In general, to obtain good yields of low molecular weight products from a solvent and monomer, the alternating reactions, between monomer radical and solvent, and between solvent radical and monomer, must proceed readily in competition with both the polymerization and chain termination reactions. This condition requires that the transfer constant of the solvent be near or greater than unity, and is met most easily when one component is an electron donor in the transition state and the other an electron acceptor. With allylic monomers, reactive solvents and strong polar effects reduce termination by degradative chain transfer, and the situation is analogous to the acceleration of the polymerization of allyl acetate by maleic anhydride, the strong alternating effect greatly extending the kinetic chain length.[25] Monomers with conjugated substituents, with reactive double bonds and unreactive radicals,[11d,26] will have smaller transfer constants for the same solvent than the unconjugated aliphatic monomers (*cf.* Table IV). Accordingly, only the most reactive solvents such as bromotrichloromethane[7] or carbon tetrabromide,[27] with transfer constants near unity, give 1:1 products with styrene, while a wider range of solvents is effective with aliphatic monomers.[13] The broken line in Fig. 1 plots results for styrene and carbon tetrachloride (transfer constant = 0.0115) at 76°.[3d] The low transfer constant prevents reaction of many solvent molecules per peroxide decomposed, although consumption of styrene is higher than for any other monomer shown.

(25) P. D. Bartlett and K. Nozaki, THIS JOURNAL, **68**, 1495 (1946).

(26) K. Nozaki, *Disc. Faraday Soc.*, **2**, 337 (1947).

(27) C. H. Bamford and M. J. S. Dewar, *ibid.*, **2**, 314 (1947); J. W. Breitenbach and H. Karlinger, *Monatsh.*, **82**, 245 (1951).

SCHENECTADY, NEW YORK

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, LINGNAN UNIVERSITY]

Halogenation of Chelated Aryl Alkyl Ketones. I. Bromination of 2-Acetylnaphthol and Several of its Derivatives

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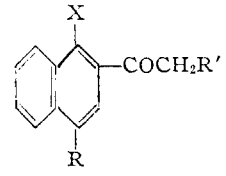
The finding that 4-nitro-2-acetylnaphthol is resistant to bromination led to a reinvestigation of the bromination of 2-acetylnaphthol. The results confirm literature reports that with excess bromine, the 4-bromo-2-acetylnaphthol formed is subsequently further brominated in the side chain, but if first isolated, it is found to resist bromination under identical previous conditions of solvent and temperature. This resistance to bromination is ascribed to chelation effects. Experimental evidence in support of this theory, and conditions under which the compound can be successfully brominated, are described.

During the course of unpublished early work on the naphthoquinone antimalarials,[3] one of us (F.C.C.) found that 4-nitro-2-acetylnaphthol (II) unexpectedly resisted bromination even under somewhat forcing conditions,[4] an observation which was not investigated further at the time. In resuming study of the problem, we were unable to reconcile the behavior of II with the seemingly straightforward α-bromination of 4-bromo-2-acetylnaphthol (III) (made from 2-acetylnaphthol (I)) as reported in the literature.[5,6] For, although the nitro compound might be expected to undergo bromination less readily than the bromo derivative because of the greater electron attraction of the nitro group, as studies by Evans, Morgan and Watson[7] of the bromination rates of various nuclear substituted acetophenones indicate, the extreme unreactivity of 4-nitro-2-acetylnaphthol in the reaction seemed implausible based merely on this difference. An alternative explanation, that the nitro group exercises some unique effect, was even less attractive. We therefore decided to re-study the bromination and dibromination of 2-acetylnaphthol as a starting point in this investigation



Napthols (X = OH)	Methyl ethers (X = OCH_3)	Acetates (X = $OCOCH_3$)	R	R′
I	VI	X	H	H
II			NO_2	H
III	VII	XI	Br	H
IV	VIII	XII	Br	Br
V	IX	XIII	H	Br

Our results indeed confirm the previous reports that I is readily brominated at room temperature to 4-bromo-2-acetylnaphthol (III), and by excess bromine to α,4-dibromo-2-acetylnaphthol (IV). But we discovered that III does not react further with bromine under the identical previous conditions[8] of temperature and solvent if the compound is first isolated. This apparent anomaly becomes clarified when the reactions involved in the dibromination of I are examined

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(2) Based on the M.S. Thesis of Yen-shang Yang, Lingnan University, 1950.

(3) L. F. Fieser, M. T. Leffler and co-workers, THIS JOURNAL, **70**, 3151 (1948).

(4) In CCl_4 at room temperature, and under reflux; in acetic acid at room temperature, and under reflux. Alkaline bromination was not tried, as the α-mono-bromo compound was desired.

(5) K. Fries and R. Frellstedt, *Ber.*, **54**, 715 (1921).

(6) M. Akram, R. D. Desai and A. Kamal, *Proc. Indian Acad. Sci.*, **11A**, 139 (1940).

(7) D. P. Evans, V. G. Morgan and H. B. Watson, *J. Chem. Soc.*, 1167 (1935).

(8) At reflux temperature in acetic acid, bromination does proceed (see experimental).

$$I \xrightarrow[(1)]{Br_2} III + HBr \xrightarrow[(2)]{Br_2} IV + HBr$$

It is seen that step 2 proceeds in a medium that contains HBr formed in step 1 and thus the conditions are not identical when initially isolated III is treated with bromine. That this analysis is sound was demonstrated by the successful bromination of III at room temperature when HBr was introduced into the solvent.

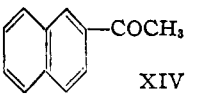
Thus, the resistance to bromination applies to the bromo- as well as to the nitro-4-substituted derivatives of 2-acetylnaphthol, and is likely to be a general characteristic of a group of compounds. It seems logical to attribute the behavior to the interaction between the *o*-substituted phenolic and the side chain keto groups, as another example of the effect of chelation on chemical reactivity.[9,10] This chelation would produce an effect of a considerably greater order than the lowered bromination rate of propiophenone and other higher homologs of acetophenone found by Evans,[11] which he explained on the basis of an interaction of a β-hydrogen atom with the keto group.[12] The coördination so postulated involves a hydrogen atom bound to carbon and would exercise a relatively small effect and, in fact, Evans and Gordon[13] state that "the ketones in their normal condition are not regarded as having a hydrogen bond," but that "the hydrogen bond is formed simultaneously with the approach of the attacking ion, and is therefore present in the transition complex." The situation is quite different in the ketones under study in our work, which are very probably chelated in their ground states.

The key steps in the acid-catalyzed bromination of ketones are generally considered to be[14]

$$RCOCH_3 \xrightarrow[(1)]{H^+} R{-}\overset{\overset{+OH}{\|}}{C}{-}CH_3 \xrightarrow[(2)]{A^-} R{-}\overset{\overset{OH}{|}}{C}{=}CH_2 + HA$$

Chelation would oppose the formation of the intermediate ion and lower the bromination rate.[15] The added H^+ acts to break up the chelate, favors the formation of the ion and allows the bromination to proceed. The successful bromination of III in refluxing acetic acid[8] conforms with the chelation postulate, inasmuch as at elevated temperatures the more labile chelate and the greater dissociation of acetic acid should be favorable factors for reaction.

The bromination behavior of the methyl ethers and acetates of 2-acetylnaphthol (I) and 4-bromo-2-acetylnaphthol (III), respectively, in which chelation is absent, lends further support to the chelation theory. None of these compounds requires added acid for their α-bromination. The methyl ether VI with an unsubstituted 4-nuclear position undergoes ring bromination with the first mole of bromine, while the corresponding acetate X is brominated in the side chain.[16] This is consistent with the relative nuclear-activating properties of the methoxy and acetoxy groups in substitution reactions. The methoxy group, a moderately powerful *o,p*-activating group promotes 4-bromination in VI, whereas the presence of the acetoxy group in X results in reaction in the side chain,[17] as occurs with 2-acetonaphthone[18] (XIV).



XIV

Further bromination of previously isolated methyl ether VII contrasts strikingly with that of the corresponding free naphthol III, in that α-bromination will take place readily at room temperature, requiring no added acid. The acetate XI is also side-chain brominated to yield α,4-dibromo-2-acetylnaphthyl acetate (XII) without added acid, as would be expected according to this theory.

The sum of this experimental evidence indicates that the resistance to α-bromination of the free naphthol can be attributed to chelation. Consequently this behavior is expected of other chelated compounds of this general type, and the rate of reaction should be a measure of the stability of the chelates. A substituent in the ring should have discernible influence on the stability of the chelate, and a correlation between the effect of the substituent on that stability and its electronic properties in other reactions is of interest. We should expect that the 4-nitro would form a more stable chelate than the 4-bromo derivative chiefly on the basis of the greater electron-withdrawal power of the former group. Qualitatively we have evidence that this is true, for the bromo compound is brominated in refluxing acetic acid whereas the nitro compound is not.[4] We have prepared a series of 4-substituted-2-acetylnaphthol derivatives for rate studies, and will report our results subsequently.

(9) H. B. Watson, "Modern Theories of Organic Chemistry," Oxford University Press, London, England, 1941, pp. 241–254.

(10) Dr. H. P. Kung of this Department originally suggested the chelation hypothesis, but agreed that the explanation seemed inadequate, for at the time it was supposed that the resistance to bromination was unique for the nitro compound; it was not then known that the bromo derivative behaves similarly.

(11) D. P. Evans, *J. Chem. Soc.*, 785 (1936).

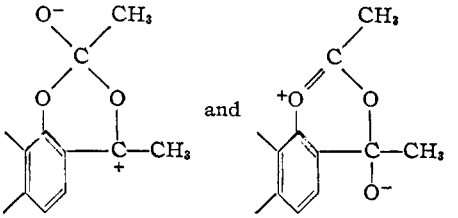
(12) E. E. Ayling (*ibid.*, 1014 (1938)), however, gives an alternate explanation in terms of a field effect.

(13) D. P. Evans and J. J. Gordon, *ibid.*, 1434 (1938).

(14) L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, p. 232.

(15) In alternate terms, chelation would increase the energy of activation (E) and presumably decrease the probability factor (P) in the reaction kinetics equation, $k = PZe^{-E/RT}$ for step 1 of the reaction.

(16) However, for smooth α-bromination of the acetates X and XI a temperature of 50° is needed. At room temperature a considerably longer reaction time is required, and the product is a mixture of the desired α-bromoacetate and III. It is conceivable that there are contributions from cyclic forms such as



(or their equivalents), resembling the structures postulated by S. Winstein and co-workers (THIS JOURNAL, **64**, 2780 (1942) and later papers), and which would give the acetate a higher activation energy.

(17) The existence of cyclic forms suggested in footnote 16 would lower the ring activation of the acetoxy group even more.

(18) C. B. Radcliffe, I. R. Sherwood and W. F. Short, *J. Chem. Soc.*, 2293 (1931).

Acknowledgment.—We are indebted to our colleagues of the Department of Chemistry of Lingnan University for valuable discussions and suggestions, and to Dr. W. G. Dauben of the University of California for his interest.

Experimental

The brominations were carried out by addition of measured volumes of 10% solutions (*e.g.*, 10 g. of bromine in 100 ml. of total solution) of bromine in one of the three solvents: chloroform, carbon tetrachloride and glacial acetic acid. These brominating solutions are referred to in the descriptions simply as bromine–solvent solutions.

Where a compound was obtained by more than one method, the identity of each of the subsequent products was further confirmed by a mixed melting point determination with the product described under a in that section.

All melting points are uncorrected.

2-ACETYLNAPHTHOL (I) was prepared by the method of Friedlander,[19] m.p. 102–103°.

Methyl ether VI was prepared according to Fries,[20] m.p. 47–49°.

Acetate X, previously prepared by Hantzsch[21] and Ullmann[22] by different methods both requiring elevated temperatures, was obtained easily in superior yield and quality as follows: 2-Acetylnaphthol (I), 3.72 g., was mixed with 25 ml. of acetic anhydride and 3 ml. of anhydrous pyridine, shaken to dissolve and allowed to stand for 18 hours at 25°. The solid which precipitated when the solution was stirred into ice-water, was filtered, washed with dilute HCl and recrystallized from commercial ethanol to give, in two crops, 4.12 g. (90%) of colorless, glistening, thin hexagonal prisms of m.p. 103–103.7° (Hantzch,[21] 107.5°; Ullmann,[22] 103.5°).

2-BROMOACETYLNAPHTHOL (V) was obtained by hydrolysis of its acetate XIII with 42% HBr in alcoholic solution, and crystallized as long yellow-green lathes, in quantitative yield, melting at 130.5–131.5° (Ullmann,[22] 124.5°).

Anal. Calcd. for $C_{12}H_9O_2Br$: C, 54.36; H, 3.42; Br, 30.15. Found: C, 54.45; H, 3.65; Br, 30.05.

Methyl ether IX was prepared from V by reaction with diazomethane in ethereal solution, as colorless needles when crystallized from dilute ethanol, m.p. 82–83°.

Anal. Calcd. for $C_{13}H_{11}O_2Br$: C, 55.93; H, 3.97. Found: C, 56.35; H, 4.14.

Acetate XIII (a).—To 2.28 g. of 2-acetylnaphthyl acetate (X), dissolved in 100 ml. of CCl_4, and maintained at a temperature of 50° with a Glascol heater, was added in portions of 0.5 ml., 16 ml. of bromine–CCl_4 solution, waiting for decolorization of the bromine after each addition. The solvent was removed by suction, and the resulting oil was dissolved in 15 ml. of benzene. On addition of 100 ml. of Skellysolve B and refrigerating, 2.1 g. (70%) of colorless, poorly-shaped crystals separated which melted at 78–81°, but after crystallization from Skellysolve B melted at 83–84° (Ullmann,[22] 77–87°). The product seems to be best purified through the free naphthol V.

(b).—By acetylation of the naphthol V with acetic anhydride and a catalytic amount of pyridine, the product crystallized from dilute ethanol in colorless plates, m.p. 86.5–87°.

4-BROMO-2-ACETYLNAPHTHOL (III), prepared by the method of Torrey and Brewster,[23] was long yellow-green needles, m.p. 126–127°.

Methyl Ether VII.—(a) From 2-acetylnaphthyl methyl ether (VI): Two-tenths gram of VI dissolved in 2 ml. of CCl_4, and 1.6 ml. of bromine–CCl_4 were mixed. Reaction was instantaneous and HBr was evolved. The resulting oil, after removal of solvent, was crystallized from aqueous alcohol to give colorless needles, m.p. 72–73°, 0.18 g. (65%).

Anal. Calcd. for $C_{13}H_{11}O_2Br$: C, 55.93; H, 3.97. Found: C, 56.33; H, 4.09.

(b) III was methylated by dimethyl sulfate in NaOH solution to yield a product which melted at 72–73°.

Acetate XI was prepared by acetylation of III with acetic anhydride in pyridine, yielding colorless needles of melting point 106–107° (Hantzsch,[21] 107°).

α,4-DIBROMO-2-ACETYLNAPHTHOL (IV).—(a) From I according to Akram, Desai and Kamal[6] by reaction with excess bromine in chloroform, giving short yellow needles, m.p. 149.5–150°.

(b) From 4-bromo-2-acetylnaphthol (III) at elevated temperature: When III (0.65 g.), dissolved in 6 ml. of acetic acid was mixed with 4 ml. of bromine–HOAc, and refluxed for 1 hour, short yellow needles separated on cooling, m.p. 149–150°, yield 0.62 g. (72%).

(c) From III in chloroform and added acid: To III (0.26 g.) dissolved in 3 ml. of $CHCl_3$ was added 1.6 ml. of bromine–$CHCl_3$. After the solution was saturated with HBr, the bromine color was discharged in 3 hours at room temperature. Recrystallized from ethanol, the product melted at 149–150°, 0.20 g. (58%).

(d) From 2-bromoacetylnaphthol (V): 0.26 g., in 3 ml. of CCl_4 and 1.6 ml. of bromine–CCl_4 in an instantaneous reaction. The product crystallized slowly yielding 0.28 g. (81%) of short yellow needles, m.p. 149–150°.

(e) From α,4-dibromo-2-acetylnaphthyl acetate (XII), by hydrolysis with 6 *N* aqueous HBr, in alcoholic solution, to give yellow needles, m.p. 149–150°.

Methyl Ether VIII.—(a) From 4-bromo-2-acetylnaphthyl methyl ether (VII): When VII (0.14 g.) dissolved in 2 ml. of CCl_4 was mixed with 0.8 ml. of bromine–CCl_4, reaction took place immediately and a solid separated. Recrystallized from alcohol as colorless needles it weighed 0.12 g. (67%), m.p. 143–144°.

Anal. Calcd. for $C_{13}H_{10}O_2Br_2$: C, 43.61; H, 2.72; Br, 44.62. Found: C, 43.65; H, 2.97; Br, 45.27.

(b) From α,4-dibromo-2-acetylnaphthol (IV) by reaction with diazomethane in ethereal solution, giving wooly needles, which, after crystallization from alcohol melted 143.5–144°.

(c) From 2-bromoacetylnaphthyl methyl ether (IX): Bromination in acetic acid was instantaneous and needles separated which after crystallization melted 143–144°.

Acetate XII.—(a) From 4-bromo-2-acetylnaphthyl acetate (XI): To XI (0.30 g.) dissolved in 6 ml. of CCl_4 was added 1.6 ml. of bromine–CCl_4 at 50°. After decolorization of the bromine color, solvent was removed and the residue was crystallized from alcohol to give 0.24 g. (62%) of colorless needles, m.p. 135–136°.

Anal. Calcd. for $C_{14}H_{10}O_3Br_2$: C, 43.55; H, 2.61. Found: C, 43.73; H, 2.50.

(b) From α,4-dibromo-2-acetylnaphthol (IV) by treatment with acetic anhydride and pyridine, colorless needles were obtained after final crystallization from alcohol, m.p. 135–136°.

CANTON, CHINA

(19) F. Friedlander, *Ber.*, **28**, 1946 (1895).

(20) K. Fries, *ibid.*, **54**, 711 (1921).

(21) A. Hantzsch, *ibid.*, **39**, 3096 (1906).

(22) G. Ullmann, *ibid.*, **30**, 1467 (1897).

(23) H. A. Torrey and C. N. Brewster, THIS JOURNAL, **31**, 322 (1909).