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Photobromination of Side-Chain Methyl Groups on Arenes with *N*-Bromosuccinimide —Convenient and Selective Syntheses of Bis(bromomethyl)- and (Bromomethyl)methylarenes—

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Photobromination of side-chain methyl groups on arenes with *N*-bromosuccinimide (**NBS**) was investigated. Visible light irradiation in benzene solvent was extremely effective in increasing the selectivity of the reaction and the efficiency for product purification. The photobromination of 1,4-, 1,8-, 2,3-, and 2,6-dimethylnaphthalenes, 4,4′-dimethylbiphenyl, and *p*-xylene with 2.2 mol equivalents of **NBS** quantitatively afforded the corresponding bis(bromomethyl)arenes, respectively. The (bromomethyl)methylarenes were also obtained in good yields in the photobromination reactions of the above dimethylarenes with 1.1 mol equivalents of **NBS**.

Synthesis of benzylic bromides has been extensively investigated[1] since Hoï reported the bromination of 2-methylnaphthalene with **NBS** in 1944.[2] However, thermal bromination of methyl groups on arenes with **NBS** is tedious[3] and the yields of bis(bromomethyl)arenes are often modest even with radical initiators such as benzoyl peroxide and 2,2′-azobis(methylpropanenitrile).[4,5]

Photothermal bromination reactions with molecular bromine have been also reported, but the yields of 2-(bromomethyl)naphthalene[6] and 1,2-bis(bromomethyl)benzene[7] are only around 50%. These types of reactions cannot be used as a convenient synthetic tool since they involve the too troublesome reaction procedures and work-ups of the reaction products.

These unsatisfactory results and the high synthetic potentials of bis(bromomethyl)arenes as precursors of aromatic dialdehydes and quinodimethanes[5,8] urged us to investigate photochemical bromination of dimethylarenes with **NBS**.

We have found that one or two side-chain methyl groups on dimethylarenes can be photobrominated selectively with visible light and appropriate amounts of **NBS**, and that the benzylic bromides can be facilely prepared with benzene solvent.

Experimental

Instrumental. The GC analyses were carried out on a Shimadzu GC-9A-FID apparatus with a column of 5% OV 17 on Chromosorb W (DMCS). The GC-MS analyses were carried out on a Shimadzu QP-1000 apparatus (EI, 20 eV) with a glass column of 1.5% OV 17 on Shimalite W (DMCS). The IR spectra were taken on a Shimadzu IR-420 Infrared Spectrophotometer. The NMR spectra were obtained on a JNM GX 400 FT NMR Spectrometer (400 MHz). The melting points were measured by means of a Yazawa hot plate and are uncorrected.

Materials. All the organic reagents were commercially purchased. Benzene, decalin, *p*-xylene, 1-methylnaphthalene, and 1,4-dimethylnaphthalene (**1,4-DMN**) were stirred with aq 5% H_2SO_4, washed with water, aq 5% NaOH and water, dried over $CaCl_2$ and distilled over CaH_2. 2-Methylnaphthalene, **1,8-**, **2,3-**, and **2,6-DMN's**, and 4,4′-dimethylbiphenyl (**4,4′-DMBP**) were recrystallized from ethanol twice. The purities of the above dimethylarenes were higher than 99% by GC. **NBS** (reagent special grade) was used without further purification. Acetone and acetonitrile were dried over P_2O_5. Chloroform and carbon tetrachloride were washed with water and dried over $CaCl_2$.

Table 1. Physical Constants and Spectroscopic Data of Bis(bromomethyl)arenes

Compd	mp/°C	^{1}H NMR/δ in ppm		IR/cm^{-1}
		Ar-CH_2Br	Aromatic H	
1,4-BBMN	137.2—137.7	4.33 (4H, s)	6.83—7.93 (6H, m)	1204, 764, 756
1,8-BBMN	126.2—126.8	5.30 (4H, s)	7.45—7.88 (6H, m)	1208, 837, 816, 773, 766
2,3-BBMN	125.1—125.7	4.50 (4H, s)	7.17—7.38 (6H, m)	1204, 891, 753
2,6-BBMN	146.2—146.7	4.10 (4H, s)	7.18—7.37 (6H, m)	1208, 896, 827
4,4′-BBMBP	152.3—153.0	4.53 (4H, s)	7.46 (4H, d, J=8.54 Hz) 7.54 (4H, d, J=8.54 Hz)	1205, 1100, 822, 709
1,4-BBMBZ	144.8—145.4	4.50 (4H, s)	7.39 (4H, s)	1227, 1198, 851, 753

BBMN=bis(bromomethyl)naphthalene, **4,4′-BBMBP**=4,4′-bis(bromomethyl)biphenyl, **1,4-BBMBZ**=1,4-bis(bromomethyl)benzene.

Photobromination of Dimethylarenes. A solution of a dimethylarene and **NBS** was irradiated at room temperature with a 200-W super-high-pressure mercury arc (Shimadzu BAUSCH & LOMB SP-200) directly or through a Toshiba glass filter L-39 ($\lambda_{\mathrm{irrad}} \geqq 390$ nm) while nitrogen was bubbled through.

Product Analysis. After the reaction, succinimide was removed by suction filtration from the condensed reaction mixture. All the bis(bromomethyl)arenes and the (bromomethyl)methylarenes could be identified by GC-MS.

Table 1 summarizes the physical constants and spectroscopic data of the bis(bromomethyl)arenes purified by silica-gel column chromatography or TLC (hexane–ether). As for the other products, some of their physical constants and spectral data are shown below.

1-(Bromomethyl)naphthalene: MS *m*/*z* 222 (6.5), 220 (6.5, M^+), 141 (100).

2-(Bromomethyl)naphthalene: MS *m*/*z* 222 (7.9), 220 (7.9, M^+), 141 (100).

1-(Chloromethyl)naphthalene: MS *m*/*z* 178 (17), 176 (50, M^+), 141 (100).

1-(2,2,2-Trichloroethyl)naphthalene: MS *m*/*z* 260 (7.0), 258 (7.0, M^+), 141 (100).

1-Bromomethyl-4-methylnaphthalene (**1,4-BMMN**): MS *m*/*z* 236 (8.7), 234 (8.7, M^+), 155 (100).

1-Bromomethyl-8-methylnaphthalene (**1,8-BMMN**): MS *m*/*z* 236 (9.1), 234 (8.2, M^+), 155 (100).

2-Bromomethyl-3-methylnaphthalene (**2,3-BMMN**): MS *m*/*z* 236 (16), 234 (17, M^+), 155 (100).

2-Bromomethyl-6-methylnaphthalene (**2,6-BMMN**): Mp 81.2—81.8 °C; ^{1}H NMR ($CDCl_3$) δ=2.50 (3H, s), 4.65 (2H, s), 7.31—7.78 (6H, m); IR 1378, 1209, 886, 717 cm^{-1}; MS *m*/*z* 236 (12), 234 (13, M^+), 155 (100).

4-Bromomethyl-4′-methylbiphenyl (**4,4′-BMMBP**): Mp 106.1—106.7 °C; ^{1}H NMR ($CDCl_3$) δ=2.39 (3H, s), 4.53 (2H, s), 7.44—7.55 (8H, m); IR 1398, 1388, 1205, 1128, 808, 725 cm^{-1}; MS *m*/*z* 262 (9.6), 260 (10, M^+), 181 (100).

1-Bromomethyl-4-methylbenzene (**1,4-BMMBZ**): MS *m*/*z* 186 (12), 184 (12, M^+), 105 (100).

Results and Discussion

Effect of Light Wavelength on the Photobromination of 1-Methylnaphthalene. It has been known that irradiation promotes benzylic bromination[6,7] due to photochemical cleavage of the nitrogen to bromine single bond in **NBS**. In our study, the effect of light wavelength in the photochemical bromination of aromatic methyl groups was investigated first, taking the photobromination of 1-methylnaphthalene as a simplified reaction system.

In the 1 h photobrominations in carbon tetrachloride, the 1-methylnaphthalene conversions were nearly 100%, independent of light wavelength, but the product distributions were different (Fig. 1). When λ_{irrad} was longer than 390 nm, 1-(bromomethyl)naphthalene was quantitatively obtained. On the other hand, on irradiation of UV light ($\lambda_{\mathrm{irrad}} \geqq 313$ nm), 1-(chloromethyl)naphthalene and 1-(2,2,2-trichloroethyl)naphthalene were obtained as by-products in 11 and 4% yields, respectively.

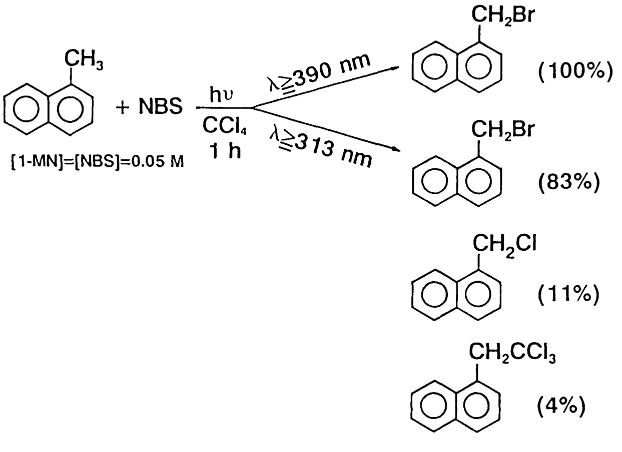


Fig. 1. Effect of light wavelength on the product distribution in the photobromination of 1-methylnaphthalene with **NBS** in carbon tetrachloride. [1-Methylnaphthalene]=[**NBS**]=0.05 mol dm^{-3}, in carbon tetrachloride, under nitrogen, 1 h.

Table 2. Solvent Effect on the Photobromination of **2,6-DMN** with **NBS**[a)]

Solvent	**2,6-DMN** conv. mol%	Products (Yield/mol%)[b)]
Decalin	18	**2,6-BMMN**[c)] (17)
CH_3CN	100	**2,6-BBMN**[d)] (88) **2,6-BBMN** isomers[e)] (12)
Acetone	100	**2,6-BBMN** (100)
CCl_4	100	**2,6-BBMN** (100)
Benzene	100	**2,6-BBMN** (100)

a) [**2,6-DMN**]=0.05 mol dm^{-3}, [**NBS**]=0.11 mol dm^{-3}, 2 h. b) Determined by GC, based on the initial concentration of the substrate. c) 2-Bromomethyl-6-methylnaphthalene. d) 2,6-Bis(bromomethyl)naphthalene. e) Naphthalene nucleus-brominated compounds.

All these facts show that the nitrogen to bromine single bond in **NBS** can be cleaved on irradiation of visible light. UV light irradiation is not desirable because it causes the incorporation of carbon tetrachloride into 1-methylnaphthalene.

Since no carbon tetrachloride decomposes on irradiation of UV light ($\lambda_{\mathrm{irrad}} \geqq 313$ nm), formation of the forementioned by-products suggests that UV light promotes the reaction of 1-naphthylmethyl radicals with carbon tetrachloride. In the subsequent reactions, only visible light was used in order to suppress formation of the by-products.

2-(Bromomethyl)naphthalene was quantitatively obtained from 2-methylnaphthalene under the same reaction conditions as for 1-methylnaphthalene. Thus, this **NBS** photobromination with visible light at ambient temperature is superior to the photothermal Br_2 bromination of 2-methylnaphthalene reported by Chapman.[6)]

Solvent Effect on the Photobromination of 2,6-DMN. Table 2 shows a solvent effect on the photobromination of **2,6-DMN**. All the solvents were unreactive under these reaction conditions, and no products from the solvents were detected by GC-MS.

In decalin, the reaction of **2,6-DMN** was very slow due to the poor solubility of **NBS**, and **2,6-BMMN** was obtained as single product. On the other hand, **2,6-DMN** was completely consumed in 2 h in acetonitrile, acetone, carbon tetrachloride, and benzene. In acetonitrile, **2,6-BBMN** was obtained in 88% yield along with its two isomers[9] with lower boiling points. These facts indicate occurrence of naphthalene nucleus bromination on the analogy of the facts that the boiling points of the bromotoluenes are lower than that of benzyl bromide. The reactions were very clean in acetone, carbon tetrachloride and benzene, and **2,6-BBMN** was almost quantitatively obtained.

Succinimide was facilely removed by suction filtration from the condensed benzene solution of the reaction mixture. The ^{1}H NMR spectrum of the reaction mixture obtained as such was superimposable on that of **2,6-BBMN**, and no absorption of the methyl or the dibromomethyl group was observed. These facts support that **2,6-BBMN** can be facilely prepared in the visible light irradiation of **2,6-DMN** with 2.2 mol equivalents of **NBS** in benzene under nitrogen. Thus, only benzene was used as solvent in the subsequent reactions.

Quantitative Preparation of Bis(bromomethyl)arenes. Under the same conditions as for **2,6-DMN** shown in Table 2, the corresponding bis(bromomethyl)arenes were obtained almost quantitatively from **2,3-**, **1,4-**, and **1,8-DMN's**, **4,4′-DMBP** and *p*-xylene.

Preparation of (Bromomethyl)methylarenes. Bromination of only one methyl group on dimethylarenes has not been achieved successfully yet, and the thermal bromination of **2,6-** and **2,7-DMN's** with **NBS** affords the corresponding bromomethyl derivatives only in 50 and 41 % yields, respectively.[3] The above (bromomethyl)methylarenes are of value because they can be precursors of hydroxymethyl- and formyl-substituted aromatic carboxylic acids. Thus, we searched for the optimum reaction conditions for the synthesis of (bromomethyl)methylarenes.

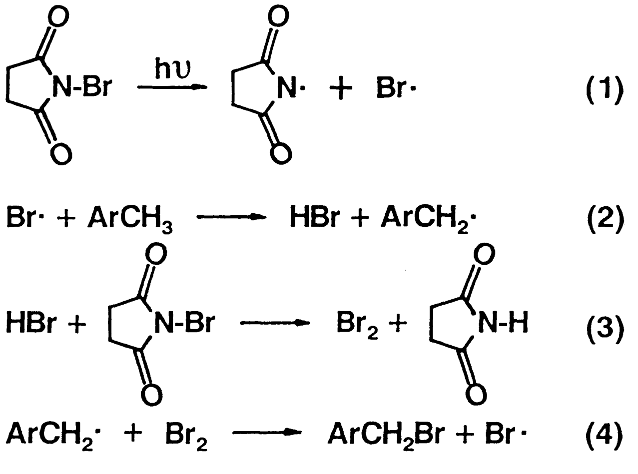
Table 3 shows that the (bromomethyl)methylarenes can be prepared in high yields with high selectivities in the 1 h photobromination reactions of the dimethylarenes with 1.1 mol equivalents of **NBS**. It can be said that the methyl groups on the (bromomethyl)methylarenes are photobrominated more slowly than those on the corresponding dimethylarenes.

Irradiation Effect on the Photobromination with NBS. Scheme 1 shows the chain mechanism for the photobromination with **NBS** which has been established by Pearson[10] and Russel.[11] Their arguments, however, have been focused only on the entity of the chain carrier, and irradiation effect has not been discussed satisfactorily. If Eqs. 2 and 4 are purely thermal and facile processes, bromination of side-chain methyl groups can proceed smoothly in the presence of the

Table 3. Selective Preparation of (Bromomethyl)methylarenes (**BMMA**)[a]

Substrate	Conv./mol%	**BMMA** (Yield/mol%)[b]
1,4-DMN	88	**1,4-BMMN** (86)
1,8-DMN	90	**1,8-BMMN** (89)
2,3-DMN	86	**2,3-BMMN** (85)
2,6-DMN	83	**2,6-BMMN** (81)
4,4′-DMBP	92	**4,4′-BMMBP** (89)
p-Xylene	93	**1,4-BMMBZ** (85)[c]

a) [Substrate]=0.05 mol dm^{-3}, [**NBS**]=0.055 mol dm^{-3}, in benzene, under nitrogen, 1 h. b) Determined by GC, based on the initial concentration of the substrate. c) 1,4-bis(bromomethyl)benzene was obtained in 7% yield. **BMMN**=(bromomethyl)methylnaphthalene, **4,4′-BMMBP**=4-bromomethyl-4′-methylbiphenyl, **1,4-BMMBZ**=1-bromomethyl-4-methylbenzene.



Scheme 1. Mechanism for the photobromination of side-chain methyl groups on arenes.

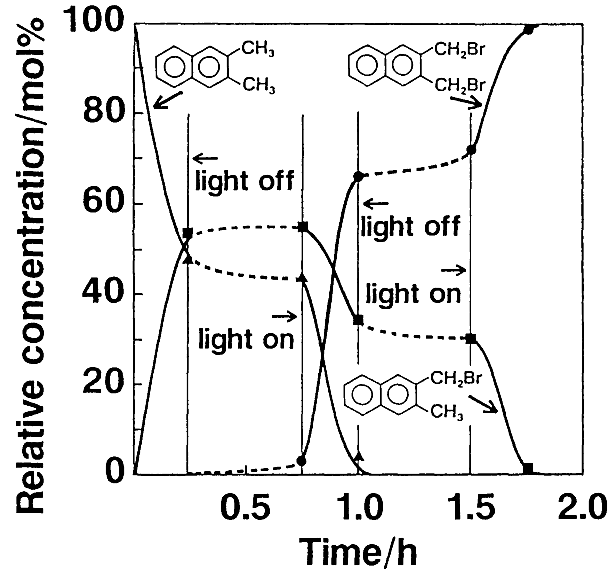


Fig. 2. Irradiation effect on the photobromination of **2,3-DMN** with **NBS** in benzene. [**2,3-DMN**]=0.05 mol dm^{-3}, [**NBS**]=0.11 mol dm^{-3}, in benzene, under nitrogen.

considerable amount of molecular bromine since Eq. 3 is a fast ionic reaction even at −86 °C.[10]

Figure 2 shows that the bromination of **2,3-DMN** virtually stops when light is cut off at the reaction time of 15 min, by when the reaction solution gets orange browned. In the case of continuous irradiation, this color dies away gradually. These findings suggest that the considerable amount of molecular bromine has been formed by the reaction time of 15 min. Without irradiation, a similar inhibition is also observed in the bromination of **2,3-BMMN**.

These facts suggest that the chain length of this reaction is not so long and that not only Eq. 1 but Eqs. 2 and 4 are promoted photochemically. As described above, the formation of 1-(chloromethyl)naphthalene and 1-(2,2,2-trichloroethyl)naphthalene in the UV light irradiation of 1-methylnaphthalene in carbon tetrachloride also indicates photochemical promotion of the halogen atom abstraction by benzylic radicals.

Conclusions

1) In the photochemical bromination of side-chain methyl groups on arenes with **NBS**, visible light irradiation in benzene is very effective in increasing the selectivity of the reaction and the efficiency for product purification.

2) Bis(bromomethyl)arenes can be obtained almost quantitatively from 1,4-, 1,8-, 2,3-, and 2,6-dimethylnaphthalenes, 4,4′-dimethylbiphenyl, and *p*-xylene (0.05 mol dm^{-3}) in their photobromination reactions with 2.2 mol equivalents of **NBS** in benzene.

3) The (bromomethyl)methylarenes can be obtained in good yields in the photobromination reactions of the above dimethylarenes (0.05 mol dm^{-3}) with 1.1 mol equivalents of **NBS** in benzene.

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9) The mass spectral data of **2,6-BBMN** are: m/z 316 (14), 314 (29), 312 (15, M$^+$), 235 (99), 233 (100), 154 (91), and those of both the **2,6-BBMN** isomers are: m/z 316 (14), 314 (26), 312 (15, M$^+$), 235 (99), 233 (100). The intense fragment peak of m/z=154, which is observed only in the mass spectrum of **2,6-BBMN**, can be assigned to $C_{12}H_{10}^+$, formed in the facile elimination of the two bromine atoms from the side-chain bromomethyl groups on the parent cation radical.

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