Tetrahedron Letters No. 29, pp 2545 - 2548.
© Pergamon Press Ltd. 1978. Printed in Great Britain.

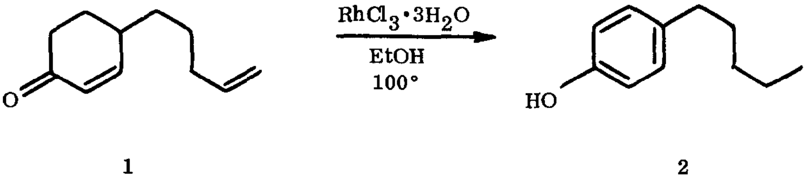
0040-4039/78/0715-2545$02.00/0

# RHODIUM-CATALYZED MIGRATION OF DOUBLE BONDS: PREPARATION OF SUBSTITUTED PHENOLS AND ANILINES

Paul A. Grieco* and Nebojsa Marinovic
Department of Chemistry, University of Pittsburgh, Pittsburgh, Pennsylvania 15260

(Received in USA 6 March 1978; received in UK for publication 25 May 1978)

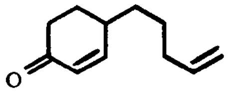
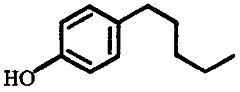
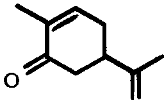
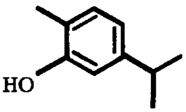
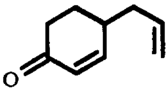
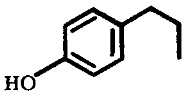
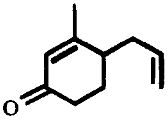
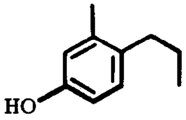
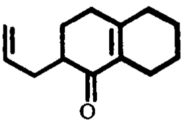
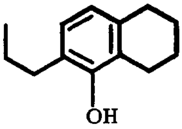
Transition metal complexes have been employed as homogeneous catalysts for the isomerization of carbon-carbon double bonds.[1] Recent reports have demonstrated the potential of rhodium complexes to bring about carbon-carbon double bond migration which is difficult to bring about otherwise.[2] We wish to report that unsaturated cyclohexenones undergo aromatization via remote double bond migration induced by rhodium chloride trihydrate (cf. eq 1). The transition metal catalyzed migration of systems such as 1 (see Table I) provides a convenient entry into a variety of substituted aromatic systems.[3]



(1)

Aromatization of carvone (Table I, entry 2) was brought about over an eight hour period in absolute ethanol containing a catalytic amount of rhodium chloride trihydrate[4] at 100°C (bath temperature) in a sealed tube. NMR analysis of the reaction product revealed the presence of an aromatic methyl group [$\delta$ 2.17 (s, 3H)] and an isopropyl group [$\delta$ 1.18 (d, 6H, J=7 Hz), 2.78 (m, 1H, ArCH-)], and the complete absence of the olefinic and enone protons of carvone. The amount of rhodium catalyst required for the conversion of carvone into 2-methyl-5-isopropylphenol was approximately 0.08 - 0.11 equiv. Less than this amount of catalyst resulted in incomplete migration and recovery of a substantial amount of starting enone. As illustrated in equation 1 the double bond need not be adjacent to the ring system. The remote double bond of 4-(4-pentenyl)-$\Delta^2$-cyclohexenone (1) migrated to afford phenol 2 in 62% yield.

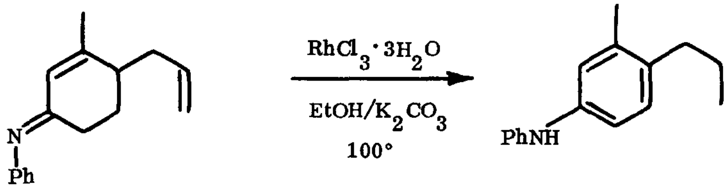
Table I. Substituted Phenols

| Entry | Starting Material | Product | Yield (%)[a] |
|---|---|---|---|
| 1 |  |  | 62 |
| 2 |  |  | 78 |
| 3 |  |  | 60 |
| 4 |  |  | 65 |
| 5 |  |  | 69 |

[a] All yields are for isolated chromatographically pure substances.

The following procedure illustrates the method. To a solution of rhodium chloride trihydrate (19 mg) in absolute ethanol (50 μl) was added carvone (100 mg, 0.66 mmol) in 125 μl of absolute ethanol. After heating at 100° (bath temperature) for 8 hr in a sealed tube under an atmosphere of nitrogen the mixture was cooled and filtered through a pad of silica gel. Chromatography of the crude product on silica gel gave 78 mg (78%) of pure 2-methyl-5-isopropylphenol.

We have observed that unsaturated imines can be aromatized giving rise to substituted aniline derivatives (Table II). Migration of the remote olefinic bond of conjugated imine 3[5] (cf. eq 2)

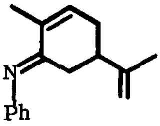
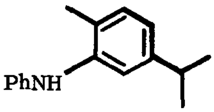
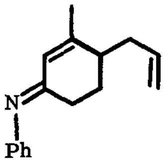
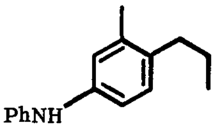
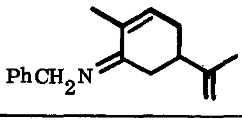
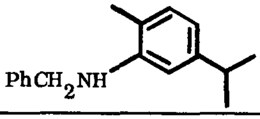


3 4

(2)

readily occurred upon treatment with rhodium chloride trihydrate in absolute ethanol containing excess anhydrous potassium carbonate at 100° in a sealed tube. In the absence of potassium carbonate hydrolysis of the imine to the enone occurred and the corresponding phenol was obtained as the major product in low yield. Under these conditions none of the diphenyl amine 4 could be detected. The anhydrous potassium carbonate serves to remove the catalytic amount of hydrogen chloride which is generated during the production of the catalytically active rhodium hydride species.[6]

Table II. Substituted Anilines

| Entry | Starting Material | Product | Yield (%)[a] |
|---|---|---|---|
| 1 |  |  | 50 |
| 2 |  |  | 51 |
| 3 |  |  | 47 |

[a] All yields are for isolated chromatographically pure substances.

The following procedure for the preparation of N-benzyl 2-methyl-5-isopropylamine is representative. A solution of the benzyl imine of carvone[5] (100 mg, 0.41 mmol) in 0.75 ml of absolute ethanol containing rhodium chloride trihydrate (16 mg) and anhydrous potassium carbonate (80 mg, 0.56 mmol) was heated at 100° in a sealed tube for 30 hr. Workup followed by chromatography on silica gel provided 47 mg (47%) of pure amine.

Acknowledgments: This work was supported by the National Cancer Institute (CA 13689) and in part by Glidden Organics.

References and Notes.

1. R. Cramer, Accounts Chem. Res., 1, 186 (1968).
2. J. F. Biellmann and M. J. Jung, J. Am. Chem. Soc., 90, 1673 (1968); A. J. Birch and G. S. R. Subba Rao, Tetrahedron Letters, 3797 (1968); E. J. Corey and J. W. Suggs, J. Org. Chem., 38, 3224 (1973); E. J. Corey and J. W. Suggs, Tetrahedron Letters, 3775 (1975); P. A. Grieco, M. Nishizawa, N. Marinovic, and W. J. Ehmann, J. Am. Chem. Soc., 98, 7102 (1976); J. Andrieux, D. H. R. Barton, and H. Patin, J. C. S. Perkin I, 359 (1977).
3. Tropolones and γ-pyridones have previously been prepared by isomerization utilizing palladium on charcoal as a catalyst [N. J. Leonard and J. W. Berry, J. Am. Chem. Soc., 75, 4898 (1953); N. J. Leonard and D. M. Locke, J. Am. Chem. Soc., 77, 1852 (1955)].
4. Rhodium chloride trihydrate [$RhCl_3 \cdot 3H_2O$] was purchased from Engelhard.
5. The conjugated unsaturated imines were prepared in benzene or ether using a slight excess of amine in the presence of molecular sieves (Linde 5A) [cf. K. Taguchi and F. Westheimer, J. Org. Chem., 36, 1570 (1971); E. P. Kyba, Org. Prep. Proced., 2, 149 (1970)]. The formation of the benzyl imine of carvone required refluxing in benzene.
6. It has been demonstrated that $RhCl_3 \cdot 3H_2O$ oxidizes ethanol generating an active rhodium hydride species and hydrogen chloride.[7]
7. J. C. Trebellas, J. R. Olechowski, H. B. Jonassen, and D. W. Moore, J. Organometallic Chem., 9, 153 (1967).