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A CATALYTIC DEHYDROGENATION ROUTE TO AZOMETHINE IMINES.

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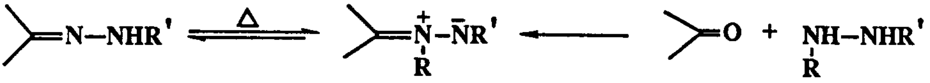
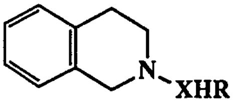
Abstract Catalytic dehydrogenation of appropriate N,N,N′- trisubstituted hydrazines with 10 mol% palladium black, ruthenium black, or Wilkinson's catalyst, in hot DMF in the presence of N-methylmaleimide occurs with high regioselectivity and leads to cycloadducts of the intermediate azomethine imines in moderate to good yield.

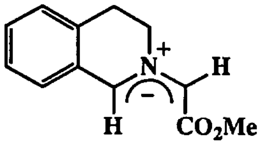
Azomethine imines (1) are available by a thermally induced 1,2-prototropic shift in hydrazones [giving (1a)],[1] or by condensation of aldehydes and ketones with 1,2-distributed hydrazines [giving (1b)].[2] A third, less well studied, approach involves the oxidation appropriate of N,N,N′- trisubstituted hydrazines with mercuric oxide[3] or by electrochemical methods.[4]



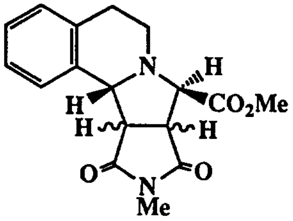
(1) a. R=H
b. R≠H



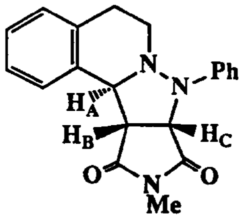
(2) a. X=CH, R=CO_2Me
b. X=N, R=Ph



(3)



(4)



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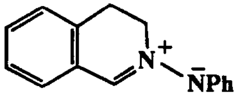
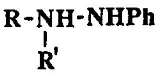


(6)

We recently reported the stereospecific formation of anti-azomethine ylides by the catalytic dehydrogenation of appropriate tertiary amines with palladium black in hot DMF e.g. (2a) → (3) → (4).[5]

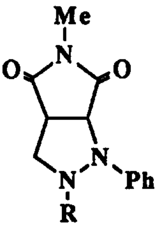
Subsequently further studies have shown that the catalytic dehydrogenation can also be achieved efficiently with both ruthenium black and Wilkinson's catalyst$[(Ph_3P)_3RhCl]$.[6]

These results encouraged us to extend these studies to appropriate hydrazines. Thus (2b) on heating (DMF, 130°C, 5h) with 10 mol% palladium black in the presence of 2 mol. of N-methylmaleimide (NMM) gives the cycloadduct (5)(40%), whilst ruthenium black (10 mol%) effects the reaction (DMF, 153°C, 20 h) in 55% yield. Wilkinson's catalyst (10 mol %) is clearly superior (DMF, 120°C, 18h) and gives (5) in 77% yield. The stereochemistry of (5) was established by n.O.e. studies. In particular irradiation of the signal for H_B effected a 7% enhancement in the signal for H_C but no enhancement in the H_A signal. Formation of (5) is assumed to proceed via (6) which is generated by a mechanism analogous to that discussed previously.[5] Excess NMM is used to regenerate the reactive metal catalyst by acting as a recipient for the hydrogen removed in the dehydrogenation step.

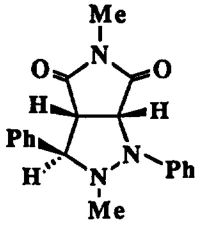


$R\text{-}\underset{R'}{N}\text{-}NHPh$

(7) a. $R=Me, R'=CH_2Ph$
- b. $R=R'=Me$
- c. $R=Me, R'=Ph$
- d. $R=Ph, R'=CH_2CH=CH_2$
- e. $R=Ph, R'=CH_2Ph$



(8) a. $R=CH_2Ph$
- b. $R=Me$
- c. $R=Ph$



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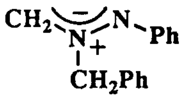


(10)

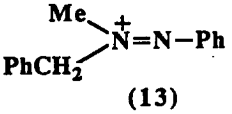
(11)

$CH_2=\overset{+}{\underset{CH_2Ph}{N}}\text{-}NHPh$

(12)

The catalytic dehydrogenation of acyclic hydrazines displays interesting regioselectivity. Thus (7a) reacts (DMF, 105-110°C) with 10 mol% of palladium black, ruthenium black or Wilkinson's catalyst in the presence of 2 mol of NMM to give cycloadduct (8a) as the major product (~60%) with only trace amounts of (9). Of the three catalysts, palladium black reacts the most cleanly. Wilkinson's catalyst is the least selective of the three, with significant amounts of an as yet unidentified product being produced. The reason for the selectivity for azomethine imine (10) as opposed to azomethine imine (11) is not immediately clear. The initial interaction with the catalyst could lead to either the iminium

(12) or diazenium (13) species. The efficacy of transition metal-hydrazine combinations for hydrogenation under mild conditions[7] suggests the diazenium species (13) is the more likely ntermediate. Deprotonation of diazenium species to azomethine imines is known to be facile even with weak bases.[8] Assuming the process proceeds via (13), the formation of (10) rather than (11) suggests deprotonation occurs on the catalyst surface and reflects surface adsorption equilibria.

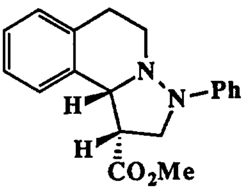


$\mathrm{Me(PhCH_2)\overset{+}{N}{=}N{-}Ph}$

(13)

PhN=NPh

(14)



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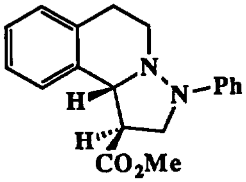

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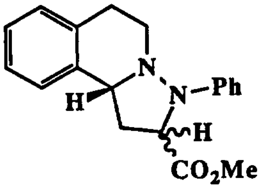

(17)

As expected the N,N-dimethylhydrazine (7b) undergoes an analogous reaction (DMF, 110°C, 16.5h) with 10 mol% palladium black and 2 mol NMM to give (8b)(61%), whilst (7c) gives (8c)(64%) under analogous conditions. In contrast, (7d) and (7e) give azobenzene (14)(88-91%) when subjected to the same treatment. In a preliminary study of regiochemistry (2b) (1 mol) was reacted with methyl acrylate(3 mol)(DMF, 120°C, 20 h) in the presence of Wilkinson's catalyst (10 mol%). The product (67%) comprised mainly a 4:5.7 mixture of (15) and (16) together with minor amounts of the two stereoisomers of the other regioisomer (17)(overall ratios 4:5.7:1.4:1).

Preparation of Cycloadduct(5) A mixture of the hydrazine (2b) (250 mg, 0.9 mmol), N-methylmaleimide (200 mg, 1.8 mmol), and tris(triphenylphosphine)rhodium chloride (82 mg, 0.09 mmol) in DMF (20 ml) was stirred and heated at 120°C fro 18 h. The solvent was then removed under reduced pressure and the residue purified by flash chromatography (SiO_2) eluting with 2:3 v/v 40-60° petroleum ether-ether. The cycloadduct (5)(280 mg, 77%), crystallised from ethyl acetate-benzene as colourless rods, m.p. 244-245°C (Found: C, 71.85; H, 5.65; N, 12.4. $C_{20}H_{19}N_3O_2$ requires C, 72.05; H, 5.75; N, 12.6%) $\delta(C_6D_6)$ 7.92(d, 1H, ArH), 7.58(d, 2H, ArH), 7.25, 7.11 and 6.48(3 x m, 6H, ArH) and 4.38(m, 1H, H_A) 3.92(d, 1H, J 8.2Hz, H_C), 2.97(t, 1H, J 8.2Hz, H_B), 2.90 and 2.75(2 x m, 2 x 1H, NCH_2), 2.45(s, 3H Me) and 2.20 and 1.85(2 x 1H, $ArCH_2$); m/z(%) 333(M^+, 100), 228(58), 221(49) and 130(23).

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