A Study on the Reactions of some Ketenes with 1-Aroyl-1*H*-pyrazoles

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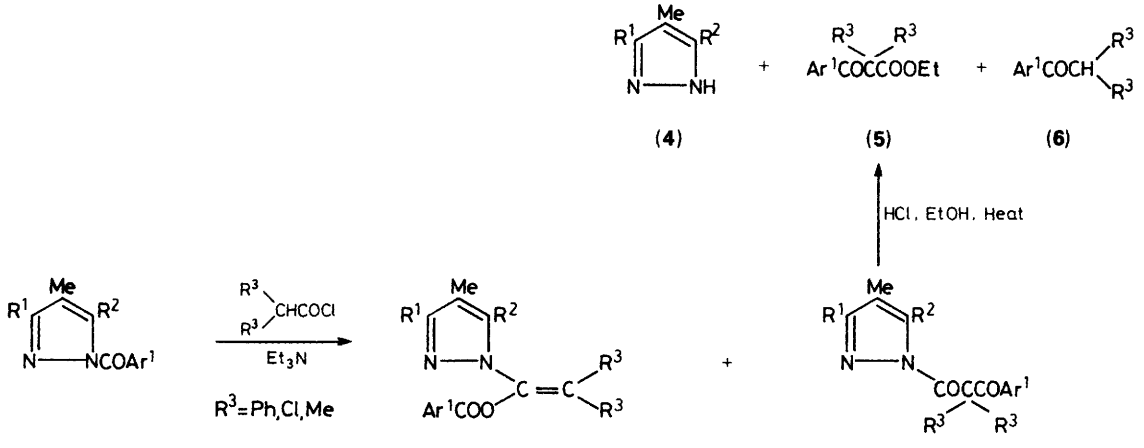
1-Aroyl-3,4,5-trimethyl-1*H*-pyrazoles (**1a–c**) react with diphenylketene (DPK) to afford the enol esters (**2**); this was confirmed by X-ray analysis. From the reaction of the pyrazoles (**1**) with dichloroketene (DCK) the pyrazolylpropanediones (**3**) are isolated, whereas from the reaction with dimethylketene (DMK) both the enol esters (**2**) and the pyrazolylpropanediones (**3**) were obtained. The hydrolysis of the products (**3**) was also studied. The corresponding pyrazolylpropanediones (**10**) and the enol esters (**11**) or their degradation products (**12**) were isolated from the reactions of the pyrazoles (**1a–c**) with some mixed anhydrides (**9**) in the presence of triethylamine. The structure of (**10e**) has also been confirmed by X-ray crystallography. Plausible schemes accounting for the formation of the products involving as a common step the quaternization of N-1 are envisaged.

Recently there has been great interest in the addition reactions of ketenes other than cycloadditions and a rich and diverse chemistry is being revealed.[1]

The reactions of thiazoles[2–4] and oxazoles[5] with ketenes lead to both cycloadducts and acyl derivatives. Recently the reaction between pyrazoles and imidazoles and (chlorocarbonyl)phenylketene to give heterocyclic betaines has been studied.[6] Also the reactions of *N*-acylated pyrazoles have been studied, as for example their arylation[7] and their oxidative coupling with alkyl acrylates in the presence of palladium acetate.[8] It is noteworthy that pyrazoles are rather inert[9] towards cycloaddition.

The chemistry of pyrazoles and especially of *N*-acylated pyrazoles, continues to attract interest[10] because of their presence in numerous biologically active compounds both natural and synthetic.

In the present work our interest was focussed on the 1-aroyl-1*H*-pyrazoles (**1**) which react with diphenylketene (DPK), dichloroketene (DCK), and dimethylketene (DMK), prepared *in situ* from the corresponding acid chlorides in the presence of triethylamine, to give different adducts depending on the ketene. Exceptions to this are the phenyl-substituted aroylpyrazoles (**1d**) and (**1e**) which were inert towards DPK and DMK but reacted smoothly with DCK (Scheme 1). From the reactions of (**1a–c**) with DPK the enol esters (**2**) were isolated in good yield (60–70%), whereas from the reaction with DCK the products



a; $R^1 = R^2 = Me$, $Ar^1 = Ph$
b; $R^1 = R^2 = Me$, $Ar^1 = p\text{-}MeC_6H_4$
c; $R^1 = R^2 = Me$, $Ar^1 = p\text{-}ClC_6H_4$
d; $R^1 = Me$, $R^2 = Ph$, $Ar^1 = p\text{-}MeC_6H_4$
e; $R^1 = Ph$, $R^2 = Me$, $Ar^1 = p\text{-}MeC_6H_4$

a; $R^1 = R^2 = Me$, $R^3 = Ar^1 = Ph$
b; $R^1 = R^2 = Me$, $R^3 = Ph$, $Ar^1 = p\text{-}MeC_6H_4$
c; $R^1 = R^2 = Me$, $R^3 = Ph$, $Ar^1 = p\text{-}ClC_6H_4$
d; $R^1 = R^2 = R^3 = Me$, $Ar^1 = Ph$
e; $R^1 = R^2 = R^3 = Me$, $Ar^1 = p\text{-}MeC_6H_4$
f; $R^1 = R^2 = R^3 = Me$, $Ar^1 = p\text{-}ClC_6H_4$

a; $R^1 = R^2 = Me$, $R^3 = Cl$, $Ar^1 = Ph$
b; $R^1 = R^2 = Me$, $R^3 = Cl$, $Ar^1 = p\text{-}MeC_6H_4$
c; $R^1 = R^2 = Me$, $R^3 = Cl$, $Ar^1 = p\text{-}ClC_6H_4$
d, $R^1 = R^2 = R^3 = Me$, $Ar^1 = Ph$
e; $R^1 = R^2 = R^3 = Me$, $Ar^1 = p\text{-}MeC_6H_4$
f; $R^1 = R^2 = R^3 = Me$, $Ar^1 = p\text{-}ClC_6H_4$
g; $R^1 = Me$, $R^2 = Ph$, $R^3 = Cl$, $Ar^1 = p\text{-}MeC_6H_4$
h; $R^1 = Ph$, $R^2 = Me$, $R^3 = Cl$, $Ar^1 = p\text{-}ClC_6H_4$

Scheme 1.

Table 1. Physical, spectral, and analytical data for 1-(3,4,5-trimethyl-1*H*-pyrazolyl)vinyl benzoates (**2**) and 1-(3-arylpropyl-1,3-dioxopropyl)-1*H*-pyrazoles (**3**).[a]

Compound	Yield (%)	M.p.[b] (°C)	ν_{max} (Nujol)/cm^{-1} (C=O)	δ_H($CDCl_3$)	Formula	Elemental analysis (%) Found (required) C	H	N
(2a)	57	155–157	1 720	1.80 (3 H, s), 1.92 (3 H, s), 2.22 (3 H, s), 6.85–7.60 (13 H, m), 7.88–8.14 (2 H, m)	$C_{27}H_{24}N_2O_2$	79.5 (79.38)	6.15 (5.92)	6.6 (6.86)
(2b)	71	153–155	1 725	1.77 (3 H, s), 1.88 (3 H, s), 2.17 (3 H, s), 2.35 (3 H, s), 6.68–7.48 (12 H, m), 7.88 (2 H, d, *J* 9 Hz)	$C_{28}H_{26}N_2O_2$	79.6 (79.59)	6.3 (6.20)	6.5 (6.63)
(2c)	70	149–151	1 725	1.77 (3 H, s), 1.89 (3 H, s), 2.18 (3 H, s), 6.65–7.50 (12 H, m), 7.90 (2 H, d, *J* 9 Hz)	$C_{27}H_{23}ClN_2O_2$	73.2 (73.22)	5.3 (5.23)	6.25 (6.32)
(2d)	33	Oil	1 730[c]	1.59 (3 H, s), 1.81 (3 H, s), 1.91 (3 H, s), 2.16 (3 H, s), 2.27 (3 H, s), 7.10–7.65 (3 H, m), 7.80–8.20 (2 H, m)	$C_{17}H_{20}N_2O_2$	71.9 (71.80)	7.0 (7.09)	10.0 (9.85)
(2e)	28	Oil	1 740[c]	1.60 (3 H, s), 1.82 (3 H, s), 1.91 (3 H, s), 2.18 (3 H, s), 2.28 (3 H, s), 2.33 (3 H, s), 7.27 (2 H, d, *J* 8 Hz), 8.06 (2 H, d, *J* 8 Hz)	$C_{18}H_{22}N_2O_2$	72.65 (72.45)	7.5 (7.43)	9.2 (9.39)
(2f)	38	Oil	1 740[c]	1.63 (3 H, s), 1.83 (3 H, s), 1.93 (3 H, s), 2.19 (3 H, s), 2.29 (3 H, s), 7.41 (2 H, d, *J* 9 Hz), 8.07 (2 H, d, *J* 9 Hz)	$C_{17}H_{19}ClN_2O_2$	64.05 (64.05)	6.2 (6.01)	8.9 (8.79)
(3a)	58	98–100	1 730, 1 700	1.79 (3 H, s), 1.94 (3 H, s), 2.48 (3 H, s), 7.20–7.45 (3 H, m), 7.84–7.95 (2 H, m)	$C_{15}H_{14}Cl_2N_2O_2$	55.6 (55.40)	4.5 (4.34)	8.75 (8.61)
(3b)	58	135–136	1 740, 1 680	1.82 (3 H, s), 1.97 (3 H, s), 2.38 (3 H, s), 2.51 (3 H, s), 7.22 (2 H, d, *J* 8.5 Hz), 7.85 (2 H, d, *J* 8.5 Hz)	$C_{16}H_{16}Cl_2N_2O_2$	56.35 (56.65)	5.0 (4.75)	8.3 (8.26)
(3c)	72	149–151	1 740, 1 690	1.80 (3 H, s), 1.98 (3 H, s), 2.52 (3 H, s), 7.42 (2 H, d, *J* 9 Hz), 7.73 (2 H, d, *J* 9 Hz)	$C_{15}H_{13}Cl_3N_2O_2$	50.3 (50.10)	3.7 (3.64)	7.8 (7.79)
(3d)	51	91–93	1 710, 1 675	1.71 (6 H, s), 1.75 (3 H, s), 1.92 (3 H, s), 2.47 (3 H, s), 7.15–7.45 (3 H, m), 7.60–7.82 (2 H, m)	$C_{17}H_{20}N_2O_2$	72.05 (71.80)	7.15 (7.09)	9.9 (9.85)
(3e)	36	95–97	1 705, 1 665	1.68 (6 H, s), 1.77 (3 H, s), 1.92 (3 H, s), 2.31 (3 H, s), 2.47 (3 H, s), 7.11 (2 H, d, *J* 9 Hz), 7.69 (2 H, d, *J* 9 Hz)	$C_{18}H_{22}N_2O_2$	72.55 (72.45)	7.45 (7.43)	9.25 (9.39)
(3f)	45	118–119	1 710, 1 670	1.69 (6 H, s), 1.77 (3 H, s), 1.92 (3 H, s), 2.46 (3 H, s), 7.30 (2 H, d, *J* 9 Hz), 7.73 (2 H, d, *J* 9 Hz)	$C_{17}H_{19}ClN_2O_2$	64.1 (64.05)	6.05 (6.01)	8.65 (8.79)
(3g)	81	147–149	1 740–1 690	2.03 (3 H, s), 2.28 (3 H, s), 2.55 (3 H, s), 7.12 (2 H, d, *J* 8.5 Hz), 7.24–7.56 (5 H, m), 7.80 (2 H, d, *J* 8.5 Hz)	$C_{21}H_{18}Cl_2N_2O_2$	62.95 (62.85)	4.4 (4.52)	6.9 (6.98)
(3h)	77	99–101	1 740–1 705	1.76 (3 H, s), 2.01 (3 H, s), 2.35 (3 H, s), 7.15–7.50 (5 H, m), 7.18 (2 H, d, *J* 8.5 Hz), 7.80 (2 H, d, *J* 8.5 Hz)	$C_{21}H_{18}Cl_2N_2O_2$	62.7 (62.85)	4.45 (4.52)	6.8 (6.98)

[a] Correct molecular ion peaks were observed in the mass spectra. [b] From ethanol. [c] Neat.

were the pyrazolylpropanediones (**3**) in 60–70% yield. However, when the reaction was repeated with DMK both products (**2**) and (**3**) were isolated in 28–38 and 35–50% yield respectively (Table 1).

To ascertain unambiguously the structure of the enol esters (**2**) an X-ray crystallographic analysis on (**2b**) was performed (Figure 1).

Additional proof for the characterization of compounds (**3**) was gained by their hydrolysis with alcoholic hydrochloric acid (Scheme 1), whereupon the pyrazole (**4**), the β-keto esters (**5**), and the ketones (**6**) were isolated. The ketones (**6**) are formed from the keto esters (**5**) by hydrolysis and decarboxylation, as was proved by an independent experiment.

Formation of the products (**2**) and (**3**) can be explained by assuming a process which is initiated by quaternization of the aroyl substituted nitrogen of the pyrazoles (**1**) by the ketenes to give the zwitterion (**7**) (Scheme 2). From the resonance form (**7A**) the enol esters (**2**) can be obtained, whereas from the resonance form (**7B**) the pyrazolylpropanediones (**3**) can be formed. This is consistent with both the well known charge

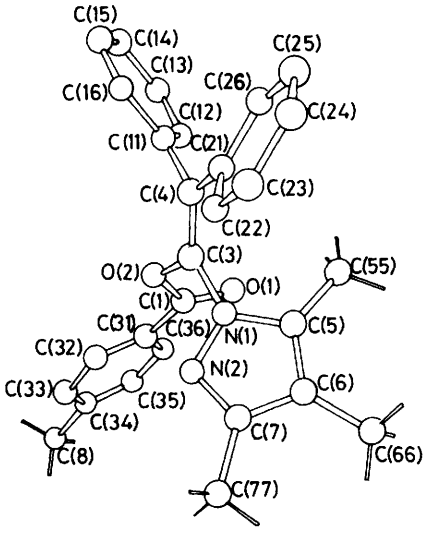
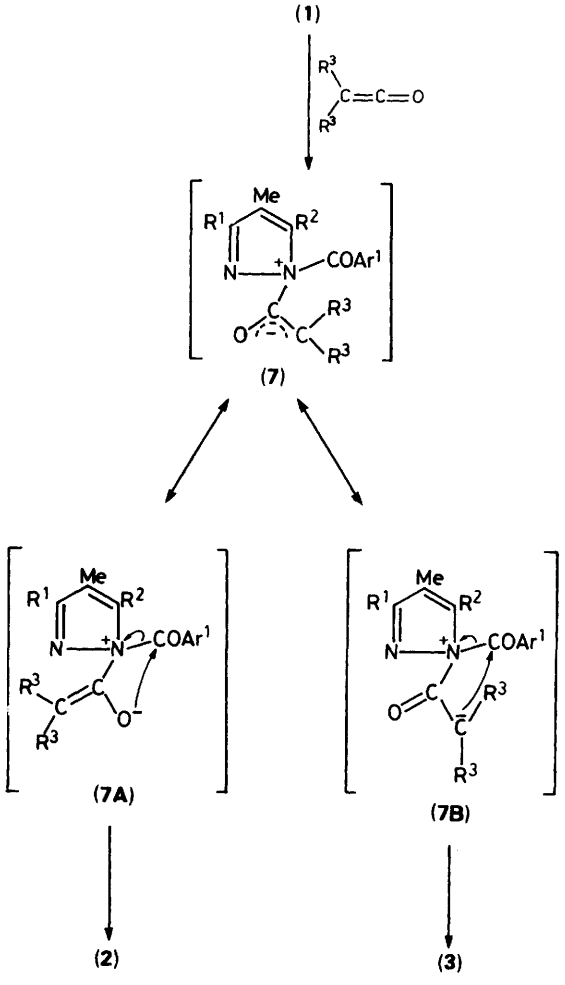
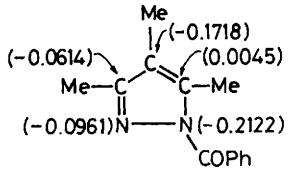


Figure 1. X-Ray molecular structure of compound (**2b**).



Scheme 2.

distribution of ketenes[11] and with the results of the charge density distribution (Figure 2) calculated by the MNDO method[12] for 1-benzoyl-3,4,5-trimethyl-1*H*-pyrazole (**1a**). This indicates that the largest negative charge is observed on the N-1 atom of the pyrazole ring (Figure 2). Electrophilic attack by the ketenes at the unsubstituted nitrogen N-2 was also



(**1a**)

Figure 2. Calculated net charges (in parentheses) for compound (**1a**).

considered as an alternative route for formation of the products (**2**) and (**3**), but such an attack is incompatible with the low charge density on this atom as indicated by the MNDO calculations (Figure 2).

Isolation of the products (**2**) and (**3**) excludes also the possibility of an initial deacylation of the aroylpyrazoles (**1**) by triethylamine followed by reaction with ketene. The possibility was also excluded by an independent experiment. In this, the aroylpyrazoles (**1**) remained unchanged when stirred with an excess of triethylamine in dichloromethane at 25 °C for 7 days, even in the presence of a few drops of water, or after the reaction mixture had been refluxed for 7 days.

Furthermore, the reactions of the aroylpyrazoles (**1a–c**) with some mixed anhydrides (**9**) in the presence of triethylamine were studied (Scheme 3). The mixed anhydrides (**9**), synthetic equivalents of acid chlorides, were prepared from the phenoxy- or *p*-chlorophenoxy-acetic acids (**8**) and toluene-*p*-sulphonyl chloride in the presence of triethylamine. Under the mild reaction conditions employed, the (**9a**) formed *in situ* reacts with the pyrazoles (**1**) in the presence of triethylamine to give the pyrazolylpropanediones (**10**) (30–50%) along with the enol esters (**11**) (25–45%). In the reaction of (**9b**) with (**1**) the pyrazolylpropanediones (**10**) were again isolated (27–45%) along with 1-[(*p*-chlorophenoxy)acetyl]pyrazole (**12**).

The structures of compounds (**10**) and (**11**), which are analogous to compounds (**3**) and (**2**) respectively, have been established by examining their analytical and spectral data (Table 2).

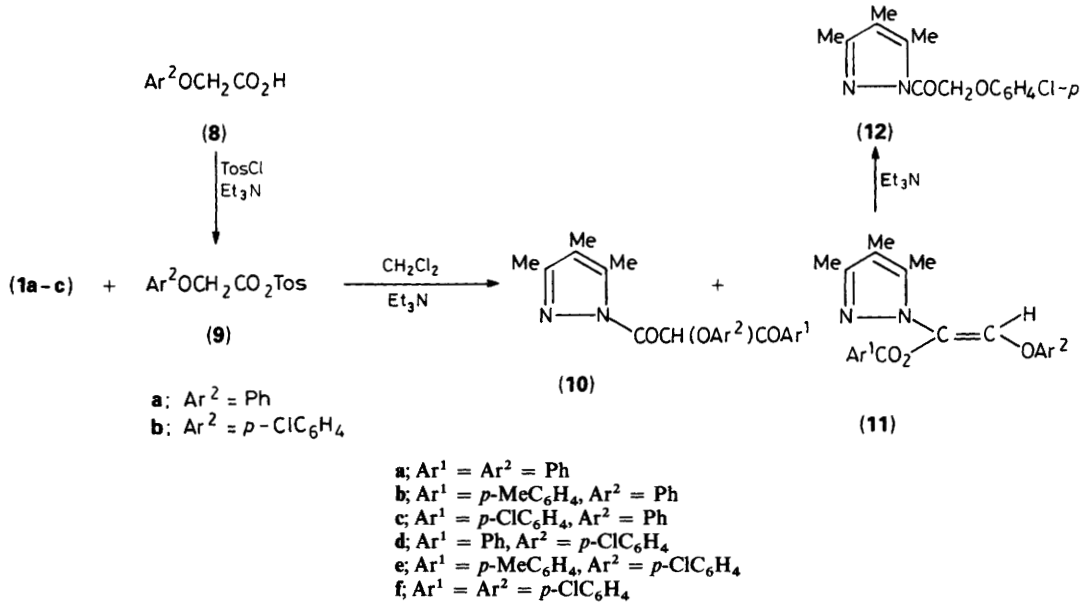
The structure of the pyrazolylpropanediones (**10**) was confirmed by an X-ray crystallographic analysis of (**10e**) (Figure 3).

For the formation of the products (**10**) and (**11**) a mechanism analogous to that shown in Scheme 2 for the ketene–aroylpyrazole reaction is possible, whereas compound (**12**) is most probably formed by degradation of the non-isolated enol esters (**11d–f**).

Experimental

M.p.s were determined on a Kofler hot-stage apparatus and are uncorrected. IR spectra were recorded as Nujol mulls on a Perkin-Elmer 297 spectrometer. ^{1}H NMR spectra were obtained on a Varian A60-A (60 MHz) spectrometer or on a Bruker Model AW 80 (80 MHz) spectrometer in $CDCl_3$ with tetramethylsilane (TMS) as internal standard. The mass spectra were obtained on a Hitachi–Perkin-Elmer RMU-6L spectrometer and elemental microanalyses were performed with a Perkin-Elmer 240 B analyser. Column chromatography was performed over Merck Kieselgel 60, particle size 0.063–0.200 mm. Light petroleum refers to that fraction of b.p. 60–80 °C.

Starting Materials.—The 1-aroyl-1*H*-pyrazoles (**1**) were prepared as previously described.[13,14] Diphenylketene (DPK), dichloroketene (DCK), and dimethylketene (DMK) were generated *in situ* by dehydrochlorination of the corresponding acid chlorides[15] with triethylamine.



a; Ar^2 = Ph
b; Ar^2 = *p*-ClC_6H_4

a; $Ar^1 = Ar^2$ = Ph
b; Ar^1 = *p*-MeC_6H_4, Ar^2 = Ph
c; Ar^1 = *p*-ClC_6H_4, Ar^2 = Ph
d; Ar^1 = Ph, Ar^2 = *p*-ClC_6H_4
e; Ar^1 = *p*-MeC_6H_4, Ar^2 = *p*-ClC_6H_4
f; $Ar^1 = Ar^2$ = *p*-ClC_6H_4

Scheme 3.

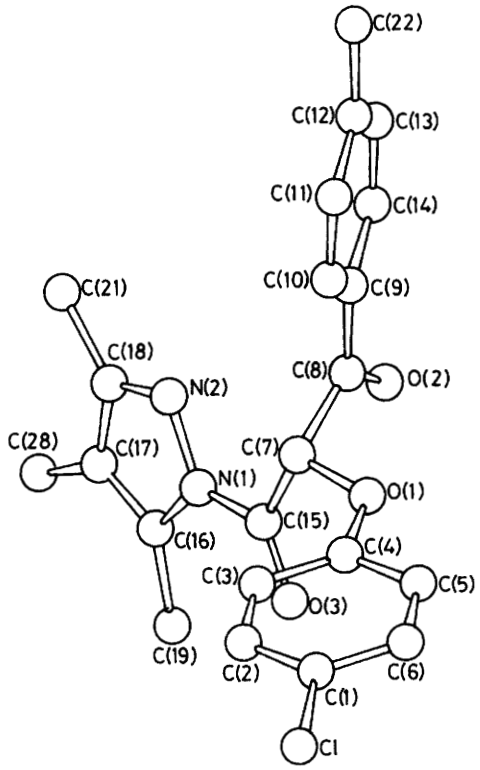


Figure 3. X-Ray molecular structure of compound (**10e**).

Reaction of 1-*Aroyl*-3,4,5-*trimethyl*-1H-*pyrazoles* (**1a–c**) *with DPK: General Procedure.*—A solution of diphenylacetyl chloride (2.0 mmol) in dry dichloromethane (5 ml) was added dropwise at room temperature for 2 h to a stirred solution of compound (**1**) (1.0 mmol) and triethylamine (2.1 mmol) in the same solvent (20 ml). The reaction mixture was stirred for 24 h and then a further quantity of triethylamine (2.1 mmol) was added followed by the dropwise addition of diphenylacetyl chloride (2.0 mmol) in dichloromethane (5 ml). The reaction mixture was stirred for a further 24 h after which it was washed with aqueous $NaHCO_3$; the organic layer was separated, dried (Na_2SO_4) and evaporated under reduced pressure. The residue was chromatographed on silica gel using ethyl acetate–light petroleum (1:10) as eluant to give the unchanged pyrazole (**1**) (~15%) and the 1-(3,4,5-trimethyl-1*H*-pyrazolyl)-2,2-diphenylvinyl benzoate (**2**) (yields are given in Table 1).

Reaction of 1-*Aroyl*-1H-*pyrazoles* (**1**) *with DCK: General Procedure.*—A solution of dichloroacetyl chloride (3.0 mmol) in dry dichloromethane (5 ml) was added dropwise at room temperature for 2 h to a stirred solution of compound (**1**) (1.0 mmol) and triethylamine (3.1 mmol) in the same solvent (20 ml). The reaction mixture was stirred for 18 h and then washed with aqueous $NaHCO_3$; the organic layer was separated, dried (Na_2SO_4), and evaporated under reduced pressure. The residue was treated with ethanol and the mixture stored in a refrigerator overnight, whereupon the 1-(3-aryl-2,2-dichloro-1,3-dioxopropyl)-1*H*-pyrazole (**3**) crystallized; compound (**3g**) was an exception and this was column chromatographed with ethyl acetate–light petroleum (1:20) as eluant.

Reaction of 1-*Aroyl*-3,4,5-*trimethyl*-1H-*pyrazoles* (**1a–c**) *with DMK: General Procedure.*—A solution of dimethylacetyl chloride (2.0 mmol) in dry dichloromethane (5 ml) was added dropwise at room temperature for 2 h to a stirred solution of the pyrazole (**1**) (1.0 mmol) and triethylamine (2.1 mmol) in the same solvent (20 ml). The reaction mixture was stirred for 4 h and then a further quantity of triethylamine (2.1 mmol) was added followed by the dropwise addition of dimethylacetyl chloride (2.0 mmol) in dichloromethane (5 ml). The reaction mixture was stirred for a further 4 h and then washed with aqueous $NaHCO_3$; the organic layer was separated, dried (Na_2SO_4), and evaporated under reduced pressure. The residue was chromatographed on silica gel using ethyl acetate–light petroleum (1:10) as eluant to give in order of elution: 1-(3-aryl-2,2-dimethyl-1,3-dioxopropyl)-3,4,5-trimethyl-1*H*-pyrazole (**3**) and 1-(3,4,5-trimethyl-1*H*-pyrazolyl)-2,2-dimethylvinyl benzoate (**2**).

Acid Hydrolysis of (**3a**).—A solution of (**3a**) (0.204 g, 0.5 mmol) in ethanol (5 ml) and concentrated hydrochloric acid (1 ml) was refluxed 48 h, after which it was made alkaline (10%

Table 2. Physical, spectral, and analytical data for 3,4,5-trimethyl-1-(3-aryl-2-aryloxy-1,3-dioxopropyl)-1*H*-pyrazoles (**10**), 1-(3,4,5-trimethyl-1*H*-pyrazolyl)-2-aryloxyvinyl benzoates (**11**), and 1-[(4-chlorophenoxy)acetyl]-3,4,5-trimethyl-1*H*-pyrazole (**12**).[a]

Compound	Yield (%)	M.p.[b] (°C)	ν_{max} (Nujol)/cm^{-1} (C=O)	δ_H($CDCl_3$)	Formula	Elemental analysis (%) Found (required) C	H	N
(10a)	31	68[b]	1 745, 1 690	1.88 (3 H, s), 2.02 (3 H, s), 2.50 (3 H, s), 6.90–7.62 (9 H, m), 7.97–8.09 (2 H, m)	$C_{21}H_{20}N_2O_3$	72.45 (72.39)	5.95 (5.79)	8.0 (8.04)
(10b)	49	126–128[b]	1 740, 1 690	1.89 (3 H, s), 2.04 (3 H, s), 2.40 (3 H, s), 2.51 (3 H, s), 6.86–7.37 (10 H, m), 7.90 (2 H, d, *J* 9 Hz)	$C_{22}H_{22}N_2O_3$	73.15 (72.91)	5.95 (6.12)	7.65 (7.73)
(10c)	29	Oil	1 740, 1 690[c]	1.89 (3 H, s), 2.04 (3 H, s), 2.51 (3 H, s), 6.77–7.53 (10 H, m), 7.94 (2 H, d, *J* 9 Hz)	$C_{21}H_{19}ClN_2O_3$	*d*		
(10d)	44	109–111[e]	1 740, 1 690	1.90 (3 H, s), 2.06 (3 H, s), 2.51 (3 H, s), 6.70–7.70 (8 H, m), 7.96–8.20 (2 H, m)	$C_{21}H_{19}ClN_2O_3$	65.95 (65.88)	5.1 (5.00)	7.4 (7.32)
(10e)	40	146–147[e]	1 740, 1 700	1.90 (3 H, s), 2.06 (3 H, s), 2.51 (3 H, s), 2.45 (3 H, s), 6.87–7.42 (7 H, m), 7.93 (2 H, d, *J* 8.5 Hz)	$C_{22}H_{21}ClN_2O_3$	66.6 (66.58)	5.3 (5.33)	6.95 (7.06)
(10f)	27	132–134[e]	1 730, 1 685	1.92 (3 H, s), 2.08 (3 H, s), 2.50 (3 H, s), 6.98 (2 H, d, *J* 9 Hz), 7.07 (1 H, s), 7.28 (2 H, d, *J* 9 Hz), 7.47 (2 H, d, *J* 9 Hz), 8.01 (2 H, d, *J* 9 Hz)	$C_{21}H_{18}Cl_2N_2O_3$	60.1 (60.44)	4.3 (4.35)	6.8 (6.71)
(11a)	44	84–86[b]	1 745	1.88 (3 H, s), 2.18 (3 H, s), 2.34 (3 H, s), 6.74 (1 H, s), 6.93–7.64 (8 H, m), 8.02–8.27 (2 H, m)	$C_{21}H_{20}N_2O_3$	72.4 (72.39)	5.75 (5.79)	8.15 (8.04)
(11b)	25	Oil	1 740[c]	1.90 (3 H, s), 2.18 (3 H, s), 2.35 (3 H, s), 2.38 (3 H, s), 6.74 (1 H, s), 6.91–7.39 (9 H, m), 8.03 (2 H, d, *J* 9 Hz)	$C_{22}H_{22}N_2O_3$	7.75 (72.91)	6.2 (6.12)	7.8 (7.73)
(11c)	23	87–89[b]	1 740	1.91 (3 H, s), 2.18 (3 H, s), 2.34 (3 H, s), 6.72 (1 H, s), 6.92–7.50 (9 H, m), 8.05 (2 H, d, *J* 9 Hz)	$C_{21}H_{19}ClN_2O_3$	65.7 (65.88)	5.05 (5.00)	7.0 (7.32)
(12)	*f*	144–146[e]	1 740	1.92 (3 H, s), 2.20 (3 H, s), 2.48 (3 H, s), 5.38 (2 H, s), 7.00 (2 H, d, *J* 9 Hz), 7.40 (2 H, d, *J* 9 Hz)	$C_{14}H_{15}ClN_2O_2$	60.5 (60.32)	5.45 (5.42)	10.15 (10.65)

[a] Correct molecular ion peaks were observed in the mass spectra. [b] From ether–light petroleum. [c] Neat. [d] Unstable compound not analysed. [e] From ethanol. [f] In 11, 20, and 24% yield from (**1a**), (**1b**), and (**1c**) with (**9b**) respectively.

NaOH; pH 8) and extracted with CH_2Cl_2 (30 ml). The organic layer was dried and evaporated and the residue was chromatographed on a silica gel column with ethyl acetate–light petroleum (1:20) as eluant to give the following: α,α-dichloroacetophenone (**6a**) (0.046 g, 49%) identified by comparison of spectral properties with those of the literature;[16] ethyl α,α-dichlorobenzoylacetate (**5a**) (0.012 g, 9%) identified by comparison of spectral properties with those in the literature;[17] and (**4a**) (0.036 g, 65%), m.p. 137–139 °C (lit.,[14] 138–139 °C).

Analogous products were isolated from hydrolysis of (**3d**), (**3e**), and (**3g**).

Reaction of (**1a–c**) *with* (**9a**) *in the Presence of* Et_3N: *General Procedure*.—A solution of phenoxyacetic acid (**8a**) (0.46 g, 3.0 mmol), toluene-*p*-sulphonyl chloride (0.57 g, 3.0 mmol), and triethylamine (0.61 g, 6.0 mmol) in anhydrous dichloromethane (15 ml) was stirred at room temperature for 10 min. To this solution the pyrazole (**1**) (1.0 mmol) was added in anhydrous dichloromethane (2 ml), and the solution was stirred at room temperature for 24 h. A further quantity of phenoxyacetic acid–toluene-*p*-sulphonyl chloride–Et_3N solution, prepared as above, was added and stirring was continued for 24 h. The reaction mixture was then washed with 5% aqueous $NaHCO_3$ (20 ml) and water (20 ml) and dried. The solvent was evaporated and the residue was chromatographed on a silica gel column with ethyl acetate–light petroleum of slowly increasing polarity, as eluant to give the following compounds in elution order. Unchanged starting material (**1**) (~5%); the 3,4,5,-trimethyl-1-(3-aryl-1,3-dioxo-2-phenoxypropyl)-1*H*-pyrazole (**10**); the 1-(3,4,5-trimethyl-1*H*-pyrazolyl)-2-phenoxyvinyl benzoate (**11**).

Reaction of (**1a–c**) *with* (**9b**) *in the Presence of* Et_3N: *General Procedure*.—The same procedure described for the reaction of (**1**) with (**9a**) was followed, starting with (4-chloro)phenoxyacetic acid (0.52 g, 3.0 mmol) and (**1**) (1.0 mmol). The reaction mixture was separated on a silica gel with ethyl acetate–hexane (1:10) as eluant to give the following: unchanged starting material (**1**) (~14%); 1-[(4-chlorophenoxy)acetyl]-3,4,5-trimethyl-1*H*-pyrazole (**12**); and 1-[3-aryl-2-(4-chlorophenoxy)-1,3-dioxopropyl]-3,4,5-trimethyl-1*H*-pyrazole (**10**).

X-Ray Structure Determination

Compound (**2b**).—*Crystal data*. $C_{28}H_{26}N_2O_2$, M = 422.53, monoclinic, a = 9.770(1), b = 10.548(2), c = 23.695(3) Å,

Table 3. Fractional atomic co-ordinates ($\times 10^4$) with estimated standard deviations in parentheses for compound (**2b**).

	x	*y*	*z*
N(1)	9 225(2)	4 078(2)	1 208.7(7)
N(2)	10 144(2)	3 364(2)	950.6(8)
O(1)	6 287(2)	4 341(2)	625.1(7)
O(2)	7 377(2)	2 673(1)	1 073.3(6)
C(1)	6 590(2)	3 242(2)	616.0(9)
C(3)	8 187(2)	3 461(2)	1 458.2(9)
C(4)	8 016(2)	3 498(2)	2 003.0(9)
C(5)	9 494(3)	5 342(2)	1 183(1)
C(6)	10 614(3)	5 464(3)	903(1)
C(7)	10 975(3)	4 224(3)	769(1)
C(8)	5 233(3)	−31(3)	−1 310(1)
C(11)	6 754(3)	2 964(2)	2 202(1)
C(12)	5 451(3)	3 303(3)	1 945(1)
C(13)	4 281(3)	2 821(4)	2 144(2)
C(14)	4 420(4)	2 012(4)	2 598(2)
C(15)	5 700(4)	1 678(3)	2 857(2)
C(16)	6 882(3)	2 146(3)	2 664(1)
C(21)	9 073(2)	4 068(2)	2 442.3(9)
C(22)	10 477(3)	3 887(2)	2 431(1)
C(23)	11 442(3)	4 432(3)	2 837(1)
C(24)	11 022(3)	5 151(3)	3 262(1)
C(25)	9 650(4)	5 331(3)	3 287(1)
C(26)	8 664(3)	4 785(3)	2 879(1)
C(31)	6 198(2)	2 344(2)	149.9(9)
C(32)	6 871(3)	1 213(2)	117(1)
C(33)	6 552(3)	433(2)	−354(1)
C(34)	5 552(3)	768(3)	−794(1)
C(35)	4 866(3)	1 892(3)	−755(1)
C(36)	5 179(3)	2 698(2)	−291(1)
C(55)	8 626(3)	6 323(2)	1 415(1)
C(66)	11 275(3)	6 685(3)	745(1)

Table 4. Selected intramolecular distances (Å) and angles (°) with estimated standard deviations in parentheses for compound (**2b**).

(*a*) Bonds			
N(1)–N(2)	1.378(2)	N(1)–C(3)	1.402(3)
N(1)–C(5)	1.362(3)	N(2)–C(7)	1.328(4)
O(1)–C(1)	1.197(3)	O(2)–C(1)	1.378(2)
O(2)–C(3)	1.397(2)	C(1)–C(31)	1.465(3)
C(3)–C(4)	1.325(3)	C(4)–C(11)	1.490(3)
C(4)–C(21)	1.489(3)	C(5)–C(6)	1.362(4)
C(5)–C(55)	1.489(4)	C(6)–C(7)	1.402(4)
C(6)–C(66)	1.511(4)	C(7)–C(77)	1.514(4)
C(8)–C(34)	1.512(4)		
(*b*) Angles			
N(2)–N(1)–C(3)	119.1(2)	N(2)–N(1)–C(5)	112.0(2)
C(3)–N(1)–C(5)	128.9(2)	N(1)–N(2)–C(7)	103.6(2)
C(1)–O(2)–C(3)	117.3(2)	O(1)–C(1)–O(2)	121.4(2)
O(1)–C(1)–C(31)	126.8(2)	O(2)–C(1)–C(31)	111.8(2)
N(1)–C(3)–O(2)	112.3(2)	N(1)–C(3)–C(4)	126.3(2)
O(2)–C(3)–C(4)	121.2(2)	C(3)–C(4)–C(11)	121.1(2)
C(3)–C(4)–C(21)	121.7(2)	C(11)–C(4)–C(21)	117.1(2)
N(1)–C(5)–C(6)	106.6(2)	N(1)–C(5)–C(55)	122.7(2)
C(6)–C(5)–C(55)	130.6(2)	C(5)–C(6)–C(7)	105.5(2)
C(5)–C(6)–C(66)	126.9(3)	C(7)–C(6)–C(66)	127.6(3)
N(2)–C(7)–C(6)	112.3(2)	N(2)–C(7)–C(77)	119.4(3)
C(6)–C(7)–C(77)	128.3(3)	C(4)–C(11)–C(12)	121.0(2)
C(4)–C(11)–C(16)	119.8(2)	C(4)–C(21)–C(22)	121.6(2)
C(4)–C(21)–C(26)	120.0(2)	C(1)–C(31)–C(32)	121.8(2)
C(1)–C(31)–C(36)	118.6(2)	C(8)–C(34)–C(33)	120.5(2)
C(8)–C(34)–C(35)	121.2(2)		

$\beta = 97.87(2)°$, $V = 2\,418.8(5)$ Å^3 (by least-squares on diffractometer angles for 15 automatically centred reflections, Mo–K_α, Zr-filtered radiation, $\lambda = 0.710\,69$ Å), space group $P2_1/c$, $Z = 4$, $D_m = 1.15$ g cm^{-3}. Crystal dimensions 0.25 × 0.31 × 0.41 mm, $\mu = 0.4$ cm^{-1}.

Data collection and processing. Nicolet $P2_1$ diffractometer, $\omega/2\theta$ mode, scan width 1.8°(2θ) plus α_1–α_2 separation, scan speed 2–20° 2θ/min, $2\theta_{max} = 47°$, reflections measured/unique/R_{merg} 4 260/3 591/0.021 observed with $I > 1.3\sigma(I)$

Table 5. Fractional atomic co-ordinates ($\times 10^4$) with estimated standard deviations in parentheses for compound (**10e**).

	x	*y*	*z*
Cl	6 154.7(4)	−3 556.8(5)	2 567.6(3)
N(1)	5 026(1)	2 739(1)	4 206.6(6)
N(2)	4 931.1(9)	2 603(1)	4 774.8(6)
O(1)	6 729.2(8)	361(1)	4 177.6(6)
O(2)	1 867.5(9)	2 449(1)	5 099.0(6)
O(3)	6 053(1)	2 034(2)	3 494.4(6)
C(1)	6 292(1)	−2 383(2)	3 053.5(8)
C(2)	5 626(1)	−1 733(2)	3 224.2(9)
C(3)	5 738(1)	−793(2)	3 602.7(9)
C(4)	6 530(1)	−538(2)	3 800.0(8)
C(5)	7 194(1)	−1 217(2)	3 628.4(8)
C(6)	7 080(1)	−2 140(2)	3 251.2(9)
C(7)	6 092(1)	1058(2)	4 426.6(8)
C(8)	6 525(1)	1 618(2)	4 960.1(8)
C(9)	6 533(1)	952(2)	5 515.6(8)
C(10)	6 357(1)	−237(2)	5 543.4(9)
C(11)	6 380(1)	−830(2)	6 070(1)
C(12)	6 556(2)	−240(2)	6 590.0(9)
C(13)	6 733(2)	935(2)	6 559.5(9)
C(14)	6 734(2)	1 530(2)	6 032.0(9)
C(15)	5 801(1)	1 979(2)	3 994.0(8)
C(16)	4 827(1)	3 688(2)	3 936.6(9)
C(17)	4 309(1)	4 154(2)	4 339.4(9)
C(18)	4 396(1)	3 454(2)	4 851.1(8)
C(19)	4 994(2)	4 046(3)	3 321(1)
C(20)	3 763(2)	5 223(2)	4 272(1)
C(21)	3 954(2)	3 597(2)	5 425(1)
C(22)	6 534(2)	−887(3)	7 167(1)

Table 6. Selected intramolecular distances (Å) and angles (°) with estimated standard deviations in parentheses for compound (**10e**).

(*a*) Bonds			
Cl–C(1)	1.752(2)	N(1)–N(2)	1.379(2)
N(1)–C(15)	1.381(2)	N(1)–C(16)	1.387(2)
N(2)–C(18)	1.310(2)	O(1)–C(4)	1.378(2)
O(1)–C(7)	1.417(2)	O(2)–C(8)	1.207(2)
O(3)–C(15)	1.212(2)	C(7)–C(8)	1.542(3)
C(7)–C(15)	1.516(3)	C(8)–C(9)	1.478(3)
C(12)–C(22)	1.511(4)	C(16)–C(17)	1.351(3)
C(16)–C(19)	1.488(3)	C(17)–C(18)	1.422(3)
C(17)–C(20)	1.511(3)	C(18)–C(21)	1.499(3)
(*b*) Angles			
N(2)–N(1)–C(15)	118.9(1)	N(2)–N(1)–C(16)	111.4(2)
C(15)–N(1)–C(16)	129.8(2)	N(1)–N(2)–C(18)	104.7(1)
C(4)–O(1)–C(7)	120.0(1)	Cl–C(1)–C(2)	119.9(2)
Cl–C(1)–C(6)	118.6(2)	O(1)–C(4)–C(3)	125.1(2)
O(1)–C(4)–C(5)	114.5(2)	O(1)–C(7)–C(8)	102.8(1)
O(1)–C(7)–C(15)	110.5(1)	C(8)–C(7)–C(15)	111.5(2)
O(2)–C(8)–C(7)	119.0(1)	O(2)–C(8)–C(9)	123.1(2)
C(7)–C(8)–C(9)	117.9(2)	C(8)–C(9)–C(10)	122.7(2)
C(8)–C(9)–C(14)	119.0(2)	C(11)–C(12)–C(22)	120.2(2)
C(13)–C(12)–C(22)	121.7(2)	N(1)–C(15)–O(3)	122.1(2)
N(1)–C(15)–C(7)	114.9(1)	O(3)–C(15)–C(7)	123.0(2)
N(1)–C(16)–C(17)	106.0(2)	N(1)–C(16)–C(19)	123.7(2)
C(17)–C(16)–C(19)	130.3(2)	C(16)–C(17)–C(18)	106.1(2)
C(16)–C(17)–C(20)	127.5(2)	C(18)–C(17)–C(20)	126.4(2)
N(2)–C(18)–C(17)	111.8(2)	N(2)–C(18)–C(21)	120.6(2)
C(17)–C(18)–C(21)	127.5(2)		

2 620, three reflections monitored periodically showed <3.0% intensity fluctuation, Lp but no absorption correction performed, $\Delta\rho_{max}/\Delta\rho_{min}$ = 0.21/−0.14 eÅ^{-3}.

Structure analysis and refinement. Direct methods,[18] full-matrix least squares refinement[18] with all non-H atoms anisotropic and hydrogens isotropic. Final R/R_w 0.041/0.048. Weighting scheme $w = [\sigma^2(F_o) + 0.0008\ F_o^2]$, with $\sigma(F_o)$ from counting statistics. Methyl groups refined as rigid groups with hydrogens riding on C-atoms at 1.00 Å, and thermal parameters tied to a free variable. All other H-atoms were located from Fourier maps and then were refined isotropically.

Compound (**10e**).—*Crystal data.* $C_{22}H_{21}ClN_2O_3$, M = 369.87, orthorhombic, a = 16.109(1), b = 11.407(1), c = 22.825(2) Å, V = 4 194.1(5) Å^3 (by least-squares on diffractometer angles for 15 automatically centred reflections, Cu-K_α, Ni-filtered radiation, λ = 1.541 78 Å, space group Pb_{cn}, Z = 8, D_m = 1.24 g cm^{-3}. Crystal dimensions 0.35 × 0.38 × 0.42 mm, μ = 17.09 cm^{-1}.

Data collection and processing. Nicolet P2$_1$ diffractometer, ω/2θ mode, scan width 1.8°(2θ) plus α_1–α_2 separation, scan speed 2–18° (2θ), $2\theta_{max}$ = 125°, reflections measured/unique/R_{merg} 3 625/3 266/0.019 observed with $I > 2.5\sigma(I)$ 2 839, three reflections monitored periodically showed <3% intensity fluctuation, Lp and analytical absorption performed,[18] I_{min}/T_{max} 0.58/0.62, $\Delta\rho_{max}/\Delta\rho_{min}$ = 0.23/−0.32 eÅ^{-3}.

Structure analysis and refinement. Direct methods,[18] full-matrix least squares refinement[18] with all non-H atoms anisotropic and hydrogens isotropic. Final R/R_w 0.034/0.041. Weighting scheme $w = [\sigma^2(F_o) + 0.001\ F_o^2]$ with $\sigma(F_o)$ from counting statistics. Methyl groups refined as rigid groups with hydrogens riding on C-atoms at 1.01 Å, and thermal parameters tied to a free variable. All other H-atoms were located from Fourier maps and then were refined.

The distortion observed in bond angles around atom (C-4) is analogous to that previous observed,[19] considering that the group of atoms C-7, 7-H, C-15, C-8 in (**10e**) is not unlike a methyl group.

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References

1 H. R. Seikaly and T. Tidwell, *Tetrahedron*, 1986, **42**, 2587.
2 A. Dondoni, A. Medici, and C. Venturoli, *J. Org. Chem.*, 1980, **45**, 621; A. Medici, P. Pedrini, C. Venturoli, and A. Dondoni, *ibid.*, 1981, **46**, 2790.
3 A. Dondoni, G. Fantin, M. Fogagnolo, A. Medici, and P. Pedrini, *Heterocycles*, 1984, **21**, 453; A. Medici, G. Fantin, M. Fogagnolo, P. Pedrini, A. Dondoni, and G. D. Adreetti, *J. Org. Chem.*, 1984, **49**, 590.
4 M. E. Hassan, *Bull. Soc. Chim. Belg.*, 1985, **94**, 149; C. Jenny, R. Prewo, J. H. Bieri, and H. Heimgartner, *Helv. Chim. Acta*, 1986, **69**, 1424.
5 A. Dondoni, G. Fantin, M. Fogagnolo, A Mastellari, A. Medici, and P. Pedrini, *J. Org. Chem.*, 1984, **49**, 3478.
6 K. T. Potts, P. M. Murphy, and W. R. Kuehnling, *J. Org. Chem.*, 1988, **53**, 2889.
7 C. Chiriac and I. Zugrăvescu, *Rev. Roumaine Chim.*, 1970, **15**, 1201; R. A. Olofson and R. V. Kendall, *J. Org. Chem.*, 1970, **35**, 2246.
8 T. Itahara, K. Kawasaki, and F. Ouseto, *Bull. Chem. Soc. Jpn.*, 1984, **57**, 3488.
9 J. Elguero, in 'Comprehensive Heterocyclic Chemistry,' eds. A. R. Katritzky and C. W. Rees, Pergamon Press, Oxford, 1984, vol. 5, p. 247.
10 R. S. Scharma, R. B. Pathak, and S. C. Bahel, *J. Indian Chem. Soc.*, 1985, **62**, 625; H. Carlsohn, U. C. Hipler, A. Breuer, A. Schuetz, H. Schuetz, and M. Hartmann, *Pharmazie*, 1983, **38**, 823.
11 L. Chosez, M. J. O'Donnel, in 'Pericyclic Reactions,' eds. A. P. Marchand and R. E. Lehr, Academic Press, New York, 1977, vol. 2, p. 79.
12 M. J. S. Dewar and W. Thiel, *J. Am. Chem. Soc.*, 1977, **99**, 4899.
13 S. Papadopoulous and J. Stephanidou-Stephanatou, *Liebigs Ann. Chem.*, 1985, 1697.
14 J. Elguero and R. Jacquier, *Bull. Soc. Chim. Fr.*, 1966, 2832; E. J. Völker and J. A. Moore, *J. Org. Chem.*, 1969, **34**, 3639.
15 C. Smith and W. Lewcock, *Chem. Ber.*, 1912, **45**, 2358; E. E. Blaise, *Bull. Soc. Chim. Fr.*, 1914, **15**, 729; E. C. Taylor, A. McKillop, and G. H. Hawks, *Org. Synth.*, 1972, **52**, 36.
16 R. N. McDonald and R. C. Cousins, *J. Org. Chem.*, 1980, **45**, 2976.
17 S. K. Gupta, *J. Org. Chem.*, 1973, **38**, 4081.
18 G. M. Sheldrick, 'SHELX76 Program for Crystal Structure Determination,' Univ. of Cambridge, England, 1976.
19 G. Salem, S. E. Filippakis, A. Hountas, and A. Terzis, *Acta Crystallogr., Sect. C*, 1986, **42**, 1581.

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