-di(1-benzimidazolyl)-2-propen-1-one (VIII) was obtained. Similarly, methyl 3,3-di(1-benzimidazolyl)acrylate (IX) and 3,3-di(1-benzimidazolyl)acrylonitrile (X) were synthesized in good yields from methyl 3-(1-benzimidazolyl)acrylate (III) and 3-(1-benzimidazolyl)acrylonitrile (IV), respectively.

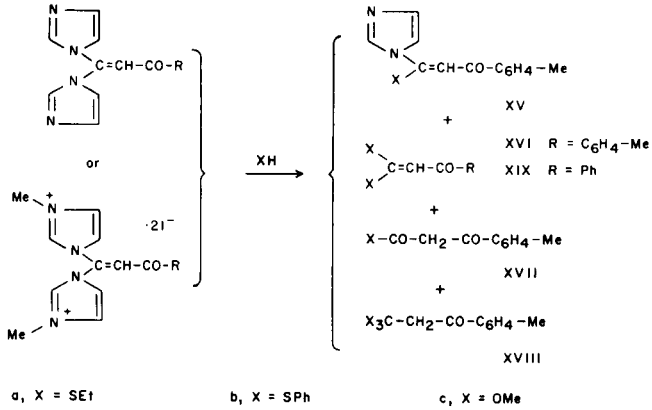
To summarize, this preparative reaction was interpreted as follows. Step a: the 1,4-addition reaction of azole to 2-halo- or 3-halo-2-alken-1-ones, step b: the elimination of hydrogen halide, step c: the addition of bromine, step d: the elimination of hydrogen bromide, and step e: the repetition of steps a and b. At this point these steps could be rearranged without any substantial change. That is, step a: the addition of bromine on the 3-halo-2-alken-1-ones, step b: the elimination of hydrogen halide, step c: the 1,4-addition reaction of azole, step d: the elimination of hydrogen halide, and step e: the repetition of step c and d. Actually, 1-(4-methylphenyl)-2,3-dibromo-3-chloropropan-1-one (XI) was obtained by the bromination on 1-(4-methylphenyl)-3-chloro-2-propen-1-one. By the treatment with imidazole in the presence of triethylamine, XI gave 1-(4-methylphenyl)-3,3-di(1-imidazolyl)-2-propen-1-one (XII) quantitatively.

Furthermore, in order to activate the reaction with nucleophiles, XII was treated with methyl iodide in a sealed tube at 100° to afford the di[1-(3-methyl)imidazolium] salt (XIV).

Nucleophilic Reaction.

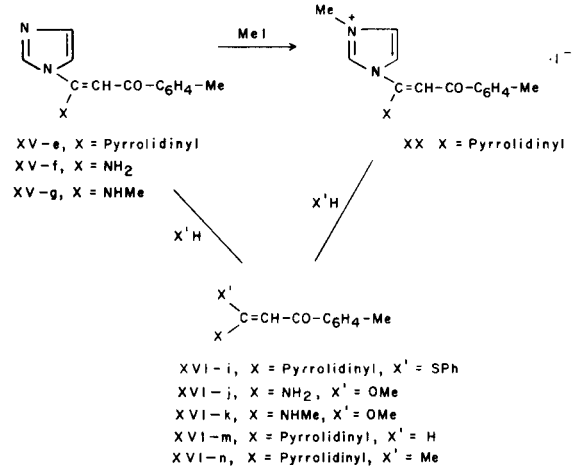
The nucleophilic reaction of 3-(1-azolyl)-2-alken-1-ones and their related compounds has been studied to afford predominantly the 3-hetero-substituted 2-alken-1-ones by

Scheme 3



a, X = SEt b, X = SPh c, X = OMe
d, X = NH-C6H4-OMe e, X = Pyrrolidinyl f, X = NH2
g, X = NHMe h, X = NHEt

Scheme 4



the replacement of azolyl group with nucleophiles. By the quaterization of azolyl group with methyl iodide, the nucleophilic reaction of 3-(1-azolyl)-2-alken-1-ones was accelerated and occurred even with the compound having rather weak nucleophilicity.

As the typical 3,3-di(1-azolyl)-2-alken-1-ones and their methiodide salts, compound XII and XIV were treated with various nucleophiles shown in Table 1. In the case of thiols such as ethylthiol and phenylthiol, the corresponding (4-methyl)benzoylketene dithioacetals (XVI-a,b) were formed from XII and XIV by the replacement of two imidazolyl groups with thio functions.

When XII was treated with methanol in the presence of either triethylamine or sodium methoxide, methyl 3-(4-methylphenyl)-3-oxopropionate (XVII-c) was obtained after usual work up. Since XVII-c was considered to be

Table 1

Yields of the Nucleophilic Reaction of XII, XIII and XIV

Compound	Nucleophile	Yields of Products (%) XV	XVI or XIX	XVII	XVIII
XII	EtSH	0	66	0	0
XII	PhSH	0	50	0	0
XII	4-$MeOC_6H_4NH_2$	61	0	0	0
XII	Pyrrolidine	89	0	0	0
XII	NH_3	64	0	0	0
XII	$MeNH_2$	61	0	0	0
XII	$EtNH_2$	43	0	0	0
XII	MeOH	0	0	trace	0
XII	MeONa	0	0	27	0
XII	MeONa [a]	0	0	0	69
XIII	EtSH	0	60	0	0
XIII	PhSH	0	52	0	0
XIV	EtSH	0	67	0	0
XIV	PhSH	0	78	0	0
XIV	4-$MeC_6H_4NH_2$	0	61	0	0
XIV	MeOH	0	0	50	0
XIV	MeONa	0	0	17	0

[a] Isolation without using water.

formed by the hydrolysis during the work up, the product from the reaction of XII with methanol was attempted to be isolated without quenching by water. After removal of the solvent from the reaction mixture, 3-(4-methylphenyl)-1,1,1-trimethoxy-3-propanone (XVIII-c) was obtained by the distillation. Indeed, XVIII-c, which was formed by the replacement of the imidazolyl group with two molar amounts of methanol and the 1,4-addition reaction of methanol, was easily hydrolyzed into XVII-c. However, (4-methyl)benzoylketene dimethylacetal (XVI-c) could not be detected under any condition. This type reaction was also observed in XIV with methanol.

In the reaction of XIV with *p*-anisidine, a similar ketene derivative, (4-methyl)benzoylketene di(4-methoxyphenyl)-aminal (XVI-d), was obtained. However, XII gave 1-(4-methylphenyl)-3-(4-methoxyphenyl)amino-3-(1-imidazolyl)-2-propen-1-one (XV-d) in good yield. This showed that the one portion of imidazolyl group in XII was replaced by amino group and further replacement reaction did not go on under the usual conditions. A similar tendency was observed in the case of XII with secondary amines such as pyrrolidine. Also one portion of the imidazolyl groups was replaced by ammonia and primary amines such as methylamine and ethylamine to afford 3-amino (XV-f), 3-methylamino- (XV-g) and 3-ethylamino-1-(4-methylphenyl)-3-(1-imidazolyl)-2-propen-1-ones (XV-h) in aprotic solvent.

However the reaction of XII with ammonia, methylamine and ethylamine in methanol, the solvolysis of intermediates XV-f, XV-g and XV-h were observed, and 3-amino (XVI-j), and 3-methylamino-1-(4-methylphenyl)-3-methoxy-2-propen-1-one (XVI-k) were obtained as well as XV-f, XV-g and XV-h, respectively. For clarifying this reaction process, XV-g was treated with methanol in the presence of triethylamine, and XVI-k was obtained predominantly. This fact suggested that the remaining imidazolyl group in XV retained the activity for the replacement reaction by nucleophiles. Therefore, the nucleophilic reaction of 3-pyrrolidinyl-1-(4-methylphenyl)-3-(1-imidazolyl)-2-propen-1-one (XV-e) was carried out. Furthermore, the methiodide salt (XX) of XV-e, which was easily prepared by the treatment of XV-e with methyl iodide, was subjected to the nucleophilic reaction. The reaction of either XV-e or XX with methanol and phenylthiol afforded the corresponding ketene derivatives. In the case with sodium borohydride and methylmagnesium iodide, 3-pyrrolidinyl-2-alken-1-ones were obtained also by the replacement of imidazolyl group with nucleophiles.

Conclusion.

By two different methods 2-alken-1-ones, 3,3-di(1-azolyl)-2-alken-1-ones were prepared in moderate yield. These compounds were very useful precursors for ketene derivative such as thioacetals and aminals by reaction with various nucleophiles. This nucleophilic reaction was accelerated by pretreatment with methyl iodide.

EXPERIMENTAL

Materials.

According to the methods reported in previous papers [1,2,3], 1-(4-methylphenyl)-3-(1-benzimidazolyl)-2-propen-1-one (II), methyl 3-(1-benzimidazolyl)acrylate (III) and 3-(1-benzimidazolyl)acrylonitrile (IV) were prepared.

1-(4-Methylphenyl)-3-(1-benzimidazolyl)-2-propen-1-one (II).

Compound II had mp 208-209° (from benzene), yield 59%; ir: 1660, 1605, 1580; nmr: δ 2.48 (s, 3H), 7.3-8.6 (m, 11H).

Anal. Calcd. for $C_{17}H_{14}N_2O$: C, 77.84; H, 5.37; N, 10.67. Found: C, 77.82; H, 5.40; N, 10.75.

Methyl 3-(1-Benzimidazolyl)acrylate (III).

Compound III had mp 110.5-111.5° (from benzene-hexane), yield 40%; ir: 1715, 1650; nmr: δ 3.75 (s, 3H), 6.33 (d, 1H, J = 14 Hz), 8.20 (d, 1H, J = 14 Hz), 8.23 (s, 1H), 7.2-8.0 (m, 4H).

Anal. Calcd. for $C_{11}H_{10}N_2O_2$: C, 65.33; H, 4.98; N, 13.85. Found: C, 65.27; H, 4.93; N, 13.88.

3-(1-Benzimidazolyl)acrylonitrile (IV).

Compound IV had mp 197.5-198.5° (from ethanol), yield 86%; ir: 2220, 1640; nmr: δ 5.78 (d, 1H, J = 14 Hz), 7.85 (d, 1H, J = 14 Hz), 8.15 (s, 1H), 7.2-8.0 (m, 4H).

Anal. Calcd. for $C_{10}H_7N_3$: C, 70.99; H, 4.17; N, 24.83. Found: C, 71.09; H, 4.15; N, 25.01.

Bromination of II, III and IV.

To the anhydrous chloroform solution (25 ml) of II, III or IV (5 mmoles) was added the chloroform solution (5 ml) of bromine (5 mmoles) at room temperature. After stirring for 1 hour, the mixture of triethylamine (1 ml) and chloroform (25 ml) was added at room temperature. The stirring was continued for 1 hour and then the reaction mixture was washed with water, dried over anhydrous magnesium sulfate. The reaction residue was recrystallized.

1-(4-Methylphenyl)-2-bromo-3-(1-benzimidazolyl)-2-propen-1-one (V).

Compound V had mp 169-171° (from benzene-hexane) as the mixture of *E* and *Z* isomers, yield 68%; ir: 1650, 1620; nmr: δ 2.38 and 2.41 (s, 3H), 8.12 and 8.99 (s, 1H), 6.9-7.8 (m, 9H).

Anal. Calcd. for $C_{17}H_{13}BrN_2O$: C, 59.84; H, 3.84; N, 8.21. Found: C, 59.84; H, 3.88; N, 8.17.

Methyl 3-(1-Benzimidazolyl)-2-bromoacrylate (VI).

The product was the mixture of *E* and *Z* isomer (ratio was 1:1), yield 99%. The mixture was chromatographed on silica gel with benzene-ethyl acetate (5:1).

The *E*-Isomer had mp 138.5-139.5° (from benzene-hexane); ir: 1720, 1630; uv: 267 (ε 11800), 307 (ε 9100); nmr: δ 3.93 (s, 3H), 8.67 (s, 1H), 9.20 (s, 1H), 7.2-8.0 (m, 4H).

Anal. Calcd. for $C_{11}H_9BrN_2O_2$: C, 46.99; H, 3.22; N, 9.96. Found: C, 46.93; H, 3.17; N, 9.96.

The *Z*-isomer had mp 126-127° (from benzene-hexane); ir: 1715, 1610; uv: 264 (ε 19800), 301 (ε 15500); nmr: δ 3.87 (s, 3H), 7.78 (s, 1H), 8.47 (s, 1H), 7.3-8.0 (m, 4H).

Anal. Calcd. for $C_{11}H_9BrN_2O_2$: C, 46.99; H, 3.22; N, 9.96. Found: C, 46.96; H, 3.21; N, 9.99.

3-(1-Benzimidazolyl)-2-bromoacrylonitrile (VII).

Compound VII had mp 165.5-166.5° (from ethanol) as the mixture of *E* and *Z* isomer, yield 51%; ir: 2240, 1640; nmr: δ 7.90 and 8.81 (s, 1H), 8.16 and 9.03 (s, 1H), 7.3-8.1 (m, 4H).

Anal. Calcd. for $C_{10}H_6BrN_3$: C, 48.41; H, 2.43; N, 16.93. Found: C, 48.21; H, 2.39; N, 17.06.

Preparation of VIII, IX and X.

The mixture of V, VI or VII (1 mmole) and the corresponding azole (1 mmole) in anhydrous benzene (25 ml) was refluxed for 7 hours in the presence of diazabicycloundecane (DBU) (163 mg). The reaction mixture was washed with water, dried over anhydrous magnesium sulfate, and concentrated. The residue was purified by silica gel column chromatography and recrystallization.

1-(4-Methylphenyl)-3,3-di(1-benzimidazolyl)-2-propen-1-one (VIII).

Compound VIII had mp 85.5-87° dec (from benzene-hexane), yield 50%; ir: 1660, 1600; nmr: δ 2.33 (s, 3H), 6.9-7.8 (m, 14H), 7.87 (s, 1H).

Anal. Calcd. for $C_{24}H_{18}N_4O\cdot0.5H_2O$: [8] C, 74.77; H, 4.94; N, 14.47. Found: C, 74.88; H, 4.93; N, 14.36.

Methyl 3,3-Di(1-benzimidazolyl)acrylate (IX).

Compound IX had mp 153.5-154.5° (from benzene-hexane), yield 66%; ir: 1720, 1640; nmr: δ 3.63 (s, 3H), 6.21 (s, 1H), 8.00 (s, 1H), 8.18 (s, 1H), 6.5-8.0 (m, 8H).

Anal. Calcd. for $C_{18}H_{14}NO_2$: C, 67.91; H, 4.43; N, 17.60. Found: C, 68.07; H, 4.43; N, 17.53.

3,3-Di(1-benzimidazolyl)acrylonitrile (X).

Compound X had mp 135-136° (from benzene-hexane), yield 21%; ir: 2230, 1640; nmr: δ 5.72 (s, 1H), 8.00 (s, 1H), 8.38 (s, 1H), 6.6-8.1 (m, 8H).

Anal. Calcd. for $C_{17}H_{11}N_5\cdot0.33C_6H_6$: [8] C, 73.29; H, 4.21; N, 22.50. Found: C, 73.31; H, 4.22; N, 22.37.

Preparation of XII.

The carbon tetrachloride solution (5 ml) of bromine (2.1 g) was added dropwise to the carbon tetrachloride solution (15 ml) of 1-(4-methylphenyl)- or 1-phenyl-3-chloro-2-propen-1-one at −10°. The reaction mixture was stirred for 1 hour and then concentrated. The residue was dissolved in anhydrous benzene (30 ml) accompanied with imidazole (2.0 g) and triethylamine (6 ml). After refluxing for 2 hours, the reaction mixture was quenched with water, and the aqueous layer was extracted with dichloromethane. The combined organic solution was washed with water and dried over anhydrous magnesium sulfate. After removal of the solvent, the reaction residue was chromatographed on silica gel with chloroform-acetone-ethanol mixture (100:40:16) and recrystallized.

1-(4-Methylphenyl)-3,3-di(1-imidazolyl)-2-propen-1-one (XII).

Compound XII had mp 113-114.5° (from benzene-hexane), yield 99%; ir: 1665, 1600; nmr: δ 2.43 (s, 3H), 6.84 (s, 1H), 6.95-7.95 (m, 10H).

Anal. Calcd. for $C_{16}H_{14}N_4O$: C, 69.04; H, 5.07; N, 20.13. Found: C, 69.06; H, 5.03; N, 20.30.

1-Phenyl-3,3-di(1-imidazolyl)-2-propen-1-one (XIII).

Compound XIII had mp 131-132.5° (from benzene-hexane), yield 52%; ir: 1665, 1600; nmr: δ 6.87 (s, 1H), 6.9-8.1 (m, 11H).

Anal. Calcd. for $C_{15}H_{12}N_4O$: C, 68.16; H, 4.57; N, 21.19. Found: C, 68.35; H, 4.59; N, 21.19.

Methylation to Methiodide Salt XIV of XII.

Compound XII was dissolved in methyl iodide, and heated at 100° for 10 minutes in a sealed tube. The reaction mixture was concentrated and the residue was recrystallized from ethanol, mp 220-222° dec, yield 95%; nmr: δ 2.44 (s, 3H), 4.04 (s, 6H), 8.29 (s, 2H), 1.3-8.2 (m, 9H).

Anal. Calcd. for $C_{18}H_{20}I_2N_4O$: C, 38.45; H, 3.58; N, 9.96. Found: C, 38.08; H, 3.61; N, 9.96.

Nucleophilic Reaction of XII, XIII and XIV.

The mixture of XII, XIII or XIV (1 mmole) and the nucleophiles (10 mmoles) in methanol or anhydrous benzene (8 ml) was stirred at room temperature for 2 hours in the presence of triethylamine (1 ml). The reaction mixture was quenched by water, and extracted with dichloromethane. The organic layer was dried over anhydrous magnesium sulfate and concentrated. The residue was chromatographed on silica gel with benzene-ethyl acetate mixture. The yields of the products were summarized in Table 1.

1-(4-Methylphenyl)-3,3-di(ethylthio)-2-propen-1-one (XVI-a).

Compound XVI-a had mp 91-92° (from hexane); ir: 1595; nmr: δ 1.36 (t, 3H, J = 7 Hz), 1.42 (t, 3H, J = 7 Hz), 2.39 (s, 3H), 3.07 (q, 2H, J = 7 Hz), 3.09 (q, 2H, J = 7 Hz), 6.87 (s, 1H), 7.27 and 7.88 (AB-q, 4H, J = 8 Hz).

Anal. Calcd. for $C_{14}H_{18}OS_2$: C, 63.11; H, 6.81. Found: C, 63.10; H, 6.81.

1-(4-Methylphenyl)-3,3-di(phenylthio)-2-propen-1-one (XVI-b).

Compound XVI-b had mp 161-162° (from hexane); nmr: δ 2.28 (s, 3H), 6.50 (s, 1H), 7.0-7.8 (m, 14H).

Anal. Calcd. for $C_{22}H_{18}OS_2$: C, 72.89; H, 5.00. Found: C, 73.07; H, 5.06.

1-(4-Methylphenyl)-3,3-di(4-methoxyphenyl)amino-2-propen-1-one (XVI-d).

Compound XVI-d had mp 142-143° (from benzene-hexane); nmr: δ 2.35 (s, 3H), 3.82 (s, 6H), 5.40 (s, 1H), 6.8-7.8 (m, 12H).

Anal. Calcd. for $C_{24}H_{24}N_2O_3$: C, 74.20; H, 6.22; N, 7.21. Found: C, 74.20; H, 6.21; N, 7.21.

1-(4-Methylphenyl)-3-(4-methoxyphenyl)amino-3-(1-imidazolyl)-2-propen-1-one (XV-d).

Compound XV-d had mp 155.5-156.5° (from benzene-hexane); ir: 1620; nmr: δ 2.38 (s, 3H), 3.70 (s, 3H), 6.07 (s, 1H), 6.75 (s, 4H), 6.9-8.0 (m, 8H).

Anal. Calcd. for $C_{20}H_{19}N_3O_2$: C, 72.05; H, 5.74; N, 12.60. Found: C, 72.31; H, 5.77; N, 12.56.

1-(4-Methylphenyl)-3-pyrrolidinyl-3-(1-imidazolyl)-2-propen-1-one (XV-e).

Compound XV-e had mp 136-136.5° (from benzene-hexane); ir: 1625, 1600; nmr: δ 1.8-2.1 (m, 4H), 2.33 (s, 3H), 3.1-3.6 (m, 4H), 5.78 (s, 1H), 6.95-7.9 (m, 7H).

Anal. Calcd. for $C_{17}H_{19}N_3O$: C, 72.57; H, 6.80; N, 14.93. Found: C, 72.58; H, 6.82; N, 14.96.

1-(4-Methylphenyl)-3-amino-3-(1-imidazolyl)-2-propen-1-one (XV-f).

Compound XV-f had mp 182.5-183° (from ethanol); ir: 1590; nmr: δ 2.40 (s, 3H), 6.30 (s, 1H), 7.24 (s, 1H), 7.35 and 8.03 (AB-q, 4H, J = 9 Hz), 7.95 (s, 1H), 8.55 (s, 1H), 9.4 (broad s, 1H).

Anal. Calcd. for $C_{13}H_{13}N_3O$: C, 68.70; H, 5.76; N, 18.49. Found: C, 68.50; H, 5.76; N, 18.41.

1-(4-Methylphenyl)-3-methylamino-3-(1-imidazolyl)-2-propen-1-one (XV-g).

Compound XV-g had mp 124-125° (from benzene-hexane); nmr: δ 2.38 (s, 3H), 2.90 (d, 3H, J = 5 Hz), 5.89 (s, 1H), 7.2-7.4 (m, 4H), 7.7-8.0 (m, 3H), 10.7 (broad s, 1H).

Anal. Calcd. for $C_{14}H_{15}N_3O$: C, 69.68; H, 6.26; N, 17.41. Found: C, 69.65; H, 6.27; N, 17.36.

1-(4-Methylphenyl)-3-ethylamino-3-(1-imidazolyl)-2-propen-1-one (XV-h).

Compound XV-h had mp 111.5-112.5° (from benzene-hexane); nmr: δ 1.18 (t, 3H, J = 7 Hz), 2.33 (s, 3H), 3.33 (m, 2H), 5.85 (s, 1H), 7.0-7.4 (m, 4H), 7.6-7.9 (m, 3H), 10.2 (broad s, 1H).

Anal. Calcd. for $C_{15}H_{17}N_3O$: C, 70.56; H, 6.71; N, 16.45. Found: C, 70.53; H, 6.66; N, 16.63.

1-Phenyl-3,3-di(ethylthio)-2-propen-1-one (XIX-a).

Compound XIX-a had mp 47-48° (from hexane); nmr: δ 1.31 (t, 3H, J = 8 Hz), 1.35 (t, 3H, J = 8 Hz), 2.99 (q, 2H, J = 8 Hz), 3.00 (q, 2H, J = 8 Hz), 6.79 (s, 1H), 7.0-8.1 (m, 5H).

Anal. Calcd. for $C_{13}H_{16}OS_2$: C, 61.86; H, 6.39. Found: C, 61.73; H, 6.41.

1-Phenyl-3,3-di(phenylthio)-2-propen-1-one (XIX-b).

Compound XIX-b had a mp of 136-137° (from hexane); nmr: δ 6.52 (s, 1H), 7.0-7.9 (m, 15H).

Anal. Calcd. for $C_{21}H_{16}OS_2$: C, 72.38; H, 4.62. Found: C, 72.26; H, 4.62.

Alcoholysis of XII and XIV.

Method A.

The alcoholic solution (7 ml) of XII or XIV (1 mmole) was stirred at room temperature for 2 hours in the presence of sodium methoxide or triethylamine (10 mmoles). The reaction mixture was quenched with water, and extracted with dichloromethane. The organic layer was dried over anhydrous magnesium sulfate and concentrated. The product was identified with methyl 3-(4-methyl)phenyl-3-oxopropionate (XVII-c) by the spectral and chromatographic data.

Method B.

After stirring for 2 hours at room temperature, the mixture of XII (2 mmoles) and sodium methoxide (10 mmoles) in methanol (7 ml) was quenched with ammonium chloride. The inorganic precipitate was filtered off and the filtrate was concentrated. The residue was dissolved in dichloromethane and filtered again. The dichloromethane solution was concentrated and distilled under reduced pressure.

1-(4-Methylphenyl)-3,3,3-trimethoxy-1-propanone (XVIII-c).

Compound XVIII-c had bp 30-85° (10 mm Hg); ir: 1680, 1600; nmr: δ 2.53 (s, 3H), 3.25 (s, 2H), 3.28 (s, 9H), 7.20 and 7.89 (AB-q, 4H, J = 8.2 Hz).

Anal. Calcd. for $C_{13}H_{18}O_4$: C, 65.52; H, 7.61. Found: C, 65.46; H, 7.60.

Methylation to the Methiodide Salt XX-e.

The mixture of XV-e (1 mmole) and methyl iodide (2.1 g) was heated for 15 minutes at 100° in a sealed tube. The reaction mixture was dissolved in warm ethanol and crystallized, yield 71%, mp 199-200° (from ethanol); 1625, 1600, 1565, 1540; nmr: δ 2.0-2.3 (m, 4H), 2.38 (s, 3H), 3.3-3.7 (m, 4H), 4.09 (s, 3H), 5.90 (s, 1H), 7.21 and 7.83 (AB-q, 4H, J = 8 Hz), 7.65 (s, 2H), 9.36 (s, 1H).

Anal. Calcd. for $C_{18}H_{22}N_3OI \cdot 0.33H_2O$: [8] C, 50.36; H, 5.32; N, 9.79. Found: C, 50.39; H, 5.16; N, 9.84.

Nucleophilic Reactions of XV-e, XV-f, XV-g and XX-e.

The mixture of XV-e, XV-f, XV-g or XX-e (1 mmole) and the nucleophiles (10 mmoles) in methanol (8 ml) was stirred for 2 hours at room temperature in the presence of triethylamine (1 ml). The reaction mixture was worked up as usual.

1-(4-Methylphenyl)-3-pyrrolidinyl-3-phenylthio-2-propen-1-one (XVI-i).

Compound XVI-i had mp 85-86° (from hexane), yield 31% (from XV-e) and 36% (from XX-e); nmr: δ 1.28 (t, 3H, J = 7.5 Hz), 1.8-2.1 (m, 4H), 2.34 (s, 3H), 2.98 (q, 2H, J = 7.5 Hz), 3.4-3.7 (m, 4H), 5.55 (s, 1H), 71.5 and 7.76 (AB-q, 4H, J = 8 Hz).

Anal. Calcd. for $C_{20}H_{21}NOS$: C, 74.26; H, 6.54; N, 4.33. Found: C, 74.32; H, 6.53; N, 4.34.

1-(4-Methylphenyl)-3-amino-3-methoxy-2-propen-1-one (XVI-j).

Compound XVI-j had mp 95-96° (from hexane), yield 45% (from XV-f); nmr: δ 2.31 (s, 3H), 3.69 (s, 3H), 5.39 (s, 1H), 7.26 and 7.76 (AB-q, 4H, J = 8 Hz).

Anal. Calcd. for $C_{11}H_{13}NO_2$: C, 69.09; H, 6.85; N, 7.32. Found: C, 69.22; H, 6.85; N, 7.36.

1-(4-Methylphenyl)-3-methylamino-3-methoxy-2-propen-1-one (XVI-k).

Compound XVI-k had mp 78-79° (from hexane), yield 49% (from XV-g); nmr: δ 2.36 (s, 3H), 2.90 (d, 3H, J = 5 Hz), 3.83 (s, 3H), 5.42 (s, 1H), 7.24 and 7.82 (AB-q, 4H, J = 8 Hz).

Anal. Calcd. for $C_{12}H_{15}NO_2$: C, 70.22; H, 7.36; N, 6.82. Found: C, 70.22; H, 7.37; N, 6.81.

Reaction of XV-e with Sodium Borohydride.

The mixture of XV-e (1 mmole) and sodium borohydride (3 mmoles) in ethanol (7 ml) was stirred for 2 hours at room temperature. The product was identified with 1-(4-methylphenyl)-3-pyrrolidinyl-2-propen-1-one (XVI-m) by the spectral and chromatographic data, yield 47%.

Reaction of XV-e with Methylmagnesium Iodide.

To the ether solution (5 ml) of methylmagnesium iodide (10 mmoles) was added XV-e (1 mmole) in THF (10 ml). The mixture was stirred for 3 hours at room temperature. After usual work up, the product was identified with 1-(4-methyl)phenyl-3-pyrrolidinyl-2-buten-1-one (XVI-n) by the spectral and chromatographic data, yield 39%.

REFERENCES AND NOTES

[1] C. Kashima and T. Tajima, *Synthesis,* 880 (1980).

[2] C. Kashima, T. Tajima and Y. Omote, *J. Heterocyclic Chem.,* in press.

[3] C. Kashima, M. Shimizu and T. Tajima, *Heterocycles,* **15**, 961 (1981).

[4] C. Kashima, T. Tajima, M. Shimizu and Y. Omote, *J. Heterocyclic Chem.,* **19**, 1325 (1982).

[5] C. Kashima, N. Yoshiwara, S. Shirai and Y. Omote, *Chem. Letters,* 1455 (1982).

[6] C. Kashima, Y. Konno, N. Yoshiwara and T. Tajima, *J. Heterocyclic Chem.,* **19**, 1535 (1982).

[7] C. Kashima, T. Tajima and Y. Omote, *Heterocycles,* submitted.

[8] The compounds VIII, X, and XX-e were unstable, when the solvent was eliminated from the solvated crystals.