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Synthesis and Thermal Decomposition of 3-Aroyl-4-aryl-2-pyrazolines[#]

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Summary. 3-Aroyl-4-aryl-2-pyrazolines (**21**–**40**) have been synthesized by the reaction of α,β-unsaturated ketones (**1**–**20**) with diazomethane. These 2-pyrazolines gave β-methyl-α,β-unsaturated ketones (**41**–**46**) on thermal denitrogenation.

Keywords. 1,3-Dipolar cycloaddition; β-Methyl-α,β-unsaturated ketones; 2-Pyrazolines; α,β-Unsaturated ketones.

Darstellung und thermische Zersetzung von 3-Aroyl-4-aryl-2-pyrazolinen

Zusammenfassung. Die Umsetzung der α,β-ungesättigten Ketone **1**–**20** mit Diazomethan lieferte die 3-Aroyl-4-aryl-2-pyrazoline **21**–**40**. Durch thermische Stickstoffabspaltung entstanden die β-Methyl-α,β-ungesättigten Ketone **41**–**46**.

Introduction

Synthesis of pyrazolines by the reaction of diazoalkanes with α,β-unsaturated carboxylic acid derivatives is well established in the literature [1–4]. However, concerning the reaction of α,β-unsaturated ketones and diazomethane, several conflicting data have been published. It has been described that the reaction of chalcone with diazomethane affords 3-benzoyl-4-phenyl-1-pyrazoline (type **A** in Scheme 2) as a primary product which is converted into 3-benzoyl-4-phenyl-2-pyrazoline (type **B** in Scheme 2) on gentle heating [5]. Later, *Ghate et al.* [6] assumed that this reaction afforded 4-benzoyl-3-phenyl-1-pyrazoline (type **C** in Scheme 2), but no spectral data were provided to corroborate the supposed structure of the product. The reaction of substituted chalcones with diazomethane was subsequently studied by *Sayed* and *Kjosen* [7], but – maybe as a consequence of the misinterpretation of the ^{1}H NMR spectra – 5-benzoyl-4-phenyl-2-pyrazolines were reported as the products. On the other hand, the preparation of 4-aryl-3-(2-furoyl)-2-pyrazolines, starting from furyl analogues of chalcones without the isolation or detection of the appropriate 1-pyrazoline isomers, has been published [8]. The 1,3-dipolar cycloaddition of exocyclic α,β-unsaturated ketones with diazomethane

[#] Dedicated to Prof. Dr. *F. Sauter* on the occasion of his 65th birthday

has also been investigated in detail [9–14]. We have found that the reaction of 3-arylidenechromanones, -flavanones, -1-thiochromanones, -1-thioflavanones, 2-arylidene-1-indanones, and -1-tetralones afforded only those regioisomers of spiro-1-pyrazolines where the methylene group is connected to the β carbon atom of the respective α,β-unsaturated ketone [10–12]. The assumption that the reaction of some 3-arylideneflavanones and diazomethane yielded such spiro-2-pyrazolines in which the methylene moiety of the diazomethane was connected to the α carbon [13, 14] certainly results from a misinterpretation of the ^{1}H NMR spectra or from the neglection of other spectroscopic measurements necessary for the structure elucidation. These compounds should actually be spiro-2-pyrazolines obtained by the isomerization of the other regioisomer spiro-1-pyrazoline where the methylene group is connected to the β carbon atom as in our cases [10–12] caused by methanol or impurities present. We have detected that spiro-1-pyrazolines obtained from our above mentioned exocyclic α,β-unsaturated ketones can easily be isomerized into the corresponding spiro-2-pyrazolines on treatment with acid [11, 12]. Based on all these results it appears that, although there are quite a lot of experimental data published in the chemical literature, several aspects of the reaction of α,β-unsaturated ketones with diazoalkanes should be reinvestigated or investigated by using newer substrates.

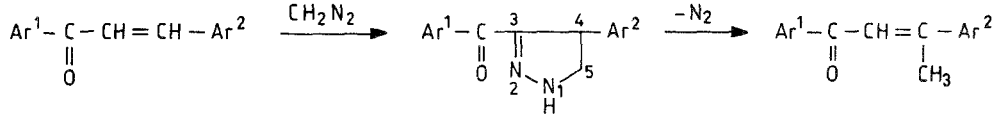
Results and Discussion

Trying to verify the correctness of the conflicting literature data discussed above, we formerly had reinvestigated the 1,3-dipolar cycloaddition of chalcones with diazomethane [15]; the structures of the reaction products have been elucidated by UV, IR, ^{1}H and ^{13}C NMR spectroscopy. These detailed spectroscopic studies unequivocally proved that the isolated reaction product was 3-aroyl-4-aryl-2-pyrazoline in each case. If the reaction progress was monitored by thin-layer chromatography (TLC), a new product (possibly the respective 1-pyrazoline isomer) could be detected which disappeared by spontaneous rearrangement into 2-pyrazoline when isolated as homogeneous single substance by removal of the solvent under reduced pressure. Thus, this reaction of chalcones is regioselective, providing 3-aroyl-4-aryl-2-pyrazolines as the only isolable products irrespective of the substituents of both aromatic rings.

In continuation of our previous study [15], a series of chalcones (**1–20**) were allowed to react with diazomethane in a mixture of anhydrous CH_2Cl_2 and diethyl ether at *ca.* 0 °C. 3-Aroyl-4-aryl-2-pyrazolines **21–40** have been obtained as homogeneous products (Scheme 1), the structures of which have been elucidated by means of spectroscopic measurements (*vide infra*).

The reaction of α,β-unsaturated ketones **1–20** with diazomethane can lead to two kinds of 1-pyrazolines (types **A** and **C** in Scheme 2) which then can be isomerized into the appropriate 2-pyrazolines (types **B** and **D** in Scheme 2).

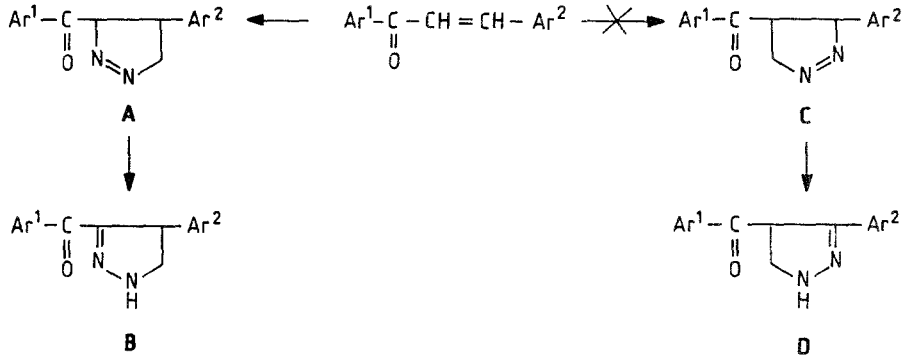
In the ^{1}H NMR spectra of compounds measured either in $CDCl_3$ or in *DMSO*-d_6, three protons gave a very similar ABX spin system. A triplet at 4.10–4.20 ppm can be assigned to the hydrogen atom connected to C-4. The chemical shifts of the two doublet–doublet signals of two other protons depend on the deshielding effect of the aryl group at position 4 (*cf.* Table 2), but unequivocally prove the presence of a CH_2 group. The measured geminal coupling constants were 11–12 Hz, whereas the vicinal ones amounted to 10–11 Hz and 5.5–6.0 Hz, respectively.



1–20 **21–40** **41–46**

Scheme 1

1, **21**, **41**: Ar^1 = phenyl, Ar^2 = 1-naphthyl; **2**, **22**: Ar^1 = 3-bromophenyl, Ar^2 = 2-naphthyl; **3**, **23**: Ar^1 = 4-methoxyphenyl, Ar^2 = 9-anthracenyl; **4**, **24**: Ar^1 = 4-bromophenyl, Ar^2 = 9-anthracenyl; **5**, **25**: Ar^1 = 2-furyl, Ar^2 = 2-naphthyl; **6**, **26**, **42**: Ar^1 = 1-naphthyl, Ar^2 = phenyl; **7**, **27**: Ar^1 = 1-naphthyl, Ar^2 = 4-chlorophenyl; **8**, **28**: Ar^1 = 1-naphthyl, Ar^2 = 9-anthracenyl; **9**, **29**: Ar^1 = 1-naphthyl, Ar^2 = 3-chromonyl; **10**, **30**, **43**: Ar^1 = 2-naphthyl, Ar^2 = phenyl; **11**, **31**: Ar^1 = 2-naphthyl, Ar^2 = 4-methoxyphenyl; **12**, **32**: Ar^1 = 2-naphthyl, Ar^2 = 4-chlorophenyl; **13**, **33**: Ar^1 = 2-naphthyl, Ar^2 = 3-chromonyl; **14**, **34**, **44**: Ar^1 = 2-phenanthrenyl, Ar^2 = phenyl; **15**, **35**: Ar^1 = 3-phenanthrenyl, Ar^2 = 4-chlorophenyl; **16**, **36**: Ar^1 = 3-phenanthrenyl, Ar^2 = 2,4-dichlorophenyl; **17**, **37**, **45**: Ar^1 = 3-phenanthrenyl, Ar^2 = 9-anthracenyl; **18**, **38**: Ar^1 = 9-phenanthrenyl, Ar^2 = phenyl; **19**, **39**, **45**: Ar^1 = Ar^2 = 9-phenanthrenyl; **20**, **40**: Ar^1 = 9-phenanthrenyl, Ar^2 = 9-anthracenyl.



Scheme 2

These ^1H NMR spectral characteristics correspond to a 2-pyrazoline structure (*cf.* types **B** and **D** in Scheme 2). The 2-pyrazoline character has also been corroborated by the ^{13}C NMR spectra of some selected substances (Table 3). A further confirmation of the 2-pyrazoline structure has been provided by their IR spectra measured as KBr discs.

The NH band (Table 1) characteristic for the 2-pyrazoline was observed between 3350 and 3260 cm^{-1}. The C=O band measured at 1593–1631 cm^{-1} allows to differentiate the two possible 2-pyrazoline structures (types **B** and **D** in Scheme 2) since these values indicate that a strong hydrogen bond should exist in the solid state. Moreover, the presence of a non-conjugated carbonyl group as in 2-pyrazoline type **D** would show an IR band at about 1680 cm^{-1} which was not observed in any of the spectra.

Thus, the cycloaddition of the chalcones **1**–**20** and diazomethane is regioselective, providing 3-aroyl-4-aryl-2-pyrazolines **21**–**40** as sole isolable products irrespective of the bulkiness and/or the electronic influence of the two aryl moieties of the starting α,β-unsaturated ketones. Therefore, our previous findings with substituted chalcones [15] are valid for the analogous α,β-unsaturated ketones as well.

Thermal decomposition of both 1-pyrazolines and 2-pyrazolines is a well known denitrogenation reaction and a convenient procedure for the preparation of

cyclopropane derivatives [2, 4, 16–23]. However, the thermal denitrogenation of pyrazolines obtained by the reaction of α,β-unsaturated ketones and diazoalkanes has received less attention [5, 9, 24]. Thermal decomposition of 3-benzoyl-4-phenyl-2-pyrazoline has been shown to afford β-methylchalcone (dypnone) [5]; spiro-1-pyrazoline (obtained by the reaction of 2-benzylidene-3-phenyl-1-indanone and diazomethane gave a β-methyl-α,β-unsaturated ketone as well [9]. Previously, we investigated the thermal decomposition of spiro-1-pyrazolines [24] synthesized by the 1,3-dipolar cycloaddition of exocyclic α,β-unsaturated ketones with diazomethane [10–12]. It has been found that, depending on the stereochemistry of the starting spiro-1-pyrazolines, the major product of the thermal decomposition was either a cyclopropane derivative or a β-methyl-α,β-unsaturated ketone [24]. Based on these results, it seemed expedient to investigate the thermal decomposition of the 2-pyrazolines synthesized in our present study.

When 3-aroyl-4-aryl-2-pyrazolines **21**, **26**, **30**, **34**, **37**, and **39** were heated slightly

Table 1. Physical constants and IR data of compounds **21–46**

	M.p. (°C)	Yield (%)	Molecular formula[a]	ν(C=O) (cm^{-1})	ν(NH) (cm^{-1})
21	177–178	80.0	$C_{20}H_{16}N_2O$	1606	3287
22	158–159	57.9	$C_{20}H_{15}BrN_2O$	1601	3263
23	243–244	84.2	$C_{25}H_{20}N_2O_2$	1620	3266
24	227–228	74.4	$C_{24}H_{17}BrN_2O$	1621	3285
25	175–176	82.7	$C_{18}H_{14}N_2O_2$	1593	3274
26	161–162	66.6	$C_{20}H_{16}N_2O$	1622	3268
27	137–138	71.8	$C_{20}H_{15}ClN_2O$	1622	3297
28	172–173	76.0	$C_{28}H_{20}N_2O$	1620	3328
29	150–151	59.8	$C_{23}H_{16}N_2O_3$	1622	3258
30	178–179	86.6	$C_{20}H_{16}N_2O$	1631	3263
31	220–221	66.5	$C_{21}H_{18}N_2O_2$	1630	3286
32	195–196	77.8	$C_{20}H_{15}ClN_2O$	1631	3260
33	181–182	73.6	$C_{23}H_{16}N_2O_3$	1622	3280
34	230–231	85.7	$C_{24}H_{18}N_2O$	1621	3350
35	197–198	72.9	$C_{24}H_{17}ClN_2O$	1619	3302
36	201–202	90.4	$C_{24}H_{16}Cl_2N_2O$	1610	3278
37	212–213	80.0	$C_{32}H_{22}N_2O$	1624	3342
38	226–227	79.6	$C_{24}H_{18}N_2O$	1610	3291
39	147–148	66.6	$C_{32}H_{22}N_2O$	1621	3318
40	250–251	75.5	$C_{32}H_{22}N_2O$	1624	3341
41	80–81	62.3	$C_{20}H_{16}O$	1660	–
42	74–75	69.4	$C_{20}H_{16}O$	1657	–
43	112–113	70.8	$C_{20}H_{16}O$	1652	–
44	124–125	63.7	$C_{24}H_{18}O$	1652	–
45	185–186	59.3	$C_{32}H_{22}O$	1658	–
46	78–79	57.4	$C_{32}H_{22}O$	1652	–

[a] Elemental analyses (C, H, N) were in good agreement with calculated values

above their melting points, compounds **41–46** could be prepared (*cf.* Scheme 1 and Tables 1 and 2) as the major products of the thermal denitrogenation. The characteristic singlet signal between 2.60 and 2.82 ppm (=C–CH_3) and the singlet at approx. 7.07–7.36 ppm (=CH–) unequivocally prove the β-methyl-α,β-unsaturated ketone structure of substances **41–46**. The conjugated enone character has also been corroborated by the ν(C=O) band at about 1652–1660 cm^{-1}. Thus, the major product of the thermal decomposition of these 2-pyrazolines is a β-methyl-α,β-unsaturated ketone accompanied by some non-isolable minor components detected by TLC.

Table 2. ^1H NMR spectroscopic data of compounds **21–46**

	Solvent	δ (ppm)
21	A	3.66 (dd, 1H), 4.19 (t, 1H), 5.40 (dd, 1H), 6.52 (s, NH), 7.21–8.22 (m, 12 arom. H)
22	A	3.81 (dd, 1H), 4.21 (t, 1H), 4.80 (dd, 1H), 6.54 (s, NH), 7.23–8.29 (m, 11 arom. H)
23	B	3.79 (s, 3H), 3.84 (t, 1H), 4.40 (dd, 1H), 6.21 (dd, 1H), 6.91–9.39 (m, 13 arom. H)
24	B	3.91 (t, 1H), 4.49 (dd, 1H), 6.22 (dd, 1H), 7.84–9.76 (m 13 arom. H)
25	B	3.68 (dd, 1H), 4.13 (t, 1H), 4.72 (dd, 1H), 6.67–9.13 (m, 10 arom. H)
26	A	3.72 (dd, 1H), 4.07 (t, 1H), 4.70 (dd, 1H), 7.21–8.06 (m, 12 arom. H)
27	A	3.76 (dd, 1H), 4.12 (t, 1H), 4.69 (dd, 1H), 7.26–8.05 (m, 11 arom. H)
28	A	4.15 (t, 1H), 4.43 (dd, 1H), 6.31 (dd, 1H), 7.27–8.62 (m, 16 arom. H)
29	A	3.75 (dd, 1H), 4.03 (t, 1H), 4.71 (dd, 1H), 7.34–8.23 (m, 11 arom. H + CH)
30	A	3.78 (dd, 1H), 4.09 (t, 1H), 4.71 (dd, 1H), 7.19–8.75 (m, 12 arom. H)
31	B	3.58 (dd, 1H), 3.71 (s, 3H), 4.08 (t, 1H), 4.57 (dd, 1H), 6.85–9.02 (m, 11 arom. H)
32	A	3.71 (dd, 1H), 4.08 (t, 1H), 4.68 (dd, 1H), 7.18–8.77 (m, 11 arom. H)
33	A	3.77 (dd, 1H), 4.03 (t, 1H), 4.76 (dd, 1H), 6.72 (s, NH), 7.36–8.83 (m, 11 arom. H + CH)
34	B	3.63 (dd, 1H), 4.12 (t, 1H), 4.64 (dd, 1H), 7.24–9.16 (m, 14 arom. H)
35	A	3.71 (dd, 1H), 4.09 (t, 1H), 4.69 (dd, 1H), 6.56 (s, NH), 7.31–9.61 (m, 13 arom. H)
36	A	3.62 (dd, 1H), 4.17 (t, 1H), 5.12 (dd, 1H), 6.58 (s, NH), 7.03–9.70 (m, 12 arom. H)
37	B	3.98 (t, 1H), 4.53 (dd, 1H), 6.34 (dd, 1H), 7.42–9.71 (m, 18 arom. H)
38	B	3.69 (dd, 1H), 4.20 (t, 1H), 4.68 (dd, 1H), 7.30–9.16 (m, 14 arom. H)
39	A	3.58 (dd, 1H), 4.08 (t, 1H), 5.39 (dd, 1H), 6.62 (s, NH), 7.46–8.77 (m, 18 arom. H)
40	B	4.02 (t, 1H), 4.56 (dd, 1H), 6.37 (dd, 1H), 7.40–9.73 (m, 18 arom. H)
41	A	2.69 (s, 3H), 7.06 (s, 1H), 7.36–8.02 (m, 12 arom. H)
42	A	2.68 (s, 3H), 7.07 (s, 1H), 7.39–8.56 (m, 12 arom. H)
43	A	2.62 (s, 3H), 7.31 (s, 1H), 7.40–8.51 (m, 12 arom. H)
44	A	2.70 (s, 3H), 7.35 (s, 1H), 7.43–8.76 (m, 14 arom. H)
45	A	2.60 (s, 3H), 7.25 (s, 1H), 7.38–9.12 (m, 18 arom. H)
46	A	2.82 (s, 3H), 7.12 (s, 1H), 7.30–8.76 (m, 18 arom. H)

Table 3. Selected ^{13}C NMR spectroscopic data of 3-aroyl-4-aryl-2-pyrazolines[a]

	Solvent	δ (ppm)			
		C=O	C-3	C-4	C-5
22	B	184.0	148.7	47.3	57.7
23	B	184.0	149.3	42.6	55.3
24	B	184.4	148.7	42.1	55.7
26	B	189.6	150.4	46.5	58.4
27	B	189.5	149.9	45.9	58.2
35	B	185.7	149.4	46.9	57.5
36	B	185.5	147.6	44.3	56.3
40	B	185.1	149.8	41.2	56.3

[a] ^{13}C NMR signals of all aromatic carbon atoms have been observed but have not been assigned to the particular atom

Experimental

^{1}H and ^{13}C NMR spectra were recorded on a Bruker WP 200 SY spectrometer at 200/50 MHz in $CDCl_3$ (A) or in *DMSO*-d_6 (B) (internal standard *TMS*, $\delta = 0.0$ ppm) at room temperature. The IR spectra (KBr discs) were measured with a Perkin-Elmer 16 PC instrument. TLC was performed on Kieselgel 60 F_{254} (Merck) using hexane:acetone (7:3 v/v) or toluene:ethyl acetate (4:1 v/v) as eluents. Starting materials **1–20** were synthesized by the alkaline-catalyzed condensation of the appropriate aromatic aldehydes and aryl methyl ketones according to known procedures [25–27].

General procedure for the synthesis of 2-pyrazolines (**21–40**)

The appropriate α,β-unsaturated ketone (**1–20**; 5 mmol) and diazomethane (10 mmol) were dissolved in a 1:1 v/v mixture of anhydrous CH_2Cl_2 and diethyl ether (100 ml). The solution was left to stand in refrigerator for 48 h; then the solvent was evaporated *in vacuo* and the residue was crystallized from methanol to afford compounds **21–40** (Scheme 1 and Tables 1–3).

General procedure for the preparation of β-methyl-α,β-unsaturated ketones (**41–46**)

3-Aroyl-4-aryl-2-pyrazolines **21**, **26**, **30**, **34**, **37**, and **39** (1.0 mmol) were heated slightly above their melting points (*ca.* 20 °C) for 30 min and the disappearance of the starting material was monitored by TLC. The purification of the crude reaction products was performed by column chromatography on a silica gel (Merck) column using hexane:acetone (7:3 v/v) as eluent to afford compounds **41–46** (Scheme 1 and Tables 1 and 2).

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