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The Generation and Reactions of 3,4-Didehydro-2*H*-[1]benzopyran, A Highly Strained Heterocycle.

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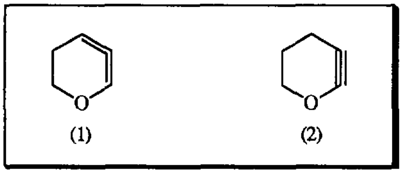
Abstract: Reaction of 3,4-dibromo-2,2,6,8-tetramethyl-2*H*-[1]benzopyran with either organolithium reagents or magnesium generates the novel aryne, 3,4-didehydro-2*H*-[1]benzopyran. Cycloaddition with dienes gives access to the dibenzo[*b,d*]pyran system.

INTRODUCTION

The generation and reactions of benzyne have been extensively studied.[1] Mention can be made of halogenoaromatic compounds,[2] benzenediazonium-2-carboxylate,[3] diphenyliodonium-2-carboxylate[4] and 1-aminobenzotriazole and related compounds[5] as well established precursors of arynes, whilst *o*-trimethylsilylphenyl triflate[6] and the recently introduced phenyl[*o*-(trimethylsilyl)phenyl]iodonium triflate[7] yield benzyne under mild conditions. Heteroarynes[8] based on pyridine,[9] thiophene,[10] furan[11] and their benzologues[12] have been confirmed. 3-Halogenocoumarins yield mixtures of the 3- and 4-substituted coumarin on reaction with piperidine, implicating the intermediacy of 3,4-didehydrocoumarin.[13] The base promoted elimination of HBr from 5-bromo-3,4-dihydropyran is facile and leads to 3,4-didehydrodihydropyran (1) rather than the heteroaryne (2). The reaction of the strained allene (1) with a range of ketone enolates has been studied.[14]



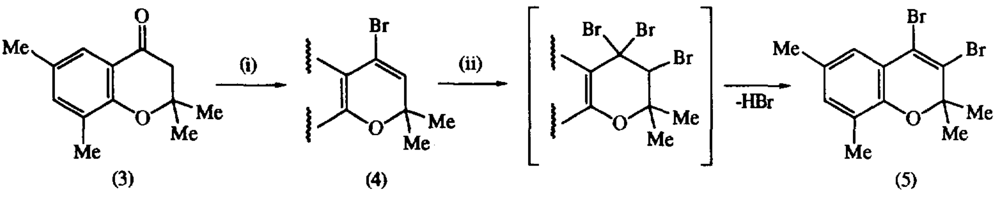
(1) (2)

We now report our work on the generation and reactions of 3,4-didehydro-2*H*-[1]benzopyran, a novel heteroaryne or highly strained alkyne, derived from a 2*H*-[1]benzopyran.

DISCUSSION

We have shown that 4-bromo-2*H*-[1]benzopyrans afford the 4-lithio derivatives on treatment with n-butyllithium and that the lithium compounds react normally with a range of electrophilic species.[15] However, 3-bromo-2*H*-[1]benzopyrans spontaneously ring open with n-butyllithium, subsequently yielding allenes.[16]

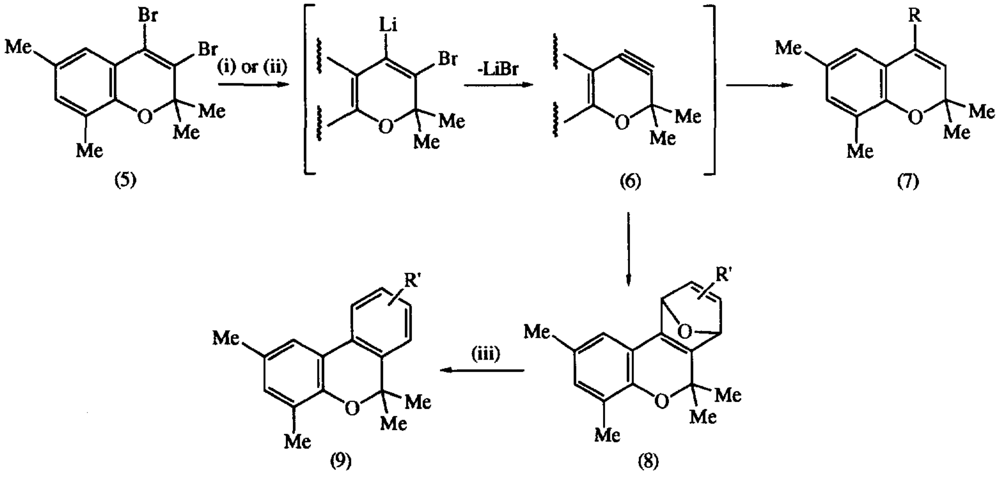
It was of interest to observe the behaviour of 3,4-dibromo-2*H*-[1]benzopyrans towards n-butyllithium. 3,4-Dibromo-2,2,6,8-tetramethyl-2*H*-[1]benzopyran (5) was obtained from the readily available 2,3-dihydro-2,2,6,8-tetramethyl-4*H*-[1]benzopyran-4-one (3) by conversion to 4-bromo-2,2,6,8-tetramethyl-2*H*-[1]benzopyran (4) using PBr_3.[15] Subsequent addition of bromine was accompanied by elimination of HBr, affording (5) in good yield (Scheme 1); the 6- and 8-methyl substituents prevent the usual facile bromination in the aromatic ring.[17]



Reagents and conditions: (i) excess PBr_3, Δ; (ii) Br_2, $CHCl_3$, RT.

Scheme 1

The reaction of (5) with an excess of n-butyllithium afforded 4-n-butyl-2,2,6,8-tetramethyl-2*H*-[1]benzopyran (7, R = n-Bu) in moderate yield together with some of the 4-unsubstituted 2*H*-[1]benzopyran (7, R = H). Similar products resulted with other alkyl lithium compounds and with phenyllithium, leading to the novel 2*H*-[1]benzopyrans (7, R = tBu, Me, Ph). Alkyl substitution in the 4-position is confirmed by reference to the chemical shift of 3-H (δ 5.39 - 5.61), similar to that for 3-H in 2,2-dimethyl-2*H*-[1]benzopyran (δ 5.46), whereas 4-H resonates at δ 6.21. These values are typical for a wide range of 2*H*-[1]benzopyrans.[18] It appears that following halogen metal exchange, loss of LiBr occurred and nucleophilic addition to an intermediate aryne completed the reaction sequence (Scheme 2).



Reagents and conditions: (i) excess RLi, THF, N_2, RT; (ii) excess Mg, substituted furan, THF, N_2, Δ; (iii) Zn, AcOH, warm.

Scheme 2

Cycloaddition reactions of arynes are well documented and in particular the use of furan to intercept any arynes generated during a reaction has become a standard technique.[19] Such a reaction features in the first total synthesis of the angucycline antibiotic C104,[20] whilst the introduction of a furyl side chain into an *o*-halogenoaniline has allowed the synthesis of the tetrahydrobenzazepine skeleton through the intramolecular capture of an intermediate aryne.[21] However, when furan was present throughout the reaction of (5) with n-butyllithium, no adduct could be isolated. It seems that the nucleophilic attack of n-butyllithium on the aryne (6) resulting in (7, R = n-Bu) is preferred to cycloaddition under these experimental conditions.

An alternative approach to the *o*-halogenophenyl carbanion precursor of benzyne utilises the reaction of magnesium with a 1,2-halogenobenzene.[22] When (5) was treated with Mg in THF in the presence of substituted furans, either the cycloadducts (8)[23] or the fully aromatic dibenzo[*bd*]pyrans (9)[24] were obtained in good yields, confirming the intermediacy of the 3,4-didehydro-2*H*-[1]benzopyran species (6) (Scheme 2). Aromatisation of the cycloadducts (8) was accomplished by treatment with zinc in acetic acid.[25]

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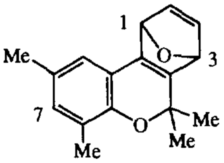
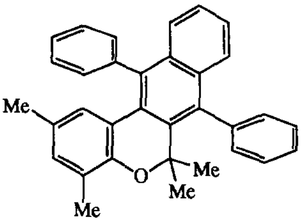
23. 1,3-Etheno-1,3-dihydro-4,4,6,8-tetramethyl-4*H*-furo[3,4-*c*][1]benzopyran (48%) as pale yellow needles from light petroleum (b.p. 60 - 80 °C), m.p. 110.5 - 111.5 °C; υ_{max}/(Nujol) 1605, 1251, 1190, 1155, 935; δ_H (250 MHz, $CDCl_3$), 1.22 (3H, s, 4-Me), 1.64 (3H, s, 4-Me), 2.14 (3H, s, Ar-Me), 2.25 (3H, s, Ar-Me), 5.39 (1H, s,1-H†), 5.75 (1H, s, 3-H†), 6.67 (1H, s, Ar-H), 6.80 (1H, s, Ar-H), 7.10-7.12 (2H, AB system, CH=CH); δ_C 15.8, 20.5, 24.3, 28.1, 78.3, 81.6, 82.5, 118.2, 119.7, 125.0, 129.1, 131.1, 142.6, 143.4, 144.1, 146.7, 148.9; (Found C, 80.1, H, 7.2. $C_{17}H_{18}O_2$ requires C, 80.3, H, 7.1 %). [† assignments may be reversed].



24. 7,12-Diphenyl-2,4,6,6-tetramethyl-6*H*-benzo[*e*]naphtho[2,3-*c*]pyran (87%), obtained from (5) and 1,3-diphenylisobenzofuran, as pale yellow crystals from ethyl acetate/hexane, m.p. 225 - 226 °C; υ_{max}/(Nujol) 1599, 1248, 1153; δ_H (250 MHz, $CDCl_3$), 1.13 (3H, s, 6-Me), 1.38 (3H, s, 6-Me), 1.95 (3H, s, Ar-Me), 2.24 (3H, s, Ar-Me), 6.43 (1H, s, Ar-H), 6.77 (1H, s, Ar-H), 6.95 (1H, m, Ar-H), 7.34 - 7.83 (13H, m, Ar-H); (Found M^+, 440.2140; C, 89.9; H, 6.4. $C_{33}H_{28}O$ requires M^+, 440.2140; C, 90.0; H, 6.4 %).



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