Cyclization and Rearrangement Processes Resulting from Bromination of 3-Benzylcycloalkenes

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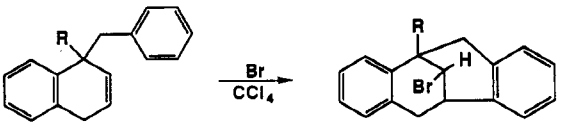
We previously reported that reaction of 1,1-dibenzyl-1,4-dihydronaphthalene (**1a**) with bromine in carbon tetrachloride yielded neither the expected product from addition of bromine to the isolated double bond nor products from carbocation rearrangements. Instead, compound **2a** was formed in high yield.[1]



1 a R = $CH_2C_6H_5$
1 b, R = CH_3

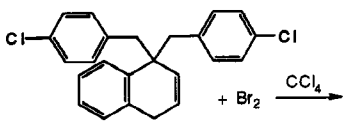
2 a R = CH_2-C_6H_5
2 b, R = CH_3

Formation of **2a** represents a unique example of Friedel–Crafts-like alkylation of a nearly unactivated benzene ring in the absence of strong acid catalysts. Aside from its surprising nature, the reaction is of interest as a novel and simple approach to the formation of the bicyclo[3.3.1]-nonane ring system.

We have now examined the reactions of bromine with several additional cycloalkene derivatives, each bearing at least one benzyl group in an allylic position of the alicyclic ring.

Reaction of bromine with 1-benzyl-1-methyl-1,4-dihydronaphthalene (**1b**) yielded the Friedel–Crafts product **2b** as the only detectable product, demonstrating that the presence of a second benzyl group is not necessary for the cyclization to take place.

Unlike the reactions of the unsubstituted benzyl derivatives **1a** and **1b**, addition of bromine to a carbon tetrachloride solution of their *p*-chlorobenzyl analog **3**



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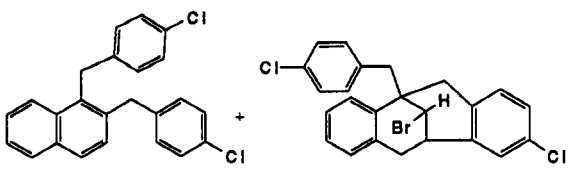
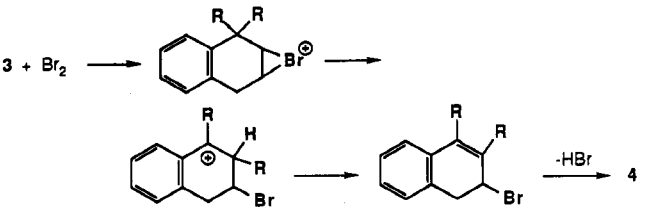


4 5

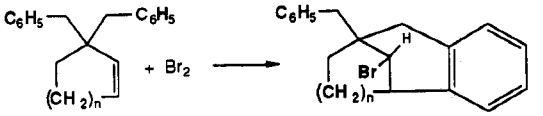
yielded a mixture of two products. The principal product (52% isolated yield) was a bromine-free compound, identified from its spectra and analysis as 1,2-bis(4-chlorobenzyl)naphthalene (**4**). This product is presumably formed by loss of hydrogen bromide from an intermediate 1,2-dihydronaphthalene derivative.



The minor product (33% isolated yield) from reaction of **3** with bromine was the Friedel–Crafts cyclization product **5**. Formation of **5** demonstrates that the initially formed bromonium ion can attack even a chlorinated aromatic ring at a position meta to a chlorine atom. However, the presence of the deactivating substituent slows down the rate of cyclization (in carbon tetrachloride solution) sufficiently to allow a Wagner–Meerwein shift of the *p*-chlorobenzyl group to compete with the Friedel–Crafts process.

In an attempt to increase the yield of **5**, the bromination of **3** was carried out in a somewhat more polar solvent, acetonitrile. This worked beautifully, as an essentially quantitative yield of **5** was obtained, with no detectable formation of **4**! However, the reason why the Wagner–Meerwein shift is suppressed in acetonitrile is not immediately obvious.

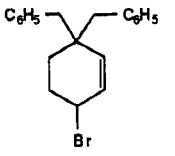
Reaction of bromine with 3,3-dibenzylcyclopentene and 3,3-dibenzylcyclohexene again usually yielded Friedel–Crafts cyclization products **6** and **7** in high yields. However,



n = 1, 2

6, n = 1
7, n = 2

when 1 equiv of bromine was very slowly added to a carbon tetrachloride solution of 3,3-dibenzylcyclohexene, a crude product whose spectra suggested it to be 3,3-dibenzyl-6-bromocyclohexene (**8**) was formed instead of the expected



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cyclization product. Rapid addition of the bromine or addition of more than 1 mol of bromine (taking advantage of the fact that addition of bromine to double bonds in nonpolar solvents is second order in bromine concentration)[2] completely eliminates this side reaction.

Experimental Section

Mp's and bp's are corrected. ^1H NMR spectra were taken in deuteriochloroform solutions unless otherwise noted, on Varian XL-200 or Hitachi R-1200 instruments. IR spectra were taken on a Perkin-Elmer 1600 FTIR spectrometer. Elemental analyses were performed by the University of Massachusetts Microanalytical Laboratory.

1-Benzyl-1-methyl-1,4-dihydronaphthalen-2-one. A solution of potassium *tert*-butoxide (3.00 g, 27.1 mmol) in 50 mL of *tert*-butyl alcohol was cooled in ice and stirred, and 1-methyl-

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(1) Miller, B.; Shi, X. *J. Org. Chem.* **1992**, *57*, 1677.
(2) Freeman, F. *Chem. Rev.* **1975**, *75*, 439.

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2-tetralone (3.94 g, 24.6 mmol) was added. After 10 min, benzyl chloride (3.40 g, 26.9 mmol) was added in five portions. The mixture was stirred with cooling for 0.5 h and then stirred at room temperature for 14 h. Water was added and the mixture extracted with ether. The organic layer was washed twice with brine, dried over magnesium sulfate, and filtered and the solvent evaporated to yield a viscous brown oil. The product crystallized on addition of petroleum ether and was recrystallized from methanol to give **1-benzyl-1-methyl-1,4-dihydronaphthalen-2-one** (5.20 g, 20.8 mmol, 85%) as colorless crystals, mp 76.5–77.5 °C. ^{1}H NMR: δ 1.56 (s, 3 H), 2.33–2.55 (m, 4 H), 2.87 (d, J = 12.7 Hz, 1 H), 3.41 (d, J = 12.7 Hz, 1 H), 6.55–6.75 (m, 2 H), 6.95–7.40 (m, 7 H). IR (KBr): 1707, 1560, 1492, 1454, 1419, 1155, 1085, 769, 756, 743, 705 cm^{-1}. Anal. Calcd for $C_{18}H_{18}O$: C, 86.40; H, 7.20. Found: C, 85.94; H, 7.37.

1-Benzyl-2-methyl-1,4-dihydronaphthalen-2-one *p*-Toluenesulfonylhydrazone. A mixture of 1-benzyl-1-methyl-2-tetralone (5.59 g, 22.0 mmol), *p*-toluenesulfonylhydrazine (10.20 g, 54.8 mmol), and 1 mL of hydrochloric acid in 80 mL of methanol was heated under reflux for 36 h. Evaporation of the solvent left a viscous brown oil. Chromatography on silica gel, eluting with mixtures of methylene chloride and petroleum ether ranging from 50% to 75% (v/v) methylene chloride, yielded **1-benzyl-2-methyl-1,4-dihydronaphthalen-2-one *p*-toluenesulfonylhydrazone** (6.30 g, 14.0 mmol, 69%) as white needles, mp 133.5–134.5 °C (from ether). ^{1}H NMR: δ 1.53 (s, 3 H), 2.40 (s, superimposed on a multiplet, totalling 7 H), 2.85 (d, J = 12.8 Hz, 1 H), 3.14 (d, J = 12.8 Hz, 1 H), 6.35–6.55 (m, 2 H), 6.94–7.28 (m, 9 H), 7.79 (bs, 1 H), 7.94 (d, J = 8.34, 2 H). IR (KBr): 3213, 1493, 1452, 1402, 1333, 1018, 814, 765, 706, 692, 669, 611, 550 cm^{-1}. Anal. Calcd for $C_{25}H_{26}H_2O_2S$: C, 71.77; H, 6.22; N, 6.70; S, 7.66. Found: C, 71.86; H, 6.30; N, 6.81; S, 7.47.

1-Benzyl-1-methyl-1,4-dihydronaphthalene. A suspension of 1-benzyl-1-methyl-1,4-dihydronaphthalen-2-one *p*-toluenesulfonylhydrazone (2.93 g, 7.01 mmol) in 20 mL of anhydrous ether was stirred under a nitrogen atmosphere and cooled in ice while a 1.4 M solution of methylithium in ether (10.0 mL, 14.0 mmol) was added over a 30-min period. Stirring was continued for an additional 1.5 h. Water was added, the layers were separated, the organic layer was washed with water, dried over magnesium sulfate, and filtered, and the solvent was evaporated. The resulting brown oil was chromatographed on silica gel, eluting with a 12% (v/v) mixture of methylene chloride in petroleum ether, to give **1-benzyl-1-methyl-1,4-dihydronaphthalene** (0.94 g, 4.02 mmol, 57%) as a colorless oil which crystallized on standing, mp 58.0–59.0 °C. ^{1}H NMR: δ 1.49 (s, 3 H), 2.75–2.97 (m, 4 H), 5.40–5.97 (m, 2 H), 6.65–7.50 (m, 9 H). IR: 1494, 1452, 751, 735, 700, 610 (sh), and 572 (sh) cm^{-1}. Anal. Calcd for $C_{18}H_{18}$: C, 92.31; H, 7.69. Found: C, 92.41; H, 7.70.

Reaction of Bromine with 1-Benzyl-1-methyl-1,4-dihydronaphthalene. A solution of bromine (374 mg, 2.34 mmol) in 3 mL of carbon tetrachloride was added slowly to a stirred solution of 1-benzyl-1-methyl-1,4-dihydronaphthalene (300 mg, 1.28 mmol) in 10 mL of carbon tetrachloride cooled in an ice–salt bath. The reaction mixture was washed with aqueous sodium thiosulfate solution and then with water and dried over magnesium sulfate. Filtration and evaporation of the solvent left a yellow solid, whose NMR spectrum was unchanged on recrystallization. Recrystallization from absolute ethanol yielded bromide **2b** (0.32 g, 1.02 mmol, 80%) as a white solid, mp 163–164 °C. ^{1}H NMR: δ 6.84–7.45 (m, 8 H), 4.71 (d, J = 4.26 Hz, 1 H), 3.90 (dd, J = 16.85, 5.62 Hz, 1 H), 3.59 (m, 1 H), 3.15 (d, J = 16.79 Hz, 1 H), 3.01 (d, J = 16.79 Hz, 1 H), 2.82 (d, J = 16.85 Hz, 1 H). IR (KBr): 1382, 1307, 1238, 1180, 894, 808, 732, 708, 578 cm^{-1}. Anal. Calcd for $C_{18}H_{17}Br$: C, 69.01; H, 5.43; Br, 25.26. Found: C, 68.58; H, 5.32; Br, 26.19.

Reaction of Bromine with 1,1-Bis(4-chlorobenzyl)-1,4-dihydronaphthalene (3). (a) In Carbon Tetrachloride Solution. A solution of **3**[3] (0.25 gg, 0.66 mmol) in 6 mL of carbon tetrachloride was cooled in ice and stirred while a solution of bromine (0.12 g, 0.75 mmol) in 2 mL of carbon tetrachloride was added slowly. Evolution of hydrogen bromide was immediate. Aqueous sodium thiosulfate solution was added, and the layers were separated. The aqueous layer was extracted with methylene chloride, the combined organic layers were washed with water and dried over magnesium sulfate, and the solvent was evaporated to yield a white solid. Thick-layer chromatography on a 20- × 20-cm silica gel plate, developed with petroleum ether, yielded two products. 1,2-bis(4-chlorobenzyl)naphthalene (0.13 g, 0.34 mmol, 52% R_f = 0.24) was obtained as white crystals (from absolute ethanol), mp 92–93 °C. ^{1}H NMR: δ 4.08 (s, 2 H), 4.40 (s, 2 H), 6.80–7.51 (m, 8 H), 7.71–7.91 (m, 3 H). IR (KBr): 1490, 1452, 1092, 1015, 815, 799, 754 cm^{-1}. Anal. Calcd for $C_{24}H_{18}Cl_2$: C, 76.37; H, 4.78; Cl, 18.83. Found: C, 75.86; H, 4.91; Cl, 18.69.

Bromide **5** (0.10 g, 0.22 mol, 33%, R_f = 0.17) was obtained as white crystals, mp 162–163 °C (from absolute ethanol). ^{1}H NMR: δ 2.81 (d, J = 16.62 Hz, 1 H), 2.83 (d, J = 17.03 Hz, 1 H), 3.40–3.55 (m, 3 H), 3.99 (dd, J = 17.03, 5.50 Hz, 1 H), 4.68 (d, J = 4.02 Hz, 1 H), 6.75 (d, J = 8.24 Hz, 1 H), 6.93–7.36 (m, 7 H), 7.54–7.64 (m, 3 H). IR (KBr): 1489, 1450, 1429, 1406, 1170, 1090, 1015, 916, 841, 798, 780, 762, 720 cm^{-1}. Anal. Calcd for $C_{24}H_{19}Cl_2Br$: C, 62.93; H, 4.15; Cl, 15.48; Br, 17.44. Found: C, 62.69; H, 4.27; Cl, 15.56; Br, 17.62.

(b) In Acetonitrile Solution. A solution of bromine (62.4 mg, 0.39 mmol) in 1 mL of acetonitrile was added in one portion to a stirred solution of cycloalkene **3** (0.10 g, 0.26 mmol) in 10 mL of anhydrous acetonitrile. The reaction was worked up as described above to give a pale yellow solid whose spectra were identical with those of **5**. Recrystallization from ethanol yielded **5** (0.104 g, 0.227 mmol, 86%) as a white solid.

2,2-Dibenzylcyclopentanone *p*-Toluenesulfonylhydrazone. A mixture of 2,2-dibenzylcyclopentanone (1.61 g, 6.06 mmol), *p*-toluenesulfonylhydrazine (3.42 g, 18.2 mmol), and concd hydrochloric acid (1 mL) in 60 mL of methanol was heated under reflux for 2 h and then stirred at room temperature for an additional 22 h. The mixture was filtered and the solid product recrystallized from methanol to yield **2,2-dibenzylcyclopentanone *p*-toluenesulfonylhydrazone** (2.02 g, 4.62 mmol, 76%) as a white powder, mp 201–202 °C. ^{1}H NMR: δ 1.02–1.35 (m, 2 H), 1.56–1.92 (m, 4 H), 2.41 (s, 3 H), 2.70 (d, J = 12.9 Hz, 2 H), 3.07 (d, J = 12.9 Hz, 2 H), 6.75–7.54 (m, 12 H), 8.01 (d, J = 8.7 Hz, 2 H). IR (KBr): 3217, 1327, 1161, 915, 769, 754, 705, 670, 560, 546 cm^{-1}. Anal. Calcd for $C_{22}H_{28}O_2N_2S$: C, 72.22; H, 6.48; N, 6.48; S, 7.41. Found: C, 71.97; H, 6.45; N, 6.48; S, 7.44.

2,2-Dibenzylcyclopentyl Xanthate. A suspension of lithium aluminum hydride (1.00 g, 26.3 mmol) in 40 mL of anhydrous ether was stirred at room temperature under nitrogen, and a solution of 2,3-dibenzylcyclohexanone (1.70 g, 6.44 mmol) in 5 mL of anhydrous ether was added slowly. After completion of the addition the mixture was heated under reflux for 1 h. The mixture was cooled in ice, and 1 M hydrochloric acid was added carefully. The layers were separated, and the ether layer was washed with water and dried over magnesium sulfate. Evaporation of the solvent yielded 1.70 g of 2,2-dibenzylcyclopentanol, which was dissolved in 6 mL of anhydrous diglyme and added to a suspension of sodium hydride (0.50 g, 12.8 mmol) in 20 mL of a 1:1 (v/v) mixture of anhydrous ether and anhydrous diglyme. Stirring was continued until evolution of hydrogen ended (about 10 min after completion of the addition), and carbon disulfide (3.41 g, 76.7 mmol) was added over a 10-min period. The mixture was stirred at room temperature for 20 min and then under reflux for 0.5 h. It was cooled to room temperature, methyl iodide (6.79 g, 47.9 mmol) was added, and the mixture was heated under reflux for 0.5 h. It was then cooled to room temperature, poured into 60 mL of 1 M hydrochloric acid, and extracted with ether. The ether layer was washed with brine and then with water and dried over magnesium sulfate and the solvent evaporated. The residual oil was chromatographed on silica gel, eluting with 5% methylene chloride in petroleum ether, to give **2,2-dibenzylcyclopentyl xanthate** (1.71 g, 4.78 mmol, 75%) as a viscous, colorless oil. ^{1}H NMR: δ 2.47–2.90 (m, 6 H), 2.55 (s, 3 H), 2.69 (s, 2 H), 2.90 (s, 2 H), 5.40–5.67 (m, 1 H), 6.95–7.30 (m, 10 H). IR (neat): 1494, 1453, 1220, 1069, 1019, 964, 753, 703 cm^{-1}. Anal. Calcd for $C_{21}H_{24}OS_2$: C, 70.79; H, 6.74. Found: C, 70.79; H, 6.83.

3,3-Dibenzylcyclopentene. (a) From 2,2-Dibenzylcyclopentanone *p*-Toluenesulfonylhydrazone. Methyllithium in ether (1.4 M, 6.00 mL, 8.33 mmol) was reacted with a suspension of 2,2-dibenzylcyclopentanone *p*-toluenesulfonylhydrazone (1.80 g, 4.17 mmol) and the reaction worked up as described for the

(3) Miller, B.; Shi, X. *J. Org. Chem.*, in press.

preparation of 3,3-dibenzylcyclohexene. Chromatography of the crude product on alumina, eluting with a 7:3 (v/v) mixture of petroleum ether and methylene chloride, yielded **3,3-dibenzylcyclopentene** (0.95 g, 3.83 mmol, 92%) as a colorless oil. ^{1}H NMR: δ 1.76 (s, 4 H), 2.72 (d, J = 13.1 Hz, 2 H), 2.74 (d, J = 13.1 Hz, 2 H), 5.59 (s, 2 H), 6.64–7.30 (m, 10 H). IR (neat): 1602, 1494, 1454, 1030, 755, 735, 700 cm^{-1}. Anal. Calcd for $C_{19}H_{20}$: C, 91.94; H, 8.06. Found: C, 91.74; H, 8.16.

(b) From 2,2-Dibenzylcyclopentyl Xanthate. Powdered 2,2-dibenzylcyclopentyl xanthate (1.70 g, 4.78 mmol) was maintained under an atmosphere of nitrogen and heated at 135–145 °C for 1 h. The spectra of the product indicated that little reaction had occurred, so the xanthate was then heated at 145–165 °C for 1 h and at 160–170 °C for 0.5 h. Chromatography on Woelm neutral alumina (activity I), eluting with petroleum ether, yielded 3,3-dibenzylcyclopentene (0.8 g, 3.23 mmol, 68%) as a colorless oil.

Reaction of Bromine with 3,3-Dibenzylcyclopentene. A solution of 3,3-dibenzylcyclopentene (0.67 g, 2.70 mmol) in 10 mL of carbon tetrachloride was cooled in an ice bath, and a solution of bromine (0.45 g, 2.82 mmol) in 5 mL of carbon tetrachloride was added slowly. Evolution of hydrogen bromide was immediate. After 5 min the reaction mixture was washed with sodium thiosulfate solution and then with water and dried over magnesium sulfate. The solvent was evaporated to yield a pale yellow oil, which was chromatographed on neutral alumina, eluting with 5% methylene chloride in petroleum ether. Bromide **6** (0.70 g, 2.10 mmol, 79%) was obtained as a colorless viscous oil. ^{1}H NMR: δ 1.55–1.86 (m, 2 H), 1.95–2.03 (m, 1 H), 2.50–2.70 (m, 2 H), 2.99 (d, J = 1.3.51 Hz, 1 H, superimposed on another 1 H signal), 3.10 (d, J = 13.51 Hz, 1 H), 3.38 (d, J = 6.23 Hz, 1 H), 4.45 (s, 1 H), 6.9–7.1 Hz (m, ca. 4 H), 7.1–7.4 (m, ca. 5 H). IR (neat): 1603, 1582, 1490, 1453, 1231, 1209, 1182, 1155, 924, 774, 760, 748, 720, 703, 592 (sh), 564 (sh) cm^{-1}. Anal. Calcd for $C_{19}H_{19}Br$: C, 69.73; H, 5.81; Br, 24.46. Found: C, 69.52; H, 5.75; Br, 24.31.

2,2-Dibenzylcyclohexanone *p*-Toluenesulfonylhydrazone. A mixture of 2,2-dibenzylcyclohexanone (7.41 g, 26.6 mmol), *p*-toluenesulfonylhydrazine (9.90 g, 53.2 mmol), and 1.0 mL of concd hydrochloric acid in 70 mL of methanol was stirred at room temperature for 20 h. The mixture was then filtered, and the solid product was recrystallized from methanol to yield **2,2-dibenzylcyclohexanone *p*-toluenesulfonylhydrazone** (5.20 g, 11.7 mmol, 44%) as white crystals, mp 155.5–157.0 °C. ^{1}H NMR: δ 1.50 (m, 4 H), 2.17 (t, J = 7.14 Hz, 2 H), 2.40 (s, 3 H), 2.67 (d, J = 13.5 Hz, 2 H), 3.06 (d, J = 13.5 Hz, 2 H), 6.97–7.31 (m, 12 H), 7.85 (d, J = 8.3 Hz, 2 H). IR (KBr): 3202, 1323, 1162, 761, 705, 667, 564 cm^{-1}. Anal. Calcd for $C_{27}H_{30}N_2O_2S$: C, 72.65; H, 6.73; N, 6.29; S, 7.17. Found: C, 72.74; H, 6.79; N, 6.30; S, 7.33.

3,3-Dibenzylcyclohexene. A suspension of 2,2-dibenzylcyclohexanone *p*-toluenesulfonylhydrazone (4.88 g, 10.9 mmol) in 100 mL of anhydrous ether was stirred and cooled to 0 °C while being maintained under an atmosphere of nitrogen. A 1.4 M solution of methyllithium in ether (1.56 mL, 21.9 mmol) was added slowly over the course of 0.5 h. The cooling bath was removed and stirring continued for another 0.5 h. Water was added, the layers were separated, and the ether layer was washed with water, dried over magnesium sulfate, and filtered. The solvent was evaporated to yield a pale yellow oil. Chromatography on silica gel, eluting with petroleum ether, yielded **3,3-dibenzylcyclohexene** (2.72 g, 10.3 mmol, 95%) as a white solid, mp 43.5–44.0 °C. ^{1}H NMR: δ 1.48 (m, 4 H), 1.71 (m, 2 H), 2.65 (d, J = 13.7 Hz, 2 H), 2.71 (d, J = 13.7 Hz, 2 H), 5.43–5.79 (m, 2 H), 7.20 (m, 10 H). IR (KBr): 1491, 1448, 762, 701 cm^{-1}. Anal. Calcd for $C_{20}H_{22}$: C, 91.60; H, 8.40. Found: C, 91.57; H, 8.47.

Reaction of Bromine with 3,3-Dibenzylcyclohexene. A solution of bromine (62 mg, 0.39 mmol) in 1 mL of carbon tetrachloride was rapidly added to a solution of 3,3-dibenzylcyclohexene (50 mg, 0.19 mmol) in 4 mL of carbon tetrachloride. The mixture was washed with sodium thiosulfate solution and with water, dried over magnesium sulfate, and filtered and the solvent evaporated to yield 60 mg of a white solid. Recrystallization from absolute ethanol (which resulted in no change in the NMR spectrum of the product) yielded bromide **7** (36.3 mg, 0.11 mmol, 56%) as white needles, mp 125–125.5 °C. ^{1}H NMR: δ 1.24–1.63 (m, 2 H), 1.9–1.1 (m, 1 H), 2.35–2.55 (m, 1 H), 2.63 (d, J = 17.69 Hz, 1 H), 2.70 (d, J = 13.30 Hz, 1 H), 2.86 (d, J = 13.39 Hz, 1 H), 3.34 (dd, J = 3.31, 1.53 Hz, 1 H), 4.59 (d, J = 1.45 Hz, 1 H), 6.85–7.10 (m, ca. 4 H), 7.1–7.4 (m, ca. 5 H). IR (KBr): 1493, 1451, 1198, 768, 758, 724, 706, 676, 546, 454 cm^{-1}. Anal. Calcd for $C_{20}H_{21}Br$: C, 70.38; H, 6.16; Br, 23.46. Found: C, 70.12; H, 6.07; Br, 23.71.

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