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3,4-DIDEHYDROPYRIDINE PLUS CYCLOPENTADIENE: [2+2] OR [4+2]-CYCLOADDITION ?

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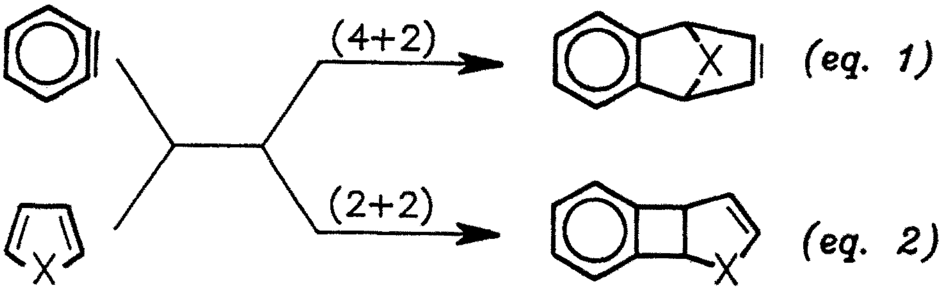
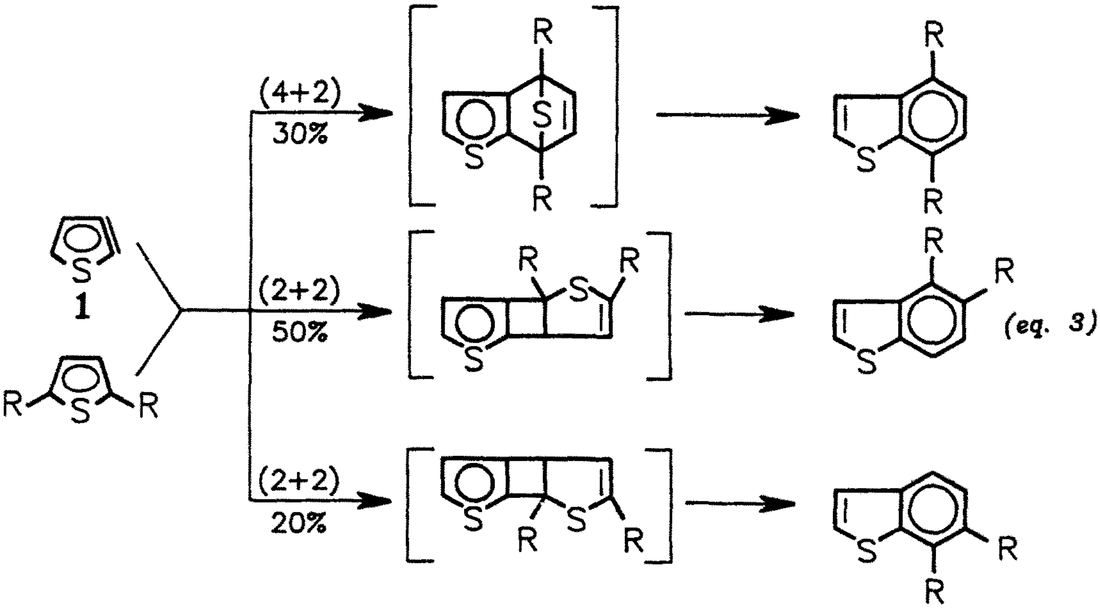
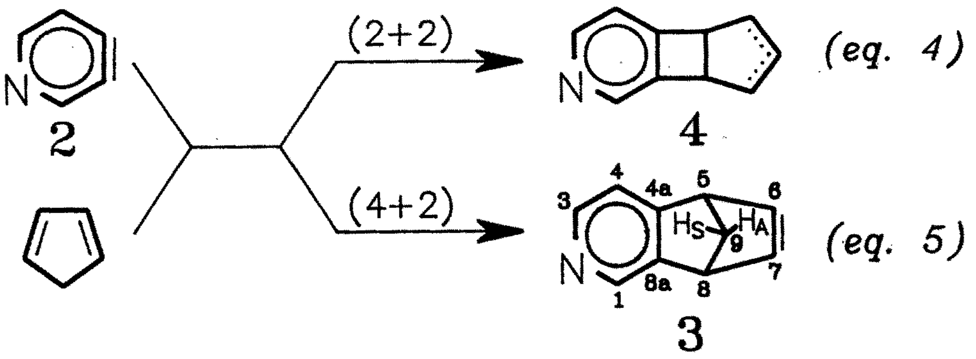
Abstract: 3,4-Didehydropyridine (2) generated from two precursors (6 and 7) of the diazonium carboxylate 5 reacts with cyclopentadiene to give the [4+2]-cyclo-addition product 3 rather than the [2+2]-adduct 4 proposed in the literature. The structure of 3 was supported by complete proton and carbon NMR assignments made with the aid of decoupling and 2D experiments.

Since its original recognition by Wittig[2], the high dieneophilic reactivity of arynes in [4+2]-cycloaddition (Diels-Alder) reactions (eq. 1) has become the basis of the single most useful diagnostic method for the detection of these reactive intermediates.[3] Although arynes will also undergo [2+2]-cycloadditions with themselves,[4] simple alkenes,[5] and even certain acyclic 1,3-dienes (eq. 2, X = no bond),[6] this path is, as expected,[7] usually avoided with cyclic, 1,3-conjugated dienes.

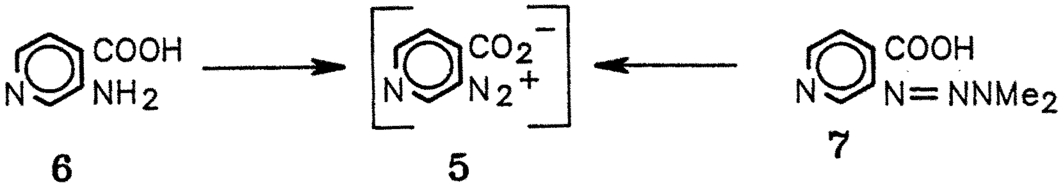


The two apparent exceptions to this generalization are the reactions of the hetarynes[8] 2,3-didehydrothiophene (1) and 3,4-didehydropyridine (2) with various substituted thiophenes (eq. 3)[9] and with cyclopentadiene (eq. 4),[10] respectively.





Whereas the former exception appears to arise from that aryne's ring size and/or heteroatom proximity,[11] no such structural features are present in the latter case. In fact, since the type of aryne precursor (an- *o*-diazonium carboxylate) and diene used are well-studied and known to generally lead to [4+2]-cycloaddition,[3] the reported[10] [2+2]-cycloaddition reactivity of 3,4-didehydropyridine (eq. 4) remains anomalous. Although these older results have been questioned previously,[8,12] recent studies[13] have also failed to yield the known[14,15] Diels-Alder adduct (3) expected from the [4+2]-cycloaddition reaction (eq. 5). We now wish to report, however, that cyclopentadiene does in fact react with 3,4-didehydropyridine (2) to give 5,8-dihydro-5,8-methanoisoquinoline (3) as the only basic product.



Instead of also[10] using the isolated and explosive pyridine-3-diazonium-4-carboxylate (5),[16] this precursor of the hetaryne 2 was generated and reacted *in situ* by the aprotic diazotization[17] of 3-aminoisonicotinic acid (6)[18] or even more conveniently by the solution-phase thermolysis of the recently developed[19] masked diazonium carboxylate, 3-(3,3-dimethyltriazen-1-yl)-pyridine-4-carboxylic acid (7), a pyridine analogue of the Nakayama reagent.[20] In the presence of cyclopentadiene either of the above methods gave a water insoluble basic oil in up to 16% yield (unoptimized) which according to GC/MS analysis is a single substance with $M^+=143$. Although the fragmentation pattern is very similar to that of benznorbornadiene[21,22] (Table I) this similarity has been considered previously to be insufficient to distinguish a norbornene such as (3) from an isomeric bicyclo[3.2.0]hept-2-ene such as (4).[23] While the similarity of the picrate melting point and most, but not all, of the NMR parameters (Table II) to those previously published[15] for samples of 3 prepared by a route which could not conceivably lead to the [2+2]-adduct 4 further suggested that the [4+2]-adduct 3 had indeed been formed (eq. 5), conclusive evidence in the form of the complete proton and carbon NMR assignments shown in Table II was obtained from 2-D COSY and ^{1}J-HETCOR NMR spectra[24] and decoupling studies.

Table I. Mass Spectral Parameters for 3 and Benzonorbornadiene[a]

Ion	3[b]	Benzonorbornadiene[c]
M^+	143 (100)	142 (91)
M-H	142 (90)	141 (100)
$M-C_2H_2$	117 (21)	116 (17)
$M-H-C_2H_2$	116 (20)[d]	115 (37)
M-H-HCN	115 (57)	
$M-H-2C_2H_2$	90 (14)[e]	89 (8)
C_7H_5	89 (27)	89 (8)
C_5H_3	63 (31)	63 (16)
C_5H_2	62 (12)	62 (7)
C_4H_3	51 (15)	51 (9)
C_4H_2	50 (14)	50 (7)
C_3H_3	39 (26)	39 (13)

[a] selected ions reported as m/e (rel. int.) including all those between 39 and M+ with rel. int. > 10; [b] taken at 70 eV on a Finnegan 1020 OWA instrument; [c] taken from ref. 21; [d] may also contain M-HCN; [e] may also contain $M-HCN-C_2H_2$.

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Table II. NMR Parameters[a] for 5,8-Dihydro-5,8-methanoisoquinoline (3).

	^1H[b]			^{13}C[c]	
Position[d]	This Work	Ref. 15	Position	This work	Ref. 15[e]
1	8.39s	8.35s	1	141.3	141.3
3	8.21d(4.7)	8.15d(5.0)	3	146.5	146.5
4	7.20d(4.6)	7.10d(5.0)	4	117.6	117.5
			4a	161.7	161.6
5	3.92m[f]	3.79brs	5	50.2	50.2
6	6.74ddd(5.4,3.2,1.2)[g]	6.70dq(5.4,3.0)	6	141.9	141.8
7	6.81ddd(5.4,3.2,1.2)[g]		7	143.4	143.3
8	3.97m[f]	3.81m	8	48.0	47.9
			8a	147.1	147.0
9s	2.24dm[i]	1.83dt[h](7.3,1.6)	9	70.2	70.2
9a	2.35dt(7.4,1.6)[j]	2.36dt(7.3,2.6)			

[a] In $CDCl_3$, ppm relative to TMS=0; [b] 300 MHz; <u>observed</u> splittings > 1.0 Hz given in parentheses; [c] 75 MHz; [d] carbon attachment of protons verified by ^1J-HECTOR experiment; the twelve COSY correlations of proton shifts are designated by connecting brackets; [e] assignments from this work as described in text; [f] collapses to a q(1.8) of an ABX system on decoupling both H-6 and H-7; when the decoupling frequency favors H-6, only H-5 is decoupled; [g] collapses to a d(5.4) on irradiating the H-5 and H-8 signals; [h] this value is probably a misprint since in several closely related derivatives (ref. 15) and benzonorbornadienes (L. Paquette, A. Varadarajan, and L.D. Burke, J. Am. Chem. Soc., 1986, 108, 8032) to the Δδ of the bridge protons is never more than 0.25 and averaging only 0.10; [i] collapses to a dt(7.5, 1.6) on decoupling H-6 and H-7 and to a brd(7.5) on decoupling H-5 and H-8; [j] collapses to a sharp d(7.5) on decoupling H-5 and H-8 but unaffected when H-6 and H-7 are decoupled.

The pyridine carbons at positions 1, 3, and 4 were assigned by correlation (^{1}J-HETCOR) with the attached hydrogen atoms whose expected[25-27] relative chemical shifts (H-1 and H-3 lower field than H-4) and multiplicities (H-1 singlet, H-3 and H-4 doublets) permitted their easy identification. This was supported by the COSY correlations (Table II) which, not surprisingly, lacked only the correlation between H-1 and H-3 since $J_{2,6}$ for pyridines is often at or near zero.[28] The quaternary carbons were easily recognized by their lower intensities and assigned to positions 4a and 8a as shown by analogy to several other 3,4-annelated pyridines[25,26] all of which also had the former carbon resonance at 13-14 ppm lower field than the latter. In contrast to many benzonorbornadienes[29] it is possible to assign the bridgehead carbon resonances based on the generalization that the higher field one arises from the carbon attached to the β-position of the pyridine ring.[30] By means of the ^{1}J-HETCOR this analysis leads to the indicated proton assignment which is not directly available by comparison with the ^{1}H-NMR spectra of 3,4-dialkylpyridines[25,27] whose benzylic protons are usually unresolved. The bridge proton resonances were assigned as in the benzonorbornadiene series[31,32] so that the one which appears at higher field, displays the most coupling, and correlates with the olefinic protons (COSY) is syn to the aromatic ring. Also as in substituted benzornorbornadienes[29] the assignment of the olefinic carbon resonances is difficult, but the COSY experiment shows that each bridgehead proton is correlated with only one of the olefinic protons as shown in Table II. If it is reasonably assumed that this correlation is between protons which not only have the larger coupling constants as expected[33] but also are separated by three (H-5 to H-6 and H-7 to H-8) rather than four (H-5 to H-7 and H-6 to H-8) bonds,[34] then it is possible to assign the olefinic protons and, through the ^{1}J-HETCOR, the attached carbons as shown in Table II.

From the above results it can therefore be concluded that 3,4-didehydropyridine (2) does in fact react with cyclopentadiene to give the [4+2]-adduct, 5,8-dihydro-5,8-methanoisoquinoline (3). The relatively low yield may simply indicate that optimum reaction conditions have not yet been achieved since other [4+2]-cycloadditions of the hetaryne 2 generated from the diazonium carboxylate 5 have been shown to be very sensitive to reaction conditions.[16] Alternatively, the low yield may reflect a competitive unimolecular decompositon of the hetaryne 2 as has been demonstrated in the gas phase[35] or more recently in inert gas matrices.[36] This question warrants examination because of the synthetic potential of the hetaryne 2 as a source of interesting molecules.[14,15,37]

EXPERIMENTAL

5,8-Dihydro-5,8-methanoisoquinoline (3). An evacuated sealed tube containing 1.9g(29.4mmol) of freshly cracked cyclopentadiene, 120mg(0.62mmol) of the triazine 7,[19] and 5ml of acetonitrile was heated at 130° for 4hr. GC/MS analysis of the resulting black solution using naphthalene as an internal standard indicated the formation of the product 3 in 16% yield. In a preparative scale experiment carried out with 1.59g of 7 in refluxing acetonitrile in the presence of trichloracetic acid according to the general procedure described for the Nakayama reagent,[20] this same product was isolated by adding 5% HCl to the reaction mixture, washing with ether, basifying with 5% NaOH, reextracting with ether, and drying the latter ether extracts over anhydrous MgSO$_4$. Evaporation of the solvent left a dark oil which was passed through a short silica gel column with hexane/CHCl$_3$ gradient elution to give 3 as a colorless oil in 6% yield after evaporation of the solvent. This oil gave a single peak on GC-analysis and had the same retention time and mass spectrum (Table I) as the previous sample. The NMR parameters are shown in Table II. Addition of picric acid in ethanol gave a picrate, mp.136-137° (lit.[14] 135-137°).

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