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4-AZA-2,7-DIMETHYL-[1-*H*]CYCLOPROPA[b]-NAPHTHALENE. THE FIRST NITROGEN ANALOGUE OF A CYCLOPROPANAPHTHALENE

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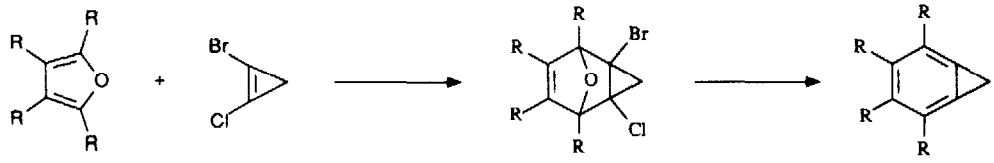
Summary. The title compound **1** is synthesized *via* Diels-Alder addition of 4-aza-2,7-dimethyl-isobenzofuran (**5**) to 1,2-bromochlorocyclopropene and aromatization of the adduct **6** with low-valent titanium.

Introduction

Although the chemistry of cycloproparenes has developed considerably over the recent years[1,2], the number of isolated heterocyclic derivatives is limited to three[3,4], and only one of them contains nitrogen. The conventional methods for synthesis of cycloproparenes are not generally applicable for preparation of heterocyclic derivatives, because often the required starting materials are not as readily available as in the series of isocyclic analogues, or do not lend themselves to the same reaction sequences. In the past, we have synthesized cycloproparenes mainly from dienes or *o*-quinodimethanes and cyclopropenes[5], but this approach appeared inadequate for heterocyclic compounds. Accordingly a variant of this methodology was developed, based on cycloaddition of furans or isobenzofurans to 1,2-dihalogenocyclopropenes[6] in order to construct the molecular framework (Scheme 1). For the aromatization of the adducts which, in general have *exo*-configuration, we exploited the observation that low-valent titanium[8] is not only capable to effect deoxygenation of 1,4-epoxybenzenes[9], but also to reduce vicinal dihalides to alkenes[10]. Indeed, these two transformations could be combined in a single reaction step using McMurry's reagent[6]. Accordingly, in model studies, cyclopropa[b]naphthalene and its 2,7-diphenyl derivative were prepared from the appropriate adducts in yields of 60 and 72%, respectively. The procedure worked also for 2-methyl-benzocyclopropene, but in this case the cycloproparene was contaminated by an equal amount of a 1,6-dihalogeno-2-methylcycloheptatriene[6].

Scheme 1

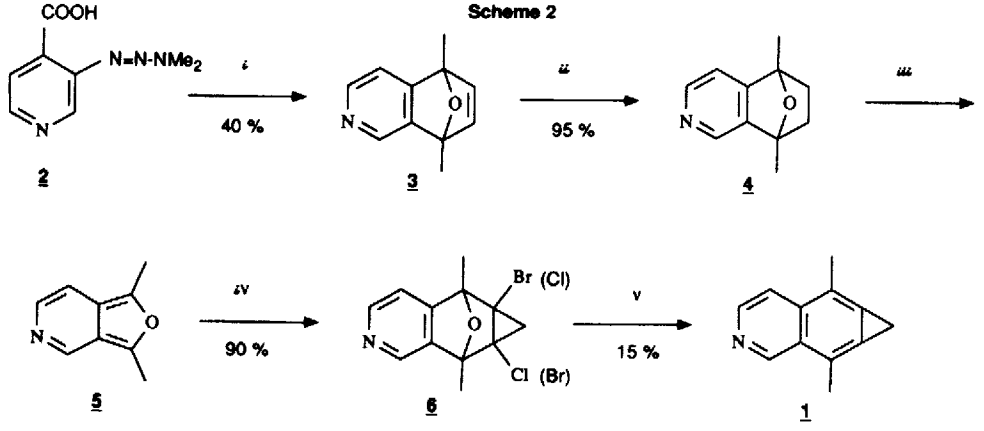


Synthesis of 4-aza-2,7-dimethyl-[1-*H*]cyclopropa[b]naphthalene

The application of this synthetic plan to 4-aza-2,7-dimethyl-cyclopropa[b]naphthalene (**1**) is shown in Scheme 2. 3-Pyridyne, prepared either from 3-bromopyridine[11] or, better, by decomposition of 3-(3,3-dimethyltri-

azen-1-yl)-pyridine-4-carboxylic acid[12] (2), was intercepted *in situ* with 2,5-dimethylfuran. The isolated double bond of the cycloadduct 3[13] was reduced by catalytic hydrogenation, and the resulting product 4[14] subjected to flash pyrolysis[15] at 600° to afford the aza-isobenzofuran 5. Although the latter was sufficiently stable to be characterized spectroscopically,[16] it was reacted without purification with 1,2-bromochlorocyclopropene[17]. *exo*-configuration is assigned to the adduct 6 on the grounds of the chemical shift of the hydrogen *syn* to the oxygen

Scheme 2



i) 2,5-dimethylfuran, 120°. ii) Pd/C, EtOH. iii) 600°.
iv) 1,2-bromochlorocyclopropene (excess), -78° to 10°. v) $TiCl_3$ / BuLi

bridge (δ = 2.70 ppm) in analogy to other adducts of cyclopropenes to furans for which the stereochemistry is unambiguously established[7]. The aromatization step of 6 to 1 with low-valent titanium (generated from $TiCl_3$ with BuLi) turned out to be much less satisfactory than in the isocyclic series. Despite of much efforts for variation of the reagent[19] and optimization of the reaction conditions, the desired cyclopropparene could only be obtained in a modest yield of 15% at best. The above sequence was also applied to the parent 4-aza-cyclopropa[b]naphthalene. No difficulties were encountered for the first four steps; however, the aromatization of 6 lacking the methyl substituents produced so far only decomposition products.

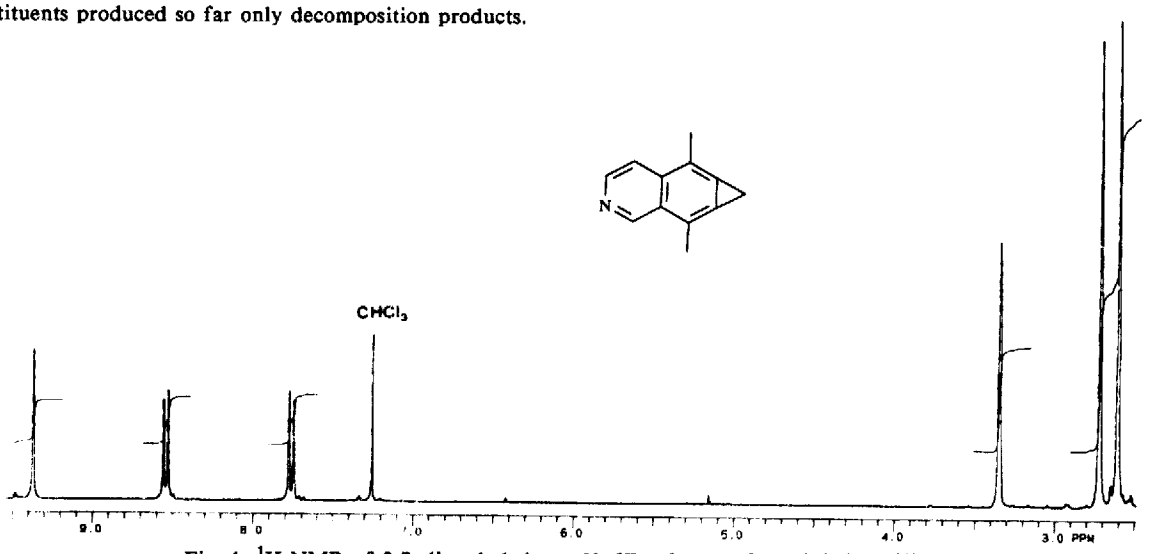


Fig. 1. ^1H NMR of 2,7-dimethyl-4-aza-[1-*H*]cyclopropa[b]naphthalene (1)

4-Aza-2,7-dimethyl-cyclopropa[b]naphthalene (1) has m.p. 86 - 88°. The ^{1}H-NMR, shown in Fig. 1, exhibits the typical pattern for isoquinolines in the aromatic region, and the CH_2 signals of the cyclopropene in the expected range[1]. The ir-vibration, characteristic for cycloproparenes[1] occurs at 1745 cm^{-1}, and the principal uv absorptions are found at 228 (15800); 279 (1900) and 323 (1300) nm. In the ms, the molecular ion gives rise to the base peak[20]. Fig. 2 shows the ^{13}C-NMR spectrum of **1**[21] in comparison to that of the isocyclic cyclopropa[b]naphthalene and isoquinoline[22]. The assignments are made on the grounds of analogies with other cycloproparenes but are considered tentative at least with respect to the quaternary carbons.

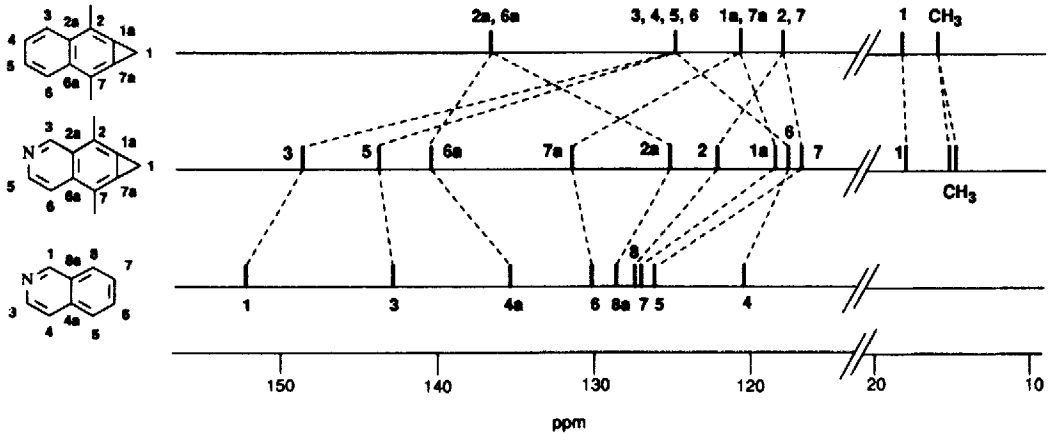


Fig. 2. ^{13}C NMR of 1, [1-*H*]cyclopropa[b]naphthalene and isoquinoline

Studies to extend this approach towards synthesis of the unsubstituted analogue of **1**, and to other heterocyclic cycloproparenes continue in this laboratory.

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[13] Data of **3**: M.P.: 81-82°; ^{1}H-NMR: ($CDCl_3$, 200 MHz): 8.3 (m, 2H), 7.095 (m, 1H), 6.76 (AB, 2H, ^{3}J=5.4 Hz, δ_A=6.8, δ_B=6.72), 1.95 (s, 3H), 1.88 (s, 3H). IR ($CHCl_3$): 3015 (s), 2980 (s), 2920 (m), 1600 (m), 1580 (w), 1455 (m), 1420 (m), 1385 (s), 1300 (m), 1240 (m), 1230 (s), 1005 (m), 855 (s), 830 (s). M.S.: ($C_{11}H_{11}NO$): 173 (M^+, 16), 172 (5), 158 (9), 147 (27), 132 (21), 131 (100), 130 (88), 115 (8), 103 (17), 91 (4), 77 (32), 63 (14), 51 (41).

[14] Data of **4**: M.P.: 68°; ^{1}H-NMR ($CDCl_3$, 200 MHz): 8.48 (d, 1H, ^{3}J=4.76 Hz), 8.4 (sl, 1H), 7.09 (dxd, 1H, ^{3}J=4.76, ^{5}J=0.95 Hz), 1.96 (m, 2H), 1.86 (s, 3H), 1.8 (s, 3H), 1.52 (m, 2H). IR ($CHCl_3$): 3010 (m), 2980 (s), 2950 (m), 2870 (w), 1610 (m), 1440 (m), 1390 (s), 1350 (m), 1220 (m), 1100 (s), 1030 (m), 930 (m), 840 (s). M.S.: $C_{11}H_{13}NO$): 175 (M^+ 0.6), 160 (6), 148 (20), 147 (100), 146 (54), 132 (47), 117 (17), 104 (13), 77 (17), 63 (9), 51 (29).

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[16] ^{1}H-NMR ($CDCl_3$, 200 MHz): 8.815 (sl, 1H), 7.62 (d, 1H, ^{3}J=6.66 Hz), 6.94 (dxd, 1H, ^{3}J=6.66 Hz, ^{5}J=1.1 Hz), 2.65 (s, 3H), 2.54 (s, 3H).

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[18] Data of **6**: M.P. 42°; ^{1}H-NMR (CD_2Cl_2, 200 MHz): 8.5 (m, 2H), 7.25 (m, 1H), 2.7 (d, 1H, ^{2}J=7.3 Hz), 1.77 (2s, 3H), 1.73 (2s, 3H), 1.65 (2d, 1H, ^{2}J=7.3 Hz). IR ($CHCl_3$): 3010 (m), 2990 (m), 2860 (m), 1610 (m), 1570 (s), 1420 (m), 1380 (s), 1325 (m), 1270 (s), 1150 (s), 1050 (s), 880 (m). M.S. ($C_{12}H_{11}BrClNO$): 224 (18), 222 (26), 220 (20), 180 (30), 178 (100), 177 (34), 142 (26), 115 (21), 77 (10), 63 (20), 51 (20).

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[20] m.s.:169 (M^+, 100); 168 (54); 167 (60); 154 (69); 141 (20); 139 (12); 127(16); 115 (20); 84 (10); 63 (16); 51 (15). High resolution ms : calc. 169.08915; found 169.08891

[21] ^{13}C NMR: C(1) 18.1; C(1a) 118.6; C(2) 121.9; C(2a) 125.1; C(3) 148.7; C(5) 142.8; C(6) 117.8; C(6a) 140.4; C(7) 116.9; C(7a) 131.5; CH_3 15.4/15.2 ppm.

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