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Neighboring group effect of five-membered heteroaromatic rings for π-facial selectivity in the reactions of fused isopropylidenenorbornene systems with electrophilic reagents

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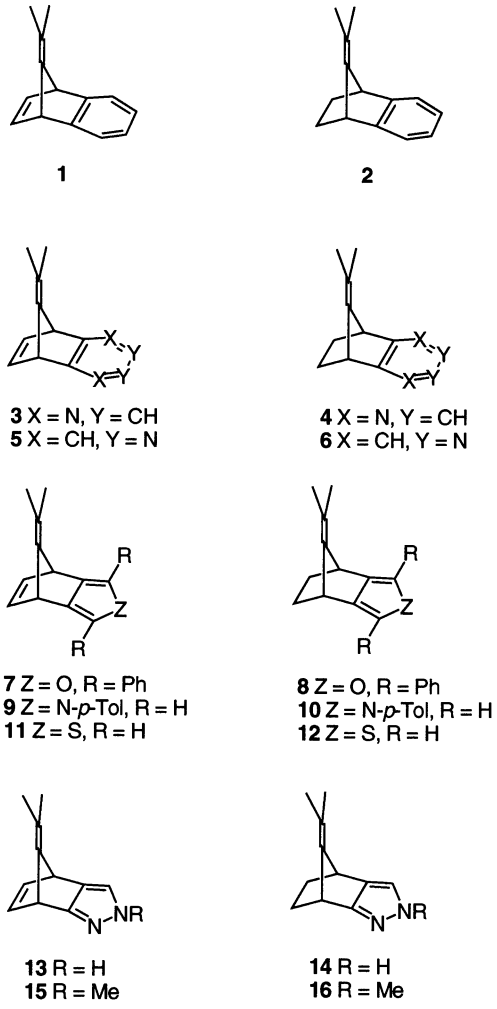
Abstract—The electrophilic reactions of novel isopropylidenenorbornadienes and isopropylidenenorbornenes fused with a furan, pyrrole, thiophene, and pyrazole ring with 1,2,4-triazole-3,5-(4*H*)-dione, *m*-chloroperbenzoic acid, dichlorocarbene, and *N*-bromosuccinimide (NBS) indicated that the neighboring group effect of the five-membered heteroaromatic rings was, unexpectedly, almost similar to that of a benzene ring except for the reaction with NBS.

1. Introduction

Although numerous experimental and theoretical studies on the π-facial stereoselectivity have been reported,[1] essentially no attention has been paid to the possible control of π-facial selectivity by a neighboring heteroaromatic ring. Recently, we reported the electrophilic reactions of isopropylidenenorbornadienes **3** and **5**, and isopropylidenenorbornenes **4** and **6**, fused with six-membered heteroaromatic rings such as pyridazine and pyrazine.[2] In these reactions, the predominant *syn* selectivity, which can not be attained by the benzene-fused congeners **1** and **2**,[3] was realized probably due to the positive electrostatic potential field over the electron-deficient heteroaromatic rings. On the other hand, five-membered heteroaromatics are generally recognized to be electron-excessive, and the higher *anti* preference than the benzene-fused congeners might be expected in the electrophilic reactions of isopropylidenenorbornenes fused with these rings. In due course of our studies on the neighboring group participation of heteroaromatic rings,[4–11] we wish to describe here the syntheses of isopropylidenenorbornadienes and isopropylidenenorbornenes **7**–**16** fused with a furan, pyrrole, thiophene, and pyrazole ring, and the reactions of them with 4-phenyl-1,2,4-triazole-3,5(4*H*)-dione (PTAD), *m*-chloroperbenzoic acid (MCPBA), dichlorocarbene, and *N*-bromosuccinimide (NBS), in order to clarify the neighboring group effect of the five-membered heteroaromatics for the π-facial selectivity (Scheme 1).



Scheme 1.

Keywords: π-facial selectivity; neighboring group effect; electrophilic reaction; isopropylidenenorbornene; heteroaromatic ring.

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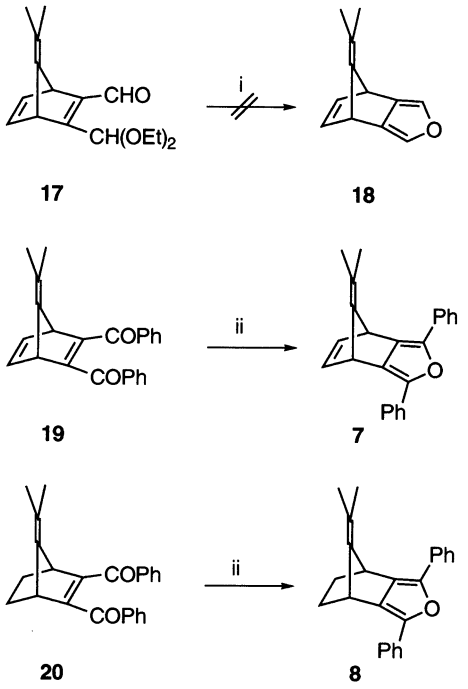


Scheme 2. *Reagents and conditions*: (i) $NaBH_4$, EtOH, rt; Amberlyst-15, CH_2Cl_2, rt; (ii) $P(OEt)_3$, *o*-dichlorobenzene, reflux.

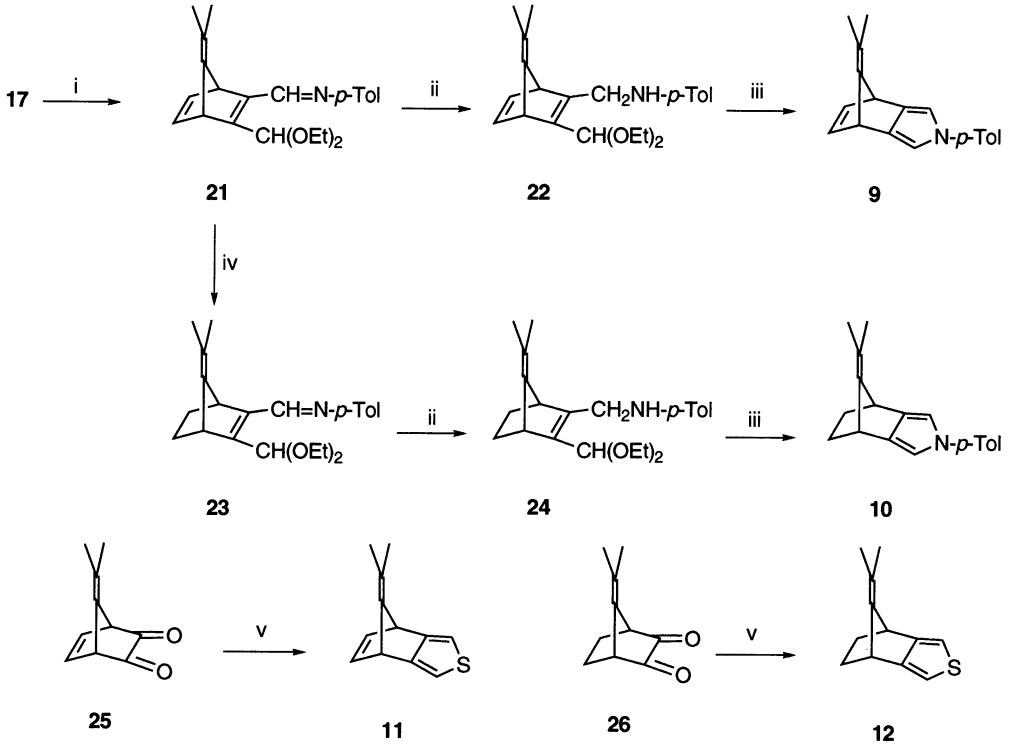
1.1. Synthesis of the fused isopropylidenenorbornene derivatives

We have reported the synthesis of the norbornadienes fused with furans, pyrroles, thiophenes,[8–10] and pyrazoles.[11] Thus, the analogous synthetic pathways would be promising for the synthesis of the isopropylidenenorbornene derivatives.

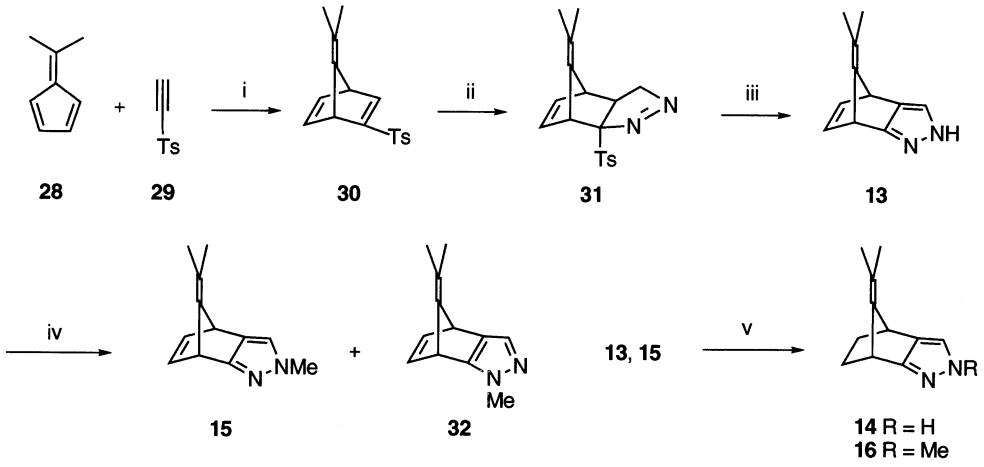
Our initial attempt to synthesize the furan **18** by treatment of the aldehyde **17** with sodium borohydride, followed by the acid-induced cyclization with Amberlyst-15, resulted in the formation of a trace amount of oil. The ^1H NMR spectrum of the oil exhibiting δ=1.50 (6H, s), 4.28 (2H, t, J=2 Hz), 6.76 (2H, t, J=2 Hz), and 7.01 (2H, s) seemed to be assignable to **18**, but we could not obtain enough amount of **18** for the full characterization. Thus, we turned to the synthesis of the diphenyl-substituted furan **7**. The reductive cyclization of 2,3-dibenzoyl-7-(1-methylethylidene) bicyclo-[2.2.1]hepta-2,5-diene (**19**) in the presence of triethyl phosphite provided the fused diphenylfuran **7** in 26% yield. A similar treatment of **20** with triethyl phosphite gave **8** in 69% yield (Scheme 2).

For the synthesis of the fused pyrroles **9** and **10**, the aldehyde **17** was treated with *p*-toluidine to give the imine **21**. The reduction of **21** with sodium borohydride, and the subsequent treatment with silica gel in benzene at room temperature successfully provided the pyrrole **9** in 11% overall yield from **21**. On the other hand, the initial hydrogenation of **21** in the presence of Pd/C, and the successive treatments with sodium borohydride and silica gel afforded the fused isopropylidenenorbornene **10** in 41% overall yield from **21**. In these reactions, we encountered difficulty in purification of the intermediates **22**–**24**, and we used them to the next step without purification.

The thiophene-fused isopropylidenenorbornadiene **11** (17%) and isopropylidenenorbornene **12** (19%) were, respectively, prepared by the double-Wittig reactions of the



Scheme 3. *Reagents and conditions*: (i) *p*-toluidine, $MgSO_4$, CH_2Cl_2, rt; (ii) $NaBH_4$, EtOH, rt; (iii) SiO_2, PhH, rt; (iv) H_2, Pd/C, AcOEt, rt; (v) $(Ph_3P^+CH_2)_2S$ $2Cl^-$ (**27**), BuLi, Et_2O, −78°C to rt.



Scheme 4. *Reagents and conditions*: (i) PhH, reflux; (ii) CH_2N_2, Et_2O–CH_2Cl_2, 0°C; (iii) NaH, THF, 0°C; (iv) NaH, MeI, THF, rt; (v) H_2, Pd/C, AcOEt, rt.

isopropylidenenorbornene-2,3-dione **25** and isopropylidenenorbornane-2,3-dione **26** with the ylide, which was derived from dimethyl thioether-α,α′-bisphosphonium dichloride (**27**) (Scheme 3).

The pyrazole-fused isopropylidenenorbornadiene **13** was synthesized by a sequence of the Diels–Alder reaction of 6,6-dimethylfulvene (**28**) and ethynyl *p*-tolyl sulfone (**29**) giving **30**, the 1,3-dipolar cycloaddition reaction of **30** with diazomethane, and the elimination of toluenesulfenic acid from **31** with sodium hydride in THF. When the fused pyrazole **13** was treated with sodium hydride and methyl iodide, the 2-methyl isomer **15** and the 1-methyl isomer **32** were obtained in 41 and 31% yields, respectively. The hydrogenation of **13** or **15** in the presence of Pd/C underwent the selective reduction of the endocyclic double bond to give **14** or **16** (Scheme 4).

1.2. Electrophilic reactions of fused isopropylidenenorbornene derivatives

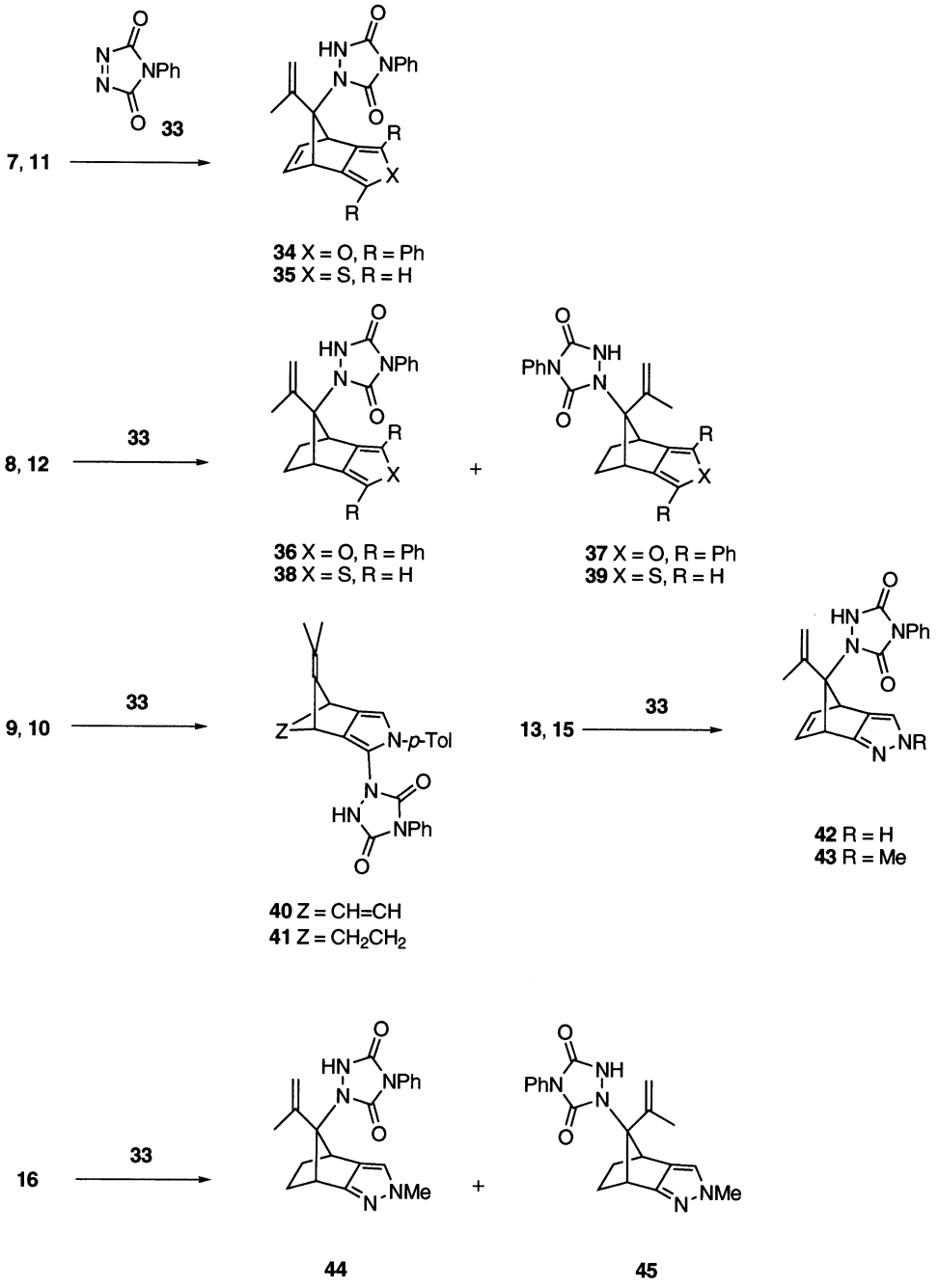
The reactions of the fused isopropylidenenorbornene derivatives with PTAD, MCPBA, dichlorocarbene, and NBS were investigated. The products and the ratios of *syn* and *anti* isomers in these reactions are summarized in Table 1.

On treatment with PTAD, the furan- and thiophene-fused isopropylidenenorbornadiene **7** and **11**, respectively, provided the ene-reaction products **34** and **35**, where PTAD attacks exclusively from the *syn* face with respect to the heteroaromatic rings. Although isopropylidenebenzonorbornadiene **1** was reported to give a single ene-reaction product on treatment with PTAD, the stereochemistry was ambiguous.[12] In contrast, the stereochemistry of the ene-reaction products **34** and **35** was clearly determined as being *syn* by the observations of NOEs between the olefinic protons at the 5- and 6-positions and the methyl group by the NOE differential spectroscopy.

The exclusive *syn* preference of these reactions was assumed to be due to the existence of the endocyclic double bond, that would stabilize a transition state of the reaction by bishomoaromatic interaction of the π-systems. Thus, the reactions of the fused isopropylidenenorbornenes **8** and **12**, where the endocyclic double bond potentially involved in such stabilization is absent, were investigated. In these reactions, a mixture of *syn* and *anti* products **36** and **37**, or **38** and **39** was obtained with *anti* preference as expected. Assignments of *syn* and *anti* configuration of the products were determined by the NOE measurements. Unfortunately, the reaction of the fused pyrroles **9** and **10** with PTAD gave the substitution products **40** and **41**, respectively, and no ene-reaction was observed. Similar reactions of the pyrazole-fused isopropylidenenorbornadienes **13** and **15** with PTAD gave only *syn* isomers **42** and **43**, while the fused isopropylidenenorbornene **16** gave a mixture of *syn* and *anti* isomers **44** and **45** in a ratio of 9:91 with *anti*

Table 1. Products and ratios of the *syn* and *anti* isomers in the electrophilic reactions of the fused isopropylidenenorbornenes

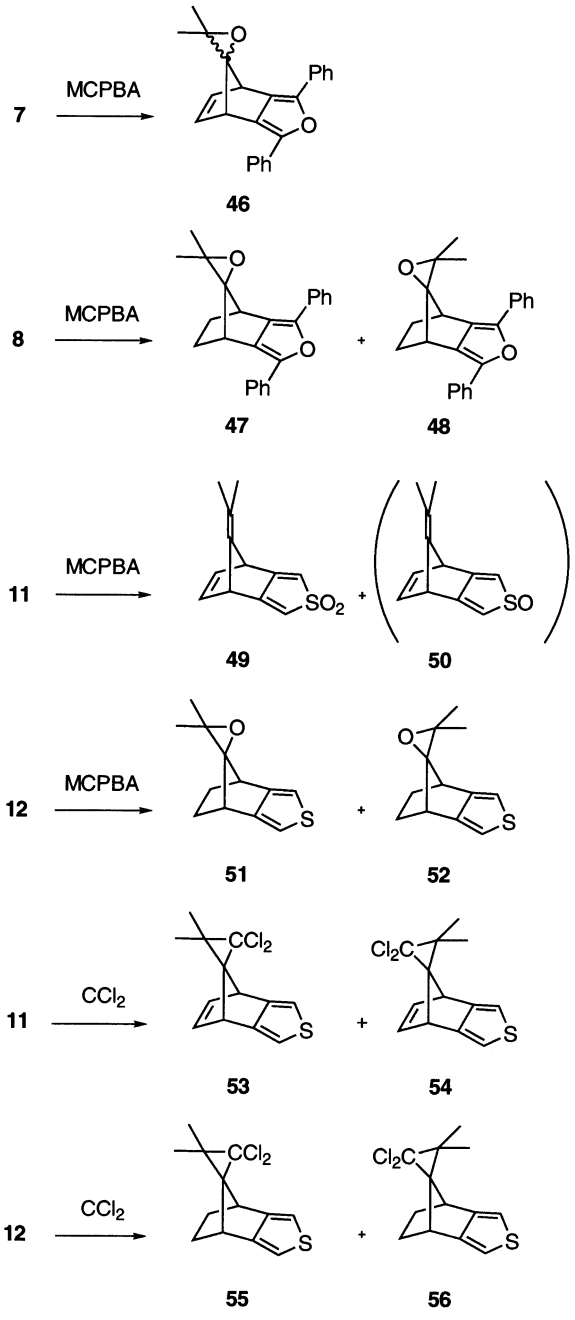
Substrates	Products			
	PTAD (*syn*/*anti*)	MCPBA (*syn*/*anti*)	CCl_2 (*syn*/*anti*)	NBS (*syn*/*anti*)
7	**34** (100:0)	**46**	–	–
8	**36**+**37** (21:79)	**47**+**48** (14:86)	–	**58** (0:100)
9	**40**	–	–	–
10	**41**	–	–	**60**
11	**35** (100:0)	**49**	**53**+**54** (61:39)	–
12	**38**+**39** (28:72)	**51**+**52** (18:82)	**55**+**56** (62:38)	**59** (0:100)
13	**42** (100:0)	–	–	–
15	**43** (100:0)	–	–	–
16	**44**+**45** (9:91)	–	–	–
2[3]	19:81	17:83	65:35	19:81



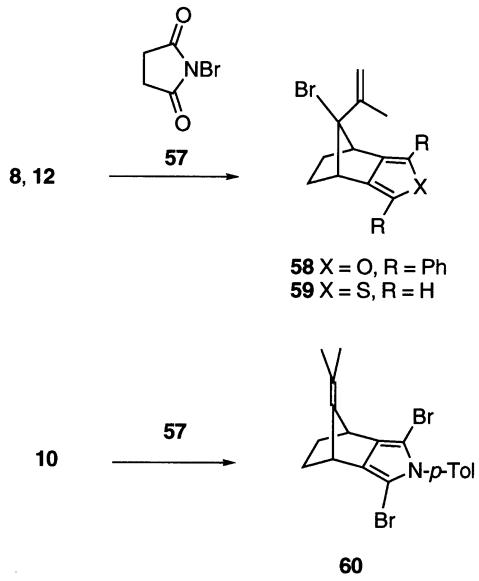
Scheme 5.

preference. Stereochemical assignment for the inseparable mixture of **44** and **45** was based on the ^{1}H chemical shifts of the methyl and methylene protons at isopropenyl group: the chemical shifts of the methyl (δ=1.74) and the methylene (δ=4.92 and 5.06) groups in the *anti* isomer **45** are shielded compared to those of the *syn* isomer **44** (δ=1.90 for CH_3 and δ=5.18 and 5.22 for $=CH_2$) due to the shielding effect of the aromatic pyrazole ring (Scheme 5).

Although the epoxidation reaction of the furan **7** with MCPBA gave the epoxide **46** as a single stereoisomer, the yield was very low (11%) and the stereochemistry of **46** could not be determined. Treatment of **8** with MCPBA provided a mixture of *syn* and *anti* epoxides **47** and **48** in a ratio of 14:86 albeit in low yield (26%). In these reactions, we could not isolate any other products, but a by-product bearing benzoyl groups seemed to be formed possibly by an oxidative ring-cleavage of the furan ring. Epoxidation of the thiophene **12** with MCPBA provided a mixture of *syn* and *anti* epoxides **51** and **52** with *anti* preference. The stereochemistry of the epoxides was based on the ^{1}H chemical shifts of the methyl group: an epoxide bearing the shielded methyl group (δ=1.30) was assigned to be the *anti* epoxide **52**, with respect to the *syn* epoxide **51** (δ=1.37 for CH_3). To our surprise, the reaction of the thiophene-fused isopropylidenenorbornadiene **11** with MCPBA unexpectedly produced the thiophene *S*,*S*-dioxide **49** and no epoxidation at the isopropylidene moiety was observed. We also



Scheme 6.



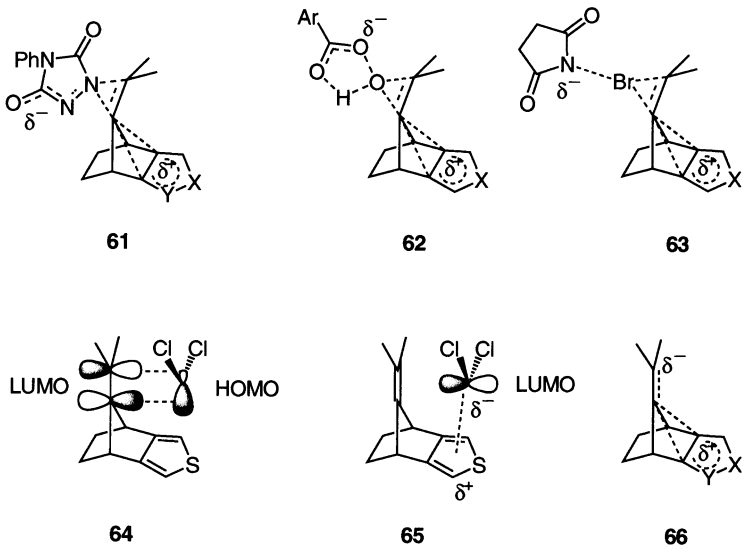
Scheme 7.

obtained a solid, the structure of which could be assigned to the thiophene *S*-oxide **50** judging from the ^{1}H NMR and mass spectra. However, the compound **50** is thermally labile as generally recognized for thiophene *S*-oxides,[13,14] and the reproducibility of **50** was rather low. Thus, we could not make a full characterization for **50**. The thiophenes **11** and **12** reacted with dichlorocarbene, which was generated by the thermolysis of sodium trichloroacetate, to give the *syn* isomers **53** and **55** as major components, respectively. Since no isomerization between *syn* and *anti* adducts was observed under the reaction conditions, the major *syn* adducts are considered to be kinetically controlled products (Scheme 6).

In contrast to these reactions described above, the reactions of the fused furan **8** and thiophene **12** with NBS exclusively produced the *anti* ene-reaction products **58** and **59**, respectively. The NOE measurements of **58** or **59** exhibited no NOE between the methyl group and the proton at the 5-position, in contrast to the fact that the NOEs are clearly observed for most of the *syn* isomers formed by other reactions. Furthermore, the ^{1}H chemical shifts of the methyl group (δ=1.79 for **58** and δ=1.75 for **59**) are almost identical to those of the *anti* isomers of the ene-reaction products with PTAD (δ=1.79 for **37** and δ=1.71 for **39**). These results are suggestive of the *anti* configuration of the products. We again observed the formation of the substitution product **60** on treatment of the fused pyrrole **10** with NBS (Scheme 7).

The variations in *syn* and *anti* ratios depending on the fused heteroaromatic rings and the electrophilic reagents would be attributed to the relative stability of the corresponding transition states. The *anti* ratios for the reactions of **8** and **12** with PTAD as well as that of **12** with MCPBA are approximately equal or slightly less compared to those of the benzene-fused analog **2** (Table 1). The *anti* preference of the reactions with PTAD and MCPBA would be ascribed to the neighboring group effect of five-membered heteroaromatic rings stabilizing the transition states by the bishomoaromatic interaction (**61** and **62**).[2,3] The pyrazole ring of **16** seems to be most effective for the formation of the *anti* isomer.

The addition reactions of dichlorocarbene would take place by a HOMO–LUMO interaction (**64**). At the same time, an electrostatic interaction between the electron-deficient carbon center of the carbene and the electron-rich thiophene ring would account for *syn* preference of the reactions (**65**).[3] Our calculations on the fused thiophene **12** and the fused benzene **2** by the PM3 method indicated no significant difference of the electrostatic potential fields between these compounds,[15] which would account for a similar *syn*/*anti* selectivity of the reactions.



Scheme 8.

The exclusive *anti* preference in the reactions with NBS can be explained as follows: the bromine–nitrogen bond in the transition state **63** is almost dissociated and the developed cationic charge on the bromine atom would be effectively stabilized by five-membered heteroaromatic rings. The effect seems to be rather stronger than that of a benzene ring, due to the electron-excessive heteroaromatic rings (Scheme 8).

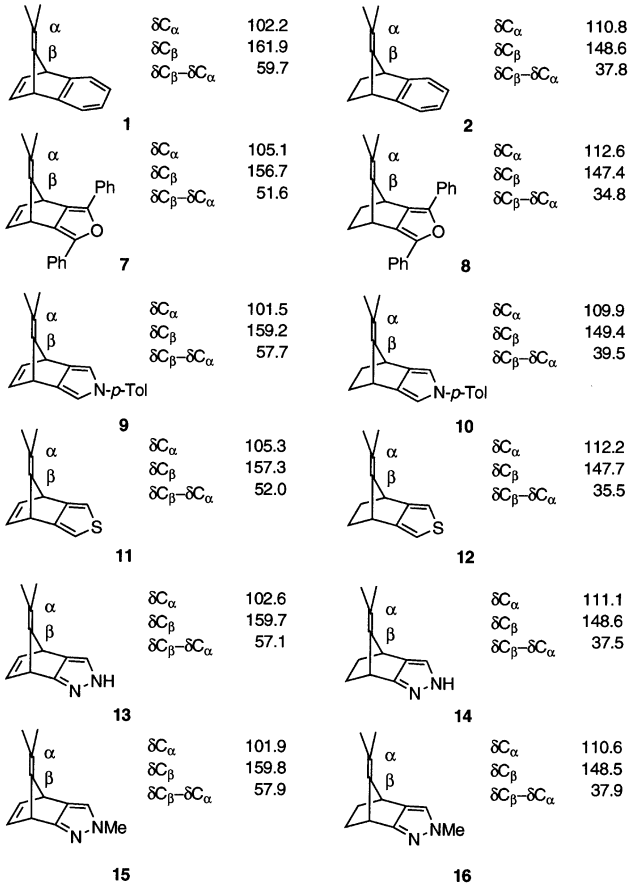


Figure 1. ^{13}C Chemical shifts of the exocyclic double bonds in the fused isopropylidenenorbornene derivatives **1**, **2**, and **7**–**16**.

One index to evaluate the through-space interaction between heteroaromatic rings and the isopropylidene moiety at the ground state as depicted in **66** is the difference in the ^{13}C chemical shifts of the olefinic carbons at isopropylidene group.[16–19] (Fig. 1) The chemical shift differences of the fused furan **8** and thiophene **12** are slightly smaller than that observed for **2**, whereas those of the fused pyrrole **10** and pyrazole **16** show larger values. Unfortunately, we could not clarify the π-facial selectivity of the fused pyrroles, but the trend in the difference of the ^{13}C chemical shifts is qualitatively comparable with that of the π-facial selectivity observed in the reaction with PTAD, probably because the transition state in the reactions with PTAD would resemble to the nature of the ground state.

Previously, the neighboring group participation of five-membered heteroaromatic rings has been demonstrated rather effective for the electrophilic addition reactions of fused norbonradienes.[10,11] Therefore, we had presumed, in the beginning, that the increasing *anti* selectivity in the electrophilic reactions of fused isopropylidenenorbornene derivatives could be expected for the fused five-membered heteroaromatics compared to that of the benzene-fused congener. However, the neighboring group effect of five-membered heteroaromatic rings for the π-facial selectivity was found to be almost similar to that of a benzene ring, except for the reaction with NBS. Further studies would be necessary to clarify the reason why the effect of the five-membered rings is comparable.

2. Experimental

2.1. General

All mps were determined with a Yanagimoto hot-stage apparatus. IR spectra were obtained with a JEOL Diamond-20 spectrometer. NMR spectra were recorded

with a JEOL JNM-LA400 (^{1}H: 400 MHz, ^{13}C: 100 MHz) spectrometer using TMS as internal standard. *J* values are given in Hz. Assignments of the ^{1}H and ^{13}C signals are based on DEPT, H–H COSY, and C–H COSY measurements. Mass spectra were measured with a Shimadzu GCMS-QP1000EX spectrometer operating in the electron impact mode (70 eV). Elemental analyses were performed with a Perkin–Elmer Model 240 apparatus. High-resolution mass spectra (HR-MS) were taken with a JEOL DX-300 spectrometer. MPLC separations were carried out by a YAMAZEN YFLC-600-10V system with a YAMZEN Ultra Pack® Column (Si-40B, silica gel). Solvents were dried and purified by standards methods. Yields are based on the isolated products with sufficient purity.

2.1.1. 4,7-Dihydro-8-(1-methylethylidene)-1,3-diphenyl-4,7-methanoisobenzofuran (7). A solution of 2,3-dibenzoyl-7-(1-methylethylidene)bicyclo[2.2.1]hepta-2,5-diene[2] (**19**) (170 mg, 0.5 mmol) and triethyl phosphite (0.25 cm^3, 1.5 mmol) in *o*-dichlorobenzene (5 cm^3) was refluxed for 30 min under a nitrogen atmosphere. The mixture was concentrated and the residue was separated by TLC (silica gel, hexane–ethyl acetate 5/1) to give **7** (42 mg, 26%): orange prisms (from ethanol); mp 168.5–169.5°C; IR (KBr) 3008, 2974, 1601, 1493, 1444 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.62 (6H, s, CH_3), 4.57 (2H, s, 4-H and 7-H), 6.89 (2H, s, 5-H and 6-H), 7.23 (2H, m), 7.40 (4H, m), 7.72 (4H, m); ^{13}C NMR ($CDCl_3$) δ=19.5 (CH_3), 44.7 (C-4 and C-7), 105.1 (C-9), 124.0, 126.7, 128.6, 131.4, 134.0 (C-3a and C-7a), 141.2 (C-1 and C-3), 141.4 (C-5 and C-6), 156.7 (C-8); MS *m*/*z* (rel intensity) 324 (100, M^+), 309 (15, $M-CH_3$), 105 (39, COPH), 77 (51, Ph). Found: C, 88.92; H, 6.35%. Calcd for $C_{24}H_{20}O$: C, 88.85; H, 6.21%.

2.1.2. 4,5,6,7-Tetrahydro-8-(1-methylethylidene)-1,3-diphenyl-4,7-methanoisobenzofuran (8). A solution of 2,3-dibenzoyl-7-(1-methylethylidene)bicyclo[2.2.1]hept-2-ene[2] (**20**) (340 mg, 1 mmol) and triethyl phosphite (0.5 cm^3, 3 mmol) in *o*-dichlorobenzene (10 cm^3) was refluxed for 1 h under a nitrogen atmosphere. The mixture was concentrated and the residue was passed through a short column (silica gel, benzene). The eluent was concentrated and the resulting solid was collected by suction to give **8** (230 mg, 69%): a white solid (from methanol); mp 184–185°C; IR (KBr) 2997, 2966, 1603, 1493, 1444, 1109, 1061 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.52 (2H, dm, *J*=7 Hz, 5-H_{endo} and 6-H_{endo}), 1.68 (6H, s, CH_3), 2.02 (2H, dm, *J*=7 Hz, 5-H_{exo} and 6-H_{exo}), 4.05 (2H, t, *J*=2 Hz, 4-H and 7-H), 7.22 (2H, m), 7.40 (4H, m), 7.72 (4H, m); ^{13}C NMR ($CDCl_3$) δ=20.3 (CH_3), 22.7 (C-5 and C-6), 38.8 (C-4 and C-7), 112.6 (C-9), 124.0, 126.4, 128.6, 131.7, 132.0, 140.5 (C-1 and C-3), 147.4 (C-8); MS *m*/*z* (rel intensity) 326 (100, M^+), 311 (15, $M-CH_3$), 298 (97, $M-CH_2CH_2$), 105 (21, COPh), 77 (34, Ph). Found: C, 88.35; H, 6.78%. Calcd for $C_{24}H_{22}O$: C, 88.31; H, 6.79%.

2.1.3. *N*-[3-(Diethoxymethyl)-7-(1-methylethylidene)bicyclo[2.2.1]hepta-2,5-dien-2-yl]methylidene-*N*-(*p*-tolyl)-amine (21). A mixture of 3-(diethoxymethyl)-7-(1-methylethylidene)bicyclo[2.2.1]hepta-2,5-diene-2-carbaldehyde[2] (**17**) (1.31 g, 5 mmol), *p*-toluidine (0.54 g, 5 mmol), and anhydrous magnesium sulfate (0.5 g) in chloroform (10 cm^3) was stirred at room temperature for 30 min. The mixture was concentrated and the residue was separated by column chromatography (alumina, hexane–ethyl acetate 5/1) to give **21** (0.87 g, 49%): a slightly yellow solid (from hexane); mp 100.5–101.5°C; IR (KBr) 2974, 2925, 2914, 2881, 1624, 1572, 1504, 1336, 1281, 1180, 1122, 1092, 1053, 1022 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.21 (3H, t, *J*=7 Hz, CH_3), 1.22 (3H, t, *J*=7 Hz, CH_3), 1.50 (3H, s, CH_3), 1.53 (3H, s, CH_3), 2.34 (3H, s, CH_3), 3.42–3.60 (4H, m, OCH_2), 4.26 (1H, t, *J*=2.5 Hz, 4-H), 4.81 (1H, t, *J*=2.5 Hz, 1-H), 5.45 (1H, s, CH), 6.91 (1H, m, 5-H), 7.02 (2H, m, 6-H), 7.06 (2H, d, *J*=8.5 Hz), 7.15 (2H, d, *J*=8.5 Hz), 8.66 (1H, S, CH=N); ^{13}C NMR ($CDCl_3$) δ=15.2 (CH_3), 18.4 (CH_3), 18.7 (CH_3), 21.0 (CH_3), 50.2 (C-1), 52.5 (C-4), 61.1 (OCH_2), 61.2 (OCH_2), 98.7 (C), 99.1 (CH), 121.0, 129.7, 135.4, 141.9 (C-5), 142.6 (C-6), 150.2, 151.1, 154.2 (CH=N), 159.7, 161.1; MS *m*/*z* (rel intensity) 351 (17, M^+), 322 (100, M−Et), 306 (18, M−OEt), 118 (32, CH=N-tolyl). Found: C, 78.57; H, 8.61; N, 4.00%. Calcd for $C_{23}H_{29}NO_2$: C, 78.60; H, 8.32; N, 3.98%.

2.1.4. 4,7-Dihydro-8-(1-methylethylidene)-2-(*p*-tolyl)-4,7-methano-2*H*-isoindole (9). To a solution of the imine **21** (0.53 g, 1.5 mmol) in ethanol (20 cm^3) was added sodium borohydride (0.08 g, 2 mmol), and the mixture was stirred at room temperature for 30 min. The mixture was concentrated and benzene (30 cm^3) was added to the residue. The organic phase was washed with water and brine prior to drying with Na_2SO_4. Insoluble materials were removed by filtration, and the filtrate was stirred at room temperature for 1 h in the presence of silica gel (1.5 g). After removal of the solvent, the residue was separated by column chromatography (silica gel, dichloromethane) to give **9** (0.20 g, 11%): colorless plates (from ethanol); mp 136–137°C; IR (KBr) 3008, 2974, 1601, 1493, 1444 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.59 (6H, s, CH_3), 2.32 (3H, s, CH_3), 4.32 (2H, t, *J*=2 Hz, 4-H and 7-H), 6.77 (2H, s, 1-H and 3-H), 6.87 (2H, t, *J*=2 Hz, 5-H and 6-H), 7.12 (2H, d, *J*=8.5 Hz, tolyl), 7.17 (2H, d, *J*=8.5 Hz, tolyl); ^{13}C NMR ($CDCl_3$) δ=19.3 (CH_3), 20.8 (CH_3), 44.7 (C-4 and C-7), 101.5 (C-9), 109.9 (C-1 and C-3), 119.7, 129.8, 133.7 (C-3a and C-7a), 136.2, 139.1, 143.0 (C-5 and C-6), 159.2 (C-8); MS *m*/*z* (rel intensity) 261 (100, M^+), 91 (31, C_7H_7). Found: C, 87.54; H, 7.40; N, 5.19%. Calcd for $C_{19}H_{19}N$: C, 87.31; H, 7.33; N, 5.36%.

2.1.5. 4,5,6,7-Tetrahydro-8-(1-methylethylidene)-2-(*p*-tolyl)-4,7-methano-2*H*-isoindole (10). Under a hydrogen atmosphere, a mixture of the imine **21** (1.05 g, 3 mmol) and Pd/C (10%, 25 mg) in ethyl acetate (40 cm^3) was stirred at room temperature for 4 h. Insoluble materials were removed by filtration through celite, and the filtrate was concentrated to give the imine **23** as a yellow oil; ^{1}H NMR ($CDCl_3$) δ=1.22 (3H, t, *J*=7 Hz), 1.23 (3H, t, *J*=7 Hz), 1.33 (2H, m), 1.58 (3H, s), 1.61 (3H, s), 1.82 (2H, m), 2.32 (3H, a), 3.49–3.69 (5H, m), 4.08 (1H, m), 5.41 (1H, s), 7.04 (2H, d, *J*=8 Hz), 7.13 (2H, d, *J*=8 Hz), 8.60 (1H, s); ^{13}C NMR ($CDCl_3$) δ=14.9, 15.0, 19.1, 19.4, 20.7, 25.7, 26.6, 42.3, 44.7, 60.4, 61.4, 98.3, 109.2, 120.7, 129.3, 134.0, 144.9, 145.3, 150.2, 152.7, 154.1; MS *m*/*z* (rel intensity) 353 (3, M^+), 296 [100, $M-CH_3-C(CH_3)_2$], 250 [70, $M-CH(OEt)_2$].

To the crude **23** was added ethanol (40 cm^3) and sodium

borohydride (0.15 g, 4 mmol), and the mixture was stirred at room temperature for 1 h. The mixture was concentrated and benzene (50 cm^3) was added to the residue. The organic phase was washed with water and brine prior to drying with Na_2SO_4. Insoluble materials were removed by filtration, and the filtrate was stirred at room temperature for 14 h in the presence of silica gel (12 g). After removal of the solvent, the residue was separated by column chromatography (silica gel, benzene) to give **10** (0.32 g, 41% from **21**): colorless plates (from methanol); mp 122–122.5°C; IR (KBr) 2991, 2968, 2931, 2863, 1523, 1338, 1028 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.32 (2H, dm, J=6.5 Hz, 5-H_{endo} and 6-H_{endo}), 1.64 (6H, s, CH_3), 1.88 (2H, dm, J=6.5 Hz, 5-H_{exo} and 6-H_{exo}), 2.32 (3H, s, CH_3), 3.76 (2H, m, 4-H and 7-H), 6.70 (2H, s, 1-H and 3-H), 7.14 (2H, d, J=8.5 Hz, tolyl), 7.19 (2H, d, J=8.5 Hz, tolyl); ^{13}C NMR ($CDCl_3$) δ=20.2 (CH_3), 20.8 (CH_3), 29.1 (C-5 and C-6), 38.7 (C-4 and C-7), 108.2 (C-1 and C-3), 109.9 (C-9), 119.9, 129.9, 133.8, 134.2 (C-3a and C-7a), 139.2, 149.4 (C-8); MS *m/z* (rel intensity) 263 (35, M^+), 248 (52, M−CH_3), 235 (100, M−CH_2CH_2). Found: C, 86.82; H, 7.95; N, 5.29%. Calcd for $C_{19}H_{21}N$: C, 86.65; H, 8.04; N, 5.32%.

2.1.6. 4,7-Dihydro-8-(1-methylethylidene)-4,7-methano-2-benzothiophene (11). To a mixture of dimethyl thioether-α,α′-bis(triphenylphosphonium) dichloride[20] (**27**) (3.93 g, 6 mmol) in ether (840 cm^3) was added butyl lithium (1.63 M hexane solution, 7.4 cm^3, 12 mmol) during 10 min at room temperature under a nitrogen atmosphere, and the mixture was stirred at room temperature for 4 h. The mixture was cooled to −78°C, and a solution of 7-(1-methylethylidene)bicyclo[2.2.1]hept-5-ene-2,3-dione[21] (**25**) (0.97 g, 6 mmol) in ether (25 cm^3) was added. The mixture was warmed up to room temperature and further stirred for 60 h. The reaction mixture was poured into water and the organic phase was separated. The aqueous layer was extracted with ether, and the combined organic phases were washed with water prior to drying with Na_2SO_4. After removal of the solvent, the residue was separated by MPLC (hexane–dichloromethane 10/1) to give **11** (0.19 g, 17%): colorless needles (from methanol); mp 87.5–88°C; IR (KBr) 3091, 3066, 3012, 2968, 2925, 2908, 1369, 1346, 1290, 1219 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.56 (6H, s, CH_3), 4.22 (2H, t, J=2 Hz, 4-H and 7-H), 6.66 (2H, s, 1-H and 3-H), 6.79 (2H, t, J=2 Hz, 5-H and 6-H); ^{13}C NMR ($CDCl_3$) δ=19.2 (CH_3), 46.8 (C-4 and C-7), 105.3 (C-9), 110.8 (C-1 and C-3), 142.2 (C-5 and C-6), 151.6 (C-3a and C-7a), 157.3 (C-8); MS *m/z* (rel intensity) 188 (100, M^+), 173 (60, M−CH_3), 134 (22, 2-benzothiophene). Found: C, 76.25; H, 6.56%. Calcd for $C_{12}H_{12}S$: C, 76.55; H, 6.42%.

2.1.7. 4,5,6,7-Tetrahydro-8-(1-methylethylidene)-4,7-methano-2-benzothiophene (12). To a mixture of dimethyl thioether-α,α′-bis(triphenylphosphonium) dichloride (**27**) (2.26 g, 3.5 mmol) in ether (700 cm^3) was added butyl lithium (1.63 M hexane solution, 4.3 cm^3, 7 mmol) during 10 min at room temperature under a nitrogen atmosphere, and the mixture was stirred at room temperature for 6 h. The mixture was cooled to −78°C, and a solution of 7-(1-methylethylidene)bicyclo[2.2.1]heptane-2,3-dione[22] (**26**) (0.57 g, 3.5 mmol) in ether (50 cm^3) was added. The mixture was warmed up to room temperature and further stirred for 36 h. The reaction mixture was poured into water and the organic phase was separated. The aqueous layer was extracted with ether, and the combined organic phases were washed with water prior to drying with Na_2SO_4. After removal of the solvent, the residue was separated by MPLC (hexane) and the resulting oil was distilled (bath temperature 100°C, 0.5 Torr) with a Kugelrohr apparatus to give **12** (0.11 g, 19%): colorless rods; mp 56–58°C; IR (KBr) 3005, 2962, 2933, 2861, 1369, 1358, 1286 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.31 (2H, dm, J=7 Hz, 5-H_{endo} and 6-H_{endo}), 1.61 (6H, s, CH_3), 1.88 (2H, dm, J=7 Hz, 5-H_{exo} and 6-H_{exo}), 3.76 (2H, t, J=2.5 Hz, 4-H and 7-H), 6.71 (2H, s, 1-H and 3-H); ^{13}C NMR ($CDCl_3$) δ=20.1 (CH_3), 28.1 (C-5 and C-6), 41.3 (C-4 and C-7), 110.5 (C-1 and C-3), 112.2 (C-9), 147.7 (C-8), 149.3 (C-3a and C-7a); MS *m/z* (rel intensity) 190 (41, M^+), 175 (100, M−CH_3), 162 (80, M−CH_2CH_2). Found: C, 75.96; H, 7.62%. Calcd for $C_{12}H_{14}S$: C, 75.74; H, 7.41%.

2.1.8. 7-(1-Methylethylidene)-2-(*p*-tolylsulfonyl)bicyclo-[2.2.1]hepta-2,5-diene (30). A solution of 6,6-dimethylfulvene[23] (**28**) (0.75 g, 7 mmol) and ethynyl *p*-tolyl sulfone[24] (**29**) (0.90 g, 5 mmol) in benzene (20 cm^3) was refluxed for 48 h. After removal of the solvent, the residue was separated by column chromatography (silica gel, CH_2Cl_2). The resulting solid was collected by suction and washed with hexane to give **30** (1.02 g, 71%): colorless needles (from hexane–ethyl acetate 1/1); mp 108–109°C; IR (KBr) 3027, 2979, 2911, 2854, 1546, 1311, 1297, 1174, 1149 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.32 (3H, s, CH_3), 1.42 (3H, s, CH_3), 2.43 (3H, s, CH_3), 4.15 (1H, m, 1-H), 4.27 (1H, m, 4-H), 6.74 (2H, m, 5-H and 6-H), 7.31 (2H, d, J=8 Hz), 7.51 (1H, dd, J=3 and 1 Hz, 3-H), 7.69 (2H, d, J=8 Hz); ^{13}C NMR ($CDCl_3$) δ=18.2 (CH_3), 18.4 (CH_3), 21.6 (CH_3), 50.6 (C-1), 51.8 (C-4), 99.4 (C-8), 127.8, 129.7, 136.2, 141.0 (C-5 or C-6), 142.2 (C-6 or C-5), 144.1, 151.6 (C-3), 156.8 (C-2), 162.2 (C-7); MS *m/z* (rel intensity) 286 (40, M^+), 271 (17, M−CH_3), 131 (44, M−Ts), 106 (13, **28**), 91 (100, C_7H_7), 65 (31, C_5H_5). Found: C, 71.41; H, 6.28%. Calcd for $C_{17}H_{18}O_2S$: C, 71.30; H, 6.34%.

2.1.9. 4,7-Dihydro-8-(1-methylethylidene)-4,7-methano-2*H*-indazole (13). A solution of diazomethane in Et_2O (30 cm^3), prepared from *N*-methyl-*N*-nitrosourea (2.06 g, 20 mmol), was added to a solution of **30** (858 mg, 3 mmol) in dichloromethane (100 cm^3) at 0°C. The mixture was stirred at room temperature for 1 h. A small amount of acetic acid was added to destroy excess diazomethane. The mixture was concentrated, and the resulting solid was collected by suction and washed with methanol to give the crude adduct **31** (728 mg): a tan solid; mp 148–150°C; ^1H NMR ($CDCl_3$) δ=1.34 (3H, s, CH_3), 1.49 (3H, s, CH_3), 2.48 (3H, s, CH_3), 2.75 (1H, dd, J=8 and 2 Hz, 3a-H), 3.26 (1H, m, 4-H or 7-H), 3.75 (1H, m, 7-H or 4-H), 4.19 (1H, dd, J=19 and 3 Hz, 3-H_{exo}), 4.33 (1H, dd, J=19 and 8 Hz, 3-H_{endo}), 6.46 (2H, t, J=2 Hz, 5-H and 6-H), 7.40 (2H, d, J=8 Hz), 7.83 (2H, d, J=8 Hz); ^{13}C NMR ($CDCl_3$) δ=19.8 (CH_3), 19.9 (CH_3), 21.8 (CH_3), 42.8 (C-3a), 48.7 (C-4 or C-7), 49.2 (C-7 or C-4), 80.4 (C-3), 116.1 (C-7a), 123.2 (C-9), 129.6, 129.8, 133.1 (C-5 or C-6), 134.7, 138.2 (C-6 or C-5), 141.2 (C-8), 145.3; MS *m/z* (rel intensity) 328 (5, M^+), 313 (5, M−CH_3), 300 (3, M−N_2), 286 (3, M−CH_2N_2), 222 (16, M−**28**), 106 (45, **28**), 91 (100, C_7H_7).

A mixture of the crude adduct **31** (728 mg) and sodium

hydride (60%, 196 mg, 5 mmol) in THF (3 cm^3) was stirred at 0°C for 2 h. Aqueous ammonium chloride (10 cm^3) was added and the product was extracted with dichloromethane. The organic phase was washed with water and brine prior to drying with Na_2SO_4. After removal of the solvent, the resulting solid was collected by suction to give **13** (314 mg, 61% from 30): colorless needles (from diethyl ether); mp 152–153°C; IR (KBr) 3166 (NH), 3068, 3014, 2997, 2908, 2852, 1577, 1560, 1479, 1438, 1396, 1369, 1286, 1272, 1211, 1166, 1157, 1141, 1083, 1076, 1020 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.56 (6H, s, CH_3), 4.34 (1H, d, J=3 Hz, 4-H or 7-H), 4.36 (1H, d, J=3 Hz, 7-H or 4-H), 6.89 (1H, dd, J=5.5 and 3 Hz, 5-H or 6-H), 6.92 (1H, dd, J=5.5 and 3 Hz, 6-H or 5-H), 7.26 (1H, s, 3-H); ^{13}C NMR ($CDCl_3$) δ=19.0 (CH_3), 19.2 (CH_3), 43.8 (C-4 or C-7), 45.2 (C-7 or C-4), 102.6 (C-9), 118.7 (C-3), 129.8 (C-3a), 142.4 (C-5 or C-6), 144.6 (C-6 or C-5), 159.7 (C-8), 168.2 (C-7a); MS m/z (rel intensity) 172 (74, M^+), 157 (100, $M-CH_3$), 144 (32, $M-N_2$). Found: C, 76.57; H, 6.97; N, 16.10%. Calcd for $C_{11}H_{12}N_2$: C, 76.71; H, 7.02; N, 16.27%.

2.1.10. *N*-Methylation reaction of 13. To a mixture of sodium hydride (60%, 106 mg, 2.6 mmol) in THF (7 cm^3) was added a solution of **13** (278 mg, 1.6 mmol) in THF (7 cm^3) and the mixture was stirred at room temperature for 20 min. Methyl iodide (572 mg, 4 mmol) was added and the mixture was stirred at room temperature for 6 h. Water was added and the products were extracted with dichloromethane. The organic phase was washed with water and brine prior to drying with Na_2SO_4. After removal of the solvent, the residue was separated by column chromatography (silica gel, benzene–ethyl acetate 1/2) to give 4,7-dihydro-2-methyl-8-(1-methylethylidene)-4,7-methano-2*H*-indazole (**15**) (123 mg, 41%) and 4,7-dihydro-1-methyl-8-(1-methylethylidene)-4,7-methano-1*H*-indazole (**32**) (94 mg, 31%).

15: a colorless liquid; bp 130°C (bath temperature, 5 Torr), IR (neat) 3010, 2975, 2869, 1570, 1455, 1446, 1373, 1290 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.56 (6H, s, CH_3), 3.74 (3H, s, N-CH_3), 4.30 (1H, m, 4-H or 7-H), 4.32 (1H, m, 7-H or 4-H), 6.88 (1H, m, 5-H or 6-H), 6.92 (1H, m, 6-H or 5-H); ^{13}C NMR ($CDCl_3$) δ=19.0 (CH_3), 19.2 (CH_3), 38.1 (N–CH_3), 44.1 (C-4 or C-7), 45.4 (C-7 or C-4), 101.9 (C-9), 121.2 (C-3), 130.2 (C-3a), 142.7 (C-5 or C-6), 144.8 (C-6 or C-5), 159.8 (C-8), 167.7 (C-7a); MS m/z (rel intensity) 186 (100, M^+), 185 (59, M−H), 171 (85, $M-CH_3$). Found: C, 77.41; H, 7.83; N, 15.30%. Calcd for $C_{12}H_{14}N_2$: C, 77.38; H, 7.58; N, 15.04%.

32: a white solid (from hexane); mp 111.5–116°C; IR (KBr) 3012, 2977, 2933, 2908, 1540, 1440 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.54 (6H, s, CH_3), 3.85 (3H, s, N–CH_3), 4.31 (2H, m, 4-H and 7-H), 6.88 (1H, m, 5-H or 6-H), 7.07 (1H, m, 6-H or 5-H), 7.11 (1H, s, 3-H); ^{13}C NMR ($CDCl_3$) δ= 18.8 (CH_3), 19.0 (CH_3), 37.4 (N–CH_3), 45.0 (C-4 or C-7), 45.4 (C-7 or C-4), 99.9 (C-9), 130.2 (C-3), 133.8 (C-3a), 141.9 (C-5 or C-6), 147.2 (C-6 or C-5), 159.0 (C-8), 161.4 (C-7a); MS m/z (rel intensity) 186 (67, M^+), 185 (50, M−H), 171 (100, $M-CH_3$). Found: C, 77.61; H, 7.73; N, 15.18%. Calcd for $C_{12}H_{14}N_2$: C, 77.38; H, 7.58; N, 15.04%.

2.1.11. 4,5,6,7-Tetrahydro-8-(1-methylethylidene)-4,7-methano-2*H*-indazole (14). A mixture of **13** (52 mg, 0.3 mmol) and Pd/C (10%, 2 mg) in ethyl acetate (15 cm^3) was stirred under a hydrogen atmosphere at room temperature for 24 h. Insoluble materials were removed by filtration through celite, and the filtrate was concentrated. Recrystallization of the resulting solid from ether provided **14** (22 mg, 42%) as colorless needles: mp 150–151°C; IR (KBr) 3139 (NH), 3039, 2997, 2865, 1581, 1471, 1461, 1407, 1371, 1298, 1272, 1160, 1147, 1114, 1079, 1022 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.26 (2H, m, 5-H_{endo} and 6-H_{endo}), 1.62 (3H, s, CH_3), 1.63 (3H, s, CH_3), 1.90 (2H, m, 5-H_{exo} and 6-H_{exo}), 3.83 (1H, d, J=3 Hz, 4-H or 7-H), 3.89 (1H, d, J=3 Hz, 7-H or 4-H), 7.11 (1H, s, 3-H), 9.66 (1H, br, NH); ^{13}C NMR ($CDCl_3$) δ=19.9 (CH_3), 20.1 (CH_3), 27.3 (C-5 or C-6), 28.7 (C-6 or C-5), 38.2 (C-4 or C-7), 39.1 (C-7 or C-4), 111.1 (C-9), 118.8 (C-3), 126.4 (C-3a), 148.6 (C-8), 162.6 (C-7a); MS m/z (rel intensity) 174 (21, M^+), 159 (53, $M-CH_3$), 146 (100, $M-CH_2CH_2$). Found: C, 75.65; H, 8.40; N, 16.29%. Calcd for $C_{11}H_{14}N_2$: C, 75.82; H, 8.10; N, 16.08%.

2.1.12. 4,5,6,7-Tetrahydro-2-methyl-8-(1-methylethylidene)-4,7-methano-2*H*-indazole (16). By a similar procedure to that described for **14**, treatment of **15** (174 mg, 1 mmol) with Pd/C (10%, 6 mg) in ethyl acetate (25 cm^3) under a hydrogen atmosphere provided **16** (89 mg, 50%): a white solid (from ether): mp 83–83°C; IR (KBr) 3014, 2972, 2863, 1571, 1461, 1384, 1376, 1371, 1282, 1176, 1155, 1116 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.23 (2H, m, 5-H_{endo} and 6-H_{endo}), 1.59 (6H, s, CH_3), 1.90 (2H, m, 5-H_{exo} and 6-H_{exo}), 3.77 (4H, m, N–CH_3 and 4-H or 7-H), 3.81 (1H, d, J=3 Hz, 7-H or 4-H), 6.88 (1H, s, 3-H); ^{13}C NMR ($CDCl_3$) δ=19.8 (CH_3), 20.0 (CH_3), 27.4 (C-5 or C-6), 28.8 (C-6 or C-5), 38.2 (N–CH_3), 38.4 (C-4 or C-7), 39.2 (C-7 or C-4), 110.6 (C-9), 120.6 (C-3), 126.9 (C-3a), 148.5 (C-8), 162.5 (C-7a); MS m/z (rel intensity) 188 (27, M^+), 173 (53, $M-CH_3$), 160 (100, $M-CH_2CH_2$). Found: C, 76.39; H, 8.50; N, 14.92%. Calcd for $C_{12}H_{16}N_2$: C, 76.55; H, 8.57; N, 14.88%.

2.1.13. Reaction of 7 with 4-phenyl-1,2,4-triazole-3,5(4*H*)-dione (33, PTAD). A solution of **7** (81 mg, 0.25 mmol) and 4-phenyl-1,2,4-triazole-3,5(4*H*)-dione[25] (**33**) (66 mg, 0.38 mmol) in dichloromethane (10 cm^3) was stirred at room temperature for 30 min. After removal of the solvent, the residue was separated by TLC (silica gel, benzene) to give **34** (53 mg, 17%): a slightly tan solid (from hexane–ether 1/1); mp 243.5–244.5°C; IR (KBr) 3167, 3080, 3053, 2966, 2945, 2916, 2848, 1765, 1703, 1691, 1599, 1502, 1493, 1427 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.92 (3H, s, CH_3), 4.79 (2H, br s, 4-H and 7-H), 5.03 (1H, s, =CH_2), 5.24 (1H, s, =CH_2), 6.60 (2H, t, J=2 Hz, 5-H and 6-H), 7.19–7.45 (11H, m, Ph), 7.72 (4H, m, Ph), 8.42 (1H, br, NH), NOE observed between CH_3 and 5-H; ^{13}C NMR ($CDCl_3$) δ=23.5 (CH_3), 50.0 (C-4 and C-7), 96.5 (C-8), 116.5 (=CH_2), 124.2, 125.6, 127.2, 128.2, 128.7, 129.1, 130.6, 131.1, 131.4, 137.7 (C-5 and C-6), 141.2, 143.9, 152.1 (CO), 153.6 (CO); MS m/z (rel intensity) 499 (75, M^+), 323 (100, M−**33**–H), 105 (41, COPh). Found: C, 76.73; H, 5.33; N, 8.24%. Calcd for $C_{32}H_{25}N_3O_3$: C, 76.94; H, 5.04; N, 8.41%.

2.1.14. Reaction of 11 with PTAD 33. A solution of **11**

(47 mg, 0.25 mmol) and **33** (44 mg, 0.25 mmol) in dichloromethane (10 cm^3) was stirred at room temperature for 30 min. After the removal of the solvent, the residue was separated by TLC (silica gel, dichloromethane) to give **35** (53 mg, 58%): a white solid (from methanol); mp 236–237.5°C; IR (KBr) 3157, 3062, 2916, 2852, 1766, 1693, 1502, 1433 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.86 (3H, s, CH_3), 4.39 (2H, br s, 4-H and 7-H), 5.06 (1H, br s, =CH_2), 5.15 (1H, br s, =CH_2), 6.55 (2H, t, J=2 Hz, 5-H and 6-H), 6.75 (2H, s, 1-H and 3-H), 7.35–7.49 (5H, m, Ph), 9,11 (1H, br, NH), NOE observed between CH_3 and 5-H; ^{13}C NMR ($CDCl_3$) δ=23.3 (CH_3), 51.7 (C-4 and C-7), 96.4 (C-8), 114.8 (C-1 and C-3), 116.2 (=CH_2), 125.6, 128.3, 129.0, 131.1, 138.7 (C-5 and C-6), 141.3, 149.1, 151.5 (CO), 154.1 (CO); MS *m/z* (rel intensity) 363 (3, M^+), 187 (100, M−**33**–H), 134 (27, 2-benzothiophene), 119 (16, PhNCO). Found: C, 65.94; H, 4.98; N, 11.85%. Calcd for $C_{20}H_{17}N_3O_2S$: C, 66.10; H, 4.71; N, 11.56%.

2.1.15. Reaction of 8 with PTAD 33. A solution of **8** (82 mg, 0.25 mmol) and PTAD (53 mg, 0.3 mmol) in dichloromethane (10 cm^3) was stirred at room temperature for 40 min. After removal of the solvent, the residue was separated by TLC (silica gel, benzene) to give **36** (10 mg, 8%) and **37** (38 mg, 30%).

36: a white powder (from hexane–ether 1/1); mp 288.5–289.5°C; IR (KBr) 3176, 3084, 3049, 3033, 2993, 2931, 2868, 1763, 1703, 1689, 1599, 1502, 1493, 1427 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.52 (2H, dm, J=7.5 Hz, 5-H_{endo} and 6-H_{endo}), 1.96 (3H, s, CH_3), 2.14 (2H, br d, J=7.5 Hz, 5-H_{exo} and 6-H_{exo}), 4.37 (2H, br s, 4-H and 7-H), 5.20 (1H, br s, =CH_2), 5.27 (1H, br s, =CH_2), 7.18–7.44 (11H, m, Ph), 7.72 (4H, m, Ph), 8.45 (1H, br, NH), NOE observed between CH_3 and 5-H_{exo}; ^{13}C NMR ($CDCl_3$) δ=19.7 (CH_3), 25.9 (C-5 and C-6), 44.2 (C-4 and C-7), 87.7 (C-8), 117.4 (=CH_2), 124.1, 125.6, 127.0, 128.1, 128.8, 129.0, 129.6, 130.9, 131.3, 138.4, 142.7, 151.3 (CO), 153.3 (CO); MS *m/z* (rel intensity) 501 (100, M^+), 325 (10, M−**33**–H), 105 (78, COPh), 77 (38, Ph). Found: C, 76.66; H, 5.65; N, 8.08%. Calcd for $C_{32}H_{27}N_3O_3$: C, 76.63; H, 5.43; N, 8.38%.

37: a white powder (from hexane); mp 300.5–302°C; IR (KBr) 3172, 3055, 3033, 2997, 2945, 2854, 1765, 1703, 1691, 1597, 1493, 1433 cm^{-1}; ^1H NMR ($CDCl_3$, 60°C) δ=1.67 (2H, d, J=8.5 Hz, 5-H_{endo} and 6-H_{endo}), 1.79 (3H, s, CH_3), 2.43 (2H, br s, 5-H_{exo} and 6-H_{exo}), 4.40 (2H, br s, 4-H and 7-H), 4.91 (1H, s, =CH_2), 5.11 (1H, s, =CH_2), 7.21–7.25 (2H, m, Ph), 7.34–7.52 (7H, m, Ph), 7.64 (6H, m, Ph), 9.62 (1H, br, NH); ^{13}C NMR ($CDCl_3$) δ=22.0 (CH_3), 26.7 (C-5 and C-6), 44.6 (C-4 and C-7), 84.8 (C-8), 117.3 (=CH_2), 123.8, 125.3, 126.9, 128.2, 128.8, 129.1, 131.0, 136.3, 140.2, 142.2, 151.1 (CO), 153.5 (CO), 1C missing; MS *m/z* (rel intensity) 501 (100, M^+), 325 (16, M−**33**–H), 105 (60, COPh), 77 (35, Ph). Found: C, 76.86; H, 5.67; N, 8.32%. Calcd for $C_{32}H_{27}N_3O_3$: C, 76.63; H, 5.43; N, 8.38%.

2.1.16. Reaction of 12 with PTAD 33. A solution of **12** (48 mg, 0.25 mmol) and PTAD (50 mg, 0.29 mmol) in dichloromethane (10 cm^3) was stirred at room temperature for 30 min. After removal of the solvent, the residue was separated by TLC (silica gel, dichloromethane–hexane 1/1) to give **38** (23 mg, 25%) and **39** (60 mg, 65%).

38: a white powder (from hexane); mp 229–230°C; IR (KBr) 3159, 3068, 2976, 2949, 2870, 1768, 1691, 1502, 1429 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.34 (2H, dm, J=7.5 Hz, 5-H_{endo} and 6-H_{endo}), 1.90 (3H, s, CH_3), 2.02 (2H, d, J=7.5 Hz, 5-H_{exo} and 6-H_{exo}), 3.99 (2H, s, 4-H and 7-H), 5.16 (1H, t, J=1.5 Hz, =CH_2), 5.19 (1H, br s, =CH_2), 6.80 (2H, s, 1-H and 3-H), 7.33–7.47 (5H, m, Ph), 8.57 (1H, br, NH), NOE observed between CH_3 and 5-H_{exo}; ^{13}C NMR ($CDCl_3$) δ=19.6 (CH_3), 26.0 (C-5 and C-6), 46.0 (C-4 and C-7), 87.2 (C-8), 114.0 (C-1 and C-3), 117.0 (=CH_2), 125.6, 128.1, 129.0, 131.2, 138.5, 146.8, 150.9 (CO), 153.9 (CO); MS *m/z* (rel intensity) 365 (3, M^+), 189 (100, M−**33**–H). Found: C, 65.94; H, 5.38; N, 11.46%. Calcd for $C_{20}H_{19}N_3O_2S$: C, 65.73; H, 5.24; N, 11.50%.

39: a white powder (from hexane); mp 245.5–247°C; IR (KBr) 3174, 2929, 2868, 1778, 1710, 1502, 1414, 1354 cm^{-1}; ^1H NMR ($CDCl_3$, 80°C) δ=1.45 (2H, d, J=8 Hz, 5-H_{endo} and 6-H_{endo}), 1.71 (3H, s, CH_3), 2.28 (2H, d, J=8 Hz, 5-H_{exo} and 6-H_{exo}), 4.02 (2H, br s, 4-H and 7-H), 4.88 (1H, s, =CH_2), 4.98 (1H, s, =CH_2), 6.77 (2H, s, 1-H and 3-H), 7.34–7.55 (5H, m, Ph), 8.33 (1H, br, NH); ^{13}C NMR ($CDCl_3$) δ=21.8 (CH_3), 27.1 (C-5 and C-6), 46.7 (C-4 and C-7), 83.8 (C-8), 113.7 (C-1 and C-3), 117.6 (=CH_2), 125.8, 128.5, 129.3, 131.4, 140.4, 151.5 (CO), 154.0 (CO), 1C missing; MS *m/z* (rel intensity) 365 (2, M^+), 189 (100, M−**33**-H). Found: C, 65.92; H, 5.18; N, 11.23%. Calcd for $C_{20}H_{19}N_3O_2S$: C, 65.73; H, 5.24; N, 11.50%.

2.1.17. Reaction of 9 with PTAD 33. A solution of **9** (65 mg, 0.25 mol) and **33** (53 mg, 0.3 mmol) in dichloromethane (10 cm^3) was stirred at room temperature for 30 min. The mixture was concentrated and the residue was separated by TLC (silica gel, hexane–ethyl acetate 1/1) to give **40** (46 mg, 42%): a white solid (from hexane–ether 9/1); mp 138–140°C; IR (KBr) 3490, 3006, 2920, 2854, 1778, 1722, 1711, 1516, 1502, 1408, 1336 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.53 (3H, s, CH_3), 1.57 (3H, s, CH_3), 2.32 (3H, s, CH_3), 4.29 (1H, br s, 4-H or 7-H), 4.32 (1H, br s, 7-H or 4-H), 6.52 (1H, s, 3-H), 6.84 (2H, m, 5-H and 6-H), 7.12–7.47 (9H, m); ^{13}C NMR ($CDCl_3$) δ=19.2 (2C, CH_3), 21.0 (CH_3), 44.7 (C-4 or C-7), 45.0 (C-7 or C-4), 102.4 (C-9), 113.1, 113.2 (C-3), 125.1, 125.8, 128.4, 129.1, 130.0, 131.1, 134.8, 134.9, 136.1, 137.0, 142.4 (C-5 or C-6), 143.5 (C-6 or C-5), 151.1 (CO), 153.0 (CO), 158.9 (C-8); MS *m/z* (rel intensity) 436 (100, M^+), 259 (84, M−**33**–2H), 119 (17, PhNCO), 91 (54, C_7H_7). Found: C, 74.51; H, 5.46; N, 12.91%. Calcd for $C_{27}H_{24}N_4O_2$: C, 74.29; H, 5.54; N, 12.84%.

2.1.18. Reaction of 10 with PTAD 33. A solution of **10** (66 mg, 0.25 mmol) and **33** (53 mg, 0.3 mmol) in dichloromethane (10 cm^3) was stirred at room temperature for 30 min. The mixture was concentrated and the residue was separated by TLC (silica gel, hexane–ethyl acetate 1/1) to give **41** (84 mg, 76%): a light tan solid (from hexane); mp 180–182°C; IR (KBr) 3492, 3174, 2929, 2862, 1778, 1711, 1502, 1414, 1354 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.36 (2H, m, 5-H_{endo} and 6-H_{endo}), 1.60 (3H, s,

CH_3), 1.63 (3H, s, CH_3), 1.86 (2H, m, 5-H_{exo} and 6-H_{exo}), 2.33 (3H, s, CH_3), 3.75 (1H, br d, J=3 Hz, 4-H or 7-H), 3.77 (1H, br d, J=3 Hz, 7-H or 4-H), 6.49 (1H, s, 3-H), 7.13–7.24 (4H, m), 7.34–7.47 (5H, m), 8.50 (1H, br, NH); ^{13}C NMR ($CDCl_3$) δ=20.1 (CH_3), 20.2 (CH_3), 21.0 (CH_3), 28.1 (C-5 or C-6), 28.8 (C-6 or C-5), 38.6 (C-4 or C-7), 38.9 (C-7 or C-4), 111.0 (C-1 or C-9), 111.6 (C-9 or C-1), 112.0 (C-3), 125.2, 125.8, 128.3, 129.1, 129.9, 131.1, 131.9, 132.3, 136.2, 137.1, 148.7 (C-8), 151.3 (CO), 153.0 (CO); MS *m/z* (rel intensity) 438 (3, M^+), 247 (16, M−**33**–CH_4), 119 (100, PhNCO), 91 (74, C_7H_7). Found: C, 73.71; H, 5.74; N, 12.73%. Calcd for $C_{27}H_{26}N_4O_2$: C, 73.95; H, 5.98; N, 12.78%.

2.1.19. Reaction of 13 with PTAD 33. A solution of **13** (52 mg, 0.3 mmol) and **33** (70 mg, 0.4 mmol) in dichloromethane (5 cm^3) was stirred at room temperature for 30 min. After removal of the solvent, the residue was separated by column chromatography (silica gel, benzene–hexane 1/10) to give **42** (36 mg, 35%): a white powder (from ethyl acetate); mp 168–170°C; IR (KBr) 3213, 3068, 2947, 2918, 2852, 1765, 1720, 1711, 1691, 1682, 1645, 1597, 1502, 1427, 1357, 1276, 1203, 1182, 1139, 1041, 1025 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.95 (3H, s, CH_3), 4.38 (1H, d, J=3 Hz, 4-H or 7-H), 4.94 (1H, d, J= 3 Hz, 7-H or 4-H), 5.10 (1H, br s, =CH_2), 5.28 (1H, br s, =CH_2), 6.79 (1H, dd, J=5 and 3 Hz, 5-H or 6-H), 6.86 (1H, dd, J=5 and 3 Hz, 6-H or 5-H), 7.19 (1H, s, 3-H), 7.32 (1H, m), 7.43 (4H, m), 11.10 (1H, br, NH), 11.90 (1H, br, NH), NOE observed between CH_3 and 5-H; ^{13}C NMR ($CDCl_3$) δ=23.7 (CH_3), 49.3 (C-4 or C-7), 51.0 (C-7 or C-4), 99.8 (C-8), 116.1 (=CH_2), 121.5 (C-3), 125.3, 128.0, 128.8 (C-3a), 129.0, 131.2, 137.5 (C-5 or C-6), 141.3 (=*C*Me), 142.9 (C-6 or C-5), 151.5 (CO), 154.6 (CO), 165.4 (C-7a); MS *m/z* (rel intensity) 347 (39, M^+), 303 (7, M−$CONH_2$), 172 (27, M−**33**), 171 (78, M−**33**–H), 119 (100, PHNCO). Found: C, 65.94; H, 4.84; N, 19.98%. Calcd for $C_{19}H_{17}N_5O_2$: C, 65.70; H, 4.93; N, 20.16%.

2.1.20. Reaction of 15 with 33. A solution of **15** (99 mg, 0.5 mmol) and **33** (147 mmol, 0.8 mmol) in dichloromethane (5 cm^3) was stirred at room temperature for 5 h. After removal of the solvent, the resulting solid was recrystallized from benzene to give **43** (89 mg, 46%): a white solid (from benzene); mp 139–140°C; IR (KBr) 3220, 2983, 2948, 2819, 1770, 1720, 1710, 1496, 1427, 1382 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.88 (3H, s, CH_3), 3.81 (3H, s, N–CH_3), 4.35 (1H, br s, 4-H or 7-H), 4.58 (1H, br s, 7-H or 4-H), 5.07 (1H, br s, =CH_2), 5.18 (1H, br s, =CH_2), 6.67 (1H, m, 5-H or 6-H), 6.72 (1H, m, 6-H or 5-H), 7.00 (1H, s, 3-H), 7.26–7.44 (5H, m), 8.84 (1H, br, NH), NOE observed between CH_3 and 5-H; ^{13}C NMR ($CDCl_3$) δ=23.3 (CH_3), 38.3 (N–CH_3), 49.7 (C-4 or C-7), 50.9 (C-7 or C-4), 99.8 (C-8), 116.0 (=CH_2), 124.0 (C-3), 125.4, 127.9, 128.4 (C-3a), 129.9, 131.3, 138.7 (C-5 or C-6), 141.6 (=*C*Me), 141.8 (C-6 or C-5), 152.0 (CO), 153.3 (CO), 166.4 (C-7a); MS *m/z* (rel intensity) 361 (8, M^+), 317 (6, M−$CONH_2$), 186 (19, M−**33**), 185 (100, M−**33**–H), 119 (33, PhNCO). Found: C, 66.45; H, 5.60; N, 19.48%. Calcd for $C_{20}H_{19}N_5O_2$: C, 66.47; H, 5.30; N, 19.38%.

2.1.21. Reaction of 16 and 33. A solution of **16** (53 mg, 0.3 mmol) and **33** (71 mg, 0.4 mmol) in dichloromethane (5 cm^3) was stirred at room temperature for 1 h. After removal of the solvent, and the resulting solid was collected by suction and washed with ether to give a mixture of **44** and **45** (9:91, 71 mg, 68%): a white powder (from methanol); decomp 278°C; IR (KBr) 3240 (NH), 1770, 1708, 1423, 1390 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.25–1.44 (2H, m, 5-H_{endo} and 6-H_{endo}), 1.73 (2.73H, s, **45** CH_3), 1.90 (0.27H, s, **44** CH_3), 2.04 (0.18H, m, **44** 5-H_{exo} and 6-H_{exo}), 2.28 (1.82H, m, **45** 5-H_{exo} and 6-H_{exo}), 3.80 (2.73H, s, **45** N–CH_3), 3.83 (0.27H, s, **44** N–CH_3), 4.03 (0.18H, br s, **44** 4-H and 5-H), 4.18 (1.92H, br s, **45** 4-H and 5-H), 4.89 (0.91H, s, **45** =CH_2), 5.05 (0.91H, s, **45** =CH_2), 5.15 (0.09H, s, **44** =CH_2), 5.21 (0.09H, s, **44** =CH_2), 6.91 (0.91H, s, **45** 3-H), 6.98 (0.09H, s, **44** 3-H), 7.25–7.54 (5H, m, Ph), 9.46 (1H, br, NH); ^{13}C NMR ($CDCl_3$) δ= 19.3 (**44**, CH_3), 22.1 (**45** CH_3), 25.5 (**44** C-5 or C-6), 26.5 (**45** C-5 or C-6), 27.0 (**44**, C-6 or C-5), 28.0 (**45** C-6 or C-5), 38.5 (N–CH_3), 43.9 (**44** C-4 or C-7), 44.3 (**45** C-4 or C-7), 45.0 (**44** C-7 or C-4), 45.5 (**45** C-7 or C-4), 85.2 (**45** C-8), 88.7 (**44** C-8), 116.9 (**44** =CH_2), 117.2 (**45** =CH_2), 122.3, 123.3, 124.1, 125.0, 125.5, 125.7, 127.9, 128.2, 128.9, 129.1, 131.6, 131.8, 138.9, 140.9, 151.2, 151.8, 153.4, 153.7, 160.0, 161.2; MS *m/z* (rel intensity) 363 (2, M^+), 188 (15, M−**33**), 187 (100, M−**33**–H). Found: C, 66.13; H, 5.92; N, 19.23%. Calcd for $C_{20}H_{21}N_5O_2$: C, 66.10; H, 5.82; N, 19.27%.

2.1.22. Reaction of 7 with MCPBA. A solution of **7** (81 mg, 0.25 mmol) and MCPBA (70%, 62 mg, 0.25 mmol) in dichloromethane (15 cm^3) was stirred at room temperature for 1 h. The mixture was washed with aqueous sodium sulfite, aqueous sodium carbonate, and brine prior to drying with Na_2SO_4. After removal of the solvent, the residue was separated by TLC (silica gel, benzene) to give **46** (9 mg, 11%); a white solid (from methanol); mp 140–142°C; IR (KBr) 3080, 3060, 3010, 2960, 2920, 2850, 1597, 1493, 1440, 1057 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.31 (6H, s, CH_3), 3.93 (2H, t, J=2 Hz, 4-H and 7-H), 6.83 (2H, t, J= 2 Hz, 5-H and 6-H), 7.26 (2H, m), 7.41 (4H, m), 7.71 (4H, m); ^{13}C NMR ($CDCl_3$) δ=20.7 (CH_3), 46.1 (C-4 and C-7), 65.3 (*C*Me_2), 98.5 (C-8), 124.0, 127.0, 128.8, 129.8, 131.0, 138.0 (C-5 and C-6), 142.1 (C-1 and C-3); MS *m/z* (rel intensity) 340 (11, M^+), 270 (100, M−acetone–CH_2), 105 (10, COPh). HR-MS (FAB+) Found: 341.1557. Calcd for $C_{24}H_{22}O_2$+H: 341.1542.

2.1.23. Reaction of 8 with MCPBA. A solution of **8** (82 mg, 0.25 mmol) and MCPBA (70%, 62 mg, 0.25 mmol) in dichloromethane (15 cm^3) was stirred at room temperature for 1 h. The mixture was washed with aqueous sodium sulfite, aqueous sodium carbonate, and brine prior to drying with Na_2SO_4. After removal of the solvent, the residue was separated by TLC (silica gel, benzene) to give a mixture of **47** and **48** (22 mg, 26%, **47**–**48**=14:86): a white solid (from methanol); mp 161–162°C; IR (KBr) 3080, 3060, 3035, 3024, 2999, 2976, 2937, 2860, 1599, 1493, 1446 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.35 (5.16H, s, **48** CH_3), 1.44 (0.84H, s, **47** CH_3), 1.59 (2H, m, 5-H_{endo} and 6-H_{endo}), 2.12 (0.28H, dm J=7.5 Hz, **47** 5-H_{exo} and 6-H_{exo}), 2.37 (1.72H, dm J=7.5 Hz, **48** 5-H_{exo} and 6-H_{exo}), 3.24 (2H, m, 4-H and 7-H), 7.18–7.26 (2H, m), 7.35–7.43 (4H, m), 7.69–7.72 (4H, m); ^{13}C NMR ($CDCl_3$) δ=20.8 (**47** CH_3), 21.7 (**48** CH_3), 25.3 (**47** C-5 and C-6), 26.2 (**48** C-5

and C-6), 39.0 (**47** C-4 and C-7), 39.2 (**48** C-4 and C-7), 62.3 (**47** *C*Me$_2$), 63.0 (**48** *C*Me$_2$), 86.6 (**48** C-8), 89.7 (**47** C-8), 123.9, 124.0, 126.6, 126.8, 128.2, 128.6, 128.7, 128.8, 131.3, 131.4, 141.9 (**48** C-1 and C-3), 142.3 (**47** C-1 and C-3); MS *m/z* (rel intensity) 342 (58, M^+), 271 (100, M−acetone–CH), 105 (68, COPh). Found: C, 84.28; H, 6.60%. Calcd for $C_{24}H_{22}O_2$: C, 84.18; H, 6.48%.

2.1.24. Reaction of 11 with MCPBA. A solution of **11** (47 mg, 0.25 mmol) and MCPBA (62 mg, 0.25 mmol) in dichloromethane (10 cm^3) was stirred at room temperature for 1 h. The mixture was washed with aqueous sodium sulfite, aqueous sodium carbonate, and brine prior to drying with Na_2SO_4. After removal of the solvent, the residue was purified by TLC (silica gel, benzene) to give **49** (10 mg, 20%): a white solid (from pentane); mp 205.5–206.5°C; IR (KBr) 3159, 3111, 3091, 3062, 3014, 2981, 2918, 2854, 1606, 1452, 1373, 1281, 1176, 1146, 1099, 1058 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.64 (6H, s, CH_3), 4.22 (2H, t, *J*=2 Hz, 4-H and 7-H), 6.15 (2H, s, 1-H and 3-H), 6.39 (2H, t, *J*=2 Hz, 5-H and 6-H); ^{13}C NMR ($CDCl_3$) δ=20.2 (CH_3), 44.8 (C-4 and C-7), 115.3 (C-5 and C-6), 119.4 (C-9), 136.6 (C-1 and C-3), 140.5 (C-8), 146.0 (C-3a and C-7a); MS *m/z* (rel intensity) 220 (36, M^+), 172 (65, M−2O–CH_4), 91 (100, C_7H_7). Found: C, 65.19; H, 5.60%. Calcd for $C_{12}H_{12}O_2S$: C, 65.43; H, 5.49%.

A small amount of a white solid which could be assignable to **50** was also obtained; ^{1}H NMR ($CDCl_3$) δ=1.72 (6H, s), 3.92 (2H, t, *J*=2 Hz), 6.70 (2H, s), 6.76 (2H, t, *J*=2 Hz); MS *m/z* (rel intensity) 204 (21, M^+), 175 (100, M−C_2H_5). HR-MS (FAB+) found: 205.0713. Calcd for $C_{12}H_{12}OS$+H: 205.0687.

2.1.25. Reaction of 12 with MCPBA. A solution of **12** (48 mg, 0.25 mmol) and MCPBA (70%, 87 mg, 0.35 mmol) in dichloromethane (10 cm^3) was stirred at room temperature for 1 h. The mixture was washed with aqueous sodium sulfite, aqueous sodium carbonate, and brine prior to drying with Na_2SO_4. After removal of the solvent, the residue was purified by TLC (silica gel, hexane) to give a mixture of **51** and **52** (42 mg, 81%, **51**–**52**=18:82): a white powder (from methanol); mp 121–122°C; IR (KBr) 3006, 2993, 2979, 2933, 2868, 1375, 1360, 1117 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.30 (4.92H, s, **52** CH_3), 1.37 (3.08H, m, 5-H$_{endo}$, 6-H$_{endo}$, and **51** CH_3), 2.01 (0.36H, dm, *J*=7 Hz, **51** 5-H$_{exo}$ and 6-H$_{exo}$), 2.23 (1.64H, dm, *J*=7 Hz, **52** 5-H$_{exo}$ and 6-H$_{exo}$), 2.99 (2H, m, 4-H and 7-H), 6.85 (1.64H, s, **52** 1-H and 3-H), 6.87 (0.36H, s, **51** 1-H and 3-H); ^{13}C NMR ($CDCl_3$) δ=20.7 (**51** CH_3), 21.7 (**52** CH_3), 25.5 (**51** C-5 and C-6), 26.5 (**52** C-5 and C-6), 41.2 (**51** C-4 and C-7), 41.6 (**52** C-4 and C-7), 62.3 (**51** *C*Me$_2$), 62.9 (**52** *C*Me$_2$), 85.7 (**52** C-8), 89.5 (**51** C-8), 112.6 (**52** C-1 and C-3), 113.2 (**51** C-1 and C-3), 145.3 (**52** C-3a and C-7a), 147.3 (**51** C-3a and C-7a); MS *m/z* (rel intensity) 206 (4, M^+), 178 (13, M−C_2H_4), 137 (100, M−C_2H_4–C_3H_5). Found: C, 69.80; H, 6.90%. Calcd for $C_{12}H_{14}OS$: C, 69.86; H, 6.84%.

2.1.26. Reaction of 11 with sodium trichloroacetate. To a solution of **11** (47 mg, 0.25 mmol) in a mixture of tetrachloroethylene (5 cm^3) and diglyme (5 cm^3) was added sodium trichloroacetate (46 mg, 0.25 mmol) under reflux. Sodium trichloroacetate (46 mg, 0.25 mmol) was introduced into the mixture in every 10 min and a total amount (920 mg, 5 mmol) of the sodium trichloroacetate was added. Water was added and the mixture was extracted three times with ether. The combined organic layers were washed with aqueous sodium sulfite, aqueous ammonium chloride, and brine prior to drying with Na_2SO_4. After removal of the solvent, the residue was separated by TLC (silica gel, hexane) to give **53** (24 mg, 35%) and **54** (15 mg, 22%).

53: a white powder (from methanol); mp 99–101°C; IR (KBr) 3089, 3074, 3026, 3012, 3003, 2996, 2968, 2929, 2873, 1375, 1350, 1288, 1144, 1126 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.12 (6H, s, CH_3), 3.65 (2H, t, *J*=2 Hz, 4-H and 7-H), 6.72 (2H, s, 1-H and 3-H), 6.81 (2H, t, *J*=2 Hz, 5-H and 6-H), NOE observed between CH_3 and 5-H$_{exo}$; ^{13}C NMR ($CDCl_3$) δ=19.0 (CH_3), 30.9 (*C*Me$_2$), 48.2 (C-4 and C-7), 69.2 (C-8), 76.0 (*C*Cl$_2$), 112.1 (C-1 and C-3), 140.7 (C-5 and C-6), 150.2 (C-3a and C-7a); MS *m/z* (rel intensity) 270/272/274 (1.2/0.8/0.2, M^+), 235/237 (100/39, M−Cl), 134 (44, 2-benzothiophene). Found: C, 57.64; H, 4.26%. Calcd for $C_{13}H_{12}Cl_2S$: C, 57.57; H, 4.46%.

54: a white powder (from methanol); mp 146.5–148.5°C; IR (KBr) 2993, 2958, 2925, 2852, 1373 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.29 (6H, s, CH_3), 3.60 (2H, t, *J*=2 Hz, 4-H and 7-H), 6.71 (2H, t, *J*=2 Hz, 5-H and 6-H), 6.79 (2H, s, 1-H and 3-H); ^{13}C NMR ($CDCl_3$) δ=20.2 (CH_3), 30.0 (*C*Me$_2$), 48.3 (C-4 and C-7), 70.4 (C-8), 75.7 (*C*Cl$_2$), 112.5 (C-1 and C-3), 140.8 (C-5 and C-6), 150.1 (C-3a and C-7a); MS *m/z* (rel intensity) 270/272/274 (4/2/0.5, M^+), 235/237 (100/38, M−Cl), 134 (57, 2-benzothiophene). Found: C, 57.49; H, 4.34%. Calcd for $C_{13}H_{12}Cl_2S$: C, 57.57; H, 4.46%.

2.1.27. Reaction of 12 with sodium trichloroacetate. By a similar procedure to that described above, the reaction of **12** (48 mg, 0.25 mmol) and sodium trichloroacetate (920 mg, 5 mmol) provided **55** (35 mg, 51%) and **56** (21 mg, 30%).

55: a white powder (from methanol); mp 145–146°C; IR (KBr) 2966, 2951, 2937, 2866, 1464, 1452, 1371, 1363, 1162, 1103 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.30 (6H, s, CH_3), 1.46 (2H, dm, *J*=7.5 Hz, 5-H$_{endo}$ and 6-H$_{endo}$), 1.98 (2H, dm, *J*=7.5 Hz, 5-H$_{exo}$ and 6-H$_{exo}$), 3.15 (2H, t, *J*=2 Hz, 4-H and 7-H), 6.82 (2H, s, 1-H and 3-H), NOE observed between CH_3 and 5-H$_{exo}$; ^{13}C NMR ($CDCl_3$) δ=19.0 (CH_3), 28.5 (C-5 and C-6), 29.5 (*C*Me$_2$), 43.6 (C-4 and C-7), 62.9 (C-8), 77.2 (*C*Cl$_2$), 112.1 (C-1 and C-3), 148.2 (C-3a and C-7a); MS *m/z* (rel intensity) 272/274/276 (25/17/4, M^+), 237/239 (100/38, M−Cl), 135 (83, 2-benzothiophene+H). Found: C, 56.99; H, 5.23%. Calcd for $C_{13}H_{14}Cl_2S$: C, 57.15; H, 5.16%.

56: a white powder (from methanol); mp 73–74°C; IR (KBr) 2976, 2954, 2939, 2868, 1462, 1441, 1381, 1371, 1363, 1151, 1097 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.15 (6H, s, CH_3), 1.43 (2H, dm, *J*=7.5 Hz, 5-H$_{endo}$ and 6-H$_{endo}$), 2.25 (2H, dm, *J*=7.5 Hz, 5-H$_{exo}$ and 6-H$_{exo}$), 3.12 (2H, t, *J*=2 Hz, 4-H and 7-H), 6.75 (2H, s, 1-H and 3-H); ^{13}C NMR ($CDCl_3$) δ=19.9 (CH_3), 27.6 (C-5 and C-6), 29.2 (*C*Me$_2$), 43.1 (C-4 and C-7), 61.2 (C-8), 111.7 (C-1 and C-3), 148.3 (C-3a and C-7a), 1C missing; MS *m/z* (rel intensity) 272/274/276 (14/10/3, M^+), 237/239 (81/31, M−Cl), 135 (100,

2-benzothiophene+H). Found: C, 57.23; H, 5.10%. Calcd for $C_{13}H_{14}Cl_2S$: C, 57.15; H, 5.16%.

2.1.28. Reaction of 8 with NBS. A solution of **8** (82 mg, 0.25 mmol) and NBS (53 mg, 0.3 mmol) in dichloromethane (10 cm^3) was stirred at room temperature for 20 min. Aqueous sodium sulfite was added to the mixture, and the organic phase was separated. The organic phase was washed with water and brine prior to drying with Na_2SO_4. After removal of the solvent, the resulting solid was collected by suction to give **58** (98 mg, 96%): a white powder (form hexane–ether 10/1); mp 177–179°C; IR (KBr) 3060, 3022, 2993, 2979, 2945, 2868, 1595, 1493, 1446, 1127, 1061 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.62 (2H, dm, J=8 Hz, 5-H_{endo} and 6-H_{endo}), 1.79 (3H, s, CH_3), 2.63 (2H, d, J=8 Hz, 5-H_{exo} and 6-H_{exo}), 3.88 (2H, m, 4-H and 7-H), 4.71 (1H, s, =CH_2), 4.97 (1H, s, =CH_2), 7.23 (2H, m), 7.40 (4H, m), 7.70 (4H, m); ^{13}C NMR ($CDCl_3$) δ=20.7 (CH_3), 27.7 (C-5 and C-6), 47.7 (C-4 and C-7), 82.7 (C-8), 114.3 (=CH_2), 123.8, 126.9, 128.0, 128.8, 131.0, 141.9, 144.6; MS m/z (rel intensity) 404/406 (81/84, M^+), 326 (32, M−Br), 105 (100, COPh), 77 (55, Ph). Found: C, 71.21; H, 5.09%. Calcd for $C_{24}H_{21}BrO$: C, 71.12; H. 5.22%.

2.1.29. Reaction of 10 with NBS. A solution of **10** (27 mg, 0.1 mmol) and NBS (45 mg, 0.25 mmol) in dichloromethane (10 cm^3) was stirred at room temperature for 1 h. Aqueous sodium sulfite was added to the mixture, and the organic layer was separated. The organic layer was washed with water and brine prior to drying with Na_2SO_4. After removal of the solvent, the residue was separated by TLC (silica gel, hexane) to give **60** (23 mg, 53%): a slightly yellow solid (from hexane); mp 130–132°C; IR (KBr) 2968, 2939, 2924, 2854, 1514, 1371, 1338, 1228, 1115, 1020 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.36 (2H, dm, J=6.5 Hz, 5-H_{endo} and 6-H_{endo}), 1.66 (6H, s, CH_3), 1.87 (2H, dm, J=6.5 Hz, 5-H_{exo} and 6-H_{exo}), 2.41 (3H, s, CH_3), 3.75 (2H, m, 4-H and 7-H), 7.08 (2H, br s),7.23 (2H, br s); ^{13}C NMR ($CDCl_3$) δ=20.2 (CH_3), 21.3 (CH_3), 28.1 (C-5 and C-6), 39.5 (C-4 and C-7), 92.9 (C-1 and C-3), 111.5 (C-9), 129.9, 133.8 (C-3a and C-7a), 135.3, 138.3, 147.3 (C-8), 1C missing; MS m/z (rel intensity) 419/421/423 (11/21/10, M^+), 404/406/408 (9/15/10, M−CH_3), 366/368/370 (32/100/44, M−C_4H_5). HR-MS (FAB) found: 418.9839. Calcd for $C_{19}H_{19}{}^{79}Br_2N$: 418.9885.

2.1.30. Reaction of 12 with NBS. A solution of **12** (48 mg, 0.25 mmol) and NBS (53 mg, 0.3 mmol) in dichloromethane (10 cm^3) was stirred at room temperature for 20 min. Aqueous sodium sulfite was added to the mixture, and the organic phase was separated. The organic phase was washed with water and brine prior to drying with Na_2SO_4. After removal of the solvent, the resulting solid was collected by suction to give **59** (98 mg, 97%): a white powder; mp 62°C; IR (KBr) 3089, 2997, 2976, 2922, 2871, 1639, 1444, 1373, 1360, 1109 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.42 (2H, dm, J=7.5 Hz, 5-H_{endo} and 6-H_{endo}), 1.75 (3H, s, CH_3), 2.50 (2H, dm, J=7.5 Hz, 5-H_{exo} and 6-H_{exo}), 3.61 (2H, m, 4-H and 7-H), 4.71 (1H, s, =CH_2), 4.88 (1H, s, =CH_2), 6.76 (2H, s, 1-H and 3-H); ^{13}C NMR ($CDCl_3$) δ=20.3 (CH_3), 28.0 (C-5 and C-6), 49.8 (C-4 and C-7), 81.7 (C-8), 112.9 (C-1 and C-3), 114.5 (=CH_2), 144.6, 144.8 (C-3a and C-7a); MS m/z (rel intensity) 268/270 (28/29, M^+), 189 (100, M−Br), 175 (34, M−Br–CH_2). HR-MS (FAB) found: 269.9904. Calcd for $C_{12}H_{13}{}^{81}BrS$: C, 269.9901.

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