A Mild Retro-[$_{\pi}4_s+_{\pi}2_s$] Cleavage Route to Furans and Fulvenes

By W. S. Wilson and R. N. Warrener*

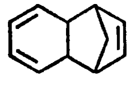
(*Department of Chemistry, Australian National University, Canberra, A.C.T.* 2600, *Australia*)

Summary A new route to β-substituted furans and fulvenes has been developed which is based on the ready thermal fragmentation of 4,5-diazatricyclo[6,2,1,$0^{2,5}$]-undeca-3,5,9-trienes.

Retro-[$_{\pi}4_s$ + $_{\pi}2_s$] (Diels–Alder) reactions are commonly used in synthesis.[1] These reactions are conducted under thermal conditions and extreme temperatures are often required to effect fragmentation.[1] This is one limitation where temperature sensitive products are the goal,[2] although this has been partly offset by flash vacuum pyrolysis techniques. This latter technique is elegantly demonstrated by the recent report by de Mayo and his co-workers on the synthesis of pentalene.[3]

We[4] and others[5] have observed that derivatives of the tricyclo[6,2,1,$0^{2,5}$]undeca-3,5,9-triene system (**1**) are particularly labile in respect to retro-[$_{\pi}4_s$ + $_{\pi}2_s$] cleavage, especially when the $_{\pi}2_s$ component becomes part of an aromatic system. We have now developed a scheme for the synthesis of β-substituted furans and fulvenes which is based on the fragmentation of the 4,5-diaza-analogue of (**1**). The features of this scheme are: (i) simple formation of the diaza-intermediate, (ii) low temperatures involved, especially in the fragmentation step, (iii) essentially quantitative conversions in each step.

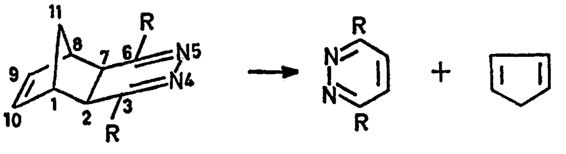
In order to evaluate the stability of the 4,5-diazatricyclo-[6,2,1,$0^{2,5}$]undeca-3,5,9-triene system, the 3,6-di-(2′-pyridyl) derivative (**3**) was prepared from the reaction of equimolar



(1)

(2)

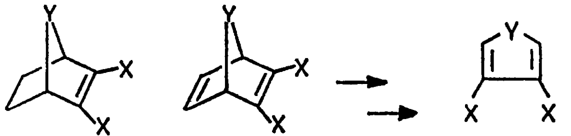
R = 2'-Pyridyl



(3) (4)

amounts of 3,6-di-(2′-pyridyl)-*s*-tetrazine and norbornadiene in $CDCl_3$ at −20°. A rapid reaction occurred and nitrogen was eliminated to yield (**3**) in quantitative yield [^1H n.m.r., δ 1·19, 1·28 (2H, AB q, *J* 9 Hz, 11-H_2), 3·40 (2H, m, 1-, 8-H), 3·54 (2H, s, 2-, 7-H), 6·50 (2H, t, 9-,10-H), 7·3—8·90 p.p.m. (8H, complex m, pyridyl)]. The lack of coupling between C-2(7) and C-1(8) supported the suggested stereochemistry, and is consistent with the *s*-tetrazine approaching from the less hindered *exo*-side. Intermediate (**3**) was stable below −10°, but above this temperature fragmentation to 3,6-di-(2′-pyridyl)pyridazine (**4**) and cyclopentadiene occurred.

In order to compare our method with the standard retro-[$_\pi4_s + {}_\pi2_s$] route used in synthesis of fulvenes[2] and furans,[6] we have chosen three reactions already reported in the literature.[2,6] The standard method involves the following steps: (a) Formation of bicyclic adduct, (**5**)—(**7**); (b) Selective hydrogenation to the dihydro-derivative (**11**)—(**13**); (c) High temperature pyrolysis (195—400°) to the 5-membered product (**8**)—(**10**) plus ethylene.



(11)-(13) (5)-(7) (8)-(10)

TABLE

Summary of conditions for conversion of 7-substituted norbornadienes into furans and fulvenes

Substituents X	Substituents Y	Dihydro-compound	Starting material	Reaction conditions	Product	^1H n.m.r. (δ p.p.m.)[a] of product
CF_3	O	(**11**)	(**5**)	room temp., $CDCl_3$ few h	(**8**)[b]	7·90 (s, vinylic)
CO_2Me	$C{=}CPh_2$	(**12**)	(**6**)	room temp., $CDCl_3$, overnight	(**9**)[c]	7·35—7·65 (m, phenyl) 6·97 (s, vinylic) 3·85 (s, OMe)
CO_2Me	$C{=}CMe_2$	(**13**)	(**7**)	50°, $CDCl_3$, 2 h	(**10**)[d]	7·16 (s, vinylic) 3·83 (s. OMe) 2·31 (s, Me)

[a] 60 MHz, $CDCl_3$, MeSi as internal standard. [b] Low boiling liquid, isolated by g.l.p.c. (carbowax 20M, fluoroport, 58°) (*m/e* 204). [c] M.p. 166°, reported[2] 165—167°, isolated by preparative layer chromatography (silica, $CHCl_3$) (*m/e* 350). [d] Unstable low-melting solid, isolated by short path distillation (*m/e* 222).

Reaction of the 7-substituted norbornadienes (**5**)—(**7**) readily occurred with the *s*-tetrazine (**2**) under mild conditions (see Table) to produce the corresponding 5-membered products (**8**)—(**10**) plus the pyridazine (**4**). ^1H N.m.r. spectroscopy showed that the conversions were quantitative, although the isolated yields were only in the range 70—90%. The spectral properties of the products were in agreement with the assigned structures (see Table). Dimethyl 6,6-dimethylfulvene-2,3-dicarboxylate was only moderately stable, and this would account for the lack of success reported by Alder and Trimborn[2] using the standard retro-[$_\pi4_s + {}_\pi2_s$] route in attempts to prepare this product.

The generality of this method is demonstrated by the synthesis of isobenzofuran,[7] isobenzofulvenes,[8a] and isoindoles.[8b]

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