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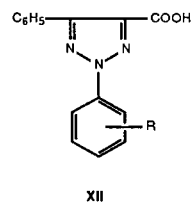
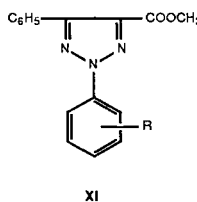
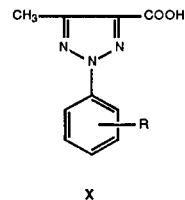
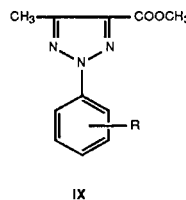
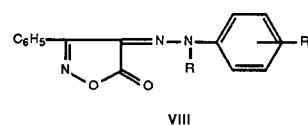
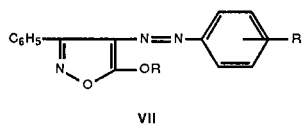
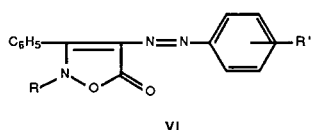
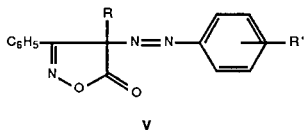
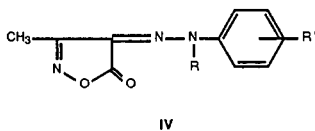
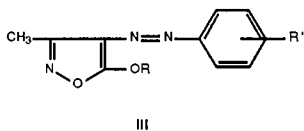
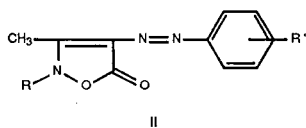
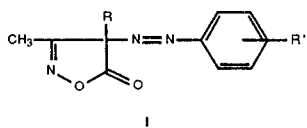
3-Methyl(or phenyl)-4-aryldiazonoisoxazol-5-ones on methylation with diazomethane afford 3-methyl(or phenyl)-4-(*N*-methylaryldiazono)isoxazol-5-ones and 3-methyl(or phenyl)-5-methoxy-4-aryldiazonoisoxazoles. The latter compounds readily rearrange to 4-methoxycarbonyl-5-methyl(or phenyl)-2-aryl-2*H*-1,2,3-triazoles.

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4-Aryldiazo-3-methylisoxazol-5-ones [1] are formally capable of existence in four tautomeric forms **I** ($R = H$), **II** ($R = H$), **III** ($R = H$) and **IV** ($R = H$). It has been established [2,3] and confirmed [4] that they exist as the phenylhydrazono tautomer **IV** ($R = H$) and this result is in accord with recent molecular orbital calculations [5]. 4-Aryldiazo-3-phenylisoxazol-5-ones likewise exist as the phenylhydrazono tautomer **VIII** ($R = H$) [5] of the four tautomeric forms **V** ($R = H$), **VI** ($R = H$), **VII** ($R = H$) and **VIII** ($R = H$). The products which are obtained by the methylation of 3-methyl- and 3-phenyl-4-aryldiazonoisoxazol-5-ones with diazomethane have been the subject of considerable uncertainty and confusion. About seventy years ago, Meyer [6] reacted 3-phenyl-4-phenylhydrazonoisoxazol-5-one **VIII** ($R = R' = H$) with diazomethane in ether and obtained two products. One product was shown to be 3-phenyl-4-(*N*-methylphenylhydrazono)isoxazol-5-one **VIII** ($R = CH_3$, $R' = H$) by unambiguous synthesis but the structure of the second product, which had mp 88° , was uncertain although it was suggested that it might be either 2-methyl-3-phenyl-4-phenylazoisoxazol-5-one **VI** ($R = CH_3$, $R' = H$) or 3-phenyl-5-methoxy-4-phenylazoisoxazole **VII** ($R = CH_3$, $R' = H$).

Since then three different groups have studied the reac-

tion and have come to different conclusions. A British group [2,3] used 3-methyl-4-(*o*-chlorophenylhydrazono)isoxazol-5-one **IV** ($R = H$, $R' = o\text{-Cl}$) and 3-methyl-4-(*m*-chlorophenylhydrazono)isoxazol-5-one **IV**, ($R = H$, $R' = m\text{-Cl}$) in their experiments and obtained three products from the reaction of each of these compounds with diazomethane. One product was considered to be the corresponding 3-methyl-4-(*N*-methyl-chlorophenylhydrazono)isoxazol-5-one **IV**, ($R = CH_3$, $R' = o\text{-Cl}$ or $m\text{-Cl}$) on spectroscopic evidence. The second product was established to have the structure of a 3-methyl-5-methoxy-4-(chlorophenylazo)isoxazole **III** ($R = CH_3$, $R' = o\text{-Cl}$ or $m\text{-Cl}$) by the absence of a carbonyl absorption in the infrared spectrum and by a methoxyl determination. The third product was assigned the structure of a 4-methoxycarbonyl-5-methyl-2-(chlorophenyl)-2*H*-1,2,3-triazole **IX** ($R = o\text{-Cl}$ or $m\text{-Cl}$) on the basis of spectroscopic evidence and a methoxyl determination and was considered to arise from the corresponding 3-methyl-5-methoxy-4-(chlorophenylazo)isoxazole **III**, ($R = CH_3$, $R' = o\text{-Cl}$ or $m\text{-Cl}$) by a transformation analogous to the thermal isomerization of certain substituted



isoxazoles to 1,2,3-triazoles [7] although no unambiguous synthesis of the 4-methoxycarbonyl-5-methyl-2-(chlorophenyl)-2*H*-1,2,3-triazoles **IX** ($R = o\text{-Cl}$ or $m\text{-Cl}$) was provided.

An Italian group used 3-methyl-4-phenylhydrazonoisoxazol-5-one **IV** ($R = R' = \text{H}$) and 3-phenyl-4-phenylhydrazonoisoxazol-5-one **VIII**, ($R = R' = \text{H}$) in their experiments with diazomethane [8]. From the former compound they obtained three products, 3-methyl-4-(*N*-methylphenylhydrazono)isoxazol-5-one **IV** ($R = \text{CH}_3$, $R' = \text{H}$), whose structure was established by unambiguous synthesis, a product of mp 54-56° considered to be 2,3-dimethyl-4-phenylazoisoxazol-5-one **II** ($R = \text{CH}_3$, $R' = \text{H}$) and a product of mp 80° considered to be 3-methyl-5-methoxy-4-phenylazoisoxazole **III** ($R = \text{CH}_3$, $R' = \text{H}$). From 3-phenyl-4-phenylhydrazonoisoxazol-5-one **VIII** ($R = R' = \text{H}$) they obtained two products as Meyer had earlier [6]. One product was identified as 3-phenyl-4-(*N*-methylphenylhydrazono)isoxazol-5-one **VIII** ($R = \text{CH}_3$, $R' = \text{H}$) by unambiguous synthesis and the second product which had mp 94-95° was considered to be 3-phenyl-5-methoxy-4-phenyl-

azoisoxazole **VII** ($R = \text{CH}_3$, $R' = \text{H}$) on spectroscopic evidence.

An Egyptian group used 3-methyl-4-(*p*-methylphenylhydrazono)isoxazol-5-one **IV** ($R = \text{H}$, $R' = p\text{-CH}_3$), 3-phenyl-4-phenylhydrazonoisoxazol-5-one **VIII** ($R = R' = \text{H}$), 3-phenyl-4-(*o*-methylphenylhydrazono)isoxazol-5-one **VIII** ($R = \text{H}$, $R' = o\text{-CH}_3$) and 3-phenyl-4-(*p*-methylphenylhydrazono)isoxazol-5-one **VIII** ($R = \text{H}$, $R' = p\text{-CH}_3$) in their experiments with diazomethane [9]. From each of the four compounds two products were obtained which were considered to be the corresponding 3-methyl (or phenyl)-4-(*N*-methylarylhydrazono)isoxazol-5-ones and 3-methyl (or phenyl)-5-methoxy-4-arylazoisoxazoles. Neither the Italian nor the Egyptian group reported evidence for the formation of triazoles of type **IX**. In view of the different results obtained by the various groups we have now undertaken a careful examination of the products obtained by reaction of seven 3-methyl-4-arylhydrazonoisoxazol-5-ones **IV** ($R = \text{H}$, $R' = \text{H}$), **IV** ($R = \text{H}$, $R' = p\text{-Cl}$), **IV** ($R = \text{H}$, $R' = m\text{-Cl}$), **IV** ($R = \text{H}$, $R' = o\text{-Cl}$), **IV** ($R = \text{H}$, $R' = p\text{-CH}_3$), **IV**, ($R = \text{H}$, $R' = m\text{-CH}_3$) and **IV** ($R = \text{H}$, $R' = o\text{-CH}_3$)

Table 1

3-Methyl-4-(*N*-methylarylhydrazono)isoxazol-5-ones and 3-Phenyl-4-(*N*-methylarylhydrazono)isoxazol-5-ones

Starting Material	Product	Yield [a]	Mp (°C)	Literature Mp (°C)	IR Carbonyl stretching (cm ⁻¹)	UV λ max (nm), log ε	NMR (δ values, ppm)
IV , $R = R' = \text{H}$	IV , $R = \text{CH}_3$, $R' = \text{H}$	48	101	102-106 [b]	1720	240, 390 (3.92, 4.19)	2.27 (s, C-CH ₃), 4.21 (s, N-CH ₃), 7.25-7.60 (m, aromatic)
IV , $R = \text{H}$, $R' = p\text{-Cl}$	IV , $R = \text{CH}_3$, $R' = p\text{-Cl}$	36	207	208 [b]	1720	242, 391 (4.01, 4.33)	2.22 (s, C-CH ₃), 4.21 (s, N-CH ₃), 7.45 (s, aromatic)
IV , $R = \text{H}$, $R' = m\text{-Cl}$	IV , $R = \text{CH}_3$, $R' = m\text{-Cl}$	31	180	180-181 [b]	1730	244, 389 (3.93, 4.28)	2.26 (s, C-CH ₃), 4.20 (s, N-CH ₃), 7.25-7.60 (m, aromatic)
IV , $R = \text{H}$, $R' = o\text{-Cl}$	IV , $R = \text{CH}_3$, $R' = o\text{-Cl}$	15	135	135-137 [b]	1725	238, 358 (3.73, 4.14)	2.18 (s, C-CH ₃), 4.18 (s, N-CH ₃), 7.25-7.65 (m, aromatic)
IV , $R = \text{H}$, $R' = p\text{-CH}_3$	IV , $R = \text{CH}_3$, $R' = p\text{-CH}_3$	41	157	157 [b]	1715	239, 396 (3.91, 4.29)	2.22 (s, C-CH ₃), 2.40 (s, aromatic CH ₃), 4.22 (s, N-CH ₃), 7.20-7.55 (m, aromatic)
IV , $R = \text{H}$, $R' = m\text{-CH}_3$	IV , $R = \text{CH}_3$, $R' = m\text{-CH}_3$	46	124	126 [b]	1720	240, 391 (3.82, 4.26)	2.22 (s, C-CH ₃), 2.42 (s, aromatic CH ₃), 4.22 (s, N-CH ₃), 7.20-7.50 (m, aromatic)
IV , $R = \text{H}$, $R' = o\text{-CH}_3$	IV , $R = \text{CH}_3$, $R' = o\text{-CH}_3$	20	163	162-164 [b]	1720	237, 363 (3.54, 4.13)	2.15 (s, C-CH ₃), 2.35 (s, aromatic CH ₃), 4.20 (s, N-CH ₃), 7.20-7.65 (m, aromatic)
VIII , $R = R' = \text{H}$	VIII , $R = \text{CH}_3$, $R' = \text{H}$	42	143	148 [b]	1720	228, 399 (4.25, 4.21)	4.24 (s, N-CH ₃), 7.25-7.96 (m, aromatic)
VIII , $R = \text{H}$, $R' = p\text{-Cl}$	VIII , $R = \text{CH}_3$, $R' = p\text{-Cl}$	34	140	140-142 [b]	1710	229, 405 (4.17, 4.20)	4.22 (s, N-CH ₃), 7.25-7.95 (m, aromatic)
VIII , $R = \text{H}$, $R' = p\text{-CH}_3$	VIII , $R = \text{CH}_3$, $R' = p\text{-CH}_3$	47	126	125-126 [b]	1720	229, 407 (4.25, 4.24)	2.35 (s, aromatic CH ₃), 4.20 (s, N-CH ₃), 7.10-7.95 (m, aromatic)

[a] Yield from reaction with diazomethane. [b] See ref [1].

and three 3-phenyl-4-arylhydrazonoisoxazol-5-ones **VIII** (R = H, R' = H), **VIII** (R = H, R' = *p*-Cl) and **VIII** (R = H, R' = *p*-CH₃) with ethereal diazomethane.

The ten compounds were each dissolved in a mixture of chloroform and ethanol and were then treated with a large excess of diazomethane in ether. The reaction mixture was allowed to stand for 2-3 days at ambient temperature by which time the starting materials had been completely methylated. The solvents were removed *in vacuo* at ambient temperature and the residue examined by nuclear magnetic resonance spectroscopy. It was apparent that in all ten cases three products had been formed. These were separated by fractional crystallisation at ambient temperature, care being taken not to use heat so as to minimize the possibility of isoxazole to triazole transformation as reported earlier by the British group [2,3].

The structures of the three products were determined in the following way. One product was shown to be the corresponding 3-methyl-4-(*N*-methylarylhydrazono)isoxazol-5-

one **IV** (R = CH₃) or 3-phenyl-4-(*N*-methylarylhydrazono)isoxazol-5-one **VIII** (R = CH₃) by comparison with authentic samples [1] (Table 1). These compounds all show a typical carbonyl stretching peak at about 1720 cm⁻¹ in their infrared spectra and have characteristic ultraviolet absorption spectra which contain two maxima at about λ 235 and 395 nm although those compounds which contain a substituent in the *ortho* position of the aryl ring, as expected, show a pronounced hypsochromic shift with reduced intensities. In the proton nuclear magnetic resonance spectra the methyl group on the hydrazono nitrogen gives a signal at δ ~ 4.20 ppm. These compounds were often the major products (~ 40% yield) from the reaction with diazomethane although where there was an *ortho* substituent on the aryl ring the yields were lower (15-20%). This result is presumably due to steric influences.

The second product was shown to be the corresponding 3-methyl-5-methoxy-4-arylazoisoxazole **III** (R = CH₃) or 3-phenyl-5-methoxy-4-arylazoisoxazole **VII** (R = CH₃) by

Table 2
3-Methyl-5-methoxy-4-arylazoisoxazoles and 3-Phenyl-5-methoxy-4-arylazoisoxazoles

Starting Material	Product	Yield [a]	Mp (°C)	Formula	Analysis Found/Calcd.			UV λ max (nm) log ε	NMR (δ values, ppm)
					C	H	N		
IV , R = R' = H	III , R = CH ₃ , R' = H	30	85 [b]	C ₁₁ H ₁₁ N ₃ O ₂	60.9 60.8	4.75 5.1	19.4 19.3	329 (4.16)	2.51 (s, C-CH ₃), 4.38 (s, O-CH ₃), 7.30-7.80 (m, aromatic)
IV , R = H, R' = <i>p</i> -Cl	III , R = CH ₃ , R' = <i>p</i> -Cl	43	94	C ₁₁ H ₁₀ ClN ₃ O ₂	52.4 52.5	3.7 4.0	17.0 16.7	335 (3.91)	2.49 (s, C-CH ₃), 4.38 (s, O-CH ₃), 7.30-7.80 (m, aromatic)
IV , R = H, R' = <i>m</i> -Cl	III , R = CH ₃ , R' = <i>m</i> -Cl	9	96 [c]	C ₁₁ H ₁₀ ClN ₃ O ₂			(d)	333 (4.25)	2.50 (s, C-CH ₃), 4.40 (s, O-CH ₃), 7.30-7.70 (m, aromatic)
IV , R = H, R' = <i>o</i> -Cl	III , R = CH ₃ , R' = <i>o</i> -Cl	46	106 [e]	C ₁₁ H ₁₀ ClN ₃ O ₂			(d)	338 (4.14)	2.51 (s, C-CH ₃), 4.39 (s, O-CH ₃), 7.15-7.65 (m, aromatic)
IV , R = H, R' = <i>p</i> -CH ₃	III , R = CH ₃ , R' = <i>p</i> -CH ₃	29	81 [f]	C ₁₂ H ₁₃ N ₃ O ₂	62.2 62.3	5.8 5.6	18.2 18.2	333 (4.30)	2.40 (s, aromatic CH ₃), 2.50 (s, C-CH ₃), 4.38 (s, O-CH ₃), 7.20-7.72 (m, aromatic)
IV , R = H, R' = <i>m</i> -CH ₃	III , R = CH ₃ , R' = <i>m</i> -CH ₃	27	66	C ₁₂ H ₁₃ N ₃ O ₂	62.5 62.3	5.3 5.6	18.2 18.2	331 (4.12)	2.40 (s, aromatic CH ₃), 2.49 (s, C-CH ₃), 4.38 (s, O-CH ₃), 7.22-7.60 (m, aromatic)
IV , R = H, R' = <i>o</i> -CH ₃	III , R = CH ₃ , R' = <i>o</i> -CH ₃	32	89 [g]	C ₁₂ H ₁₃ N ₃ O ₂	62.3 62.3	5.6 5.6	18.1 18.2	336 (4.25)	2.42 (s, aromatic CH ₃), 2.55 (s, C-CH ₃), 4.32 (s, O-CH ₃), 7.20-7.55 (m, aromatic)
VIII , R = R' = H	VII , R = CH ₃ , R' = H	29	85 [h]	C ₁₆ H ₁₃ N ₃ O ₂	68.6 68.8	5.0 4.7	15.3 15.05	337 (4.21)	4.30 (s, O-CH ₃), 7.25-8.15 (m, aromatic)
VIII , R = H, R' = <i>p</i> -Cl	VII , R = CH ₃ , R' = <i>p</i> -Cl	38	112	C ₁₆ H ₁₂ ClN ₃ O ₂	61.5 61.2	3.8 3.8	13.8 13.4	342 (4.26)	4.30 (s, O-CH ₃), 7.30-8.00 (m, aromatic)
VIII , R = H, R' = <i>p</i> -CH ₃	VII , R = CH ₃ , R' = <i>p</i> -CH ₃	35	118 [i]	C ₁₇ H ₁₅ N ₃ O ₂	69.5 69.6	5.3 5.1	14.3 14.3	340 (4.21)	2.39 (s, aromatic CH ₃), 4.30 (s, O-CH ₃), 7.20-8.20 (m, aromatic)

[a] Yield from reaction with diazomethane. [b] Ref [8] gives mp 80°. [c] Refs [3,13] give mp 96°. [d] Previously reported in literature. [e] Refs [2,3,13] give mp 104°. [f] Ref [9] gives mp 101° but structure there is probably **IX**, R = *p*-CH₃, see Table 3. [g] Ref [13] gives mp 89°. [h] Ref [8] gives mp 94-95°, ref [9] gives mp 88°. [i] Ref [9] gives mp 96°.

Table 3

4-Methoxycarbonyl-5-methyl-2-aryl-2*H*-1,2,3-triazoles and 4-Methoxycarbonyl-5-phenyl-2-aryl-2*H*-1,2,3-triazoles

Starting Material	Product	Yield [a]	Mp (°C)	Formula	Analysis Found/Calcd.			IR carbonyl stretching (cm ⁻¹)	UV λ max (nm) log ε	NMR (δ values, ppm)
					C	H	N			
IV, R = R' = H	IX, R = H	12	57 [b]	C ₁₁ H ₁₁ N ₃ O ₂	61.1 60.8	5.1 5.1	19.0 19.3	1725	280 (4.30)	2.60 (s, C-CH ₃), 4.00 (s, O-CH ₃), 7.35-8.20 (m, aromatic)
IV, R = H, R' = <i>p</i> -Cl	IX, R = <i>p</i> -Cl	15	122	C ₁₁ H ₁₀ ClN ₃ O ₂	52.7 52.5	4.3 4.0	17.1 16.7	1730	281 (4.29)	2.62 (s, C-CH ₃), 4.01 (s, O-CH ₃), 7.30-8.15 (m, aromatic)
IV, R = H, R' = <i>m</i> -Cl	IX, R = <i>m</i> -Cl	29	102 [c]	C ₁₁ H ₁₀ ClN ₃ O ₂	52.6 52.5	4.3 4.0	17.0 16.7	1725	280 (4.26)	2.60 (s, C-CH ₃), 4.01 (s, O-CH ₃), 7.35-8.15 (m, aromatic)
IV, R = H, R' = <i>o</i> -Cl	IX, R = <i>o</i> -Cl	11	90 [d]	C ₁₁ H ₁₀ ClN ₃ O ₂			[e]	1730	270 (3.92)	2.60 (s, C-CH ₃), 3.98 (s, O-CH ₃), 7.30-7.70 (m, aromatic)
IV, R = H, R' = <i>p</i> -CH ₃	IX, R = <i>p</i> -CH ₃	8	102	C ₁₂ H ₁₃ N ₃ O ₂	62.7 62.3	5.8 5.6	18.2 18.2	1725	285 (4.35)	2.43 (s, aromatic CH ₃), 2.63 (s, C-CH ₃), 4.00 (s, O-CH ₃), 7.17-8.00 (m, aromatic)
IV, R = H, R' = <i>m</i> -CH ₃	IX, R = <i>m</i> -CH ₃	6	60	C ₁₂ H ₁₃ N ₃ O ₂	62.6 62.3	5.7 5.6	18.3 18.2	1715	281 (4.26)	2.40 (s, aromatic CH ₃), 2.61 (s, C-CH ₃), 4.01 (s, O-CH ₃), 7.23-7.99 (m, aromatic)
IV, R = H, R' = <i>o</i> -CH ₃	IX, R = <i>o</i> -CH ₃	5	82	C ₁₂ H ₁₃ N ₃ O ₂	62.3 62.3	6.0 5.6	18.25 18.2	1715	270 (3.87)	2.36 (s, aromatic CH ₃), 2.60 (s, C-CH ₃), 3.98 (s, O-CH ₃), 7.15-7.75 (m, aromatic)
VIII, R = R' = H	XI, R = H	9	88	C ₁₆ H ₁₃ N ₃ O ₂	69.1 68.8	4.6 4.7	15.3 15.05	1740	284 (4.28)	3.94 (s, O-CH ₃), 7.30-8.20 (m, aromatic)
VIII, R = H, R' = <i>p</i> -Cl	XI, R = <i>p</i> -Cl	4	139	C ₁₆ H ₁₂ ClN ₃ O ₂	61.5 61.2	4.1 3.8	13.6 13.4	1725	292 (4.29)	3.99 (s, O-CH ₃), 7.40-8.20 (m, aromatic)
VIII, R = H, R' = <i>p</i> -CH ₃	XI, R = <i>p</i> -CH ₃	5	70	C ₁₇ H ₁₅ N ₃ O ₂	69.7 69.6	5.0 5.1	14.2 14.3	1730	290 (4.29)	2.40 (s, aromatic CH ₃), 3.97 (s, O-CH ₃), 7.20-8.15 (m, aromatic)

[a] Yield from reaction with diazomethane. [b] Ref [8] gives mp 54-56° but erroneously gives structure as II, R = CH₃, R' = H. [c] Ref [3] gives mp 104°. [d] Refs [2,3] give mp 90°. [e] Previously reported in literature.

elemental analysis and by the absence of a carbonyl peak in the infrared spectrum (Table 2). These compounds have a characteristic ultraviolet absorption spectra which consist of a maximum at about λ 335 nm. In the proton nuclear magnetic resonance spectra the methyl group of the 5-methoxy substituent gives a signal at δ ~ 4.35 ppm. These compounds were isolated from the reaction mixture in yields of 9-46%.

The third product was assigned the structure of the corresponding 4-methoxycarbonyl-5-methyl-2-aryl-2*H*-1,2,3-triazole (IX) or 4-methoxycarbonyl-5-phenyl-2-aryl-2*H*-1,2,3-triazole (XI) in agreement with the British group [2,3] on the basis of microanalyses and spectroscopic evidence (Table 3). These compounds all show a typical carbonyl stretching peak at about 1730 cm⁻¹ in their infrared spectra and have characteristic ultraviolet absorption spectra which consist of a maximum at about λ 285 nm although those compounds which contain a substituent in

the *ortho* position of the 2-aryl group, as expected, show a pronounced hypsochromic shift with reduced intensities. In the proton nuclear magnetic resonance spectra the methyl group of the methoxycarbonyl substituent gives a signal at δ ~ 4.00 ppm. These compounds were isolated in 4-29% yield from the reaction mixture. By way of further characterisation all ten esters listed in Table 3 were hydrolysed to the corresponding acids, namely 4-carboxy-5-methyl-2-aryl-2*H*-1,2,3-triazoles X or 4-carboxy-5-phenyl-2-aryl-2*H*-1,2,3-triazoles XII (Table 4). The acids show a typical carbonyl stretching peak at about 1690 cm⁻¹ in their infrared spectra and have a maximum at about λ 285 nm in their ultraviolet spectra although like the esters (Table 3) those compounds which contain a substituent in the *ortho* position of the 2-aryl group show a pronounced hypsochromic shift with reduced intensities.

To confirm the structures of the esters and acids listed in Tables 3 and 4, 4-carboxy-5-methyl-2-phenyl-2*H*-1,2,3-triazole X (R = H) was unambiguously synthesized essen-

Table 4

4-Carboxy-5-methyl-2-aryl-2*H*-1,2,3-triazoles and 4-Carboxy-5-phenyl-2-aryl-2*H*-1,2,3-triazoles

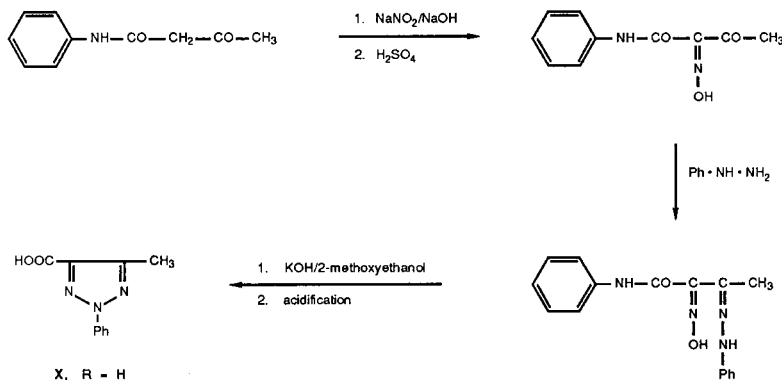
Starting Material	Product	Mp (°C)	Formula	Analysis Found/Calcd.			IR Carbonyl stretching (cm ⁻¹)	UV λ max (nm) log ε	NMR (δ values, ppm)
				C	H	N			
IX , R = H	X , R = H	204 [a]	C ₁₀ H ₉ N ₃ O ₂	59.4 59.1	4.7 4.4	20.6 20.7	1690	279 (4.27)	2.58 (s, C-CH ₃), 7.40-8.15 (m, aromatic)
IX , R = <i>p</i> -Cl	X , R = <i>p</i> -Cl	246 (b)	C ₁₀ H ₈ ClN ₃ O ₂	50.5 50.5	3.4 3.4	17.9 17.7	1690	283 (4.33)	2.55 (s, C-CH ₃), 7.40-8.10 (m, aromatic)
IX , R = <i>m</i> -Cl	X , R = <i>m</i> -Cl	204 [c]	C ₁₀ H ₈ ClN ₃ O ₂	50.9 50.5	3.4 3.4	18.0 17.7	1690	281 (4.29)	2.55 (s, C-CH ₃), 7.40-8.05 (m, aromatic)
IX , R = <i>o</i> -Cl	X , R = <i>o</i> -Cl	184	C ₁₀ H ₈ ClN ₃ O ₂	50.8 50.5	3.5 3.4	17.6 17.7	1700	270 (3.93)	2.55 (s, C-CH ₃), 7.45-7.75 (m, aromatic)
IX , R = <i>p</i> -CH ₃	X , R = <i>p</i> -CH ₃	234 [d]	C ₁₁ H ₁₁ N ₃ O ₂	60.8 60.8	5.2 5.1	19.5 19.3	1690	281 (4.31)	2.37 (s, aromatic CH ₃), 2.55 (s, C-CH ₃), 7.20-7.97 (m, aromatic)
IX , R = <i>m</i> -CH ₃	X , R = <i>m</i> -CH ₃	180	C ₁₁ H ₁₁ N ₃ O ₂	61.1 60.8	4.8 5.1	19.6 19.3	1690	280 (4.32)	2.42 (s, aromatic CH ₃), 2.58 (s, C-CH ₃), 7.18-7.90 (m, aromatic)
IX , R = <i>o</i> -CH ₃	X , R = <i>o</i> -CH ₃	159	C ₁₁ H ₁₁ N ₃ O ₂	60.55 60.8	4.8 5.1	19.5 19.3	1690	270 (3.91)	2.40 (s, aromatic CH ₃), 2.66 (s, C-CH ₃), 7.25-7.70 (m, aromatic)
XI , R = H	XII , R = H	215 [e]	C ₁₅ H ₁₁ N ₃ O ₂	67.6 67.9	4.2 4.2	15.7 15.8	1685	289 (4.31)	7.40-8.20 (m, aromatic)
XI , R = <i>p</i> -Cl	XII , R = <i>p</i> -Cl	197	C ₁₅ H ₁₀ ClN ₃ O ₂	60.3 60.1	3.1 3.3	13.9 14.0	1700	295 (4.34)	7.45-8.25 (m, aromatic)
XI , R = <i>p</i> -CH ₃	XII , R = <i>p</i> -CH ₃	210	C ₁₆ H ₁₃ N ₃ O ₂	68.8 68.8	4.8 4.7	15.2 15.05	1695	292 (4.32)	2.40 (s, aromatic CH ₃), 7.25-8.10 (m, aromatic)

[a] Literature mps range from 198-203°, for example Refs [10,11]. [b] Ref [12] gives mp 240-242°. [c] Ref [3] gives mp 207°. [d] Ref [11] gives mp 230-231°. [e] Ref [14] gives mp 208-209°.

tially as described by Klingsberg [11] starting from acetoacetanilide as outlined in Scheme 1. The acid **X** (R = H) was esterified to 4-methoxycarbonyl-5-methyl-2-phenyl-2*H*-1,2,3-triazole **IX** (R = H) with boiling methanol containing concentrated sulfuric acid. The sample of **IX** (R = H) obtained by this route was identical in all respects to

the sample obtained from the reaction of 3-methyl-4-phenylhydrazonoisoxazol-5-one **IV** (R = H, R' = H) with diazomethane. The acid **X** (R = H) obtained by hydrolysis of **IX** (R = H) was, as expected, identical to the sample obtained by the Klingsberg route.

Scheme 1



It was subsequently ascertained that the seven 3-methyl-5-methoxy-4-arylazoisoxazoles listed in Table 2 were completely converted to the corresponding 4-methoxycarbonyl-5-methyl-2-aryl-2*H*-1,2,3-triazoles (Table 3) merely by heating in boiling ethanol for one hour. Moreover solid samples of the 3-methyl-5-methoxy-4-arylazoisoxazoles which were stored at ambient temperature slowly changed to the 4-methoxycarbonyl-5-methyl-2-aryl-2*H*-1,2,3-triazoles and in some cases conversion was complete in two months. Likewise the three 3-phenyl-5-methoxy-4-arylazoisoxazoles listed in Table 2 were converted to the corresponding 4-methoxycarbonyl-5-phenyl-2-aryl-2*H*-1,2,3-triazoles (Table 3) although usually more slowly, heating in boiling ethanol for 3-8 hours being required for complete conversion. It is evident, therefore, that 3-methyl(or phenyl)-5-methoxy-4-arylazoisoxazoles are unstable compounds which are readily changed to the corresponding 4-methoxycarbonyl-5-methyl(or phenyl)-2-aryl-2*H*-1,2,3-triazoles. This very facile ring transformation serves as another example of the isomerisation of isoxazoles to 1,2,3-triazoles [15].

From these results it is clear that reaction of 3-methyl(or phenyl)-4-arylhydrazonoisoxazol-5-ones with diazomethane results in the formation of 3-methyl(or phenyl)-4-(*N*-methylarylhydrazono)isoxazol-5-ones and 3-methyl(or phenyl)-5-methoxy-4-arylazoisoxazoles but due to the instability of the latter compounds some of their rearrangement products, namely 4-methoxycarbonyl-5-methyl(or phenyl)-2-aryl-2*H*-1,2,3-triazoles are also formed during the diazomethane experiments.

It is now possible to make some important corrections to the literature. In the paper by Meyer [6] the product of mp 88° of uncertain structure from the reaction of 3-phenyl-4-phenylhydrazonoisoxazol-5-one **VIII** (R = R' = H) with diazomethane was almost certainly 4-methoxycarbonyl-2,5-diphenyl-2*H*-1,2,3-triazole **XI** (R = H), which has mp 88° (Table 3), since several fractionations and recrystallisations were required by Meyer to obtain it pure. In the paper by the Italian group [8] the compound of mp 54-56° which was isolated from the reaction of 3-methyl-4-phenylhydrazonoisoxazol-5-one **IV** (R = R' = H) with diazomethane is clearly 4-methoxycarbonyl-5-methyl-2-phenyl-2*H*-1,2,3-triazole **IX** (R = H), which has mp 57° (Table 3) and is not, as they report, 2,3-dimethyl-4-phenylazoisoxazol-5-one **II** (R = CH₃, R' = H) [*cf.* 16]. 2,3-Dimethyl-4-phenylazoisoxazol-5-one **II** (R = CH₃, R' = H), which has been unambiguously synthesised, has mp 200° [1]. The product of mp 80°, however, was correctly assigned by the Italian group as 3-methyl-5-methoxy-4-phenylazoisoxazole **III** (R = CH₃, R' = H). We obtained mp 85° (Table 2) for this compound. From the reaction of 3-phenyl-4-phenylhydrazonoisoxazol-5-one **VIII** (R = R' = H) with diazomethane the Italian group [8] obtained a product of mp 94-95° which they considered to be 3-phenyl-5-methoxy-4-phenylazoisoxazole **VII** (R = CH₃, R' = H). This compound may instead be 4-methoxycarbonyl-2,5-diphenyl-2*H*-1,2,3-triazole **XI** (R = H) which has mp 88° (Table 3) since it was obtained pure only after repeated crystallisations from boiling ethanol. In the paper by the Egyptian group [9] the compound of mp 101° which was obtained

Table 5
Fractional Crystallization of Products from Reaction with Diazomethane

Starting Material	First Solvent	Compound Least Soluble in First Solvent	Second Solvent	Compound Least Soluble in Second Solvent	Compound in Filtrate of Second Solvent
IV , R = R' = H	petrol [a]	IV , R = CH ₃ , R' = H [b]	ethanol	III , R = CH ₃ , R' = H [c]	IX , R = H [d]
IV , R = H, R' = <i>p</i> -Cl	petrol [a]	IV , R = CH ₃ , R' = <i>p</i> -Cl [b]	ethanol	III , R = CH ₃ , R' = <i>p</i> -Cl [c]	IX , R = <i>p</i> -Cl [e]
IV , R = H, R' = <i>m</i> -Cl	ethanol	IV , R = CH ₃ , R' = <i>m</i> -Cl [b]	methanol	III , R = CH ₃ , R' = <i>m</i> -Cl [f]	IX , R = <i>m</i> -Cl [g]
IV , R = H, R' = <i>o</i> -Cl	ethanol	III , R = CH ₃ , R' = <i>o</i> -Cl [h]	petrol [j]	IV , R = CH ₃ , R' = <i>o</i> -Cl [b]	IX , R = <i>o</i> -Cl [d]
IV , R = H, R' = <i>p</i> -CH ₃	petrol [a]	IV , R = CH ₃ , R' = <i>p</i> -CH ₃ [j]	petrol [a]	III , R = CH ₃ , R' = <i>p</i> -CH ₃ [k]	IX , R = <i>p</i> -CH ₃ [l]
IV , R = H, R' = <i>m</i> -CH ₃	petrol [m]	IV , R = CH ₃ , R' = <i>m</i> -CH ₃ [b]	ethanol	III , R = CH ₃ , R' = <i>m</i> -CH ₃ [c]	IX , R = <i>m</i> -CH ₃ [g]
IV , R = H, R' = <i>o</i> -CH ₃	petrol [a]	IV , R = CH ₃ , R' = <i>o</i> -CH ₃ [b]	petrol [a]	III , R = CH ₃ , R' = <i>o</i> -CH ₃ [k]	IX , R = <i>o</i> -CH ₃ [l]
VIII , R = R' = H	petrol [a]	VIII , R = CH ₃ , R' = H [b]	ethanol	VII , R = CH ₃ , R' = H [c]	XI , R = H [j]
VIII , R = H, R' = <i>p</i> -Cl	acetone	VII , R = CH ₃ , R' = <i>p</i> -Cl [n]	petrol [j]	VIII , R = CH ₃ , R' = <i>p</i> -Cl [o]	XI , R = <i>p</i> -Cl [j]
VIII , R = H, R' = <i>p</i> -CH ₃	acetone	VII , R = CH ₃ , R' = <i>p</i> -CH ₃ [b]	petrol [j]	XI , R = <i>p</i> -CH ₃ [l]	VIII , R = CH ₃ , R' = <i>p</i> -CH ₃ [b]

[a] Bp 60-100°. [b] Recrystallised from chloroform/ethanol. [c] Recrystallised from cold ethanol. [d] Recrystallised from petrol, bp 60-80°. [e] Recrystallised from petrol, bp 80-100°. [f] Recrystallised from cold methanol. [g] Recrystallised from petrol, bp 40-60°/chloroform. [h] Recrystallised from cold ethanol/chloroform. [i] Bp 60-80°. [j] Recrystallised from ethanol. [k] Recrystallised from cold petrol, bp 60-100°. [l] Recrystallised from petrol, bp 60-100°/chloroform. [m] Bp 40-80°. [n] Recrystallised from cold acetone. [o] Recrystallised from acetone.

from the reaction of 3-methyl-4-(*p*-methylphenylhydrazono)isoxazol-5-one **IV** ($R = H$, $R' = p\text{-CH}_3$) with diazomethane and which was assigned the structure 3-methyl-5-methoxy-4-*p*-methylphenylazoisoxazole **III** ($R = \text{CH}_3$, $R' = p\text{-CH}_3$) (mp 81° , Table 2) is almost certainly instead 4-methoxycarbonyl-5-methyl-2-*p*-methylphenyl-2*H*-1,2,3-triazole **IX** ($R = p\text{-CH}_3$) which we found to have mp 102° (Table 3). Likewise the compound of mp 96° which was obtained by the Egyptian group [9] from the reaction of 3-phenyl-4-(*p*-methylphenylhydrazono)-isoxazol-5-one **VIII** ($R = H$, $R' = p\text{-CH}_3$) with diazomethane and which was assigned the structure of 3-phenyl-5-methoxy-4-*p*-methylphenylazoisoxazole **VII** ($R = \text{CH}_3$, $R' = p\text{-CH}_3$) is almost certainly impure since we obtained mp 118° (Table 2) for this compound. The rearrangement product 4-methoxycarbonyl-5-phenyl-2-*p*-methylphenyl-2*H*-1,2,3-triazole **XI** ($R = p\text{-CH}_3$) has mp 70° .

EXPERIMENTAL

The nmr spectra refer to proton nmr spectra (60 MHz) with tetramethylsilane as internal standard. The spectra of compounds listed in Tables 1, 2 and 3 were run in deuteriochloroform and those in Table 4 in deuteriodimethylsulfoxide. Ultraviolet absorption spectra were taken in ethanol solution. Infrared spectra were run in potassium bromide discs. Microanalyses were performed by the Australian Microanalytical Service.

Reactions with Diazomethane.

The 3-methyl(or phenyl)-4-arylhydrazonoisoxazol-5-ones (10 g) were dissolved in a mixture of chloroform and ethanol (~ 750 ml) at ambient temperature and were then treated with a large excess of diazomethane in ether. The solution was allowed to stand for 2-3 days. The solvents were then removed *in vacuo* at ambient temperature. The solid residues were then fractionally crystallized at ambient temperature in the ways summarized in Table 5. Briefly, the solid residue was treated with the first solvent and the solid which did not dissolve was filtered off. In the cases where the second solvent is recorded as being the same as the first solvent in Table 5 the filtrate was partly evaporated at ambient temperature and chilled and the resultant crystals collected. The third compound was recovered from the filtrate. In the cases where the second solvent was different from the first solvent, the filtrate of the first solvent was evaporated off completely at ambient temperature and the solid residue was then treated with the second solvent. The solid which did not dissolve was filtered off. The third compound was recovered from the filtrate of the second solvent. In all cases the three compounds, which were obtained, were recrystallised further as indicated in the footnotes in Table 5.

4-Carboxy-5-methyl-2-aryl-2*H*-1,2,3-triazoles and 4-Carboxy-5-phenyl-2-aryl-2*H*-1,2,3-triazoles (Table 4).

(a) The following method is typical. The appropriate 4-methoxy-carbo-

nyl-5-methyl(or phenyl)-2-aryl-2*H*-1,2,3-triazole (1.5 g) (see Table 3) was refluxed for 5-6 hours in concentrated hydrochloric acid (30 ml) and glacial acetic acid (40 ml). The solvent was partly evaporated and the solution cooled whereupon the 4-carboxy-5-methyl(or phenyl)-2-aryl-2*H*-1,2,3-triazole precipitated. Yields were about 90%. Compounds **X** ($R = H$), **X** ($R = p\text{-Cl}$), **X** ($R = m\text{-Cl}$), **X** ($R = p\text{-CH}_3$) and **X** ($R = o\text{-CH}_3$) were recrystallized from petrol, bp $60\text{-}80^\circ/\text{chloroform}$, **X** ($R = o\text{-Cl}$) from water, **X** ($R = m\text{-CH}_3$) from petrol $40\text{-}60^\circ/\text{methanol}$, **XII** ($R = H$) from methanol/chloroform and **XII** ($R = p\text{-Cl}$) and **XII** ($R = p\text{-CH}_3$) from aqueous acetic acid.

(b) 4-Carboxy-5-methyl-2-phenyl-2*H*-1,2,3-triazole **X** ($R = H$) was also prepared by the method of Klingsberg [11] (see Scheme 1) starting from acetoacetanilide. The product obtained by this route was identical in all respects to the sample prepared by method (a) above.

4-Methoxycarbonyl-5-methyl-2-phenyl-2*H*-1,2,3-triazole **IX** ($R = H$).

4-Carboxy-5-methyl-2-phenyl-2*H*-1,2,3-triazole **X** ($R = H$) (1 g) was refluxed in methanol (20 ml) containing concentrated sulfuric acid (2 ml) for 4 hours. The mixture was cooled and the solvent partly evaporated. The solution was then diluted with excess aqueous sodium hydrogen carbonate. The resultant oil solidified on standing and the product was crystallised from petrol, bp $60\text{-}80^\circ$. The yield was 80%. The product was identical in all respects to the sample of 4-methoxy-carbonyl-5-methyl-2-phenyl-2*H*-1,2,3-triazole which was obtained from the reaction of 3-methyl-4-phenylhydrazonoisoxazol-5-one with diazomethane (see Table 3).

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