

PALLADIUM (II) CATALYSED TANDEM [2,3]-SIGMATROPIC SHIFT-1,3-DIPOLAR
CYCLOADDITION PROCESSES IN OXIME O-ALLYL ETHERS

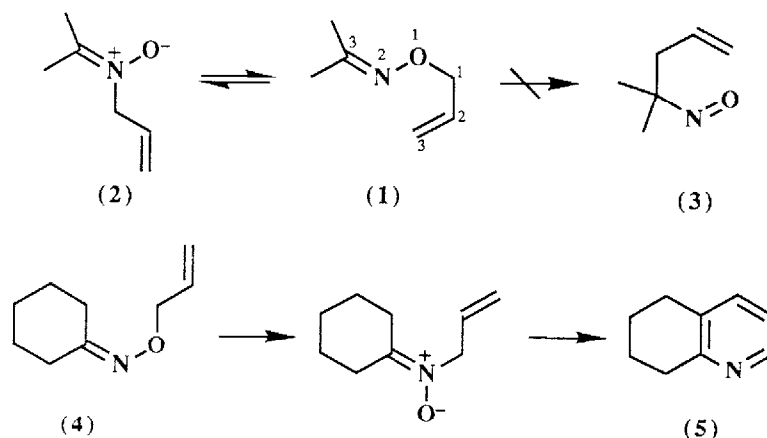
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Abstract

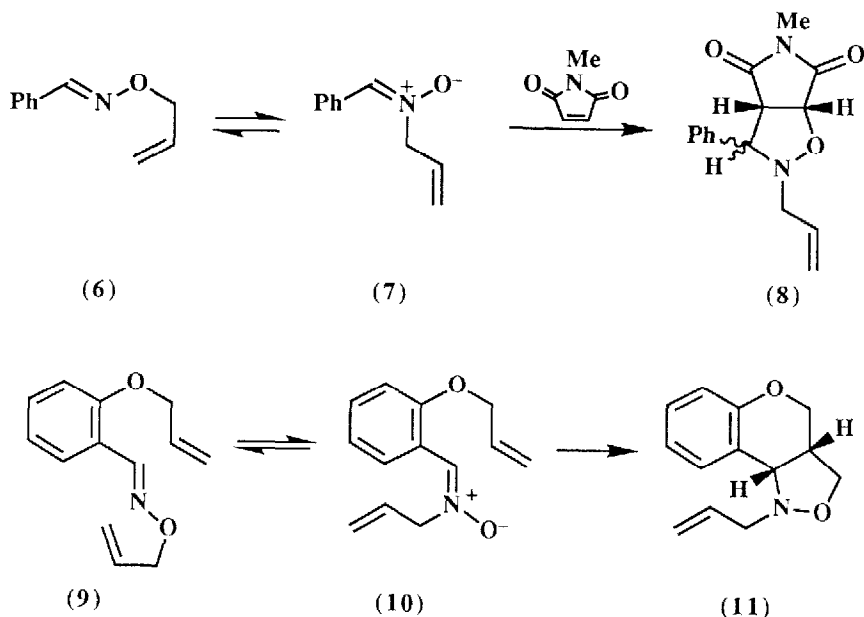
Oxime O-allyl ethers are equilibrated with the corresponding N-allyl nitrones on treatment with 10 mol% $\text{PdCl}_2(\text{MeCN})_2$ by a formal [2,3]-sigmatropic shift. The nitrones can be trapped both inter- and intra-molecularly by appropriate dipolarophiles to give cycloadducts in good to excellent yields.

O-Allyl ethers of oximes (1) are known to undergo a reversible formal [2,3]-sigmatropic shift giving N-allyl nitrones (2) to the exclusion of the alternative [3,3]-sigmatropic process (1) \rightarrow (3).¹ Subsequent work² provided e.s.r. evidence that the rearrangement (1) \rightleftharpoons (2) is, at least in part, a reversible Martynoff rearrangement,³ proceeding via a radical pair intermediate.

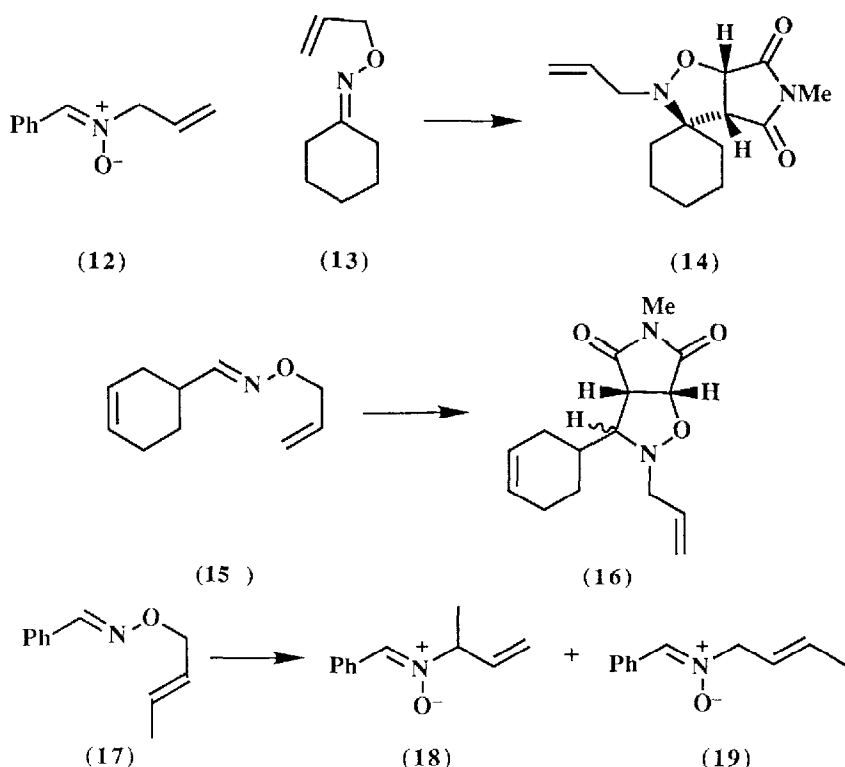


The formal [2,3]-sigmatropic shift of oxime O-allyl ethers of cyclic ketones, when conducted in the presence of air at ca. 180°C leads to 2,3-cycloalkenopyridines e.g. (4) \rightarrow (5) in poor to moderate yield.⁴ Substituent labelling of the O-allyl moiety leads to scrambling of the substituent in the 2,3-cycloalkenopyridine product consistent with a radical pair intermediate.⁴

Our interest in this process arose from a program designed to develop new tandem cycloaddition processes proceeding via 1,3-dipoles. In addition to tandem sequences involving azomethine ylides,⁵ azomethine imines,⁶ and sulphinylaminomethanide species⁷ we have developed six tandem processes involving oximes and proceeding via nitrones.⁸ Two tandem processes involving the formal [2,3]-sigmatropic shift (1) \rightleftharpoons (2) are possible in which the resultant nitrone is trapped intermolecularly, e.g. (6) \rightarrow (7) \rightarrow (8), or intramolecularly, e.g. (9) \rightarrow (10) \rightarrow (11).⁹ These two processes were selected for model studies.



When (6) was heated with N-methylmaleimide in toluene (sealed tube, 180°, 24 h) the reaction proceeded to only 27% conversion but gave a good yield (92%) of a 2:1 mixture of exo- and endo-isomers of (8). Attempts to achieve conversion of (9) to (11) under identical conditions resulted in a 90% conversion to products but afforded only a 10% yield of (11) together with unidentified products and Claisen rearrangement product. Attempts to catalyse the formal [2,3]-sigmatropic shift were more successful. Thus (6) on treatment with 15 mol % $\text{PdCl}_2(\text{MeCN})_2$ (CHCl_3 , 25°, 60 h) afforded a single nitrone (12, 70%). The stereochemistry of (12) is assigned on the basis of n.o.e. studies.¹⁰ The nitrone (12) on heating in o-dichlorobenzene (180°C, 5 h) gave a 7:1 mixture of (6) and (12). The Pd(II) catalysis could be extended to the tandem processes. Thus (6) on heating with N-methylmaleimide [CHCl_3 , 60°C, 15 mol % $\text{PdCl}_2(\text{MeCN})_2$, 24 h] afforded (8) as a 1:1 mixture of endo- and exo-isomers in 93% yield.¹¹ The conversion of (9) to (11) (50%) was achieved under analogous conditions. The lower yield in this latter case presumably reflects the tendency of aryl allyl ethers to give Pd(II)- π -allyl complexes.



Attempts to observe and/or isolate the corresponding nitron from (13) were unsuccessful. However, when the reaction [CHCl_3 , 60° , 10 mol % $\text{PdCl}_2(\text{MeCN})_2$, 6 h] was run in the presence of N-methylmaleimide the cycloadduct (14) was obtained in 96% yield. Thus the nitron \rightleftharpoons O-allyl oxime equilibrium lies very largely on the O-allyl oxime side in this case. Oxime (15) affords (16) as a ca. 1:1 mixture of endo- and exo-isomers (each of which comprises a ca. 1:1 mixture of diastereomers) under analogous conditions [CHCl_3 , 60°C , 10 mol % $\text{PdCl}_2(\text{MeCN})_2$, 7h].

The mechanism of the Pd(II) catalysed rearrangement requires further study but does not proceed simply by a cyclisation-fragmentation mechanism¹² as shown by treatment of (17) with 10 mol% $\text{PdCl}_2(\text{MeCN})_2$. The product consists of a 2:3:1 mixture of (18), (19) and an as yet unidentified product. Nitrones (18) and (19) were obtained as single stereoisomers and their configurations are assigned on the basis of n.o.e. studies¹⁰. Pd(II) and Pd(O) complexes are known to catalyse [3,3]-sigmatropic shifts.¹³

Further work is in hand to explore this process more fully.

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- 9 A sub-class of this latter process is that the dipolarophile can be located within a substituent in the allyl moiety.
- 10 N.O.e. data (C_6D_6): (12)-irradiation of $CH=N$ (δ 6.7) effects a 6.5% enhancement on the CH_2N protons (δ 3.95); (18)-irradiation of $CH=N$ (δ 6.85) effects a 14.5% enhancement on the $MeCHN$ proton (δ 3.95); (19)-irradiation of $CH=N$ (δ 6.75) effects a 5.5% enhancement on the CH_2N protons (δ 3.9).
- 11 The reaction can also be conducted at 25°C over several days.
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