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Reaction of N-Haloamide. XXVIII.[1] Preparation of N,N-Dibromourethan and Reactions of N,N-Dihaloamides with Styrene and 1,2-Dihydronaphthalenes[2]

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N,N-Dibromourethan (DBU) was prepared. The addition of DBU to styrene gave an anti-Markownikoff's adduct, (**2**). The orientation of the addition of DBU is thus similar to that of N,N-dichloro analogue (DCU) and opposed to that of N,N-dibromobenzenesulfonamide (DBBS).

Reactions of DBU, DCU, and DBBS or N,N-dibromo-*p*-toluenesulfonamide with 1,2-dihydronaphthalene were examined in which DBBS gave desired adduct, (**5**), in good yield whereas DCU and DBU gave no normal adduct but complex mixtures. Reaction of methyldihydronaphthalenes with these reagents gave similar results.

Compound (**2**) was converted to 1-bromo-2-benzenesulfonamido (**7**), and 1-alkoxy-2-benzenesulfonamido-1,2,3,4-tetrahydronaphthalenes (**8** and **9**).

Keywords——N,N-dibromourethan; N,N-dichlorourethan; styrene; 1,2-dihydronaphthalenes; addition; NMR; contact shift reagent; N,N-dibromosulfonamides; GC-mass

Previous paper on the addition of N,N-dibromobenzenesulfonamide (DBBS) to asymmetric olefins have described that the addition occurred in Markownikoff's fashion[4,5] whereas the additions of N,N-dichlorourethan (DCU) or N,N-dichlorobenzenesulfonamide (DCBS) gave adduct of opposite orientation[6–8]

Table I shows the addition mode of these N,N-dihaloamides to certain asymmetric olefins.

The distinction in the orientation of the addition of N,N-dihaloamides appears to be dependent on the difference of either the acid moieties or the halogens in the reagents. The studies on the reactivity of unknown N,N-dibromourethan (DBU) may be required to reveal this problem.

Ethyl carbamate was brominated by dropping aqueous sodium hydroxide into a solution of bromine and the carbamate in carbon tetrachloride under stirring. The crude product was purified passing through a column of silica gel to obtain an orange oil. Absence of N–H stretching band in the infrared spectrum and the active bromine measured by iodometry supported the structure of the desired N,N-dibromourethan. Since this oil was easily reversed to ethyl carbamate by exposure it in the air or by the reduction with aqueous sodium bisulfite, freshly prepared DBU was used to the studies of the addition reactions.

The reactivity of DBU was then examined on the reaction with styrene in carbon tetra-

1) Part XXVII: A. Yamasaki, H. Terauchi, and S. Takemura, *Chem. Pharm. Bull.* (Tokyo), **24**, 2841 (1976).
2) This work has been briefly presented at the Meeting of the Kinki Branch of the Pharmaceutical Society of Japan, Kobe, 1975.
3) Location: *3-4-1, Kowakae, Higashi-osaka.*
4) H. Terauchi, A. Yamasaki, and S. Takemura, *Chem. Pharm. Bull.* (Tokyo), **23**, 3162 (1975).
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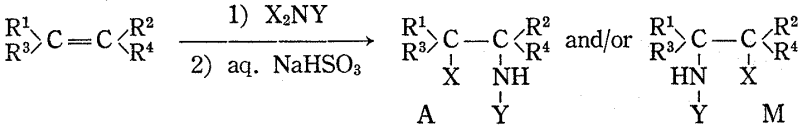
6) T.A. Foglia and D. Swern, *J. Org. Chem.*, **31**, 3625 (1966); *idem, ibid.*, **32**, 75 (1967); *idem, ibid.*, **33**, 766 (1968).
7) F.A. Daniher and P.E. Butler, *J. Org. Chem.*, **33**, 4336 (1968); F.A. Daniher, M.T. Melchiov, and P.E. Butler, *Chem. Comm.*, **1968**, 931.
8) M.S. Kharash, and H. Priestley, *J. Am. Chem. Soc.*, **61**, 3425 (1939).

Table I. Orientation of Addition of N,N-Dihaloamides to Asymmetric Olefins



Asymmetric olefins				Ratios of adducts A : M (%)			
R^1	R^2	R^3	R^4	DCU[6] A:M	DCBS[7] A:M	DBBS[4] A:M	DBU A:M
C_6H_5–	H–	H–	H–	100:0	100: 0	0:100[6]	100:0
$(CH_3)_2CH$–	H–	CH_3–	H–	100:0	—	0:100[4]	—
$(CH_3)_3C$–	H–	H–	H–	100:0	—	—	—
CH_3–	C_2H_5–	CH_3–	H–	—	—	0:100[4]	—
CH_3–	–$(CH_2)_4$–		H–	—	—	0:100[4]	—
CH_3–	H–	H–	H–	100:0	85:15	—	—

chloride. The reaction gave an anti-Markownikoff type adduct (A-type, see Table I), **2**, in 46.2% yield as a major product and 1-phenyl-1,2-dibromoethane in 7.2%. No adduct of type M was found in the reaction mixture. The structure of the adduct (**2**) was presumed by nuclear magnetic resonance (NMR) analysis; a quartet at 3.7 ppm assigned to protons of β-methylene was coupled with a triplet at 5.05 ppm assigned to a proton of α-methine with coupling constant, 7 Hz. Decoupling irradiating 5.05 ppm in addition of deuterium oxide changed the quartet of β-methylene to a singlet.

In view of the facts shown in Table I and the above result, N-bromo and sulfonyl groups in reagent seem to give M-type adduct in preference to N-chloro and carbethoxy groups.

The reaction of N,N-dihaloamides was then applied to that with 1,2-dihydronaphthalene. N,N-Dibromobenzenesulfonamide (DBBS) gave adduct of M-type, **5**, in good yield whereas DCU and DBU gave no desired addition products but complex mixtures of dehydrogenated, and halogenated products. The structure of the product (**5**), was given by agreement of its elemental analysis and analysis of NMR spectrum; the NMR in $CDCl_3$ exhibited overlapped signals assigned to C-2 and C-1 protons near 4.5 ppm which gave no effective information on the orientation of the addition, however in the presence of contact shift reagent, tris(dipivaloylmethanato)-europium-III, C-2 proton signal was shifted to 4.9 ppm as a quartet and the signal of C-1 proton to 5.1 ppm as a broad doublet separately. Decoupling experiments of them shown in Fig. 1 supported the structure of 5. The treatment of **5** with sodium hydroxide gave an aziridine compound (**6**), which was then treated with hydrobromic acid to give an isomer of **5**, compound (**7**). The structure of **7** was presumed by showing reasonable NMR and its contact shift in a similar manner as **5** (Fig. 1). The aziridine (**6**), was decomposed with alkoxides to give 1-alkoxy-2-benzenesulfonamido-1,2,3,4-tetrahydronaphthalenes (**8** and **9**).

The reaction of N,N-dibromo-*p*-toluenesulfonamide with 2-methyl-3,4-dihydronaphthalene gave a M-type adduct (**15**) in a poor yield. In its NMR spectrum, a doublet at 4.60 ppm assigned to C-1 proton coupled with a doublet of NH proton at 4.85 ppm with 9 Hz.

The reaction of DCU with dihydronaphthalene gave no desired addition product but crystals of mp 182° and an oil boiling at 75—82° in 6 mmHg. The crystals (**10**) were identified with the authentic sample of α-1,2,3,4-tetrachloro-1,2,3,4-tetrahydronaphthalene.[9] Since the oil was assumed to be still a mixture showing a complex NMR spectrum, it was analyzed by gas–liquid chromatography (GLC)–mass spectrometry to give peaks corresponding to naphthalene

9) P.B.D. De la Mare, R. Koeningsberger, J.S. Lomas, V.S. del Olms, and A. Sexton, *Rec. Trav. Chem.*, **84**(1), 109 (1965) [*C.A.*, **62**, 13101].

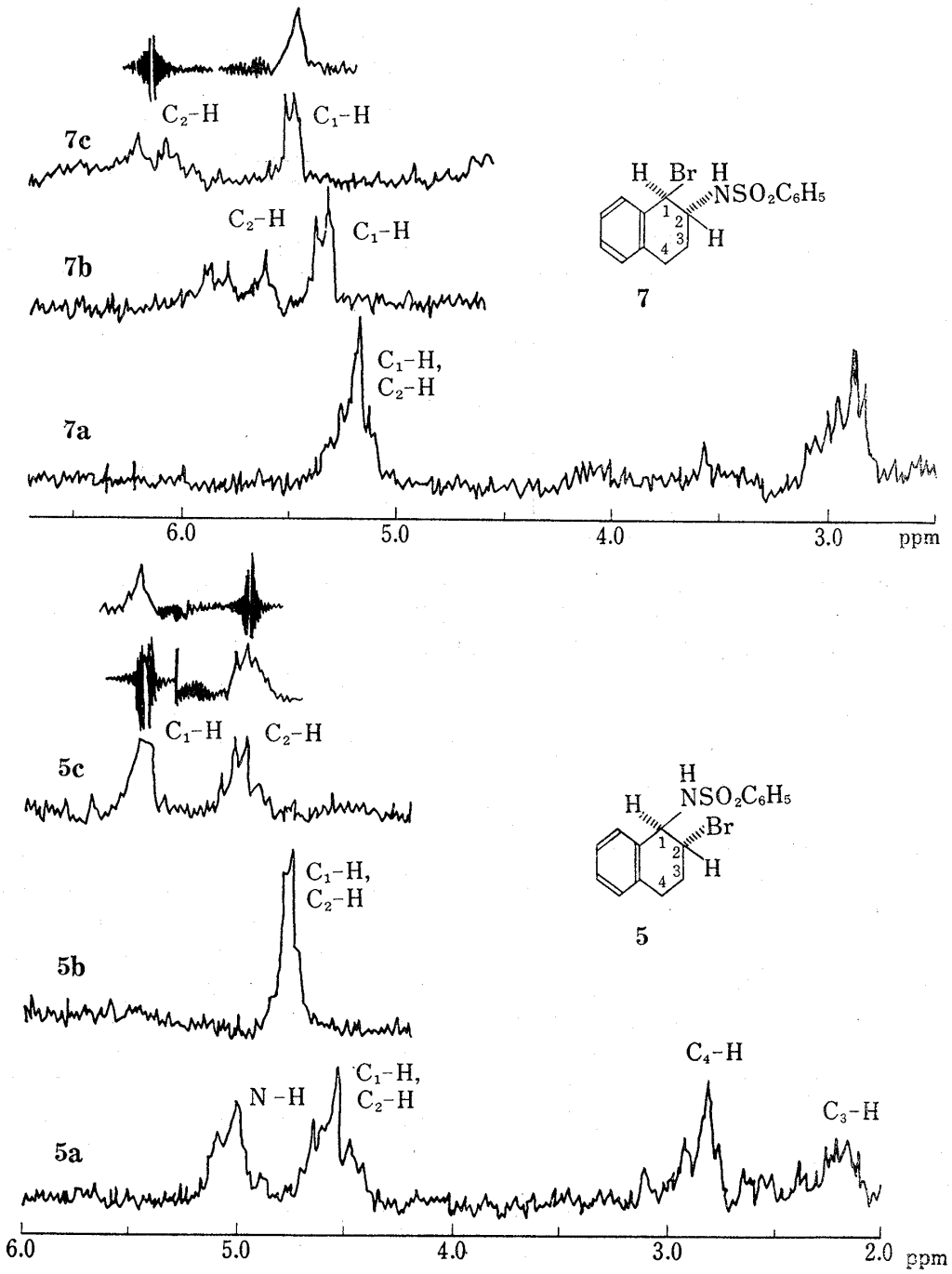


Fig. 1. Contact Shifts of Compounds **5** and **7** with $Eu(DPM)_3$ ($CDCl_3$, 60 Mc)
molar ratio (compound: Eu $(DPM)_3$): **5a** 10: 0; **5b** 10: 3; **5c** 10: 5; **7a** 10: 0; **7b** 10: 2; **7c** 10: 3

(M^+ 128), monochloronaphthalene (M^+ 162), monochloro-tetrahydronaphthalene (M^+ 166), and tetrahydronaphthalene (M^+ 132). Further studies on the structures of them were not performed.

The reactions of DBU with dihydronaphthalenes gave no normal adducts; reaction with 1,2-dihydronaphthalene (**4**) gave a small amounts of naphthalene and 1-bromo-2-carbethoxyaminonaphthalene (**11**) which hydrolyzed to known 1-bromo-2-naphthylamine,[10] and the reaction with 1-methyl-3,4-dihydronaphthalene (**12**) gave 1-methylnaphthalene, 1-methyl-2-car-

10) C. Cosiner, *Ber.*, **14**, 59 (1881).

bethoxyaminonaphthalene (**13**) which was converted to known 1-methyl-2-naphthylamine,[11] and an oily mixture. The oil was analized by GLC–mass spectrometry giving peaks corresponding to monomethylnaphthalene (M^+ 142), monobromo-methylnaphthalene (M^+ 220), dibromo-methylnaphthalene (M^+ 298), monobromo-methyl-dihydronaphthalene (M^+ 222), and dibromo-methyl-dihydronaphthalene (M^+ 300).

These distinction of reactivity between N,N-dibromosulfonamides and the other N,N-dihaloamides may be attributed to the difference of reaction mechanism. Further studies of the reactivity of these reagents are in progress.

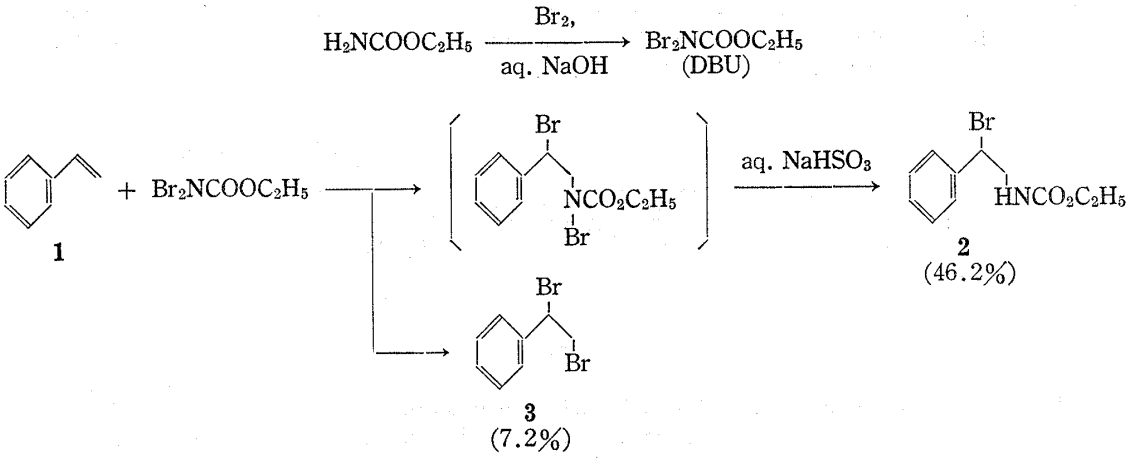


Chart 1

Experimental

Ethyl N,N-Dibromocarbamate (DBU)——Into a solution of ethyl carbamate (8.9 g, 0.1 mole) and Br_2 (12.9 ml, 0.25 mole) in CCl_4 (100 ml), aq. 4% NaOH (250 ml) was added during 30 min under stirring at room temperature. After stirring for additional 2 hr, the CCl_4-layer was dried over Na_2SO_4, and the solvent was removed *in vacuo* at 30—40°. The residue was passed through a short silica gel column eluting with CCl_4 to give an orange oil (15.6 g, 63.2%). $IR_{max}^{CCl_4}$ cm^{-1}: 1740 ($\nu_{C=O}$), 1220, 1060 (ν_{C-O}). NMR (CCl_4) δ: 4.25 (2H, q, J=7 Hz, $C\underline{H}_2CH_3$), 1.35 (3H, t, J=7 Hz, $CH_2C\underline{H}_3$). The active bromine determined by iodometry was 79.3% of the theoretical value. Exposure in a open vessel for 2 days reversed the oil to the original urethan. Reduction of the oil (1.5 g) with aq. $NaHSO_3$ at room temperature also gave urethan (0.45 g, 83%).

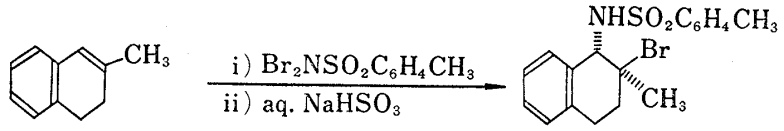
Reaction of DBU with Styrene (1)——Into a solution of styrene (6.25 g, 0.056 mole) in CCl_4 (100 ml), DBU (13.9 g, 0.056 mole) in CCl_4 (100 ml) was dropwise added during 30 min under cooling at −5° and stirring in N_2-atmosphere. After the addition of DBU, the mixture was stirred for 2 hr and allowed to stand overnight. The solution was stirred with 10% aq. $NaHSO_3$ (100 ml) for 1 hr, washed with H_2O, and dried over Na_2SO_4. The solvent was distilled *in vacuo* and the residue was chromatographed on a silica gel column to obtain major product of mp 58° (from hexane), **2**, (6.3 g, 46.2%). *Anal.* Calcd. for $C_{11}H_{14}O_2NBr$: C, 48.54; H, 5.19; N, 5.15. Found: C, 48.42; H, 5.21; N, 5.12. IR_{max}^{Nujol} cm^{-1}: 3350 (ν_{N-H}), 1700 ($\nu_{C=O}$), 1520, 930, 860 (δ_{arom}). NMR ($CDCl_3$) δ: 7.30 (5H, s, arom.), 5.05 (1H, t, J=6.8 Hz, CHBr; 1H, br, NH, overlapped), 4.1 (2H, q, J=7.1 Hz, $-OC\underline{H}_2CH_3$), 3.78 (2H, t, J=6.8 Hz, CH_2N), 1.21 (3H, t, J=7.1 Hz, $-OCH_2C\underline{H}_3$), addition of D_2O: 5.05 (1H, t, J=6.8 Hz, CHBr), 3.78 (2H, d, J=6.8 Hz, CH_2N), irradiation at 5.05 ppm: 3.78 (2H, s, CH_2N). From the other fraction of the eluate, 1,2-dibromo-1-phenylethane (**3**) was obtained, mp 72—73° (7.2%) which was identified with authentic sample[12] by mixed melting point determination.

Reaction of DBBS with 1,2-Dihydronaphthalene (4)——1,2-Dihydronaphthalene (9 g) was dissolved in CH_2Cl_2 (50 ml). DBBS (22 g) was added to this solution in small portions under stirring and ice-cooling. After additional stirring for 30 min, 10% aq. $NaHSO_3$ (75 ml) was added to the mixture and stirred for 30 min. The organic layer was separated and the aqueous layer was extracted with ether (20 ml×2). The combined solution of the CH_2Cl_2-layer and ether-extract was washed with H_2O, dried over Na_2SO_4, and the solvent was eliminated *in vacuo* to leave a solid which was recrystallized from EtOH to give crystals of **5**, mp 165° (96%). *Anal.* Calcd. for $C_{16}H_{16}O_2NSBr$: C, 52.46; H, 4.40; N, 3.82. Found: C, 52.28; H, 4.61; N, 3.55. IR_{max}^{Nujol} cm^{-1}: 3200 (ν_{NH}), 1320, 1155 (ν_{SO_2N}). NMR ($CDCl_3$): Fig. 1.

11) K. Fries and E. Hubner, Ber., **39**, 444 (1906).
12) A. Blyth and W. Hofmann, *Ann.*, **53**, 306 (1845).

Reaction of 1-Benzenesulfonamido-2-bromo-1,2,3,4-tetrahydronaphthalene (5) with Sodium Hydroxide——Into a stirred mixture of 10% aq. NaOH (5 ml) and CH_2Cl_2 (10 ml), **5** (1 g) was added in portions at room temperature. The stirring was continued for additional 1 hr. The CH_2Cl_2-layer separated was washed with H_2O and dried over Na_2SO_4. The solvent was removed *in vacuo* and the residual solid was recrystallized from CH_2Cl_2–*n*-hexane to give crystals of mp 105—106° (**6**) (62%). *Anal.* Calcd. for $C_{16}H_{15}O_2NS$: C, 71.34; H, 5.61; N, 5.20. Found: C, 71.22; H, 5.73; N, 5.21. IR_{max}^{Nujol} cm^{-1}: 1320, 1150 (ν_{SO_2N}). NMR ($CDCl_3$) δ: 2.0 (2H, m, C^3H_2), 2.7 (2H, m, C^4H_2), 3.6 (1H, m, C^2H, J=6 Hz), 3.85 (1H, d, C^1H, J=6 Hz), 7.0—8.0 (9H, m, arom.).

***trans*-1-Bromo-2-benzenesulfonamido-1,2,3,4-tetrahydronaphthalene (7)**——Compound (**6**) (0.2 g) was dissolved in $CHCl_3$ (5 ml) and 35% aq. HBr (5 ml) was dropwise added to the stirred solution at room temperature. The mixture was stirred for additional 1 hr and the $CHCl_3$-layer separated was washed with H_2O, dried over Na_2SO_4, and the solvent was eliminated *in vacuo*. The residue was quickly chromatographed through a short silica gel column eluting with $CHCl_3$–*n*-hexane (1: 1) to obtain crystals (0.2 g) of **7** which were unstable for further purification. NMR ($CDCl_3$): Fig. 1.



14 **15**

Chart 2

***trans*-1-Methoxy-2-benzenesulfonamido-1,2,3,4-tetrahydronaphthalene (8)**——Into a solution of MeONa prepared from Na (0.3 g) and dry MeOH (20 ml), compound (**6**) was added. The mixture was refluxed for 30 min, and the solvent was evaporated *in vacuo* to leave a syrup which was mixed with H_2O (20 ml) and the separated solid was filtered and recrystallized from EtOH to give crystals of mp 119° (**8**) (48%). *Anal.* Calcd. for $C_{17}H_{19}O_3NS$: C, 64.33; H, 6.03; N, 4.41. Found: C, 64.30; H, 6.06; N, 4.41. IR_{max}^{Nujol} cm^{-1}: 3200 (ν_{NH}), 1320, 1155 (ν_{SO_2N}). NMR ($CDCl_3$) δ: 1.7 (2H, m, C^3H_2), 2.7 (2H, t, J=7 Hz, C^4H_2), 3.1 (3H, s, OCH_3), 3.8 (1H, m, C^2H), 4.1 (1H, d, J=5.5 Hz, C^1H), 5.0 (1H, br, NH), 7.1—8.0 (9H, m, arom.).

***trans*-1-Ethoxy-2-benzenesulfonamido-1,2,3,4-tetrahydronaphthalene (9)**——Compound (**6**) (1 g) was added to a solution of Na (0.3 g) in dry EtOH (20 ml). The mixture was refluxed for 30 min and the solvent was evaporated under reduced pressure. To the residue, H_2O (20 ml) was added and the precipitate was filtered and recrystallized from EtOH to obtain **9**, mp 141° (51%). *Anal.* Calcd. for $C_{18}H_{21}O_3NS$: C, 65.23; H, 6.39; N, 4.23. Found: C, 65.13; H, 6.41; N, 4.35.

Reaction of N,N-Dibromo-*p*-toluenesulfonamide with 2-Methyl-3,4-dihydronaphthalene (14)——N,N-Dibromo-*p*-toluenesulfonamide (2.5 g) was added to a stirred solution of **14** (1 g) in CH_2Cl_2 (50 ml) during 30 min under cooling at 0°. The mixture was then refluxed for 30 min. The solvent was removed distillation to leave an oil which was chromatographed on a silica gel column eluting with $CHCl_3$–*n*-hexane (3: 10) to obtain crystals which were recrystallized from $CHCl_3$–*n*-hexane to give **15**, mp 164° (25%). *Anal.* Calcd. for $C_{18}H_{20}O_2NSBr$: C, 54.82; H, 5.11; N, 3.55. Found: C, 54.55; H, 5.05; N, 3.69. IR_{max}^{Nujol} cm^{-1}: 3300 (ν_{NH}), 1310, 1155 (ν_{SO_2N}). NMR ($CDCl_3$) δ: 1.90 (3H, s, C^2CH_3), 2.05 (2H, m, C^3H_2), 2.45 (3H, s, $C^{4'}CH_3$), 2.90 (2H, m, C^4H_2), 4.60 (1H, d, J=9 Hz, C^1H), 4.85 (1H, d, C^1NH), 6.3—7.8 (8H, m, arom.).

Reaction of DCU with 1,2-Dihydronaphthalene (4)——A solution of DCU (4.7 g, 0.03 mole) in CCl_4 (100 ml) was dropwise added to a stirred solution of **4** (3.9 g, 0.03 mole) in CCl_4 (100 ml) under stirring at −5° during 30 min. N_2 was bubled through into the mixture during the addition. After additional stirring for 2 hr at room temperature, the mixture was stirred with 10% aq. $NaHSO_3$ (100 ml) and the organic layer was separated. The layer was washed with H_2O and dried over Na_2SO_4. The solvent was distilled under reduced pressure and the residue was chromatographed on a silica gel column eluting with *n*-hexane to isolate an oil, bp_6 75—82°. Successive elution of the column with *n*-hexane–$CHCl_3$ (4: 1) gave crystals of mp 182° which was identified with authentic α-1,2,3,4-tetrachloro-1,2,3,4-tetrahydronaphthalene.[9] The oil, the first eluate from the column, gave single spot on a thin-layer chromatography (TLC) ($CHCl_3$). NMR ($CDCl_3$) δ: 0.9 (m, br), 1.25 (s), 1.45 (s), 1.7 (m, br), 2.75 (m, br), 6.9—8.4 (m). GC–MS[13] M^+: *m/e* 128, 162, 132, 166 (Chart 2).

Reaction of DBU with 1,2-Dihydronaphthalene (4)——The procedure carried out in the similar way as that of the reaction of DCU gave a reaction mixture which was chromatographed through a silica gel column eluting with *n*-hexane–$CHCl_3$ (4: 1) to isolate crystals of mp 77° (25%) which were identified with naphthalene by comparison of infrared (IR) and NMR spectra. From the second fraction of the elution, crystals of

13) Shimazu-LKB 9000 GC-MS. Measurement: column, 5% SE 30, 3 mm×2 m, 100—150°; accelerating volt: 3500 v; ion source: 270°; separator: 240°; ionization potential: 70 eV.

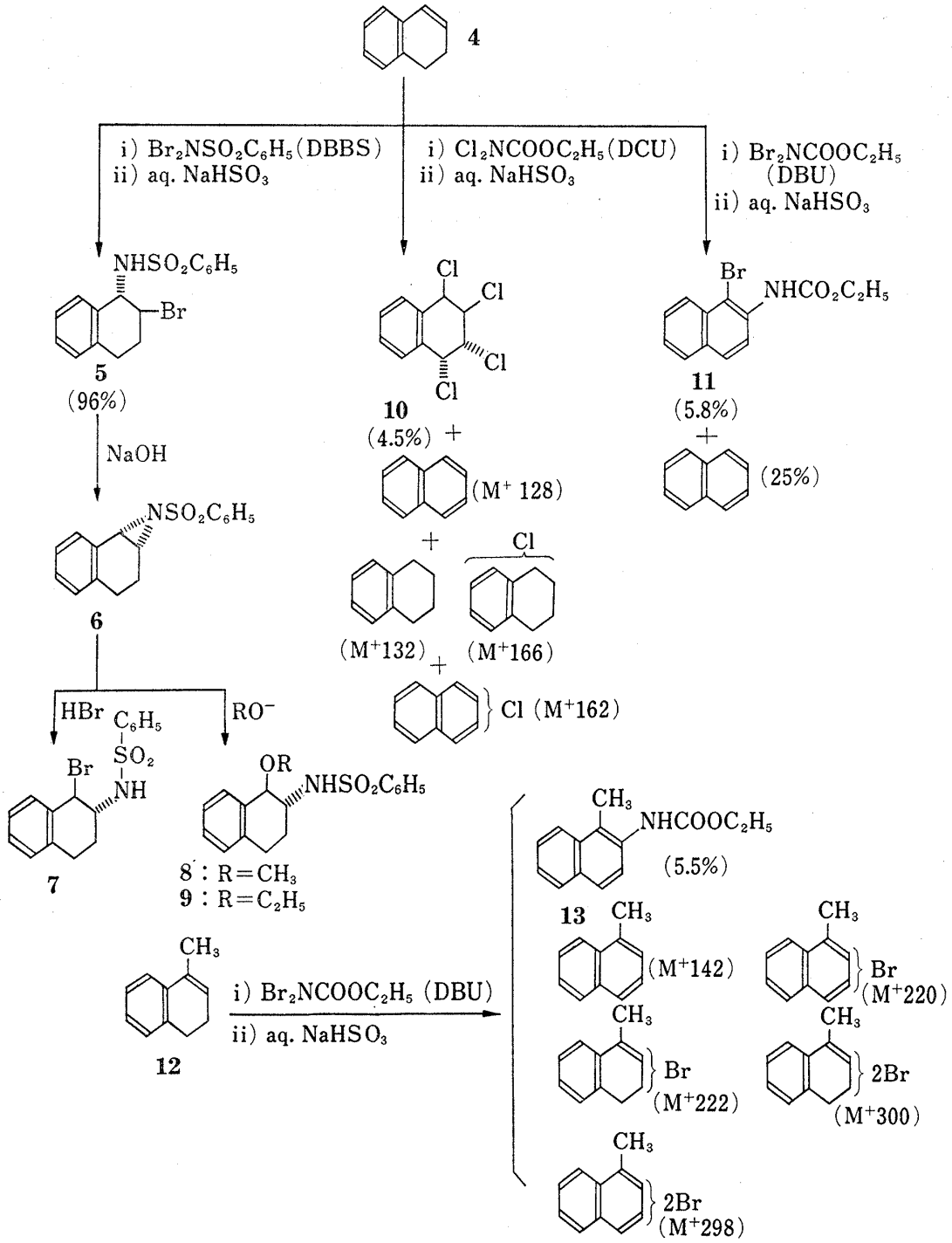


Chart 3

mp 87° (**11**) were isolated (5.8%). *Anal.* Calcd. for $C_{13}H_{12}O_2NBr$: C, 53.03; H, 4.11; N, 4.76. Found: C, 53.10; H, 4.16; N, 4.60. NMR ($CDCl_3$) δ: 1.35 (3H, t, J=7 Hz, $OCH_2\underline{CH_3}$), 4.25 (2H, q, J=7 Hz, $O\underline{CH_2}CH_3$), 7.2—8.45 (6H, m, arom; 1H, br, NH).

1-Bromo-2-naphthylamine——A mixture of **11** (0.5 g) and 20% aq. KOH (10 ml) was refluxed for 1 hr and the solution was extracted with Et_2O. The extract was washed with H_2O, dried over Na_2SO_4, and the solvent was removed *in vacuo*. The residue was recrystallized from EtOH to obtain crystals of mp 62° (0.2 g) which were identified with authentic 1-bromo-2-naphthylamine by mixed melting point determination.

Reaction of DBU with 1-Methyl-3,4-dihydronaphthalene (12)——Under cooling at −5° and N_2 atmosphere, a solution of DBU (11.4 g, 0.046 mole) in CCl_4 (100 ml) was added to a stirred solution of **12** (6.7 g, 0.046 mole) in CCl_4 (100 ml) during 30 min. Stirring was continued for additional 1.5 hr at room temperature and the mixture was allowed to stand overnight. The reaction mixture was then stirred with 10% aq. $NaHSO_3$ until KI-starch showed negative. The CCl_4-layer was washed with H_2O, dried over Na_2SO_4, and

the solvent was eliminated *in vacuo*. The residue was chromatographed on a silica gel column to obtain crystals of mp 123° (**13**, 5.5%) and an oil. Compound (**13**): *Anal.* Calcd. for $C_{14}H_{15}O_2N$: C, 73.34; H, 6.59; N, 6.11. Found: C, 73.21; H, 6.65; N, 6.08. NMR ($CDCl_3$) δ: 1.3 (3H, t, J=7 Hz, $OCH_2C\underline{H}_3$), 2.5 (3H, s, C^1CH_3), 4.2 (2H, q, J=7 Hz, $OC\underline{H}_2CH_3$), 6.5 (1H, br, NH), 7.2—8.1 (6H, m, arom.). The oil: NMR ($CDCl_3$) δ: 2.2 (m, CH_3), 2.6—2.9 (m, CH_2 and CH), 4.5 (s), 4.9 (s), 5.1 (s), 5.6 (t), 7.0—8.2 (m, arom.). GC-MS* M^+: *m/e* 142, 220, 222, 302, 300 (Chart 2).

1-Methyl-2-naphthylamine——A mixture of **13** (0.5 g) and 10% aq. NaOH (10 ml) was refluxed for 1 hr and the mixture was extracted with ether. The extract was washed with H_2O, dried (Na_2SO_4), and distilled to remove ether. The residue was recrystallized from *n*-hexane to give crystals of mp 50—51° which were identified with authentic sample of 1-methyl-2-naphthylamine[10] by mixed melting point determination.

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