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Norbornadiene-Fused Heterocycles: Syntheses and Cycloaddition Reactions of 2-Aryl-4,7-dihydro-4,7-methano-2*H*-isoindoles and 4,7-Dihydro-4,7-methanoisobenzofuran

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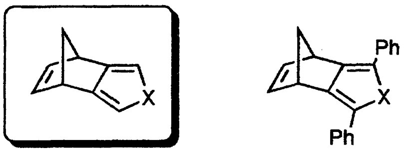
2-Phenyl- and 2-(*p*-tolyl)-4,7-dihydro-4,7-methano-2*H*-isoindole were synthesized by treatment of 3-(diethoxymethyl)bicyclo[2.2.1]hepta-2,5-diene-2-carbaldehyde with aniline or *p*-toluidine, followed by reduction with sodium borohydride and acid-catalyzed cyclization. It was concluded that the previous claim of the synthesis of methanoisoindole derivatives was incorrect. 4,7-Dihydro-4,7-methanoisobenzofuran was prepared by the reduction of the norbornadiene-monocarbaldehyde with sodium borohydride and subsequent treatment with Amberlyst-15. The *p*-tolylmethanoisoindole reacted with dimethyl acetylenedicarboxylate to give a novel 1 : 3 adduct. On the other hand, in the reaction of the methanoisobenzofuran with *N*-phenylmaleimide, spontaneous oxidation of the Diels–Alder cycloadduct took place to give exclusively its epoxide.

Five-membered heteroaromatics fused with norbornadiene such as **1**—**3** are of interest from various points of view, e.g., (a) the effect of the strain stemmed from the fusion of norbornadiene on the physical and chemical properties of the heterocyclic ring,[1)] (b) the behavior of a cationic intermediate resulted by an electrophilic attack on the double bond,[2)] and (c) the possibility of a through-space or through-bond interaction of the π-electrons between the olefin moiety and the aromatic ring to furnish an interesting photochemical transformation.[3)] However, an approach toward the norbornadiene-fused thiophene **3** by the reaction of 3,5-dimethoxy-4-oxatricyclo[5.2.1.0^{2,6}]dec-8-ene[4)] (**5**) with hydrogen sulfide has been described to be unfruitful.[5,6)] An unsuccessful attempt for the synthesis of benzonorbornadiene-fused [*c*]furan by the reaction of 2,3-dimethylene-1,4-methano-1,2,3,4-tetrahydronaphthalene with singlet oxygen also appeared.[7)] Recently, we described the syntheses of the diphenyl-substituted pyrrole, furan, and thiophene (**4**) fused at the [*c*]-bond with norbornadiene (Scheme 1), and discussed some structural and spectral properties of these molecules.[8)] We also reported the synthesis and spectral properties of an imidazole fused with 2-azanorbornene.[9)] However, it was found that reactivities of these molecules are low contrary to our expectation. For instance, the diphenyl-substituted derivatives **4** are unreactive toward *N*-phenylmaleimide or dimethyl acetylenedicarboxylate even under forcing conditions, probably due to the steric and electronic effects of the two phenyl substituents on the reactive centers.[8)] Consequently, we considered it indispensable to prepare the unsubstituted, norbornadiene-fused heterocycles **1**—**3** for the investigations on the reactivities of these molecules as well as on the spectral properties which are not perturbed by substituents. Here we wish to report the syntheses of novel 2-aryl-4,7-dihydro-4,7-methano-2*H*-isoindoles **1** and 4,7-dihydro-4,7-methanoisobenzofuran (**2**), together with their reactions with some dienophiles.



1: X = N-R
2: X = O
3: X = S

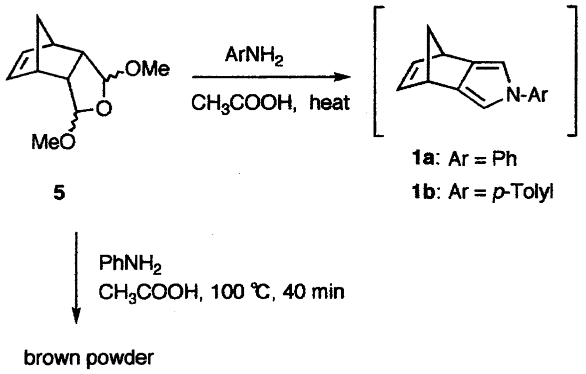
4: X = NH, O, S

Scheme 1.

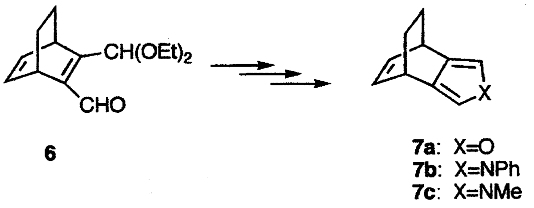
Results and Discussion

In 1970, the synthesis of 2-phenyl- and 2-(*p*-tolyl)-4,7-dihydro-4,7-methano-2*H*-isoindole (**1a** and **1b**) was reported.[10,11)] The proposed structures of the methanoisoindoles **1a** and **1b** were based only on IR spectra, elemental analyses, and unspecified ^{1}H NMR spectra. According to the conditions described in the literature,[10)] a solution of the acetal **5** in acetic acid was heated at 100 °C in the presence of aniline (Scheme 2). From this reaction mixture,we obtained brown powder exhibiting a similar decomposition point (decomp 276 °C) to that reported for **1a** (decomp 277 °C).[10,11] In the IR spectrum, a few absorptions similar to those reported for **1a** were observed. However, repeated elemental analyses of the brown powder did not agree with the structure **1a**. Moreover, the ^{1}H NMR spectrum of the powder exhibited only broad signals probably due to the formation of polymers, and no peak assignable to the methanoisoindole **1a** was observed. As our repetition materializing **1a** was unsuccessful, we turned to explore an alternative synthetic route toward the methanoisoindoles.

Since the syntheses of the furan **7a** and the pyrroles **7b** and **7c** fused with a bicyclo[2.2.2]octadiene skeleton starting from a bicyclo[2.2.2]octadiene derivative **6** have been described by Gorgues et al. (Scheme 3),[12,13] we planned to use 3-(diethoxymethyl)bicyclo[2.2.1]hepta-2,5-diene-2-carbaldehyde (**8**) as a versatile starting substance not only for the synthesis of the methanoisoindoles **1** but also for the methanoisobenzofuran **2**.



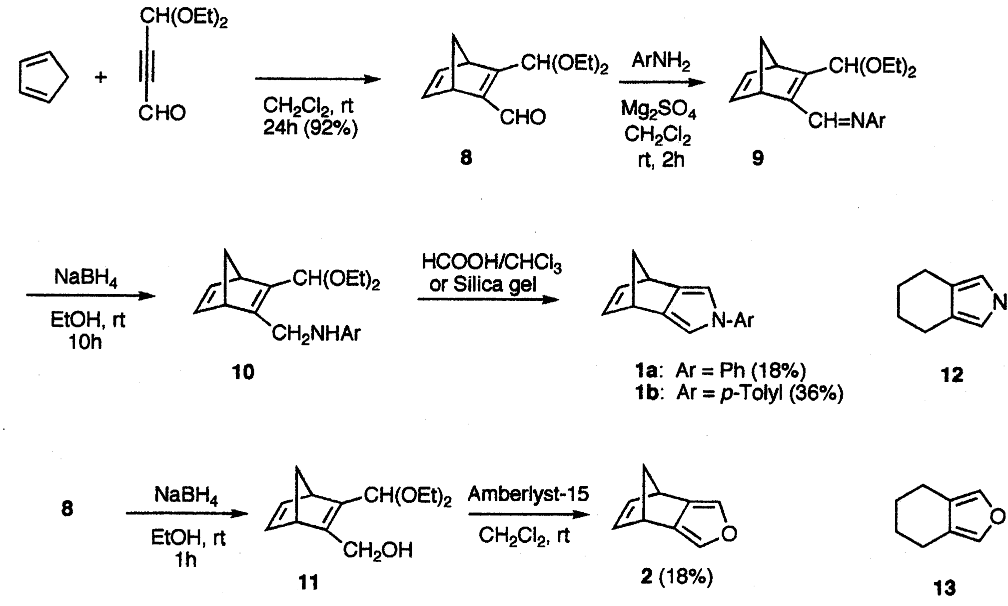
Scheme 2.



Scheme 3.

The Diels–Alder reaction of cyclopentadiene with 4,4-diethoxy-2-butynal[14] provided the norbornadiene-monocarbaldehyde **8** in 92% yield (Scheme 4). Treatment of **8** with aniline in the presence of magnesium sulfate gave the imine **9a**, which was converted to the amine **10a** by the reduction with sodium borohydride in ethanol. Since the imine **9a** and the amine **10a** were found to decompose on distillation in vacuo, they were submitted to the next steps without purification. When the amine **10a** was stirred in chloroform in the presence of formic acid, the *N*-phenylmethanoisoindole **1a** was obtained in 18% overall yield from the norbornadiene-monocarbaldehyde **8**. The *p*-tolylmethanoisoindole **1b** was formed in 36% yield from **8** when a benzene solution of the crude amine **10b** was passed through a silica-gel column. In this instance, the use of formic acid gave a lower yield of **1b**. Unfortunately, our attempt to obtain the corresponding *N*-benzyl derivative was unsuccessful: The acid-catalyzed cyclization of the corresponding amine resulted in the formation of a complex mixture.

The norbornadiene-monocarbaldehyde **8** was treated with sodium borohydride in ethanol to give the alcohol **11** which was found to be labile upon distillation. It was therefore submitted to the acid-catalyzed cyclization without purification. Various acids were examined, and the use of Amberlyst-15 in dichloromethane proved to give the best yield of the methanoisobenzofuran **2**



Scheme 4.

(18% overall yield from **8**).

The structures of the methanoisoindoles **1a** and **1b**, and the methanoisobenzofuran **2** were confirmed by ^{1}H NMR, ^{13}C NMR, and Mass spectra as well as elemental analyses. The ^{13}C NMR spectra of **1a**, **1b**, and **2** respectively show 9, 10, and 5 lines, and these observations indicate the presence of C_s symmetry in these molecules. The assignment of the ^{13}C signals was deduced from the measurement of C–H coupling constants. A noticeable feature of the ^{13}C NMR spectra of these norbornadiene-fused heterocycles is that the chemical shifts of the ring-juncture carbons are fairly deshielded when compared with those of cyclohexene-fused derivatives. The ^{13}C signals of the ring-juncture carbons for 4,5,6,7-tetrahydro-2*H*-isoindole[15] (**12**) and 4,5,6,7-tetrahydroisobenzofuran[16] (**13**) have been reported to appear at $\delta=119.3$ and $\delta=121.5$, respectively. In contrast, those of the norbornadiene-fused derivatives appear at $\delta=138.6$, 138.3, and 137.2 for **1a**, **1b**, and **2**, respectively. These deshielded signals are unambiguously assignable to the ring-juncture carbons, because similar downfield shifts have been observed for the ring-juncture carbon of benzonorbornadiene ($\delta=151.5$)[17] relative to that of 1,2,3,4-tetrahydronaphthalene ($\delta=137.0$),[18] as well as in the cases of the diphenyl-substituted norbornadiene-fused heterocycles **4**.[8] The methanoisoindoles **1a** and **1b** exhibit the melting points respectively at 92 and 141 °C, which are quite different from the values as reported in the literatures (decomp 277 °C for **1a** and decomp 213 °C for **1b**).[10,11] From these results, we conclude that the alleged structures of **1a** and **1b** in the literatures have been erroneously assigned.

When the *p*-tolylmethanoisoindole **1b** was heated in acetic acid at 100 °C for 40 min, only an intractable material was formed: **1b** was found to be unstable under the conditions employed in the claimed synthesis.[10] Treatments of **1b** with bromine or 4-phenyl-1,2,4-triazoline-3,5-dione also resulted in the formation of complex mixtures. These compounds have been reported to afford adducts with benzonorbornadiene via skeletal rearrangement of dipolar intermediates.[2,19] On the other hand, the treatment of **1b** with fourfold excess of dimethyl acetylenedicarboxylate (DMAD) in refluxing benzene afforded the 1:3 adduct **18** (40%) as yellow needles. A similar reaction with twofold excess of DMAD also resulted in the formation of the adduct **18** in 30% yield along with the recovery of **1b** (46%). In contrast, the reaction of **1b** with fourfold excess of DMAD at room temperature for 3 d gave a mixture of complex products.

The structure of **18**, totally devoid of symmetry, is based on the appearance of 32 carbon signals (^{13}C NMR), eight of which are quaternary sp^{2} carbons. These data unambiguously exclude the possibility of an isomeric structure **19**, which has only seven quaternary sp^{2} carbons. The ^{1}H NMR spectrum shows the presence of methano bridge and bridgehead protons along with six methoxy groups, one of which is rather shielded ($\delta=2.83$) by an anisotropic effect of the neighboring *p*-tolyl group. The assignments for the proton and carbon resonances (Fig. 1) are supported by the H–H COSY, H–C COSY, and HMBC measurements. The HMBC spectrum shows the correlations between H_c and C_A; H_g and C_C, C_D, C_F; and H_h and C_C, C_E. The adduct **18** was obtained as a single stereoisomer and the NOESY experiments were performed with **18**. In Fig. 2, the observed nuclear Overhauser effects are shown with curved arrows. The NOE's observed between H_a and H_e, and H_b and H_d, as well as these between H_g and H_e, and H_g and H_f support the stereochemistry of **18** as shown in Fig. 2.

The proposed mechanism for the formation of **18** is shown in Scheme 5. An approach of DMAD from the *endo*-face of the *p*-tolylmethanoisoindole **1b** provides an initial Diels–Alder adduct **14**, which undergoes the zwitterionic aza-Cope rearrangement via **15** to give a dihydroindole intermediate **16**.[20,21] Further

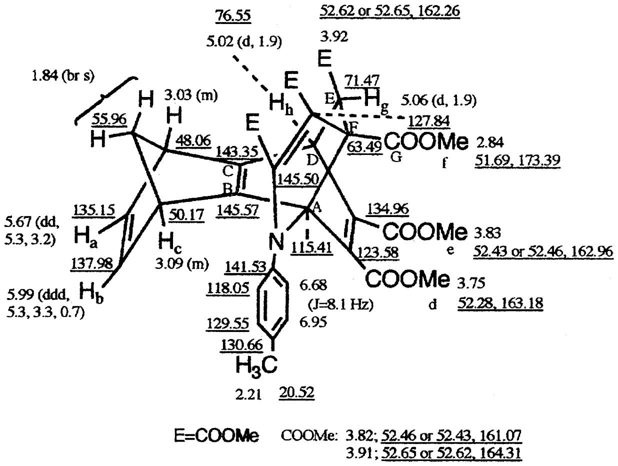


Fig. 1. ^{1}H and ^{13}C (underlined) NMR spectral data of **18**.

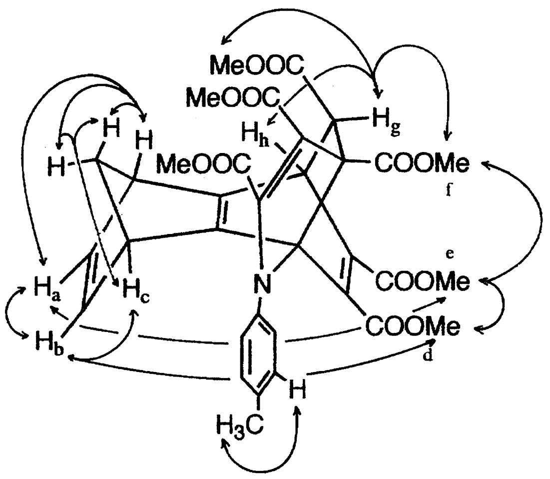
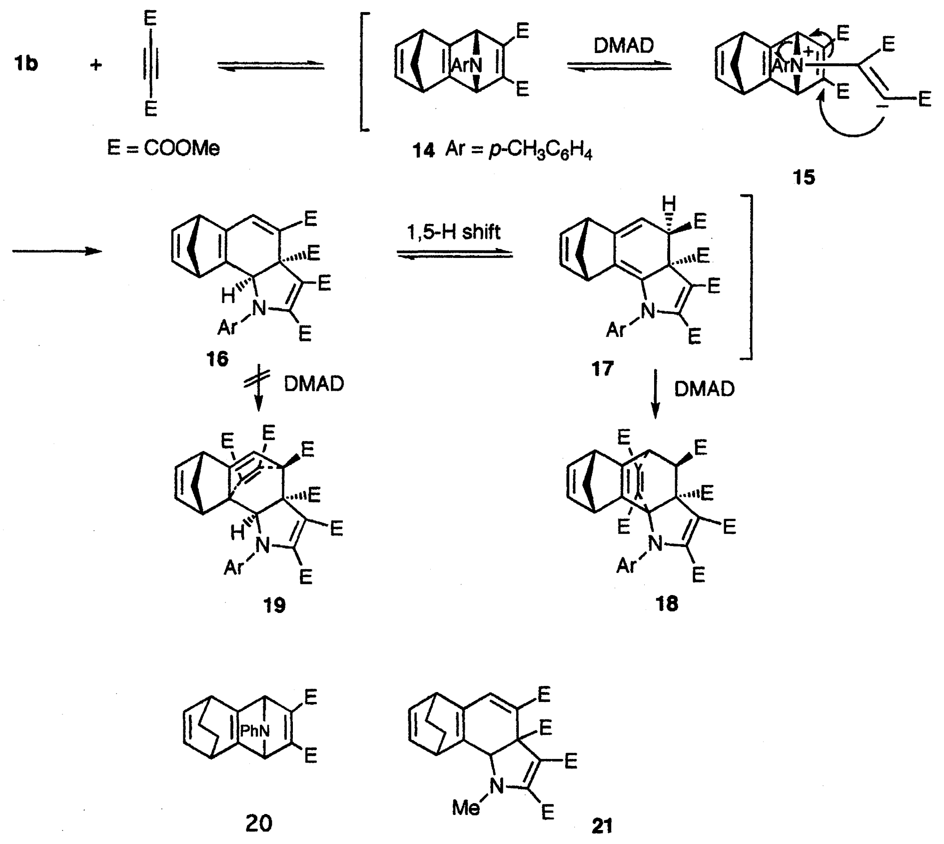


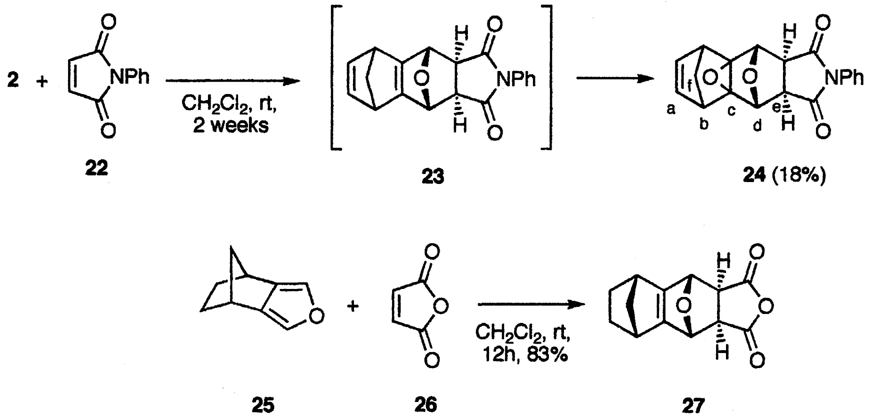
Fig. 2. Observed cross peaks in the NOESY spectrum of **18**.



Scheme 5.

1,5-prototropic shift leading to **17** and the subsequent Diels–Alder reaction with DMAD leads to the cycloadduct **18**. Previously, the reactions of the bicyclo[2.2.2]octadiene-fused pyrroles **7b** and **7c** with DMAD have been described respectively to give a 1 : 1 adduct **20** and a 1 : 2 adduct **21**, depending on the substituents on the nitrogen atom.[12] The formation of similar 1 : 2 adducts of monocyclic pyrroles with DMAD has been well recognized.[20,21] However, neither the 1 : 1 nor 1 : 2 adduct such as **14** or **16** could be isolated from the present reaction. The reason for the formation of an unusual 1 : 3 adduct should be due to the fusion of a norbornadiene skeleton. Fusion of such a constrained ring would make the 1 : 1 adduct **14** rather unstable and would favor the exocyclic diene intermediate **17** at equilibrium over its isomer **16**, as can been seen in equilibrium of isodicyclopentadiene tautomers.[22,23] It also appears that the diene moiety of **16** is too hindered to allow approach of DMAD leading to **19**.

The methanoisoindole **1b** did not react with *N*-phenylmaleimide **22** in refluxing toluene. In contrast, when the methanoisobenzofuran **2** was left at room temperature for 2 weeks in the presence of **22**, the epoxide **24** was isolated albeit in a low yield (18%) (Scheme 6). The ^{13}C NMR spectrum shows 11 signals, indicating the presence of C_s symmetry. The observation of a quater-



Scheme 6.

nary sp^3 carbon assignable to an oxirane ring (δ=67.8) supports the structure of **24**. The epoxide **24** was obtained as a single stereoisomer, and the value of the coupling constants ($J\approx 0$ Hz) between H_e and H_d indicates that the hydrogen atoms H_e take in the *endo* position. However the relative stereochemistry of the methano bridge and the oxirane ring could not be deduced from the spectral data.

In this reaction, a simple Diels–Alder cycloadduct **23** could not be isolated. The formation of the epoxide **24** appears to proceed via air-oxidation of **23** on the central double bond, which is supposed to be pyramidalized.[24] These observations are in striking contrast with the fact that the norbornene-fused furan **25** reacts with maleic anhydride to give the cycloadduct **27** in good yield, whereas an analogous oxidation has been described for cycloadduct of **25** with DMAD.[24]

Finally, we treated the acetal **5** with Lawesson's reagent or diphosphorus pentasulfide expecting to obtain the norbornadiene-fused thiophene **3**, but only intractable mixtures were formed. The norbornadiene-monocarbaldehyde **8** seems to be unsuitable as a starting material for the synthesis of **3**, and further efforts to explore a successful route toward **3** are underway in our laboratory.

Experimental

General. All the melting points were recorded with a Yanagimoto hot-stage apparatus and are uncorrected. IR spectra were obtained with a Hitachi 345 spectrometer. ^{1}H (90 MHz) and ^{13}C (22.5 MHz) NMR spectra were recorded with a JEOL-FX-90Q spectrometer with tetramethylsilane as an internal standard, and ^{1}H (500 MHz) and ^{13}C (125 MHz) NMR spectra were taken with a Bruker DRX500 spectrometer and the Bruker pulse program was used. The NOESY spectra were recorded by the phase sensitive mode with 2.6 s of mixing time. The mass spectra were measured with Shimadzu GCMS-QP1000EX spectrometer operating in the electron impact mode (70 eV). UV spectra were recorded with a Shimadzu UV-260 spectrometer. Elemental analyses were performed with a Perkin–Elmer Model 240 apparatus.

Attempted Synthesis of 2-Phenyl-4,7-dihydro-4,7-methano-2*H*-isoindole (1a).[10] A solution of 3,5-dimethoxy-4-oxatricyclo[5.2.1.0^{2,6}]dec-8-ene[4] (**5**) (0.99 g, 5 mmol) and aniline (0.47 g, 5 mmol) in acetic acid (3 cm^3) was heated at 100 °C for 40 min. The reaction mixture was extracted with dichloromethane and washed with aq NaHCO$_3$ and water. After drying with Na$_2$SO$_4$, the mixture was concentrated to give brown powder (0.90 g): Decomp 276 °C, (lit,[10] decomp 277 °C); IR (KBr) 3400, 3050, 2930,1590, 1485, 1305, 1240, 1180, 1090, 970 cm^{-1}; (lit,[10] IR 1597, 1495, 1035 cm^{-1}). The ^{1}H NMR spectrum shows only broad signals at δ=2—8. Found: C, 85.93; H, 6.63; N, 7.41%. Calcd for $C_{15}H_{13}N$: C, 86.92; H, 6.32; N, 6.76%.

3-(Diethoxymethyl)bicyclo[2.2.1]hepta-2,5-diene-2-carbaldehyde (8): A solution of cyclopentadiene (2.83 g, 18 mmol) in dichloromethane (15 cm^3) was added dropwise to a solution of 4,4-diethoxy-2-butynal[14] (5.51 g, 6 mmol) in dichloromethane (15 cm^3) at 0 °C. The reaction mixture was left at room temperature for 24 h. The solution was concentrated and the residue was distilled in vacuo to give **8** (7.11 g, 92%) as slightly yellow liquid: Bp 110—117 °C (0.5 Torr, 1 Torr=133.322 Pa); IR (neat) 2970, 2940, 2870, 1660 (CO), 1340, 1290, 1220, 1160, 1100, 1050, 680 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ=1.22 (6H, t, J=7.0 Hz, CH$_3$), 1.80—2.08 (2H, m, 7-H), 3.15—3.90 (5H, m, CH$_2$ and 4-H), 4.04 (1H, br s, 1-H), 5.49 (1H, s, CH(OEt)$_2$), 6.70—7.00 (2H, m, 5- and 6-H), 10.18 (1H, s, CHO); ^{13}C NMR (CDCl$_3$) δ=15.9 (q, CH$_3$), 48.2 (d, C-4), 52.9 (d, C-1), 61.4 (t, OCH$_2$CH$_3$), 70.9 (t, C-7), 98.8 (d, CH(OEt)$_2$), 141.5 (d, C-5 or C-6), 142.8 (d, C-6 or C-5), 152.0 (s, C-2), 170.4 (s, C-3), 187.3 (d, CHO); MS m/z (rel intensity) 222 (M$^+$; 16), 193 (M−CHO; 31), 119 (M−CH(OEt)$_2$; 50), 91 (C_7H_7; 100). Found: C, 69.87; H, 8.16%. Calcd for $C_{13}H_{18}O_3$: C, 70.24; H, 8.16%.

2-Phenyl-4,7-dihydro-4,7-methano-2*H*-isoindole (1a): A mixture of the norbornadiene-monocarbaldehyde **8** (550 mg, 2.5 mmol), aniline (264 mg, 2.8 mmol), and anhydrous magnesium sulfate (1.62 g) in chloroform (30 cm^3) was stirred at room temperature for 2 h. Insoluble materials were removed by filtration and the filtrate was concentrated to give the crude imine **9a** as yellow liquid: ^{1}H NMR (CDCl$_3$) δ=1.21 (3H, t, J=7.0 Hz, CH$_3$), 1.22 (3H, t, J=7.0 Hz, CH$_3$), 2.05 (2H, m, 7-H), 3.53 (2H, q, J=7.0 Hz, OCH$_2$), 3.55 (2H, q, J=7.0 Hz, OCH$_2$), 3.76 (1H, m, 4-H), 4.32 (1H, 1-H), 5.41 (1H, s, CH(OEt)$_2$), 6.80—7.05 (2H, m, 5- and 6-H), 7.10—7.60 (5H, m, Ph), 8.66 (1H, s, CH=N); MS m/z (rel intensity) 297 (M$^+$; 4), 268 (M−OEt; 100), 194 (M−CH(OEt)$_2$; 46), 104 (PhN=CH; 25). Attempted distillation (150 °C/1 Torr) resulted in decomposition of the product.

A solution of the crude imine **9a** and sodium borohydride (116 mg, 3.1 mmol) in ethanol (10 cm^3) was stirred at room temperature for 10 h. The reaction mixture was concentrated and extracted with chloroform. The combined extracts were washed with water and dried over Na$_2$SO$_4$. The solvent was removed in vacuo to give the crude amine **10a** as light yellow liquid: IR (neat) 3450 (NH) cm^{-1}; ^{1}H NMR (CDCl$_3$) δ=1.18 (3H, t, J=7.0 Hz, CH$_3$), 1.21 (3H, t, J=7.0 Hz, CH$_3$), 1.80—2.10 (2H, m, 7-H), 3.20—4.10 (9H, m, NCH$_2$, NH, 1-H, 4-H, and OCH$_2$), 6.50—7.40 (7H, m, 5-H, 6-H, and Ph); MS m/z (rel intensity) 299 (M$^+$; 1), 253 (M−EtOH; 1), 207 (isoindole; 100). Attempted distillation (160 °C/1 Torr) resulted in decomposition of the product.

A solution of the crude amine **10a** and formic acid (36 mg, 0.76 mmol) in chloroform (80 cm^3) was stirred at room temperature for 24 h. The mixture was washed with aq NaHCO$_3$ solution and water, and dried over Na$_2$SO$_4$. After removal of the solvent, the residue was purified by column chromatography (alumina, hexane) to give the phenylmethanoisoindole **1a** (94 mg, 18% from the norbornadiene-monocarbaldehyde **8**): Colorless needles (from hexane), mp 91—92 °C; IR (KBr) 3050, 3000, 2970, 2925, 1585, 1490, 1400, 1325, 1190, 1030, 940, 900, 865, 835, 820, 780, 755, 740, 710 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ=2.20—2.45 (2H, m, 8-H), 3.81 (2H, m, 4- and 7-H), 6.70 (2H, m, 5- and 6-H), 6.77 (2H, s, 1- and 3-H), 7.00—7.45 (5H, m, Ph); ^{13}C NMR (CDCl$_3$) δ=44.4 (dq, J=150, 7 Hz, C-4 and C-7), 68.7 (t, J=135 Hz, C-8), 110.3 (dd, J=186, 4 Hz, C-1 and C-3), 119.5 (dt, J=160, 5 Hz, C-2′), 123.9 (dt, J=161, 5 Hz, C-

4′), 129.3 (dd, J=161, 5 Hz, C-3′), 138.6 (s, C-3a and C-7a), 141.7 (t, J=7 Hz, C-1′), 142.4 (d, J=173 Hz, C-5 and C-6); MS m/z (rel intensity) 207 (M^+; 100), 103 (PhNC; 14), 77 (Ph; 77). Found: C, 86.99; H, 6.36; N, 6.92%. Calcd for $C_{15}H_{13}N$: C, 86.92; H, 6.32; N, 6.76%.

2-(*p*-Tolyl)-4,7-dihydro-4,7-methano-2*H*-isoindole (1b): By a similar procedure as described for **9a**, the reaction of the norbornadiene-monocarbaldehyde **8** (1.12 g, 5 mmol) and *p*-toluidine (536 mg, 5 mmol) gave the crude *p*-tolylimine **9b** as light yellow liquid: ^{1}H NMR ($CDCl_3$) δ=1.21 (3H, t, J=7.0 Hz, CH_3), 1.22 (3H, t, J=7.0 Hz, CH_3), 2.06 (2H, m, 7-H), 2.34 (3H, s, CH_3), 3.53 (2H, q, J=7.0 Hz, OCH_2), 3.55 (2H, q, J=7.0 Hz, OCH_2), 3.84 (1H, m, 4-H), 4.35 (1H, m, 4-H), 5.41 (1H, s, $CH(OEt)_2$), 6.80 (6H, m, 5-H, 6H, and aromatics), 8.66 (1H, s, CH=N); MS m/z (rel intensity) 311 (M^+; 5), 282 (M−Et; 100), 118 (tolyl-NCH; 21), 91 (tolyl; 58). Attempted distillation (150 °C/1 Torr) resulted in decomposition of the product.

By a similar procedure as described for **10a**, the reaction of the crude *p*-tolylimine **9b** and sodium borohydride (55 mg, 1.5 mmol) gave the crude *p*-tolylamine **10b** as a light yellow liquid; IR (neat) 3400 (NH) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.13 (3H, t, J=7.0 Hz, CH_3), 1.17 (3H, J=7.0 Hz, CH_3), 2.10 (5H, m, 7-H and $CH_3C_6H_4$), 3.00—4.00 (9H, m, 1-H, 4-H, OCH_2, NH, NCH_2), 5.20 (1H, s, $CH(OEt)_2$), 6.40—7.10 (6H, m, 5-H, 6-H, and aromatics); MS m/z (rel intensity) 313 (M^+; 3), 222 (M−tolyl; 100), 91 (tolyl; 48). Attempted distillation (170 °C/1 Torr) resulted in decomposition of the product.

A solution of the crude *p*-tolylamine **10b** in benzene was slowly passed through a column (silica gel, benzene) and the eluent was concentrated. The resulting solid was collected and washed with methanol to give the *p*-tolylmethanoisoindole **1b** (399 mg, 36% from the norbornadiene-monocarbaldehyde **8**): Colorless plates (from methanol); mp 140—141 °C, IR (KBr) 3060, 2970, 2935, 2860, 1875, 1610, 1560, 1510, 1430, 1405, 1330, 1295, 1250, 1215, 1195, 1125, 1025, 940, 835 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=2.35 (2H, m, 8H), 2.32 (3H, s, CH_3), 3.81 (2H, m, 4- and 7-H), 6.71 (2H, m, 5- and 6-H), 6.73 (2H, s, 1- and 3-H), 7.15 (4H, s, tolyl); ^{13}C NMR ($CDCl_3$) δ=20.7 (q, J=127 Hz, CH_3), 44.5 (dq, J=150, 8 Hz, C-4 and C-7), 68.9 (t, J=136 Hz, C-8), 110.4 (dd, J=185, 5 Hz, C-1 and C-3), 119.7 (dd, J=160, 5 Hz, C-2′), 129.8 (dd, J=158, 5 Hz, C-3′), 133.5 (s, C-4′), 138.3 (s, C-3a and C-7a), 139.5 (s, C-1′), 142.4 (d, C-5 and C-6); Ms m/z (rel intensity) 221 (M^+; 100), 91 (tolyl; 11), 65 (C_5H_5; 16). Found: C, 86.96; H, 6.96; N, 6.24%. Calcd for $C_{16}H_{15}N$: C, 86.84; H, 6.83; N, 6.30%.

4,7-Dihydro-4,7-methanoisobenzofuran (2): A solution of the norbornadiene-monocarbaldehyde **8** (1.73 g, 7.8 mmol) and sodium borohydride (0.61 g, 4 mmol) in ethanol (30 cm^3) was stirred at room temperature for 1 h. The reaction mixture was concentrated and extracted with dichloromethane. The combined extracts were washed with water and saturated aq NaCl solution, and dried over Na_2SO_4. Removal of the solvent gave the alcohol **11** as colorless oil: IR (neat) 3420 (OH) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.20 (3H, t, J=7.0 Hz, CH_3), 1.21 (3H, t, J=7.0 Hz, CH_3), 1.88 (1H, dt, J=6.0, 1.6 Hz, 7-H), 2.04 (1H, dt, J=6.0, 1.6 Hz), 3.18 (1H, t, J=5.8 Hz, OH), 3.30—3.70 (6H, m, CH_2), 4.31 (1H, dd, J=1.6, 0.9 Hz, 1- or 4-H), 4.37 (1H, dd, J=1.6, 0.9 Hz, 4- or 1-H), 5.23 (1H, br s, $CH(OEt)_2$), 6.74—6.92 (2H, m, 5- and 6-H); MS m/z (rel intensity) 224 (M^+; 4), 178 (M−EtOH; 32), 121 (M−$CH(OEt)_2$; 44), 103 ($CH(OEt)_2$; 90), 91 (C_7H_7; 100). Attempted distillation (121 °C/0.5 Torr) resulted in decomposition of the product.

A solution of the crude alcohol **11** in dichloromethane (70 cm^3) was added to a stirred mixture of Amberlyst-15 (8.5 g) in dichloromethane (200 cm^3) over 45 min. The reaction mixture was stirred at room temperature for 2 h. Amberlyst-15 was removed by filtration and the filtrate was concentrated. The residue was separated by column chromatography (silica gel, dichloromethane) and the crude product was distilled under vacuum with a Kugelrohr apparatus to give the norbornadiene-fused furan **2** (185 mg, 18%) as colorless liquid: Bp 110 °C (bath temp)/20 Torr; IR (neat) 3075, 3015, 2980, 2880, 1580, 1305, 990 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=2.10—2.40 (2H, m, 8-H), 3.75 (2H, m, 4- and 7-H), 6.59 (2H, m, 5- and 6-H), 6.95 (2H, s, 1- and 3-H); ^{13}C NMR ($CDCl_3$) δ=42.8 (dq, J=151, 7 Hz, C-4 and C-7), 66.5 (t, J=137 Hz, C-8), 130.6 (dd, J=202, 6 Hz, C-1 and C-3), 137.2 (s, C-3a and C-7a), 141.2 (d, J=173 Hz, C-5 and C-6); MS m/z (rel intensity) 132 (M^+; 100), 103 (M−CHO; 86), 78 (C_5H_2O; 70); UV (2,2,4-trimethylpentane) λ_{max} (log ε) 269 (1.55) nm. Found: C, 82.01; H, 6.05%. Calcd for C_9H_8O: C, 81.79; H, 6.10%.

The Reaction of the Methanoisoindole 1b with Dimethyl Acetylenedicarboxylate (DMAD): A solution of the methanoisoindole **1b** (221 mg, 1 mmol) and DMAD (568 mg, 4 mmol) in benzene (3 cm^3) was refluxed for 5 h. The solution was concentrated and methanol was added to the residue. The resulting solid was collected to give the adduct **18** (265 mg, 40%); Yellow needles (from methanol); mp 182—184 °C; IR (KBr) 1715 cm^{-1}; MS m/z (rel intensity) 647 (M^+; 8), 616 (M−OMe; 3), 585 (M−2×OMe; 4), 556 (M−tolyl), 273 (M−2×DMAD−tolyl+H; 47), 242 (m/z 273−OMe; 100); UV (CH_3OH) λ_{max} (log ε) 239 (4.23), 352 (3.38) nm. Found: C, 63.08; H, 5.25; N, 2.13%. Calcd for $C_{34}H_{33}NO_{12}$: C, 63.06; H, 5.14; N, 2.16%. ^{1}H NMR ($CDCl_3$, 500 MHz) and ^{13}C NMR ($CDCl_3$, 125 MHz) spectral data are shown in Fig. 1.

A similar reaction of **1b** (221 mg, 1 mmol) with DMAD (312 mg, 2.2 mmol) in refluxing benzene (3 cm^3) for 16 h gave the adduct **18** (198 mg, 30%) along with the recovery of **1b** (102 mg, 46%) after chromatographic separation (silica gel, benzene).

The Cycloaddition Reaction of the Methanoisobenzofuran 2 with *N*-Phenylmaleimide: A solution of the methanoisobenzofuran **2** (188 mg, 1.42 mmol) and *N*-phenylmaleimide **22** (246 mg, 1.42 mmol) in anhydrous dichloromethane (10 cm^3) was left at room temperature for 2 weeks. The solution was concentrated and the residue was separated by column chromatography (silica gel, dichloromethane) to give the epoxide **24** (82 mg, 18%): Colorless needles (from hexane); mp 223 °C (decomp); IR (neat) 1710, 1490, 1385, 1190, 1000, 850, 720, 690 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.80 (1H, m, H_f), 2.41 (1H, m, H_f), 3.08 (2H, s, H_e), 3.16 (2H, m, H_b), 4.87 (2H, s, H_d), 6.68 (2H, m, H_a), 7.20—7.70 (5H, m, Ph); ^{13}C NMR ($CDCl_3$) δ=43.5 (d, C-b), 49.6 (d, C-e), 54.7 (t, C-f), 67.8 (s, C-c), 78.9 (d, C-d), 126.6 (d, C-2′), 129.0 (d, C-3′), 129.3 (d, C-4′), 131.7 (s, C-1′), 140.2 (d, C-a), 175.0 (s, CO); MS m/z (rel intensity) 321 (M^+; 64), 173 (**22**; 25), 148 (M−**22**; 30), 66 (C_5H_6; 100). Found: C, 71.18; H, 4.73; N, 4.08%. Calcd for $C_{19}H_{15}NO_4$:

C, 71.02; H, 4.71; N, 4.36%.

References

1) M. W. Galley and R. C. Hahn, *J. Org. Chem.*, **41**, 2006 (1976).

2) S. J. Christol and G. W. Nachtigal, *J. Org. Chem.*, **32**, 3727 (1967).

3) L. A. Paquette, L. D. Burke, T. Irie, and H. Tanida, *J. Org. Chem.*, **52**, 3246 (1987).

4) K. Alder, H. Betzing, and K. Heimbach, *Justus Liebigs Ann. Chem.*, **638**, 187 (1960).

5) J. D. Wit and H. Wynberg, *Tetrahedron*, **29**, 1379 (1973).

6) H. Wynberg and A. J. H. Klunder, *Recl. Trav. Chim. Pays-Bas*, **88**, 328 (1969).

7) B. Atasoy, F. Bayrmoğlu, and T. Hokelek, *Tetrahedron*, **50**, 5753 (1994).

8) T. Kobayashi, K. Ono, H. Suda, Y. Yamashita, and H. Kato, *Bull. Chem. Soc. Jpn.*, **66**, 2707 (1993).

9) T. Kobayashi, H. Fujieda, Y. Murakami, T. Nakamura, K. Ono, S. Yamamoto, and H. Kato, *Bull. Chem. Soc. Jpn.*, **67**, 3082 (1994).

10) A. A. Ponomarev, I. A. Markushina, and G. E. Marnicheva, *Khim. Geterosikl. Soedin.*, **1970**, 1444.

11) A. A. Lebedev, I. A. Markushina, G. E. Marinicheva, and T. B. Merkulova, *Khim.-Farm. Zh.*, **15**, 38 (1981).

12) D. Stephan, A. Gorgues, and A. L. Coq, *Tetrahedron Lett.*, **29**, 1025 (1988).

13) D. Stephan, A. Gorgues, and A. L. Coq, *Tetrahedron Lett.*, **27**, 4295 (1986).

14) A. Gorgues, A. Simon, A. L. Coq, A. Hercouet, and F. Corre, *Tetrahedron*, **42**, 351 (1986).

15) M. Suzuki, H. Ohtake, Y. Kameya, N. Hamanaka, and R. Noyori, *J. Org. Chem.*, **54**, 5292 (1989).

16) J. Rühe, C. Kröhnke, T. A. Ezqerra, F. Kremer, and G. Wegner, *Ber. Bunsenges. Phys. Chem.*, **91**, 885 (1987).

17) K. Tori, T. Tsushima, H. Tanida, K. Kushida, and S. Satoh, *Org. Magn. Reson.*, **1974**, 324.

18) R. P. Thummel and D. K. Kohli, *J. Org. Chem.*, **43**, 4882 (1978).

19) W. Adam, O. D. Lucchi, and I. Erden, *Angew. Chem., Int. Ed. Engl.*, **18**, 468 (1979).

20) C. K. Lee, C. S. Hahn, and W. E. Noland, *J. Org. Chem.*, **43**, 3727 (1978).

21) W. E. Noland and C. K. Lee, *J. Org. Chem.*, **45**, 4573 (1980).

22) R. Subramanyam, P. D. Bartlett, G. Y. M. Iglesias, W. H. Watson, and J. Gallor, *J. Org. Chem.*, **47**, 4491 (1982).

23) L. A. Paquette, R. V. Williams, R. V. C. Carr, P. Charumilind, and J. F. Blount, *J. Org. Chem.*, **47**, 4566 (1982).

24) J.-P. Hagenbuch, P. Vogel, A. A. Pinkerton, and D. Schwarzenbach, *Helv. Chim. Acta*, **64**, 1818 (1981).