142 © 1985 The Chemical Society of Japan Bull. Chem. Soc. Jpn., 58, 142—145 (1985) [Vol. 58, No. 1

The α-Chlorination of Aryl Ketones with Manganese(III) Acetate in the Presence of Chloride Ion

Takehiko Tsuruta, Tetsuya Harada, Hiroshi Nishino, and Kazu Kurosawa*
Department of Chemistry, Faculty of Science, Kumamoto University, Kurokami 2-39-1, Kumamoto 860

(Received June 21, 1984)

The reaction of 2-(4-methoxyphenyl)-4-chromanone with $Mn(OAc)_3$ in the presence of LiCl gave 3,3-dichloro-2-(4-methoxyphenyl)-4-chromanone. The reactions of 2-phenyl-4-chromanone, 1-phenyl-1-propanone, 1,2-diphenylethanone, and 1-tetralone similarly yielded α,α-dichloro derivatives in good yields. 2,2,2-Trichloroacetophenones were obtained from 2,2-dichloroacetophenones, but in the absence of LiCl, 2,2-dichloroacetophenones gave 2,2,3,3-tetrachloro-1,4-butanediones. KCl, NaCl, NH_4Cl, $AlCl_3$, and $CaCl_2$ were also employed as the Cl^- ion source. Synthetic applicability and the reaction mechanisms are discussed briefly.

In a previous publication,[1] it was reported that the reaction of 4′-methoxyacetophenone with $Mn(OAc)_3$ in AcOH containing NH_4Cl yielded 2-chloro-4′-methoxyacetophenone and 2,2-dichloro-4′-methoxyacetophenone, and the reaction of the 2-chloro-4′-methoxyacetophenone with $Mn(OAc)_3$ in AcOH alone gave several dimeric compounds. This seemed to indicate that the reaction could provide a useful method for the total α-chlorination of some aryl ketones if an excess of $Mn(OAc)_3$–Cl^- is used. Therefore, the reactions of 2-phenyl-4-chromanones (**1a** and **1b**), 1-phenyl-1-propanone (**2**), 1,2-diphenylethanones (**3a** and **3b**), 1-tetralone (**4**), and 2,2-dichloroacetophenones (**5a—5d**) with $Mn(OAc)_3$ in the presence of various chloride ion sources such as LiCl, KCl, NH_4Cl, $CaCl_2$, and $AlCl_3$ in boiling AcOH were examined. These aryl ketones were chosen for the reason that they have at least one or two hydrogens at the α-position of the carbonyl function and are all enolizable ketones.

When 2-(4-methoxyphenyl)-4-chromanone (**1a**) was heated under reflux in AcOH containing $Mn(OAc)_3$ and LiCl, the products were found to be 3,3-dichloro-2-(4-methoxyphenyl)-4-chromanone (**6a**), 3-chloro-4′-methoxyflavone (**7**), and 4′-methoxyflavone (**8a**). A similar reaction of 2-phenyl-4-chromanone (**1b**) yielded 3,3-dichloro-2-phenyl-4-chromanone (**6b**) and flavone (**8b**).

The reactions of 1-phenyl-1-propanone (**2**) and 1-tetralone (**4**) gave the corresponding α,α-dichloro derivatives as the sole product.

When 1,2-bis(4-methoxyphenyl)ethanone (**3a**) was oxidized with $Mn(OAc)_3$–LiCl, the products were 2-acetoxy-1,2-bis(4-methoxyphenyl)ethanone (**13**), 1,2-bis(4-methoxyphenyl)ethanedione (**14a**), and *p*-anisic acid (**15a**). The formation of **13** can be accounted for by assuming a substitution of the chlorine atom by acetate ion in 2-chloro-1,2-bis(4-methoxyphenyl)ethanone (**16**) which may be formed as an intermediate. In fact, **16** gave **13** when heated in AcOH. 1,2-Diphenylethanone (**3b**), on the other hand, yielded the corresponding α,α-dichloro derivative (**11**) as the major product.

When 2,2-dichloro-4′-methoxyacetophenone (**5a**) was oxidized with $Mn(OAc)_3$–LiCl, it gave 2,2,2-trichloro-4′-methoxyacetophenone (**17a**) in almost quantitative yields (Table 1, Entry 7). 2,2-Dichloro-(**5b**), 2,2,4′-trichloro-(**5c**), and 2,2-dichloro-4′-methylacetophenones (**5d**) also yielded the corresponding 2,2,2-trichloroacetophenone (**17b—17d**) in excellent yields (Entries 9, 11, and 13). The reaction of **5a** with $Mn(OAc)_3$ in AcOH alone, on the contrary, resulted in the formation of a dimeric compound (**18a**) as in the reaction of 2-chloro-4′-methoxyacetophenone.[1] It was also found that **5c** gave another dimeric compound (**19**) together with **18c**.

The formation of 3,3-dichloro-2-phenyl-4-chromanones, **6a** and **6b**, has precedence. Weber and Birkner[2] have reported that the reaction of **1a** and **1b** with $CuCl_2$ for 8 h yielded **6a** (65.5%) and **6b** (27.2%), respectively. The reaction using $Mn(OAc)_3$–LiCl is certainly better than that reported because of a shorter reaction time (130 min) and a much higher yield (73% for **6a** and 74% for **6b**). It was also reported[3] that 2,2-dichloro-1-tetralone (**12**) was obtained by a two-step reaction of **4** with $FeCl_3$ (a 53% overall yield). Again this is poor when compared with ours.

In order to examine the reaction conditions in more detail, we chose 2-(4-methoxyphenyl)-4-chromanone (**1a**) as a substrate and carried out reactions under various conditions since **1a** gave several products in a previous experiment. Also, the products could be well separated on TLC. A previous study[1] revealed that the molar ratio of a substrate to $Mn(OAc)_3$ has considerable effect on the yield of products in the reaction of 4′-methoxyacetophenone with $Mn(OAc)_3$–NH_4Cl. An increase in the yield of **6a** was observed to be at the expence of **8a**, while increasing the amount of $Mn(OAc)_3$ (they stayed constant beyond the molar ratio of 1:7). In Table 2 a summary of the molar ratios and yields is presented.

Changing LiCl to other salts as a chloride ion source has some effect on the yields of the products (Table 3). It is demonstrated that KCl and NaCl are better salts and gave a much higher yield of **6a** than the other. $CaCl_2$ yielded a moderate amount of **8a**. NH_4Cl and

$AlCl_3$ were intermediary and gave *r*-3-acetoxy-*t*-2-(4-methoxyphenyl)-4-chromanone (**9**) together with **6a**, **7**, and **8a**. **9** was the major product in the reaction of **1a** with $Mn(OAc)_3$ alone (Entry 6). In the case of $AlCl_3$ it was necessary to acidify the reaction mixture with 2 M (1 M=1 mol/dm^3) hydrochloric acid to free the products from $AlCl_3$. All salts other than LiCl and $AlCl_3$ were only partially soluble in AcOH and some remained at the bottom of the flask. Although KCl gave the maximum yield of **6a**, it is better to use LiCl as the chloride ion source since KCl gives a rather poor yield in the case of 1,2-diphenylethanone (**11**, 50%).

The formation of the dimeric compound (**18a**—**d** and **19**) seems to suggest the radical nature of the reaction. The formation of **17a** in the reaction of **5a**, even in the absence of Cl^- ions (Table 1, Entry 8), indicates that **5a**, itself, could supply Cl^- ions. It can be postulated that the α-keto radical (A) produced from a 2,2-dichloroacetophenone by the action of a Mn(III) species is the common reaction intermediate both for the α-chlorination and for the formation of dimeric compounds. The intermediate A reacts with $Mn(OAc)_3/Cl^-$ to give **17a**—**d**, and in the absence of Cl^- ions dimerizes by a head-to-head coupling to give **18a**—**d** and by a head-to-tail coupling to give **19** (Scheme 1). When **19** was heated at 180 °C under reduced pressure, it isomerized to **18c**. This indicates that the dissociation of **19** to A (Ar=4-chlorophenyl) takes place and a recombination of A gives **18c**. Hydrolysis of **19** with aqueous AcOH yielded **5c** and 4-chlorobenzoic acid (**15c**). The formation of the α,α-dichloro derivatives in the reaction of other ketones can also be accounted for by the similar α-keto radical intermediates (-CO-CH- and -Co-CCl=).

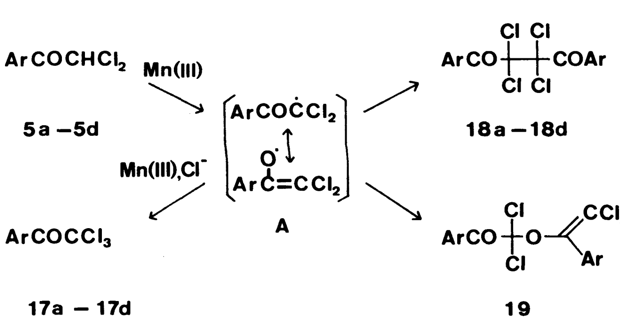
It was thus shown that the reaction of $Mn(OAc)_3$–LiCl provides a facile and extremely simple procedure for α-chlorination of aryl ketones.

Experimental

All the ^{1}H-NMR spectra were recorded with a Hitachi-Perkin-Elmer R-24 spectrometer with tetramethylsilane as the internal reference. The proton decoupled ^{13}C-FT NMR spectra were measured for deuteriochloroform solutions at 100 MHz on a JEOL FX 100 spectrometer using tetramethylsilane as the internal reference. The IR spectra were taken for chloroform solutions on a JASCO IR A-1 grating spectrometer and the UV spectra were recorded for methanol solutions with a Hitachi EPS 3T spectrophotometer. The melting points were determined with a Yanagimoto micro-melting point apparatus and were not corrected.

Materials. 2-(4-Methoxyphenyl)-4-chromanone[4] (**1a**) 2-phenyl-4-chromanone[5] (**1b**), 1,2-bis(4-methoxyphenyl)-ethanone[6] (**3a**), 1,2-diphenylethanone[7] (**3b**), 2,2-dichloro-4′-methoxyacetophenone[8] (**5a**), 2,2-dichloroacetophenone[9] (**5b**) 2,2,4′-trichloroacetophenone[10] (**5c**), and 2,2-dichloro-4′-methylacetophenone[11] (**5d**) were prepared by the method described in the literature. 1-Phenyl-1-propanone (**2**) and 1-tetralone (**4**) were commercially available (Wako Pure Chemical Industries Ltd.).

Oxidations of Aryl Ketones with $Mn(OAc)_3$-Cl^-. The general procedure for the oxidation of aryl ketones with $Mn(OAc)_3$–Cl^- was as follows. To a heated solution of $Mn(OAc)_3 2H_2O$[12] (4—9 mmol) and Cl^- (10 mmol) in AcOH (20 ml), a ketone (1 mmol) was added. The mixture was then heated under reflux until the dark color of the solution



Scheme 1.

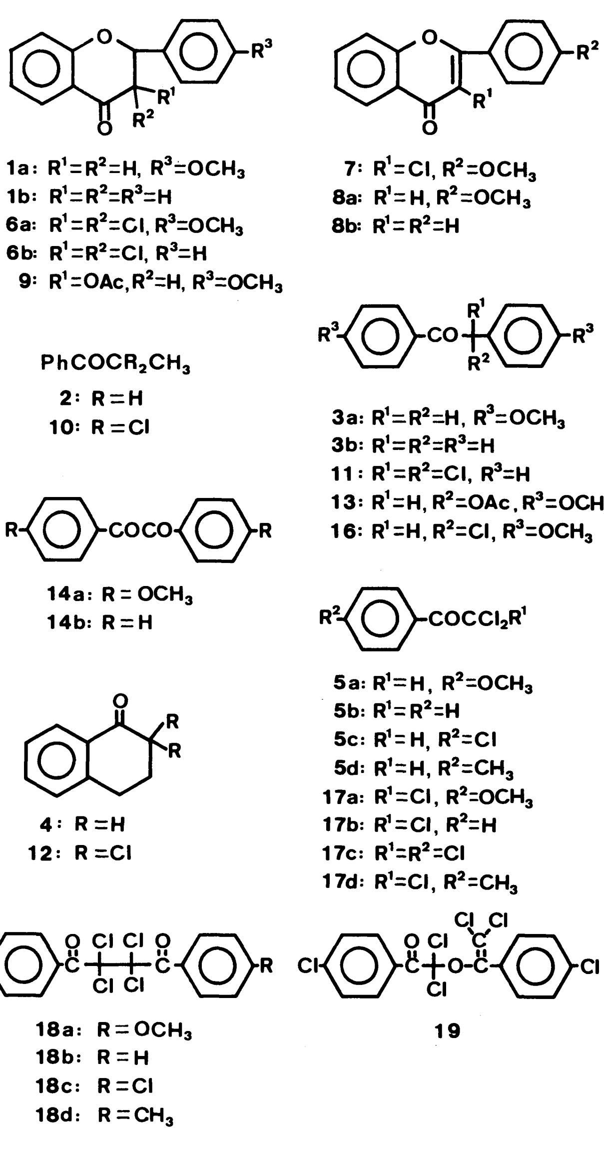


Fig. 1.

TABLE 1. REACTION OF ARYL KETONES WITH $Mn(OAc)_3$-LiCl

Entry	Substr.	Reaction conditions		Product (yield/%)[a]			
		Molar ratio of Substr : $Mn(OAc)_3$: LiCl	Time / min				
1	**1a**	1 : 7 : 10	130	**6a** (73)	**7** (6)	**8a** (12)	
2	**1b**	1 : 7 : 10	54	**6b** (74)		**8b** (9)	
3	**2**	1 : 9 : 10	180	**10** (93)			
4	**3a**	1 : 5 : 10	91		**13** (79)	**14a** (16)	**15a** (2)
5	**3b**	1 : 5 : 10	23	**11** (75)		**14b** (10)	**15b** (5)
6	**4**	1 : 5 : 10	11	**12** (78)[b]			
7	**5a**	1 : 4 : 10	180	**17a** (98)			
8	**5a**	1 : 2 : 0	95	**17a** (2)	**18a** (53)		**15a** (5)
9	**5b**	1 : 4 : 10	210	**17b** (95)			
10	**5b**	1 : 2 : 0	160		**18b** (42)		
11	**5c**	1 : 4 : 10	223	**17c** (94)			
12	**5c**	1 : 2 : 0	125		**18c** (38)	**19** (34)	
13	**5d**	1 : 4 : 10	94	**17d** (97)			
14	**5d**	1 : 2 : 0	280		**18d** (49)		

a) Yields based on the amount of substrate used. b) **4** was recovered (5%).

TABLE 2. REACTION CONDITIONS AND PRODUCT YIELDS FOR THE OXIDATION OF 2-(4-METHOXYPHENYL)-4-CHROMANONE (**1a**) WITH $Mn(OAc)_3$-LiCl

Entry	Reaction conditions		Product (yield/%)[a]		
	Molar ratio of **1a** : $Mn(OAc)_3$: LiCl	Time / min	**6a**	**7**	**8a**
1	1 : 5 : 10	48	51	5	37
2	1 : 6 : 10	128	58	6	33
3	1 : 7 : 10	130	73	6	12
4	1 : 8 : 10	144	73	6	15
5	1 : 9 : 10	197	73	7	16

a) Yields based on the amount of the substrate used.

disappeared. The reaction mixture was diluted with water (60 ml) and then extracted with benzene (30 ml) twice. The combined benzene solution was washed with an aqueous sodium hydrogencarbonate solution and then evaporated *in vacuo*. Finally, the resulting products were purified on TLC with either benzene or chloroform as the eluting solvent, and then recrystallized or distilled. Yields are summarized in Tables 1, 2, and 3.

Oxidation Products of 2-(4-Methoxyphenyl)-4-chromanone (1a). 3,3-Dichloro-2-(4-methoxyphenyl)-4-chromanone (6a): Mp 133—134 °C (lit,[2] 129—131 °C). *3-Chloro-4′-methoxyflavone (7)*: Mp 141.5—142.5 °C (lit,[2] 143—144 °C). *4′-Methoxyflavone (8a)*: Mp 157—158 °C (lit,[13] 157—158 °C). r-*3-Acetoxy*-t-*2-(4-methoxyphenyl)-4-chromanone (9)*: Colorless liquid (lit,[14] mp 96—97 °C).

Oxidation Products of 2-Phenyl-4-chromanone (1b). 3,3-Dichloro-2-phenyl-4-chromanone (6b): 141.8—142.3 °C (lit,[2] 144 °C). *Flavone (8b)*: Mp 99 °C (lit,[15] 97 °C).

2,2-Dichloro-1-phenyl-1-propanone (10): Colorless liquid (lit,[16] bp 83—87 °C/0.5 mmHg (1 mmHg=133.322 Pa)).

2,2-Dichloro-1-tetralone (12): Mp 79.5—79.9 °C (lit,[3] 79—80 °C).

Oxidation Products of 1,2-Bis (4-methoxyphenyl)ethanone (3a). 2-Acetoxy-1,2-bis(4-methoxyphenyl)ethanone (13): Mp 96.7—97 °C (lit,[17] 93.5 °C). *1,2-Bis(4-methoxyphenyl)ethanedione (14a)*: Mp 134—135.5 °C (lit,[18] 133 °C). p-*Anisic acid (15a)*: Mp 185 °C.

TABLE 3. INFLUENCE OF THE CHLORIDE ION SOURCE UPON THE OXIDATION OF 2-(4-METHOXYPHENYL)-4-CHROMANONE (**1a**) WITH $Mn(OAc)_3$-Cl^-

Entry	Reaction conditions			Produdt (yield/%)[a]				
	Salt	Molar ratio of **1a** : $Mn(OAc)_3$: Cl^-	Time / min	**6a**	**7**	**8a**	**9**	**15a**
1	KCl	1 : 7 : 10	86	78	7	9		
2	NaCl	1 : 7 : 10	61	70		7	3	
3	NH_4Cl	1 : 7 : 10	46	46	2	13	6	3
4	$AlCl_3$	1 : 7 : 3.3	46	45	1	9	10	
5	$CaCl_2$	1 : 7 : 5	63	23	27	42		
6	None	1 : 6 : 0	17			22	41	12

a) Yields based on the amount of the substrate used.

*2-Acetoxy-1,2-bis(4-methoxyphenyl)ethanone (**13**) from 2-Chloro-1,2-bis(4-methoxyphenyl)ethanone*[19] *(**16**).* A solution of **16** (128 mg) in AcOH (20 ml) was heated under reflux for 90 min. Evaporation of the solvent *in vacuo* gave **13** (136 mg, 98%), identical with an authentic sample.

*Dichloro-1,2-diphenylethanone (**11**):* Mp 62.1—62.9 °C (lit,[20] 61—62 °C). *1,2-Diphenylethanedione (**14b**):* Mp 94—95 °C. *Benzoic acid (**15b**):* Mp 120 °C.

*2,2,2-Trichloro-4′-methoxyacetophenone (**17a**):* Bp 120—125 °C (bath temp)/0.02 mmHg (lit,[21] mp 33—35.3 °C).

*2,2,2-Trichloroacetophenone (**17b**):* Bp 105—110 °C (bath temp)/0.02 mmHg (lit,[10] 145 °C/25 mmHg).

*2,2,2,4′-Tetrachloroacetophenone (**17c**):* Bp 110—115 °C (bath temp)/0.02 mmHg (lit,[22] mp 28 °C).

*2,2,2-Trichloro-4′-methylacetophenone (**17d**):* Bp 115—120 °C (bath temp)/0.02 mmHg (lit,[23] 137 °C/10 mmHg).

Oxidation of Aryl Ketones with Mn(OAc)$_3$. The general procedure for the oxidation of aryl ketones with Mn(OAc)$_3$ was virtually identical with that for the reaction with Mn(OAc)$_3$-Cl$^-$.

*2,2,3,3-Tetrachloro-1,4-bis(4-chlorophenyl)-1,4-butanedione (**18a**):* Mp 145—146 °C (lit,[1] 145—146 °C).

*2,2,3,3-Tetrachloro-1,4-diphenyl-1,4-butanedione (**18b**):* Colorless Cubes; mp 94—95 °C (from light petroleum); IR 1700 cm^{-1} (-C=O): UV λ_{max} (ε) 265 nm (20900); ^{1}H-NMR (CDCl$_3$) δ=7.2—7.6 (6H, m, H-3′, H-3″, H-4′, H-4″, H-5′, and H-5″), and 8.1—8.3 (4H, m, H-2′, H-2″, H-6′, and H-6″). Found: C, 51.04; H, 2.67%. Calcd for $C_{16}H_{10}Cl_4O_2$: C, 51.07; H, 2.68%.

*2,2,3,3-Tetrachloro-1,4-bis(4-chlorophenyl)-1,4-butanedione (**18c**):* Colorless cubes; mp 167—168 °C (from light petroleum), IR 1712 cm^{-1} (>C=O); UV λ_{max} (ε) 219^{sh} (9000) and 276 nm (27700); ^{1}H-NMR (CDCl$_3$) δ=7.48 (4H, m, H-3′, H-3″, H-5′, and H-5″), and 8.16 (4H, m, H-2′, H-2″, H-6′, and H-6″); ^{13}C-NMR δ=183.958 (>C=O), 140.100 (=C–Cl), 132.118 (2×=$\overset{|}{\mathrm{C}}$–H), 130.719 (=$\overset{|}{\mathrm{C}}$–CO), 128.405 (2×=$\overset{|}{\mathrm{C}}$–H), and 89.420 (–CCl$_2$–). Found: C, 43.09; H, 1.81%. Calcd for $C_{16}H_4Cl_6O_2$: C, 43.16; H, 1.81%.

*4,β,β-Trichloro-α-[dichloro-(4-chlorobenzoyl)methoxy]styrene (**19**):* Colorless cubes; mp 81.7—82.7 °C (from light petroleum); IR 1730 cm^{-1} (>C=O); UV λ_{max} (ε) 224^{sh} (17400) and 263 nm (15300); ^{1}H-NMR (DMSO-*d*$_6$) δ=7.64 (4H, m, H-2, H-3, H-5 and H-6), 7.69 (2H, m, H-3′ and H-5′), and 8.18 (2H, m, H-2′ and H-6′); ^{13}C-NMR δ=180.605 (>C=O), 144.788 (=$\overset{|}{\mathrm{C}}$–O–), 140.709 (=$\overset{|}{\mathrm{C}}$–Cl), 136.445 (=$\overset{|}{\mathrm{C}}$–Cl), 132.547 (2×=$\overset{|}{\mathrm{C}}$–H), 131.509 (2×=$\overset{|}{\mathrm{C}}$–H), 129.438 (=$\overset{|}{\mathrm{C}}$–CO), 128.707 (4×=$\overset{|}{\mathrm{C}}$–H). 128.2 (=$\overset{|}{\mathrm{C}}$–C(O)–), 120.486 (=CCl$_2$), and 109.765 (–CCl$_2$–). Found: C, 43.22; H, 1.81%. Calcd for $C_{16}H_8Cl_6O_2$: C, 43.16; H, 1.81%.

*2,2,3,3-Tetrachloro-1,4-bis(4-methylphenyl)-1,4-butanedione (**18d**):* Colorless cubes; mp 167.5—169.5 °C (from CCl$_4$–light petroleum); IR 1720 cm^{-1} (>C=O); UV λ_{max} (ε) 219^{sh} (7800) and 278 nm (23600); ^{1}H-NMR (CDCl$_3$) δ=2.40 (6H, s, 2×CH$_3$), 7.27 (4H, m, H-3′, H-3″, H-5′, and H-5″), and 8.16 (4H, m, H-2′, H-2″, H-6′, and H-6″). Found: C, 53.13; H, 3.44%. Calcd for $C_{18}H_{14}Cl_4O_2$: C, 53.47; H, 3.49%.

*Isomerization of 4,β,β-Trichloro-α-[dichloro-(4-chlorobenzoyl)methoxy]styrene (**19**) to 2,2,3,3-Tetrachloro-1,4-bis(4-chlorophenyl)-1,4-butanedione (**18a**).* **19** (33.9 mg) was heated in a glass tube at 180—190 °C under reduced pressure (15 mmHg) for 1 h. The product was recrystallized from light petroleum to give **18a** (28.9 mg, 85%), mp 167—168 °C.

*Hydrolysis of 4,β,β-Trichloro-α-[dichloro-(4-chlorobenzoyl)methoxy]styrene (**19**).* A mixture of **19** (73.5 mg), AcOH (2 ml), water (1 ml), and concd hydrochloric acid (0.05 ml) was heated under reflux for 2 h. After the AcOH was removed *in vacuo*, the resulting substance was separated on TLC with carbon tetrachloride as the eluting solvent to give **5c** (27.5 mg, 74%), mp 61—62 °C (lit,[10] 51 °C) and 4-chlorobenzoic acid (**15c**) (6.9 mg, 26%), mp 244.5—245.5 °C (in a sealed tube) (lit,[24] 241.5 °C).

We wish to thank Professor Hitoshi Takeshita and Associate Professor Akira Mori of the Research Institute of Industrial Science, Kyushu University, for their measurements of the ^{13}C-NMR spectra.

References

1) K. Kurosawa and K. Yamaguchi, *Bull. Chem. Soc. Jpn.*, **54**, 1757 (1981).
2) F. G. Weber and E. Birkner, *Z. Chem.*, **19**, 292 (1979).
3) Y. Nakatani and M. Matsui, *Hgr. Biol. Chem.*, **32**, 734 (1968).
4) A. Edelstein and St. v. Kostanecki, *Ber.*, **38**, 1507 (1905).
5) A. Löwenbein, *Ber.*, **42**, 2348 (1909).
6) H. Apitsch, *Ber.*, **40**, 1803 (1907).
7) C. F. H. Allen and W. E. Barker, *Org. Synth.* Coll Vol. **II**, 156 (1943).
8) F. Kunckell and F. Johanssen, *Ber.*, **31**, 169 (1898).
9) H. Gautier, *Ann. Chim. Phys.*, **14**, 345 (1888).
10) H. Gaitier, *Ann. Chim. Phys.*, **14**, 402 (1888).
11) S. K. Morita, A. N. Ganguli, N. N. Chakravarti, and R. N. Adhya, *Tetrahedron Lett.*, **1971**, 199.
12) P. J. Andrulis, Jr., M. J. S. Dewar, R. Dietz, and R. L. Hunt, *J. Am. Chem. Soc.*, **88**, 5473 (1966).
13) K. v. Auwers and L. Anschütz, *Ber.*, **54**, 1558 (1921).
14) G. W. K. Cavill, F. M. Dean, A. McGookin, B. M. Marshall, and A. Robertson, *J. Chem. Soc.*, **1954**, 4573.
15) W. Feuerstein and St. v. Kostanecki, *Ber.*, **31**, 1760 (1898).
16) M. Ballester and J. Riera, *Anales Real. Soc. Espan.*, **56**, 897 (1960). *Chem. Abstr.*, **55**, 19876c (1961).
17) R. P. Barnes and W. M. Lucas, *J. Am. Chem. Soc.*, **64**, 2258 (1942).
18) M. Bösler, *Ber.*, **14**, 322 (1881).
19) G. Henne and A. Bruglants, *Bull. Soc. Chim. Belges*, **57**, 320 (1948).
20) B. Lachowicz, *Ber.*, **17**, 1161 (1884).
21) J. Houben and W. Fischer, *Ber.*, **60**, 1759 (1927).
22) H. Gaurier, *Ann. Chim. Phys.*, **14**, 403 (1888).
23) J. Houben and W. Fischer, *J. prakt. Chem.*, **123**, 313 (1929).
24) N. V. Sidgwick ad E. K. Ewbank, *J. Chem. Soc.*, **119**, 979 (1921).