Tetrahedron. Vol. 26, pp. 2781–2786. Pergamon Press 1970. Printed in Great Britain

REACTIONS OF CUPRIC HALIDES WITH ORGANIC COMPOUNDS—VIII[1]

REACTIONS OF 9-ACYLANTHRACENES

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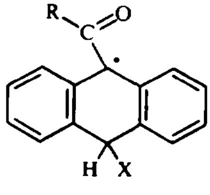
(*Received in the UK* 18 *November* 1969; *Accepted for publication* 12 *March* 1970)

Abstract—9-Acylanthracenes undergo reaction with cupric halides in chlorobenzene to give 9-acyl-10-halogenoanthracenes together with 9-halogeno- and 9,10-dihalogenoanthracenes. The products arise from ligand-transfer reactions of the cupric halide and the 9-acylanthracene at the 9- and 10-positions.

9-Acetylanthracene gives 9-bromoacetylanthracene on reaction with cupric bromide in ethyl acetate-chloroform.

CUPRIC halides have been shown to halogenate 9-alkyl-[2], 9-aryl-[2], and 9-halogeno-[3] anthracenes in the 10-position under heterogeneous conditions in carbon tetrachloride, benzene, or chlorobenzene. This study is now extended to reactions of 9-acylanthracenes with cupric halides. These reactions are of particular interest since cupric bromide in ethyl acetate/chloroform mixtures has been shown to halogenate hydroxyacetophenones in the acetyl group rather than in the nucleus.[4]

9-Acetylanthracene was found to react fairly slowly with cupric halides to give the 9-acetyl-10-halogenoanthracene together with some of the 9-halogeno- and 9,10-dihalogenoanthracene (Table 1). That the rate of reaction was fairly slow is consistent with studies on 9-arylanthracenes in which electron-withdrawing substituents were found to retard these reactions.[2] The formation of the 9-acetyl-10-halogenoanthracene is postulated to arise from ligand-transfer of halogen to the 10-position to give the intermediate radical (**1**; R = Me) which on further reaction with cupric halide affords the product. The formation of the 9-halogenoanthracene is postulated to proceed by ligand-transfer of halogen to the 9-position to give the radical (**2**; R = Me).



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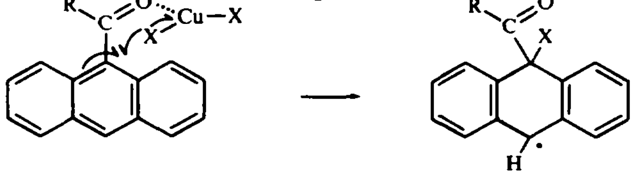

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Subsequent reaction of this with cupric halide in a second ligand-transfer reaction affords the 9-halogenoanthracene and acetyl chloride. Reaction would not normally be expected at this position on steric grounds. However, in this instance it is conceived that if co-ordination of the copper of the cupric halide were to occur thereby holding the cupric halide in the right steric environment for ligand-transfer of the halogen to occur then reaction could take place at the 9-position. The 9,10-dihalogenoanthracene is presumed to arise from subsequent reaction of the 9-halogenoanthracene with further cupric halide, a reaction which occurs readily under these conditions, rather than by subsequent reaction of 9-acetyl-10-halogenoanthracene with cupric halide. This latter reaction has been shown to proceed only very slowly under the reaction conditions and would not account for the 9,10-dihalogenoanthracene obtained.

The reaction was further investigated by studying the reaction between 9-chloroacetylanthracene and cupric chloride. The reaction, which was much slower than that of 9-acetylanthracene, gave much less of the deacylated products. Several reasons for this can be proposed. Firstly the electron density on the carbonyl oxygen of the chloroacetyl group would be reduced relative to the situation with the acetyl group thereby reducing the tendency of the copper to co-ordinate and hence decreasing the amount of reaction at the 9-position. This effect would be accentuated since the chloroacetyl group would lie further out of the plane of the anthracene ring because of the increased size of the acyl group thus reducing the conjugation of the acyl group with the aromatic system and hence reducing the electron density on the carbonyl oxygen. It could also be argued that reaction of the radical (**2**; R = Me) with cupric chloride would be expected to proceed more rapidly than that of the analogous radical derived from 9-chloroacetylanthracene since an acetyl radical or carbonium ion would be more stable than a chloracetyl radical or carbonium ion because of the electron-withdrawing effect of the chlorine. Reactions of this type have been shown to proceed more readily the more stable is the leaving group as a radical or carbonium ion.[5] Further clarification of some of these points was sought by studying the reaction of 9-trichloroacetylanthracene with cupric chloride. Unfortunately attempts to prepare this compound proved abortive.

Examination of the reactions of 9-*p*-substituted benzoylanthracenes with cupric chloride was then undertaken to make a more detailed study of the influence of electronic effects without the interference of steric effects. The rate of reaction was found to be very strongly dependent on the substituent in the benzoyl group, but the products were, within experimental error, the same in all cases (Table 1). The small amounts of deacylated products obtained indicates that the radical (**2**; R = Ar) is only formed to a small extent or if formed in greater amounts reverts reversibly to the starting material. That the same amount of deacylated products are formed in all the reactions suggests that the reasons for this may be largely steric. The 9-aroyl-10-chloroanthracenes were synthesized from the 9-aroylanthracenes and phosphorus pentachloride. The yields were lower than those obtained in the cupric chloride reactions.

Methyl 9-anthroate underwent reaction with both cupric bromide and cupric chloride to give exclusively the 10-halogenated product. Copper is known to co-ordinate less readily to a carbonyl of a carbomethoxy group than to the carbonyl of an acetyl group and hence reaction would be expected to proceed predominantly if not exclusively at the 10-position. The stability constant of copper ethyl acetoacetate is less than that of copper acetylacetone in accordance with the above contention.[6]

9-Anthraldehyde underwent reaction with cupric chloride much more slowly than did 9-acetylanthracene affording 10-chloro-9-anthraldehyde and 9,10-dichloroanthracene. The formyl group in 9-anthraldehyde lies much more nearly in the plane of the aromatic system than does the acetyl group in 9-acetylanthracene.[7,8] The electron-withdrawing resonance effect of the formyl group would thus be expected to be much more potent than that of the acetyl group thus accounting for the slower reaction.

The reaction of 9-acetylanthracene with cupric bromide in ethyl acetate-chloroform was also examined using the conditions employed by King and Ostrum[4] for the bromination of hydroxyacetophenones to hydroxyphenacyl bromides. The sole product of the reaction was 9-bromoacetylanthracene. The reaction clearly must have proceeded by a somewhat different mechanism and a possible reaction scheme is outlined. In this the cupric bromide initially co-ordinates to the carbonyl oxygen

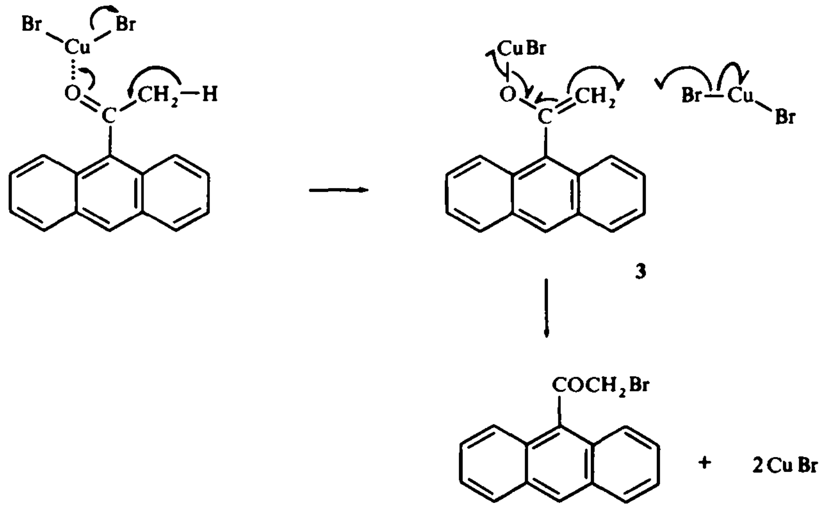

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TABLE 1. REACTION OF 9-ACYLANTHRACENES WITH CUPRIC HALIDES

9-Acylanthracene $RCOC_{14}H_9$	Cupric Halide	Time hr	Products (%)			
R	CuX_2		9–X	9, 10–X_2	9-RCO-10–X	9-RCO
CH_3	$CuBr_2$	5¼	66	6	23	3
CH_3	$CuCl_2$	9	22	12	31	27
CH_2Cl	$CuCl_2$	42	1	3·5	34	60
Ph	$CuBr_2$	2	2	7	75	12
Ph	$CuCl_2$	8½	0	8	82	7
p-$CH_3C_6H_4$	$CuCl_2$	¾	0	5	81	12
p-ClC_6H_4	$CuCl_2$	29	0	3	75	18
CH_3O	$CuBr_2$	21½	0	0	82	3
CH_3O	$CuCl_2$	24½	0	0	23	72
H	$CuCl_2$	47	0	34	39	0

TABLE 2. NEW 9-ACYL-10-CHLOROANTHRACENES

Compound 9-RCO-10-X$C_{14}H_8$		M.p.	Cryst. from	Found (%)			Formula	Calc. (%)		
R	X			C	H	X		C	H	X
CH_3	Cl	155–156°	Pet-PhH	75·3	4·5	13·8	$C_{16}H_{11}ClO$	75·4	4·3	13·95
CH_3	Br	174–175	Pet-PhH	64·6	3·6	26·5	$C_{16}H_{11}BrO$	64·2	3·7	26·7
CH_2Cl	Cl	118–119	Pet.	66·7	3·4	24·4	$C_{16}H_{10}Cl_2O$	66·5	3·5	24·6
p-$CH_3C_6H_4$	Cl	147–148	Pet.	79·7	4·8	10·5	$C_{22}H_{15}ClO$	79·9	4·5	10·7
p-ClC_6H_4	Cl	170–172	Pet.	71·4	3·5	19·6	$C_{21}H_{12}Cl_2O$	71·8	3·4	20·2

affording the bromocupric enolate of 9-acetylanthracene (3). Reaction of this with a second molecule of cupric bromide affords the product and cuprous bromide. This mechanism is essentially a variant of that proposed by Kosower for the cupric halide halogenation of enolizable ketones in dimethyl formamide.[9, 10] Cupric chloride was found to be ineffective under the same reaction conditions. 9-Benzoylanthracene was unattacked by cupric bromide under these conditions though 9-methylanthracene underwent bromination in the 10-position as it did in benzene and chlorobenzene.

EXPERIMENTAL

Light petroleum refers to the fraction b.p. 60–80°. NMR spectra were recorded in deuteriochloroform on a Perkin–Elmer R10 spectrometer operating at 60 MHz using TMS as an internal standard; IR spectra as nujol mulls unless otherwise stated on a Perkin–Elmer 525 spectrometer; UV spectra in ethanol on a Perkin–Elmer 202 spectrometer. Chromatographies were carried out using Spence Grade H alumina. Cupric bromide and cupric chloride were dried and ground as previously described.[3]

Preparation of starting and reference materials

9-Acetylanthracene,[11] 9-benzoylanthracene,[12] 9-anthraldehyde[13] and methyl 9-anthroate[14] were prepared as described in the literature.

9-*Chloroacetylanthracene.* A stirred mixture of finely ground $AlCl_3$ (15 g, 0·112 mole) and chloroacetyl chloride (12·7 g, 0·112 mole) in CS_2 (118 ml) was cooled to − 10° in an ice-salt freezing mixture.[15] To this, anthracene (20 g, 0·112 mole) was added slowly. When the addition was complete, the mixture was allowed to warm up to room temp and was then heated gently on a steam bath for 1 hr. 6N HCl was added slowly and the mixture stirred until complete separation of the two layers had been effected. The organic layer was separated off, washed with N KOH, and with water before drying ($MgSO_4$). Evaporation of the solvent left a thick reddish-black gum. This was dissolved in benzene and chromatographed on alumina. Elution with benzene gave 9-*chloroacetylanthracene*, which was crystallized from MeOH and then from light petroleum as yellow needles, (4 g, 14%), m.p. 94–95° (Found: C, 75·2; H, 4·2; Cl, 13·9. $C_{16}H_{11}ClO$ requires C, 75·45; H, 4·3; Cl, 13·9%); IR ν_{max} 1719 cm^{-1}.

9-p-*Methylbenzoylanthracene.* Anthracene (20 g, 0·112 mole) was added over 10 min to a stirred mixture of finely ground $AlCl_3$ (15 g, 0·112 mole) and P-toluoyl chloride (17·3 g, 0·112 mole) in CS_2 (118 ml).[14] When the initial vigorous reaction had subsided, the mixture was refluxed on a steam bath for 2½ hr. The reaction was worked up as before. The organic product was crystallized from EtOH and then from benzene-light petroleum as yellow cubes of 9-p-*methylbenzoylanthracene* (30 g, 91%), m.p. 193–194 (Found: C, 89·15; H, 5·5. $C_{22}H_{16}O$ requires: C, 89·2; H, 5·4%); IR ν_{max} 1660 $cm.^{-1}$ (C═O).

9-p-*Chlorobenzoylanthracene.* This was prepared as above starting with *p*-chlorobenzoyl chloride (19·6 g, 0·112 mole). The product was crystallized from EtOH and benzene–light petroleum as yellow needles of 9-p-*chlorobenzoylanthracene* (32 g, 92%), m.p. 189–191°. (Found: C, 79·3; H, 4·2; Cl, 11·6. $C_{21}H_{13}ClO$ requires: C, 79·55; H, 4·1; Cl, 11·2%); IR ν_{max} 1661 $cm.^{-1}$ (C═O).

9-*Aroyl*-10-*chloroanthracenes.* A mixture of 9-aroylanthracene (7 mmole) and PCl_5 (7 mmole) in anhyd benzene was refluxed for 24 hr. The solvent was distilled off from the mixture and the residue chromatographed on alumina. Elution with 1:1 benzene:light petroleum gave initially 9-aroyl-10-chloroanthracene, followed by mixtures of this with 9-aroylanthracene. The first reactions were crystallized from light petroleum. 9-Chloro-10-*p*-methylbenzoylanthracene and 9-chloro-10-*p*-chlorobenzoylanthracene were obtained in yields of 43% and 31% respectively (see Table 2 for physical constants).

9-*Chloro*-10-*chloroacetylanthracene.* To a stirred cooled mixture of 9-chloroanthracene (10 g, 0·047 mole) and acetyl chloride (12·14 g, 0·282 mole) in anhydrous benzene (64 ml), was added $AlCl_3$ (6·27 g, 0·094 mole) at a rate so that the temp of the mixture remained between − 5 and 0°. After the addition was complete, the mixture was stirred for a further 30 min. The mixture was then allowed to warm to 10°, and the red complex which had formed was filtered off on a sintered-glass funnel and washed well with dry benzene. The complex was added in small portions to a stirred mixture of ice and conc HCl. The crude ketone was filtered off and purified by chromatography on alumina. Elution with 1:1 benzene:light petroleum gave 9-acetyl-10-chloroanthracene (3·7 g, 27%), which was crystallized from benzene-light petroleum, m.p. 155–156°.

Reactions of 9-acylanthracenes and methyl 9-anthroate with cupric halides in chlorobenzene. A typical experiment is described. A stirred mixture of 9-benzoylanthracene (3 g, 10·6 mmole) and $CuBr_2$ (4·75 g, 21·2 mmole) in chlorobenzene (225 ml) was refluxed for 2 hr when evolution of HBr had ceased. The reaction mixture was filtered and the filtrate evaporated to dryness. The residue in 9:1 light petroleum:benzene was chromatographed on alumina. Elution with this solvent mixture gave a mixture of 9-bromo- and 9,10-dibromoanthracenes, the composition of which was determined by UV spectroscopy. Elution with 1:1 light petroleum: benzene gave 9-benzoyl-10-bromoanthracene (2·875 g, 75%), which was crystallized from light petroleum as yellow needles, m.p. and mixed m.p. 174–175°. Continued elution with this solvent gave 9-benzoylanthracene (0·65 g, 12%).

The reaction of 9-benzoylanthracene with $CuCl_2$ was carried out simularly. In one experiment, the filtrate from the reaction was fractionally distilled under reduced press. The final fractions of the solvent were analysed by GLC and shown to contain traces of benzoyl chloride. This was confirmed by treatment of these fractions with *p*-nitroaniline when benz-*p*-nitroanilide was obtained, m.p. and mixed m.p. 198–199°.

Reactions of cupric halides in ethyl acetate-chloroform. Reaction of 9-acetylanthracene

(a) *with cupric bromide.* A soln of 9-acetylanthracene (2·2 g, 10 mmole) in $CHCl_3$ (25 ml) was added to a stirred suspension of $CuBr_2$ (4·48 g, 20 mmole) in EtOAc (25 ml). The stirred mixture was refluxed until evolution of HBr ceased (2 hr). The mixture was filtered. The green filtrate was washed with water and then with $NaHCO_3$ eq, and dried (Na_2SO_4). The residue, after evaporation of the solvent, was analysed by GLC and shown to contain 9-bromoacetylanthracene (80%) and 9-acetylanthracene (20%). Crystallization from MeOH and then from light petroleum gave yellow prisms of 9-bromoacetylanthracene, m.p. 108–109° (lit.[16] 107–108·5°). NMR τ 5·36 (2H).

(b) *with cupric chloride.* The reaction was carried out as above but using $CuCl_2$ (2·69 g, 20 mmole). After 7 hr reflux, no reaction had taken place.

Reaction of 9-benzoylanthracene with cupric bromide

The reaction was carried out as above but using 9-benzoylanthracene (2·82 g, 10 mmole). No reaction had occurred after refluxing the mixture for 6 hr.

Reaction of 9-methylanthracene with cupric bromide

The reaction was carried out as above using 9-methylanthracene (1·92 g, 10 mmole). GLC analysis of the product showed it contained 9-bromo-10-methylanthracene and 9-methylanthracene.

Acknowledgement—One of us (J.A.R.) thanks the Science Research Council for a Maintenance Grant.

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