

Further Studies on Acetylenic β -Diketones, and their Conversion into 3-Chloro-4-pyrones.

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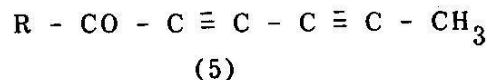
Summary: The mass spectra of 1,5-diarylpent-1-yne-3,5-diones (1a-e) is studied for the first time. The 3-chloro-4H-pyran-4-ones were obtained from the corresponding acetylenic β -diketones by the action of N-chlorosuccinimide (NCS). The intermediate 4-chloro acetylenic β -diketones (7a,d) could be cyclized to the pyrones (9a,d), which gave 3-chloro-1-hydroxy-4-pyridones (13a,d) or isoxazole derivatives (14a,d) with hydroxylamine.

Although acetylenic β -diketones are versatile intermediates in the synthesis of several heterocyclic systems [1]; yet much of their chemistry is still to be explored. Conjugated acetylenic carbonyl compounds have been very little studied by mass spectrometry [2-4]. The behaviour of the aryl substituted acetylenic β -diketones (1a-e) under electron impact was examined. The structure of the prominent peaks besides the possible fragmentation routes for these compounds are shown in Scheme-1.

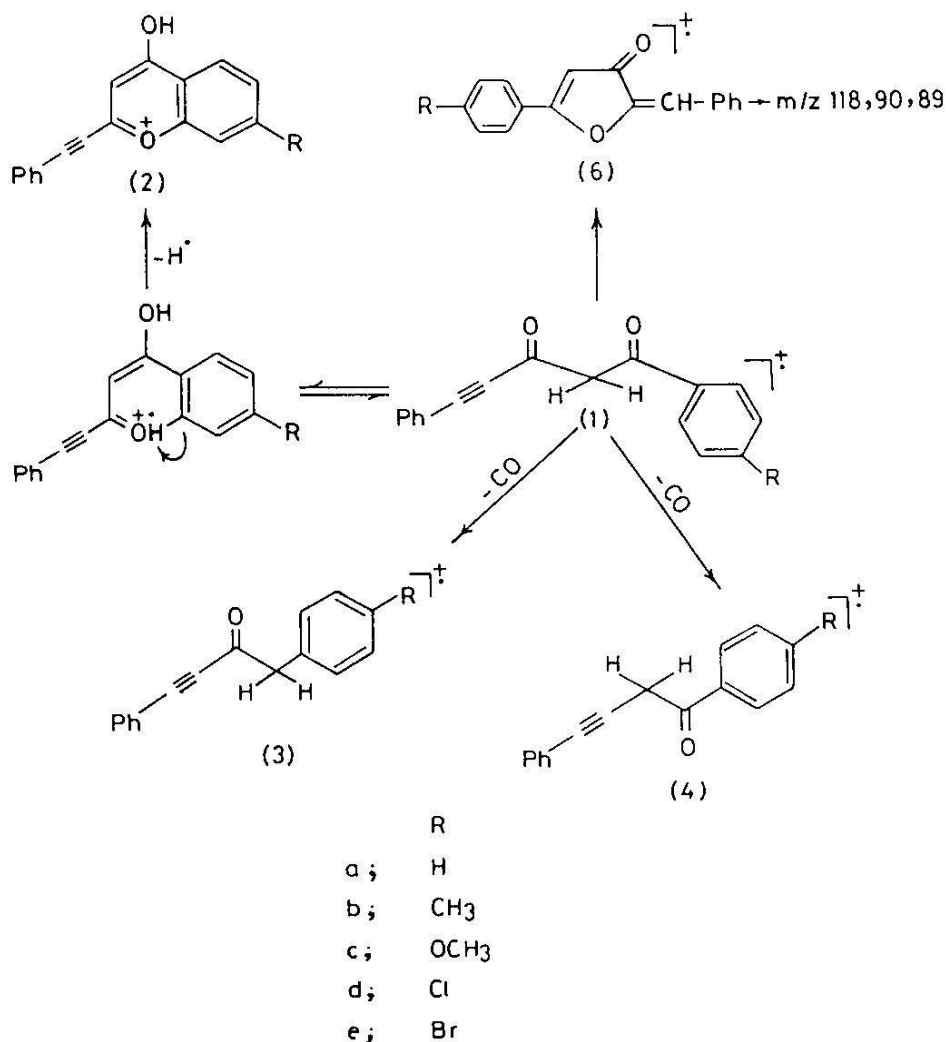
They all gave a strong molecular ion peaks which in the case of (1b,c) were the base peaks. A significant (M-1) ions were observed, except for (1d), which may be formulated as the stable oxonium ion (2) arising by loss of a hydrogen atom from the aryl phenyl ring. Similar oxonium ion structures were suggested to the (M-1) fragments in the mass spectra of benzoylacetone, and dibenzoylmethane [5].

Behaving like both β -diketones [5,6], and conjugated acetylenic ketones [2,4], loss of CO from the molecular ion is expected to be a major

fragmentation pathway for the acetylenic β -diketones (1). The (M-CO) species may be formulated either as (3) or (4). Although the possibility of the existence of the two species can not be ruled out, structure (3) having the carbonyl group conjugated with the acetylenic linkage seems to be more favourable. This conclusion is supported by the observation that the stabilizing effect of the alkynyl group considerably exceeds the effect of a phenyl group in the fragmentation of the molecular ions of α,β -acetylenic ketones [3]. Moreover, in the mass spectra of aryldiacetylenic ketones (5; R = aryl), M-CO, species are more dominating than for the alkyl analogs (5; R = alkyl), which suggests a lower energy pathway for the ejection of CO from the aryl ketones [2].



Furthermore the spectra showed strong peaks at m/z 118, 90, and 89 which characterize the spectra of 2-benzylidene-3(2H) furanones (6)[7]. Partial thermal cyclization of the acetylenic β -diketones to the furanones in the inlet system of the mass spectrometer may be assumed.



Scheme 1

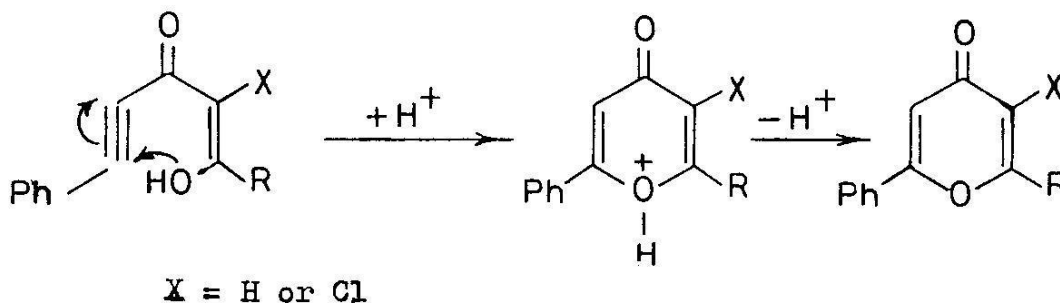
In the synthesis of chloro 4H-pyran-4-ones, direct chlorination of the pyrone ring is very limited [8]. Instead, most of the reported methods involve cyclization of chlorinated open-chain substrates [9-12]. In the present study, 3-chloro-4H-pyran-4-ones (9) were prepared from the reaction of the corresponding acetylenic β -diketones (1) with NCS. Intermediate open-chain 1,5-diarylpent-1-yne-4-chloro-3,5-diones (7a,d) initially formed were subse-

quently cyclized to the respective pyrones (9a,d). It was only in the case of (1e), that 3-chloro pyrone (9e) was directly formed.

The i.r. spectra of (7a,d) showed the dicarbonyl absorption at 1588-1595 cm^{-1} at relatively low frequency that the non chlorinated compounds (1) [13], besides the acetylenic stretching band in the range 2208-2210 cm^{-1} . No separate signal could be detected

for the H-4 proton in their ^1H -n.m.r. spectra, probably due to their existence in the chelated enol form (8).

Acid-catalysed transformation of the acetylenic β -diketones into 4H-pyran-4-ones probably involves an initial protonation of the triple bond, and subsequent cyclization. Similar mechanisms were suggested for acid-catalysed cyclization of symmetrical, and asymmetrical diacetylenic ketones into the corresponding pyrones [14].



2,6-Diaryl-3-chloro-4H-pyran-4-ones (9a,d) afforded the corresponding thiones (10a,d), thione (10d) was converted to the respective oxime (11d) (see Experimental). 1,5-Diphenyl-pent-1-yne-4-chloro-3,5-dione (7a) reacted with iodine mono-chloride with the formation of 2,6-diphenyl-3-iodo-4H-pyran-4-one (12a)[15]. Obviously displacement of chlorine by iodine atom and subsequent cyclization took place (Scheme 2).

Previously it was stated that the reaction of acetylenic β -diketones with hydroxylamine gives either 1-hydroxy-4-pyridones [1] or isoxazoles [16]. However, the reaction of 1,5-diaryl-pent-1-yne-4-chloro-3,5-diones (7a,d) with hydroxylamine in ethanol yielded a mixture of 2,6-diaryl-3-chloro-1-hydroxy-4-pyridones (13a,d), and isoxazole oximes (14a,d). Yet, isoxazole oximes were mainly formed when the above reaction was carried out in pyridine (Scheme 2).

The ^1H -n.m.r. spectra of the isoxazole oximes (14) exhibited two singlets in the ranges δ 6.32-6.87 (1 H), and δ 4.22-4.27 (1 H) assigned to H-4 isoxazole ring, and side-chain CHCl protons [17-19], respectively. Their electronic spectra showed a maximum absorption at 255-256 nm supporting the presence of 5-aryl isomer chromophore [16,20,21].

Experimental

Microanalyses were performed by the Microanalysis Unit, Cairo Univer-

sity, Cairo. I.R. spectra were measured with a Unicam SP 1025 spectrophotometer for potassium bromide pellets, and U.V. spectra were measured with a Unicam SP 800 spectrophotometer in methanol. All ^1H -n.m.r. spectra were recorded on a Varian EM-390 n.m.r. spectrometer at 90 MHz with tetramethylsilane as internal standard. Mass spectra were recorded at 70 eV with an AEI MS-9 spectrometer coupled to a DS-50 data system using a direct insertion probe for introduction of samples (source temperature 110-130°C above ambient).

1,5-Diarylpent-1-yne-3,5-diones (1a-e):

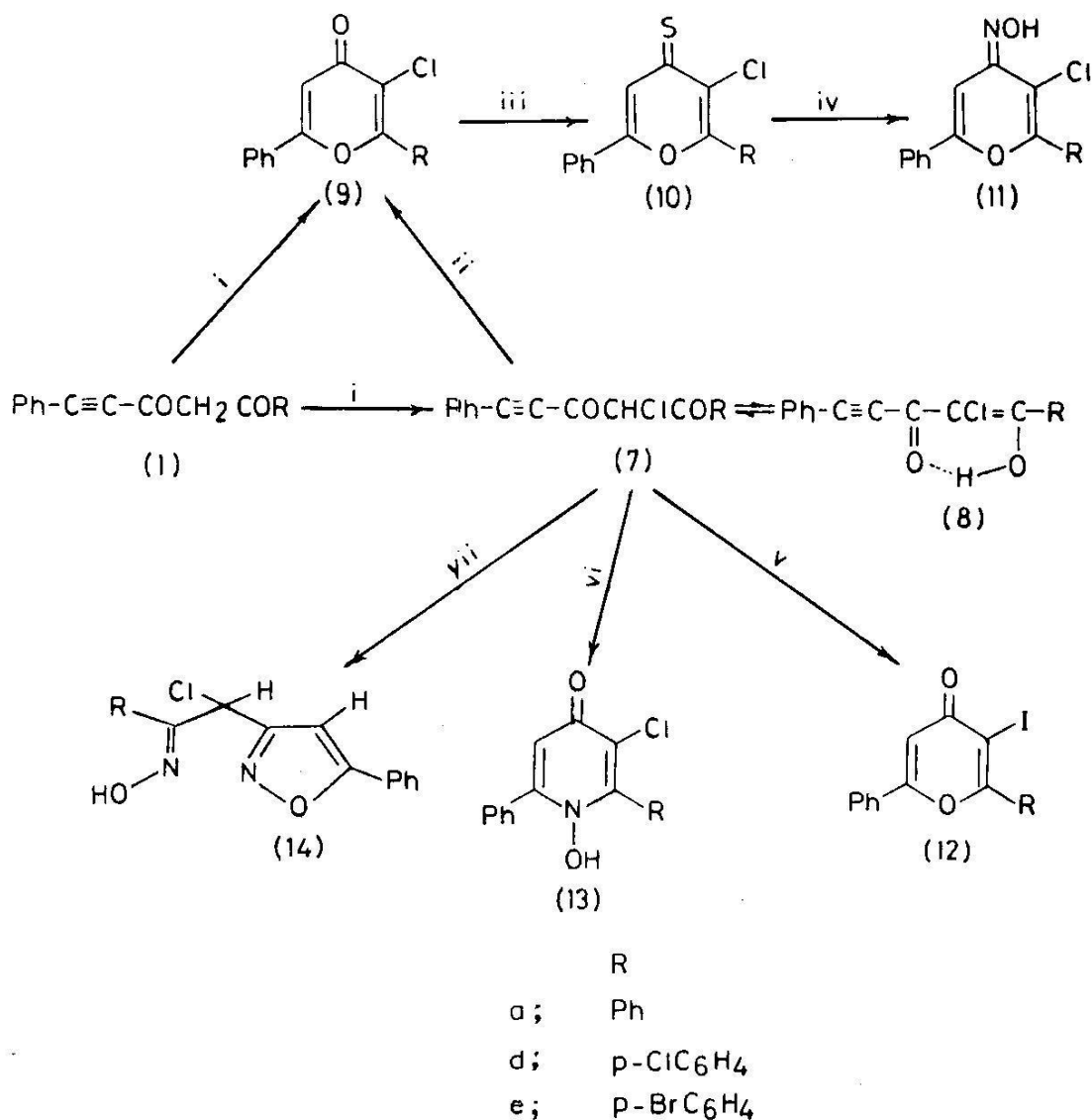
They were prepared from sodium ethoxide catalysed condensation of ethyl phenylpropionate with suitable ketones as described earlier [1,7]; ms: m/z (relative abundance) (1a): 248 (M^+ , 97%), 247 (45), 221 (20), 220

(100), 219 (3), 192 (6), 191 (11), 189 (3), 179 (5), 178 (9), 171 (4), 165 (4), 131 (4), 129 (13), 119 (3), 118 (29), 116 (3), 115 (22), 114 (3), 110 (14), 106 (4), 105 (40), 103 (9), 102 (78), 101 (3), 91 (3), 90 (29), 89 (18), 78 (6), 77 (56); **(1b)**: 262 (M^+ , 100%), 261 (56), 247 (5), 235 (9), 234 (46), 233 (5), 219 (4), 206 (6), 205 (8), 194 (2), 193 (16), 192 (39), 191 (11), 189 (3), 179 (2), 178 (6), 171 (5), 165 (2), 145 (10), 132 (3), 131 (20), 130 (5), 129 (39), 128 (3), 120 (6), 119 (63), 118 (20), 117 (6), 116 (10), 115 (17), 114 (3), 105 (4), 103 (5), 102 (22), 101 (4), 92 (4), 91 (35), 90 (8), 89 (8), 77 (8); **(1c)**: 278 (M^+ , 100%), 277 (22), 251 (6), 250 (31), 236 (5), 235 (15), 222 (5), 221 (5), 210 (4), 209 (24), 208 (45), 207 (9), 194 (4), 193 (3), 191 (2), 179 (4), 178 (7), 177 (3), 171 (3), 165 (4), 161 (20), 148 (40), 136 (8), 135 (77), 133 (6), 132 (34), 131 (30), 130 (4), 129 (32), 127 (3), 126 (3), 125 (10), 121 (2), 118 (16), 117 (9), 115 (16), 108 (8), 107 (8), 105 (6), 103 (5), 102 (12), 101 (6), 92 (15), 90 (10), 89 (15), 77 (31); **(1d)**: 284, 282 (M^+ , 7, 22%), 257 (6), 256 (32), 255 (19), 254 (100), 225 (2), 219 (2), 192 (3), 191 (16), 190 (3), 189 (5), 165 (4), 152 (2), 151 (5), 150 (2), 149 (13), 148 (2), 145 (2), 142 (3), 141 (8), 139 (26), 138 (14), 137 (5), 136 (48), 128 (11), 127 (19), 123 (3), 117 (4), 116 (3), 115 (22), 114 (5), 113 (12), 112 (3), 111 (26), 110 (2), 106 (3), 105 (38), 103 (7), 102 (75), 101 (18), 100 (5), 99 (4), 95 (68), 89 (8), 87 (5), 77 (57); **(1e)** : 328, 326 (M^+ , 90, 90%), 327

Table-1: I.R. (KBr), and 1H n.m.r. ($CDCl_3$) spectroscopic data for the 4-chloro acetylenic β -diketones, and their derivatives.

Compound	ν_{max} / cm^{-1}				1H N.m.r./ δ			
	C = S	C = N	C = O	C = C	OH	H - 5 (s)	Ar-H (m)	OH (s)
(7a)			1595	2210			7.57	
(7d)			1588	2208			7.65	
(9a) ^a			1644			6.90	7.65	
(9d)			1641			7.00	7.97	
(9e)			1660			6.90	7.57	
(10a)	2263						7.67	
(10d)	1175						7.67	
(11d) ^b		1650			3260	7.11	7.63	11.01
(13a)			1647		3480	6.95	7.70	11.47
(13d)			1646		3420	7.20	7.65	11.42

a = When the spectrum carried out in deuterated trifluoroacetic acid H-5 overlapped with aromatic protons (7.82). b = In $DMSO-d_6$.



Scheme 2. Reagents: i, NCS; ii, HCl; iii, P₂S₅; iv, NH₂OH, EtOH; v, ICl; vi, NH₂OH, EtOH; vii, NH₂OH, Pyridine

(15), 325 (15), 301 (17), 300 (100),
 299 (17), 298 (100), 195 (4), 191 (5),
 189 (3), 185 (11), 183 (13), 182 (22),
 180 (22), 157 (8), 150 (22), 149 (23),
 145 (2), 118 (13), 115 (9), 114 (2),
 109 (2), 106 (2), 105 (20), 103 (5),
 102 (57), 101 (23), 95 (5), 90 (10),
 89 (8), 77 (27).

1,5-Diarylpent-1-yne-4-chloro-3,5-diones (7) (Tables 1,2):

A mixture of 1,5-diarylpent-1-yne-3,5-diones (1a,d) (0.8 g; 0.0028 mole), NCS (0.5 g.; 0.038 mole), benzoylperoxide (0.0200 g.), and carbon tetrachloride (100 ml) was

Table-2: Analytical data for the 4-chloro acetylenic β -diketones, and their derivatives.

Compound (Formula)	M.p.(°C)	Found (%) (Required)					
		C	H	N	S	Cl	Br
(7a) (C ₁₇ H ₁₀ Cl ₂ O ₂)	75	72.1 (72.2)	3.8 3.9			12.9 12.6)	
(7d) (C ₁₇ H ₁₀ Cl ₂ O ₂)	90	64.4 (64.6)	3.1 3.2			22.0 22.2)	
(9a) (C ₁₇ H ₁₁ ClO ₂)	126	72.2 (72.2)	3.7 3.9			12.4 12.6)	
(9d) (C ₁₇ H ₁₀ Cl ₂ O ₂)	170	64.4 (64.6)	3.2 3.2			22.4 22.2)	
(9e) (C ₁₇ H ₁₀ BrClO ₂)	185	56.2 (56.4)	2.8 2.8			9.6 9.8	22.4 22.1)
(10a) (C ₁₇ H ₁₁ ClOS)	160	68.1 (68.3)	3.8 3.7		10.6 10.8	12.1 11.9)	
(10d) (C ₁₇ H ₁₀ Cl ₂ OS)	210	61.3 (61.5)	2.9 3.0		9.4 9.6	21.4 21.1)	
(11d) (C ₁₇ H ₁₁ Cl ₂ NO ₂)	255	61.4 (61.6)	3.1 3.4	4.0 4.2		21.5 21.2)	
(13a) (C ₁₇ H ₁₂ ClNO ₂)	190	68.4 (68.6)	4.2 4.0	4.6 4.7		11.7 11.9)	
(13d) (C ₁₇ H ₁₁ Cl ₂ NO ₂)	192	61.5 (61.6)	3.1 3.3	4.0 4.2		21.4 21.2)	

stirred at room temperature for twenty minutes under ultraviolet radiation. After further stirring for one hour the precipitated succinimide was filtered off, and the solvent evaporated under reduced pressure. The residual oil afforded the chloro acetylenic β -diketones (7a,d) (85-88% yield) after treatment with ethanol. They crystallised from ether in yellow needles.

2,6-Diaryl-3-chloro-4H-pyran-4-ones
(9) (Tables 1,2):

A solution of (7a,d) (25 g.; 0.0009 mole) in methanol (10 ml) containing concentrated hydrochloric acid (1 ml) was refluxed for two hours. After concentration, and cooling, the separated 3-chloro pyrones (9a,d) (70-80% yield) were crystallised from methanol in needles. Completion of the reaction was tested by T.L.C.

2-p-Bromophenyl-3-chloro-6-phenyl-4H-pyran-4-one (9e) was directly obtained (60% yield) from the reaction of (1e) with NCS as described before and crystallised from benzene-ethyl acetate (2:3) in pale yellow needles.

2,6-Diaryl-3-chloro-4H-pyran-4-thiones (10) (Tables 1,2):

They were prepared from the respective 3-chloro pyrones (9), and phosphorus pentasulphide as described earlier [22].

2-p-Chlorophenyl-3-chloro-6-phenyl-4H-pyran-4-one oxime (11d) (Tables 1,2):

This oxime was prepared from the corresponding 3-chloro thione (10d), hydroxylamine hydrochloride, and sodium acetate in ethanol as described earlier [22].

2,6-Diphenyl-3-iodo-4H-pyran-4-one (12a):

This pyrone was prepared from the respective (7a), and iodine monochloride in chloroform as described earlier [15].

(12a), needles 'm.p. 170°C (from chloroform-methanol)'; ν_{\max} (KBr) 1615; δ (CDCl₃), 6.83 (1H, s, H-5); ms : m/z (relative abundance): 374 (M⁺, 100%), 346 (36), 254 (4), 248 (11), 247 (52), 228 (28), 219 (8), 191 (20), 189 (5), 173 (10), 129 (7), 111 (5), 105 (90), 102 (20), 101 (14), 97 (8), 95 (8), 89 (10), 77 (65) (Found: C, 54.4; H, 3.0; I, 33.4. C₁₇H₁₁IO₂ requires C, 54.5; H, 3.2; I, 33.9).

2,6-Diaryl-3-chloro-1-hydroxy-4-pyridones (13) (Tables 1,2):

They were prepared from the respective 4-chloro acetylenic β -diketones (7a,d), hydroxylamine hydrochloride, and sodium acetate in ethanol as described earlier [1]. The crude products were subjected to fractional crystallisation from benzene-ethyl acetate (2:3). The pyridones (13a,d) (45-60% yield) separated first, and the isoxazole oximes (14a,d) (25-30% yield) were isolated from mother liquors.

3-(β -Aryl- β -hydroxyimino- α -chloro-ethyl)-5-phenyl-isoxazoles (14) (Tables 1,2):

They were prepared from the corresponding (7a,d), and hydroxylamine hydrochloride in pyridine as described earlier [16]. The following new compounds were thus prepared.

(14a), needles 'm.p. 155°C (from benzene-ethyl acetate)'; ν_{\max} (KBr) 3265, 1622, and 1599 cm⁻¹; λ_{\max} 255 nm (ϵ 42968); δ (CDCl₃), 9.40 (1H, s, OH), 7.57 (10H, m, Ar-H), 6.32 (1H, s, H-4), and 4.22 (1H, s, -CHCl-) (Found: C, 65.2; H, 4.3; N, 9.2; Cl, 11.2. C₁₇H₁₃ClN₂O₂ requires C, 65.3; H, 4.2; N, 9.0; Cl, 11.4).

(14d), needles ,m.p. 190°C (from benzene-ethyl acetate)'; ν_{\max} (KBr) 3212, 1604, and 1586 cm⁻¹; λ_{\max} 256 nm (ϵ 27392); δ (CDCl₃) 8.40 (1H, s, OH), 7.38 (9H, m, Ar-H), 6.87 (1H, s, H-4), and 4.27 (1H, s, -CHCl-) (Found: C, 58.8; H, 3.3; N, 8.0; Cl, 20.6. C₁₇H₁₂Cl₂N₂O₂ requires C, 59.0; H, 3.5; N, 8.1; Cl, 20.2).

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