Tetrahedron Letters,Vol.26,No.20,pp 2423-2426,1985 0040-4039/85 $3.00 + .00
Printed in Great Britain

PALLADIUM MEDIATED DEHYDROGENATION IN THE PHOTOCHEMICAL CYCLIZATION OF HETEROCYCLIC ANALOGS OF STILBENE

Viresh H. Rawal, Robert J. Jones and Michael P. Cava*
Department of Chemistry, University of Pennsylvania,
Philadelphia, PA 19104

Abstract: A method is described for the photocyclization of heterocyclic analogs of stilbene to the corresponding phenanthrene-like systems under a N_2 atmosphere, using a catalytic amount of Pd on carbon (Pd/C) as the "oxidant".

One of the most thoroughly studied and synthetically useful photochemical reactions is the phototransformation of stilbenes to phenanthrenes via a 6π-electron conrotatory electrocyclic ring closure followed by an in situ oxidation of an intermediary dihyrophenanthrene.[1] Heterocyclic analogs of stilbene also undergo this reaction, although the yields are usually lower, particularly for analogs containing electron-rich heterocycles which are easily destroyed by oxidants.

In connection with our work on the synthesis of the potent antitumor agent CC-1065, we recently reported the O_2(air) mediated photocyclizations of pyrrole containing-stilbenes.[2] While these reactions proceeded satisfactorily on a 1 mmolar scale, yields dropped considerably with preparative amounts of material (1-5g) due to oxidative destruction of the indole-like products. To overcome this problem we examined several other oxidants (e.g., air/I_2, I_2, $CuCl_2$, TCNE),[3,4,5] but found them to be unsuitable for our substrates. Success was achieved with the mild, catalytic-dehydrogenation procedure which we had developed during our work on the conversion of aporphines to dehydroaporphines.[6]

Thus when 1 was irradiated with an external light source (450W, medium pressure Hanovia lamp[7]) in refluxing acetonitrile with a catalytic amount of Pd/C (1 mmol, 200 ml, 0.10g 5% Pd/C, 3 h), we obtained in 80% yield a 3:1 mixture of two products, the major one being the desired phenanthrene, 2. The second product was found to be 1,2-di(2, N-Methylpyrryl)-ethane (3), resulting from transfer hydrogenation of the starting material.[8] By including a more powerful hydrogen acceptor, nitrobenzene, in the reaction mixture, we circumvented the competing hydrogenation, and obtained a good yield of 2. Chromatographic purification was simplified, by using a combination of *p*-nitrobenzoic acid and Et_3N. Interestingly, the reaction worked, albeit at a much slower rate, even without external heating.

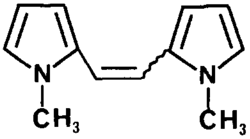
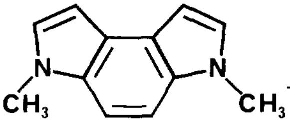
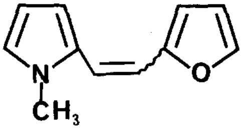
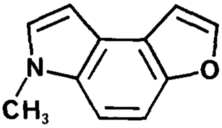
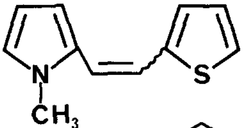
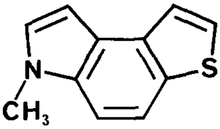
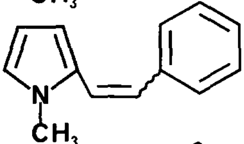
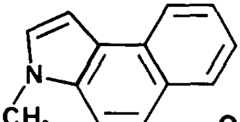
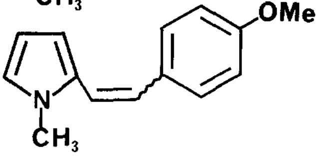
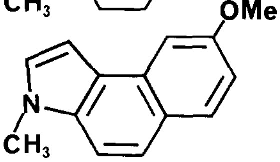
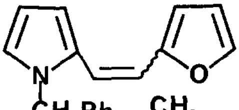
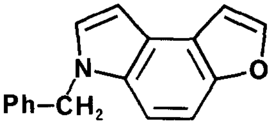
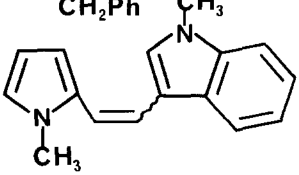
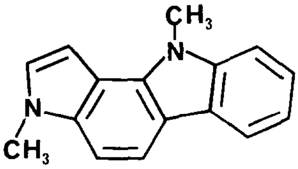
We have carried out the Pd/C mediated photocyclization of several heterocyclic analogs of stilbene (see Table). These substrates were irradiated in a two-neck, Dewar-shaped Pyrex vessel.[9] In all cases the reaction was remarkably clean, and proceeded in good yield. Furan containing systems cyclized at a much slower rate than other substrates. In contrast to the heterocyclic examples cited here, stilbene itself was not converted to phenanthrene under the same reaction conditions. We are looking into the mechanistic implications of this unexpected result. We are also investigating the use of other dehydrogenation catalysts for the photocyclization reaction.

In conclusion, stilbenoids which contain electron rich heterocycles undergo photocyclization only in poor yield using the standard oxidants; for such systems, the Pd/C protocol described here should prove to be a superior alternative.

General procedure for the Pd/C mediated photocyclization.[10]

N-Methylpyrrolo(3,2-e)-N-Methylindole, 2. A magnetically stirred solution of 4-nitro-benzoic acid (1.67g, 10.0 mmol), Et_3N (1.6 ml, 12.0 mmol), 5% Pd/C (0.5 g, Engelhardt), acetonitrile (500 ml), and 1,2-Di(2,N-methylpyrryl)ethene (1, 1.86 g, 10.0 mmol) was heated to a gentle reflux, and, after purging with N_2 for 30 min., irradiated.[7,9] The progress of the reaction was monitored by NMR spectroscopy. After complete disappearance of the starting material (ca. 16 h), the cooled solution was filtered, and the solvent was evaporated *in vacuo*. The crude product was dissolved in CH_2Cl_2, evaporated onto silica gel (30 mls), and purified by flash chromatography[11] over silica gel (100 mls; CH_2Cl_2: hexanes, 1:2), to give 2 as shiny white needles (1.56 g, 85%, mp 153-154°C).

TABLE[a,b,c]

Entry	Substrate		Reaction Time (days)	Product		Yield (%)
1		1	1		2	85
2		4	5.5		5	84
3		6	1.5		7	85
4		8	2		9	82
5		10	1		1	75
6		11	5		12	80
7		13	1		14	88

---

a) The substrates were prepared as described in ref. 2, and are mixtures of *cis* and *trans* isomers.

b) Reactions were usually carried out on 5 mmol scale. See experimental for a detailed procedure.

c) All compounds gave satisfactory spectral data (250 MHz NMR, IR, MS).

Acknowledgements: This work was supported by a grant from the National Institutes of Health (CA 36973). V. H. R. thanks the University of Pennsylvania for a Dean's Fellowship.

References and Notes

1. For an excellent current review on the photocyclization of stilbenes, see: Mallory, F. B.; Mallory, C. W. Organic Reactions, 1984, 30, 1. See also: Laarhoven, W. H. Recl. Trav. Chim. Pays-bas, 1983, 102, 185.

2. Rawal, V. H.; Cava, M. P. J. Chem. Soc., Chem. Comm., 1984, 1526.

3. Mallory, F. B.; Wood, C. S.; Gordon, J. T.; Lindquist, L. C.; Savitz, M. L. J. Am. Chem. Soc., 1962, 84, 4361.

4. Collins, D. J.; Hobbs, J. J. Chem. Ind. (London), 1965, 1725. Kellogg, R. M.; Groen, M. B.; Wynberg, H. J. Org. Chem., 1967, 32, 3093.

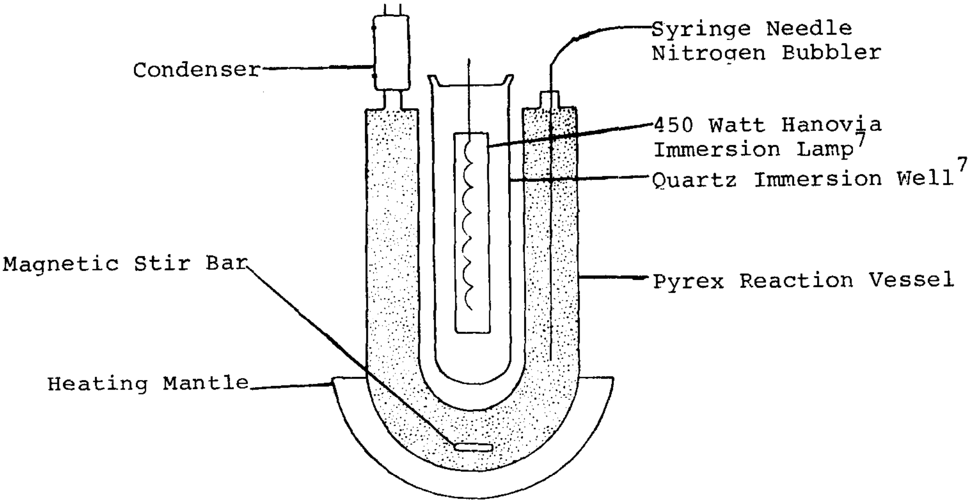
5. Bendig, J.; Beyermann, M.; Kreysig, D. Tetrahedron Lett., 1977, 3659. Bendig, J.; Beyermann, M.; Kreysig, D.; Schoneich, R.; Siegmund, M. J. Prakt. Chemie, 1978, 320, 798.

6. Cava, M. P.; Edie, D. L.; Saa, J. M. J. Org. Chem., 1975, 40, 3601. For a general review on dehydrogenation of polycyclic compounds, see: Fu, P. P.; Harvey, R. G. Chem. Rev. 1978, 78, 317.

7. Available through Ace Glass Co., Vineland, NJ.

8. Brieger, G.; Nestrick, T. J. Chem. Rev., 1974, 74, 567.

9. A schematic of the reaction setup is shown. The Dewar-shaped flask was constructed so as to hold 600 mls.



10. These stilbenoids are very light sensitive, quickly becoming dark in room light. Immediately before use, these compounds were purified by flash chromatography in a dimly lit room.

11. Still, W. C.; Kahn, M.; Mitra, A., J. Org. Chem., 1978, 43, 2923.

(Received in USA 14 February 1985)