Tetrahedron. Vol. 25, pp. 4357 to 4362. Pergamon Press 1969. Printed in Great Britain

DIRECTIVE EFFECTS IN BENZYLIC HYDROGEN ATOM ABSTRACTION—I

RADICAL BROMINATION BY 4-BROMO-2,4,6-TRI-TERT-BUTYL-2,5-CYCLOHEXADIENONE

K. H. Lee

Department of Chemistry, University of Malaya, Kuala Lumpur, Malaysia

(*Received in Japan* 31 *March* 1969; *Received in the UK for publication* 13 *May* 1969)

Abstract—Relative reactivity values in benzylic bromination of alkylbenzenes and benzyl type ethers by 4-bromo-2,4,6-tri-t-butyl-2,5-cyclohexadienone (BTBC) have been measured by intermolecular competition with benzhydryl methyl ether as reference standard at 40° in CCl_4 and are compared with results found for N-bromosuccinimide (NBS). The reactivity values for *m*- and *p*-substituted $XC_6H_4CH_2OMe$ relative to this standard toward BTBC show a polar effect with $\rho = -0.43$ correlated by σ^+ constants; a result identical to that found for NBS ($\rho = -0.45$) carried out in CH_2Cl_2. The identical ρ-values and other data support the suggestion that atomic Br is the main H-abstracting species in benzylic bromination using BTBC.

In HYDROGEN atom abstraction reactions from hydrocarbons[1] and α-substituted toluenes[2] atomic Br is known to be one of the most selective radicals. Free-radical bromination by molecular bromine tends to be complicated by an equivalent amount of hydrogen bromide formed and high HBr/Br_2 ratio.[3-5] On the other hand in bromination by N-bromosuccinimide the hydrogen bromide formed reacts rapidly[5] with the reagent to release molecular bromine and thus maintains a low concentration of hydrogen bromide. However, NBS is rather insoluble in most inert solvents, and, except in methylene chloride,[6] most of the reactions have been carried out under heterogeneous systems. The use of 4-bromo-2,4,6-tri-t-butyl-2,5-cyclohexadienone (BTBC) as an efficient and highly selective brominating agent in solution is now reported.

RESULTS AND DISCUSSION

The reaction of 4-bromo-2,4,6-tri-t-butyl-2,5-cyclohexadienone with relative reactive substrates such as ethers and ethylbenzenes can be initiated photochemically or thermally. In a reaction of benzyl methyl ether with BTBC initiated photochemically and carried out to complete consumption of the brominating agent (checked by IR at 1661 cm^{-1}) the only phenolic product was 2,4,6-tri-t-butylphenol, identified by IR and gas chromatography, there being no isomerization of the phenolic product as noted by Kennedy and Ingold[7] in reactions of some polyhalogenated 4-bromo-2,5-cyclohexadienone with alkylbenzenes. The only product from the ether was the α-bromobenzyl methyl ether which on treatment with aqueous sodium carbonate yielded benzaldehyde identified by IR and gas chromatography. Bromination of alkylbenzenes by similar reagents studied by Kennedy and Ingold[7] was also found to occur only at the benzylic position.

The results of photochemically initiated reactions of BTBC with a number of substrates in CCl_4 at 40° are presented in Table 1. With ethers the reaction time is relatively short and comparable to those found in bromination by bromotrichloromethane but somewhat longer than those observed in reactions of N-bromosuccinimide.[2] The product from *p*-chlorobenzyl methyl ether was the corresponding α-bromobenzyl methyl ether[8] which on treatment with aqueous Na_2CO_3 gave *p*-chlorobenzaldehyde. Benzaldehyde and benzophenone were formed from dibenzyl ether and benzhydryl methyl ether, respectively. With benzhydryl benzyl ether the reaction yielded a mixture of benzaldehyde and benzophenone. Under similar conditions benzaldehyde was found not to react with BTBC.

When a solution of ethylbenzene and BTBC in CCl_4 was irradiated the yellow solution turned deep green indicating that the blue 2,4,6-tri-t-butylphenoxy radical was formed. This radical has been shown[9] by ESR spectroscopy to be formed from BTBC at 50–80°. The green colour fades with time as the concentration of BTBC decreases. Similar observations in the presence of *p*-diethylbenzene were also noted. The corresponding α-bromoethylbenzenes were identified by comparison of the difference IR spectra of the reaction solution with authentic samples. All the products reported in Table 1 were estimated by IR spectrophotometry. Excellent material balance between unconsumed BTBC and 2,4,6-tri-t-butylphenol was found and the ratios of products from the substrates to the phenol were generally 96 to 102 mole %.

The highly selective nature of BTBC as a brominating agent is seen from Table 2 in which the results of competitive experiments are compared with those obtained at 40° for NBS bromination in CH_2Cl_2 solution. For comparison some of the NBS results previously reported[2b] at 80° in CCl_4 have been recalculated by the usual relative rate equation[10] and included in the Table. The reactivity values relative to benzhydryl methyl ether, K/K_{BHE}, for the NBS series are higher at 40°. This is to be expected as selectivity by a radical increases as the temperature is lowered.[11, 12] At 40° the K/K_{BHE} values for ethers are somewhat similar for the two reagents, BTBC and NBS. On the other hand the values for ethylbenzenes and cumenes differed for the two reagents, the values for BTBC being higher by a factor of 1·9 than those for NBS in the case of ethylbenzene and *p*-diethylbenzene. Kennedy and Ingold[7] have reported some nearly identical relative reactivity values for NBS and for the substituted 4-bromo-cyclohexadienones but some differing values were also found.

The similar ρ-values found for the substituent effects in the bromination of substituted toluenes by both molecular bromine and N-bromoimides have been used by Pearson and Martin[5] and also by Walling[4b] as substantive evidence for H-abstraction by atomic Br when the latter reagents were employed. The relative reactivity of *m*- and *p*-substituted benzyl methyl ethers towards atomic Br (from NBS) in CCl_4 at 80° have been found[13] to obey the Hammett equation with ρ-value of $-0{\cdot}35$ correlated by the σ^+ constants of Brown and Okamoto.[14] The reactivity of these ethers relative to benzhydryl methyl ether, K/K_{BHE}, towards BTBC in CCl_4 and NBS in CH_2Cl_2 have now been measured at 40° by IR spectrophotometry, and the results are presented in Table 3. The amount of NBS used was 40 mole % of the total substrates and in the BTBC series the irradiation times were 0·5 to 1 hr during which time 30–40 mole % of the substrates had reacted. Except for the *p*-MeO value which is higher for the NBS series, the effect of the substituents, as seen from the K/K_0 values in Table 3, tends to be similar. It was found that in bromination of substituted toluenes by molecular bromine and by a number of N-bromoimides[4, 5] the reactivity value of *p*-methoxytoluene relative to toluene varied from 5·7 to 12·6. Also the pyrolysis of BTBC in anisole gave *p*-bromo-anisole.[15] For these reasons the *p*-MeO results in the present work have been omitted from the correlation by the Hammett equation. Calculations by standard statistical methods[16] show that for the NBS series the results are better correlated by the σ^+ constants of Brown and Okamoto[14] with $\rho = -0{\cdot}45 \pm 0{\cdot}03$ ($r = 0{\cdot}984$) than by the σ constants of McDaniel and Brown[17] ($\rho = -0{\cdot}50 \pm 0{\cdot}03$; $r = 0{\cdot}968$). Almost identical results were found for the BTBC series, namely $\rho = -0{\cdot}43\,\sigma^+ \pm 0{\cdot}03$ ($r = 0{\cdot}995$) and $\rho = -0{\cdot}48\,\sigma \pm 0{\cdot}04$ ($r = 0{\cdot}988$). The ρ-value of $-0{\cdot}45$ at 40° for the NBS series is of the correct order of magnitude when compared with the previously reported value[13] of $-0{\cdot}35$ at 80°, both well correlated by the σ^+ constants typical for atomic Br.[2]

The Goldfinger mechanism of NBS bromination as applied to alkylbenzenes has been established from the nearly identical deuterium-isotope effects[3] found for α-d_1-toluenes in reactions with NBS and molecular bromine, and from the identical ρ-values obtained for the two reagents in the bromination of substituted toluenes.[5] These data have been interpreted[5] in terms of a chain mechanism involving atomic Br as the H-abstracting species. The similar ρ-values found for the substituted benzyl methyl ethers towards NBS and BTBC provide supporting evidence to the suggestion by Kennedy and Ingold[7] that atomic Br is the H-abstracting species in side-chain bromination by substituted 4-bromo-cyclohexadienone.

TABLE 1. PRODUCT STUDIES OF BTBC[a] WITH ETHERS AND HYDROCARBONS[b]

Substrates mmoles	BTBC,[a] mmoles		Irradiation time, mins	Products,[c] mmoles	
	Initial	Final		2,4,6-$Bu^tC_6H_2OH$	
$PhCH_2OMe$, 10·0	10·0	0·65	60	9·38	PhCHO, 9·22 (0·91)[d]
p-$ClC_6H_4CH_2OMe$, 10·0	7·0	0·61	45	6·27	*p*-ClC_6H_4CHO, 6·30 (0·85)[d]
Ph_2CHOMe, 10·0	7·0	1·44	45	5·58	Ph_2CO, 5·40
$(PhCH_2)_2O$, 10·0	7·0	2·36	30	4·36	PhCHO, 4·20
$PhCH_2OCHPh_2$, 10·0	7·0	2·33	45	4·64	PhCHO, 2·70; Ph_2CO, 2·00
PhEt, 30·0	15·0	0·40	360	14·24	$PhCHBrCH_3$, 14·1
p-EtC_6H_4Et, 28·0	14·0	3·63	300	9·96	*p*-$EtC_6H_4CHBrCH_3$, 9·9

[a] BTBC = 4-Bromo-2,4,6-tri-t-butyl-2,5-cyclohexadienone

[b] Reactions carried out under N_2 in CCl_4 (25 ml) at 40° by irradiation with a 275-Watt G.E. sunlamp.

[c] Products analysed by infrared spectrophotometry.

[d] Estimated before washing with aqueous Na_2CO_3.

EXPERIMENTAL

Materials. 4-Bromo-2,4,6-tri-t-butyl-2,5-cyclohexadienone was prepared[9] in almost quantitative yield and after recrystallization from light petroleum the product had m.p. 80–81° and ν_{max} (CCl_4) at 1661 and 1639 cm^{-1} (lit.[18] m.p. 80·5–81·5°). α-Bromo-*p*-diethylbenzene, b.p. 80–81 /0·2 mm, n_D^{25} 1·5474, was prepared from N-bromosuccinimide and *p*-diethylbenzene, and had a Br analysis[10] of 99·5%. The following

TABLE 2. SELECTIVITY[a] IN BROMINATION BY BTBC AND NBS

Substrates	BTBC CCl_4, 40°	K/K_{BHE}[b] NBS CH_2Cl_2, 40°	NBS CCl_4, 80°
$PhCH_2OMe$	1·40 ± 0·01	1·58 ± 0·01	1·08 ± 0·04
p-$ClC_6H_4CH_2OMe$	1·20 ± 0·02	1·38 ± 0·04	0·98 ± 0·02
$PhCH_2OCH_2Ph$	1·86 ± 0·01	2·04 ± 0·02	1·59 ± 0·04
PhEt	1·10 ± 0·01	0·58 ± 0·02	0·29 ± 0·01
p-EtC_6H_4Et	4·03 ± 0·05	2·14 ± 0·03	1·09 ± 0·02
$PhCHMe_2$	0·73 ± 0·02	0·57 ± 0·01	0·50 ± 0·01
p-$MeC_6H_4CHMe_2$	1·29 ± 0·03	1·14 ± 0·02	0·75 ± 0·02

[a] Per molecule relative to P_2CHOMe.

[b] based on analysis of products and Ph_2CO.

TABLE 3. SUBSTITUENT EFFECTS IN BROMINATION OF X—$C_6H_4CH_2OMe$ BY BTBC AND NBS AT 40°

X in X—$C_6H_4CH_2OMe$	Relative reactivity values BTBC (CCl_4) K/K_{BHE}[a]	K/K_0	NBS (CH_2Cl_2) K/K_{BHE}[a]	K/K_0
p-MeO	1·94 ± 0·09	1·39	4·30 ± 0·22	2·72
p-Me	1·76 ± 0·05	1·26	2·34 ± 0·13	1·48
p-Bu^t	1·80 ± 0·07	1·29	2·11 ± 0·08	1·34
m-Me	1·50 ± 0·04	1·07	1·66 ± 0·04	1·05
H	1·40 ± 0·01	1·00	1·58 ± 0·01	1·00
p-Cl	1·20 ± 0·02	0·86	1·38 ± 0·04	0·87
p-Br	1·18 ± 0·01	0·84	1·25 ± 0·03	0·79
m-Cl	0·94 ± 0·01	0·66	1·12 ± 0·01	0·71
m-Br	0·93 ± 0·01	0·65	1·08 ± 0·01	0·68

σ^+ correlation[b] $\rho = -0{\cdot}43 \pm 0{\cdot}03$ ($r = 0{\cdot}995$); $\rho = -0{\cdot}45 \pm 0{\cdot}03$ ($r = 0{\cdot}984$)

σ correlation[b] $\rho = -0{\cdot}48 \pm 0{\cdot}04$ ($r = 0{\cdot}988$); $\rho = -0{\cdot}50 \pm 0{\cdot}03$ ($r = 0{\cdot}968$)

[a] Based on X—C_6H_4CHO and $Ph_2C{=}O$ products, the latter from the standard substrate Ph_2CHOMe, by the infrared method.

[b] Omitting the p-MeO values (see text).

X·$C_6H_4CH_2OMe$ were prepared (Method B) from the corresponding benzyl bromides and purified as previously described[8,13] (substituent, yield, b.p./35 mm and n_D^{25}): 3-*Me*, 92%, 95–96°, 1·5020 (lit.[19] b.p. 85–86°/23 mm); 3-*Br*, 81%, 127–128°, 1·5440 (lit.[20] b.p. 116–117·5°/21 mm); 4-*Br*, 82%, 127–128°, 1·5438 (lit.[20] b.p. 124–125°/30 mm). The other substituted benzyl methyl ethers were prepared and purified in the usual manner.[8,13] CH_2Cl_2 was purified as described.[6] All other materials used were purified in the manner described.[2,6,8]

Reaction of benzyl methyl ether with BTBC. A soln of benzyl methyl ether (10 mmoles) and BTBC (7 mmoles) in CCl_4 (ca. 25 ml), in a pyrex flask with N_2 inlet, coiled condenser and drying tube, was heated at 40° in a thermostated water bath after replacing the atmosphere with N_2. The soln was maintained under a slow stream of N_2 and irradiated with a 275-Watt G.E. sunlamp for 3 hr. After washing the soln with sat Na_2CO_3aq and drying over $CaCl_2$ the IR spectrum showed strong phenolic OH (3645 cm^{-1}) and strong $>$C=O (1709 cm^{-1}) peaks and no BTBC absorption at 1661 cm^{-1} The only phenolic product was 2,4,6-tri-t-butylphenol, identified by retention time on a SE-30 on Chromosorb W column at 170° and a QF-1 on Chromosorb W column at 155° using an Aerograph 1520 gas chromatograph instrument. Unconsumed benzyl methyl ether, and benzaldehyde were resolved and identified by retention time on the QF-column at 100°.

Product studies for reactions of BTBC with benzyl ethers and alkylbenzenes. The reaction of BTBC with a number of substrates were carried out in CCl_4 at 40° as described above and the results are given in Table 1. With ethers the reaction soln was washed with sat Na_2CO_3aq and dried over $CaCl_2$. IR analyses were performed as previously described[10] using a Hilger–Watts Infrascan instrument. For estimation of benzophenone the 1275 cm^{-1} peak was used with compensating solns of 2,4,6-tri-t-butylphenol in the reference beam as the phenol absorbs weakly at 1275 cm^{-1} peak. Unconsumed BTBC was estimated using the 1661 and 1639 cm^{-1} peaks. In presence of benzophenone BTBC was determined on the 1639 cm^{-1} peak with a compensating soln of the ketone in the reference beam. Estimation of 2,4,6-tri-t-butylphenol was carried out using the 3645 cm^{-1} peak. In reactions involving ethylbenzene and *p*-diethylbenzene the spectra of the soln after reaction, compensated for unreacted hydrocarbon. BTBC and the phenol, were identical to the spectra of the corresponding authentic α-bromides. The α-bromides were estimated at 1178 and 1176 cm^{-1}, respectively, using the compensating technique after having determined the phenol.

Procedure for competitive brominations with BTBC. Solns containing equimolar amounts (7 to 10 mmoles) of the substrate, benzhydryl methyl ether (standard compound) and BTBC in CCl_4 (25 ml) at 40° were irradiated as described above until 30 to 40% of the competing substrates had reacted. With ethers as competing substrates the relative reactivity values were based on infrared determination of benzaldehydes and benzophenone (1275 cm^{-1} peak) from aliquots of the reaction soln suitably diluted, washed with sat Na_2CO_3aq and dried. In experiments in which an alkylbenzene was a competing substrate the amount of the corresponding α-bromide was assumed to be the difference between the amounts of 2,4,6-tri-t-butylphenol and benzophenone (compensating technique at 1275 cm^{-1}) found. The results given in Tables 2 and 3 were calculated by the usual relative rate equation.[10] All the results are the mean of triplicate experiments.

Procedure for competitive bromination with N-*bromosuccinimide.* For reactions in CCl_4 at 80° the previously adopted procedure was used.[2] When CH_2Cl_2 was used as solvent 4 mmoles of NBS and 5 mmoles each of the two substrates in CH_2Cl_2 (25 ml) were illuminated with a 150-Watt tungsten lamp at 40° under N_2. For IR estimation of aldehydes and benzophenone aliquots of the reaction soln was suitably diluted, washed with sat Na_2CO_3aq, and dried ($CaCl_2$). For reactions in which an alkylbenzene was one of the competing substrates, the flask was heated at 40° for a further 30 min after which aliquots of the cooled soln were evacuated at room temp and 50 mm pressure followed by estimation of the α-bromo-alkylbenzene as described before[10] Benzophenone was determined as above. All the results given in Tables 2 and 3 are the average of triplicate experiments and the material balance based on N-bromosuccinimide are usually 97 to 103%.

Acknowledgement—Valuable technical assistance in connection with this investigation and the following publications by Mr. T. B. Lim is gratefully acknowledged.

REFERENCES

[1] G. C. Fettis, J. H. Knox and A. F. Trotman-Dickenson; *J. Chem. Soc.* 4177 (1960).

[2] [a] R. L. Huang and K. H. Lee, *Ibid.* (C), 932 (1966);
[b] R. L. Huang and K. H. Lee, *Ibid.* (C), 935 (1966);
[c] E. P. Chang, R. L. Huang and K. H. Lee, *Ibid.* in press.

[3] K. B. Wiberg and L. H. Slaugh, *J. Am. Chem. Soc.* **80**, 3033 (1958).

[4] [a] C. Walling, A. L. Rieger and D. D. Tanner, *Ibid.* **85**, 3129 (1963);
[b] C. Walling and A. L. Rieger, *Ibid.* **85**, 3134 (1963).

[5] R. E. Pearson and J. C. Martin, *Ibid.* **85**, 3142 (1963).

[6] G. A. Russell and K. M. Desmond, *Ibid.* **85**, 3139 (1963).

[7] B. R. Kennedy and K. U. Ingold, *Canad. J. Chem.* **45**, 2632 (1967).

[8] R. L. Huang and K. H. Lee, *J. Chem. Soc.* 5957 (1964).

[9] V. D. Pokhodenko and N. N. Kalibabchuk, *Zh. Organ. Khim.* **2**, 1397 (1966).

[10] K. H. Lee, *Tetrahedron* **24**, 4793 (1968).

[11] K. H. Lee, *Ibid.* unpublished results.

[12] G. A. Russell, *J. Am. Chem. Soc.* **80**, 4987, 4996, 5002 (1958).

[13] R. L. Huang and K. H. Lee, *J. Chem. Soc.* 5963 (1964).

[14] H. C. Brown and Y. Okamoto, *J. Am. Chem. Soc.* **80**, 4979 (1958).

[15] M. Tsubota, *Nippon Kagaku Zasshi* **89**, 597 (1968).

[16] H. H. Jaffe, *Chem. Rev.* **53**, 191 (1953).

[17] D. H. McDaniel and H. C. Brown, *J. Org. Chem.* **23**, 420 (1958).

[18] C. D. Cook and R. C. Woodworth, *J. Am. Chem. Soc.* **75**, 6242 (1953).

[19] Y. Ogata and Y. Sawaki, *Ibid.* **88**, 5832 (1966).

[20] R. E. Lovins, L. J. Andrews and R. M. Keefer, *J. Org. Chem.* **30**, 1577 (1965).