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DIAZIRINES IN CARBENOID REACTIONS CATALYZED BY RHODIUM(II) CARBOXYLATES

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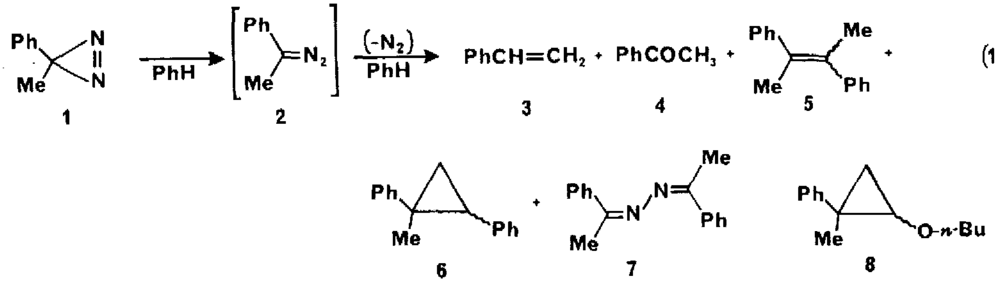
Summary: Diazo compounds formed by thermal or photolytic rearrangement of 3-alkyl-3-phenyldiazirines in the presence of catalytic amounts of rhodium(II) perfluorobutyrate are effectively directed to metal carbenoid products with minimal competition from processes which are dominant when the diazo compound is used directly or when the diazirine is decomposed in the absence of the catalyst.

The sensitivity of diazoalkanes to acids and their propensity for azine and carbene dimer formation has made them normally unsuitable for synthetic applications.[1] Transition metal catalysts that are effective in carbenoid reactions with diazo carbonyl compounds are inhibited by the by-products of diazoalkane decomposition.[2] In contrast, diazirines are stable towards acids[3] and, although they are generally unreactive towards the transition metal compounds that catalyze carbenoid reactions of diazo compounds, several examples of metal carbene and μ-bridged methylene complexes that result from diazirine decomposition have recently been reported.[4] However, since structurally diverse diazirines whose substituents range from alkyl to carbonyl undergo thermal and/or photochemical rearrangement to diazo compounds,[5] diazirines should be suitable as carbenoid precursors in transition metal catalyzed reactions, and their use should minimize competing reactions that are dominant when diazoalkanes are employed. We now report the first examples of the use of diazirines in catalytic carbenoid transformations.

3-Alkyl-3-phenyldiazirines undergo isomerization and subsequent dinitrogen extrusion with rate constants that do not differ by more than a factor of 3 at 100°C.[6] When the decomposition of 3-methyl-3-phenyldiazirine is performed in refluxing benzene over a 12 h period, styrene, acetophenone, carbene dimers, 1,2-diphenyl-1-methylcyclopropanes (from cyclopropanation of styrene) and azine are formed (eq. 1).[7] In the presence of 10 molar equivalents of *n*-butyl vinyl ether, the product mixture contains **8**,[8]



(1)

to the near exclusion of **6**, but azine and carbene dimers are also major products under both thermal and photochemical conditions (Table I). However, when these same reactions are performed in the presence of 2.0 mol % of rhodium(II) perfluorobutyrate,[9] cyclopropanation of *n*-butyl vinyl ether is the dominant reaction process. Carbene dimers and azine are minor products. In contrast, the rhodium(II) perfluorobutyrate catalyzed decomposition of 1-diazo-1-phenylethane[10,11] yields azine as the major product, and this azine strongly inhibits the catalytic action of the rhodium(II) carboxylate. Reactions were performed under dilute conditions in benzene (0.03 M) and, although dry solvents were employed and reactions were run under a nitrogen atmosphere, dioxygen could not be totally excluded so that formation of acetophenone remained a competitive process in most of these reactions.

Table I. Influence of Rhodium(II) Perfluorobutyrate on the Product Composition from the Decomposition of 3-Methyl-3-phenyldiazirine (**1**) and 1-Diazo-1-phenylethane (**2**) in Benzene Containing *n*-Butyl Vinyl Ether

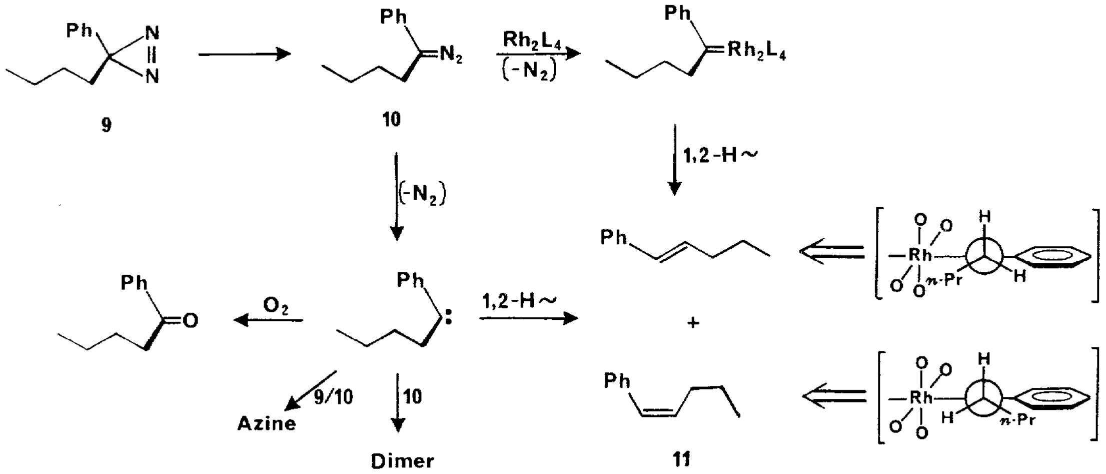
Reactant	Conditions[a]	mol % $Rh_2(pfb)_4$	$\frac{[BVE]}{[MePhCN_2]}$	Yield, % **3**	**4**	**5**	**6**	**7**	**8**	Isomer Ratio **5**	**8**[b]
1	T, 80°C[c]	—	0	11	9	26	29	25	0	1.3	—
1	T, 80°C	—	10	13	14	15	1	12	46	1.4	1.01
1	P, 30°C	—	10	4	33	21	12	14	16	1.2	1.54
1	T, 80°C	2.0	10	1	0	2	1	10	86	1.2	1.25
1	P, 30°C	2.0	10	12	5	3	1	6	73	—	1.30
2	T, 80°C[d]	—	0	3	25	35	2	34	0	1.3	—
2	T, 80°C[e]	—	10	4	42	17	3	27	7	1.4	1.42
2	25°C	2.0	10	0	12	0	0	74	14	—	1.20

[a] Reactions performed in refluxing benzene (T) for 12 h or by photolysis (P) for 4 hr in a Rayonet photochemical reactor (350 nm). [b] (*E*)/(*Z*) with trans orientation of phenyl and *n*-butoxy substituents predominant. [c] Unreacted diazo compound (20%) remained after 8 h. [d] Unreacted diazo compound (4%) remained after 8 h. [e] Unreacted diazo compound (14%) remained after 8 h.

The success of the catalytic methodology for cyclopropanation with 3-methyl-3-phenyldiazirine is based upon its rate-limiting production of the corresponding diazo compound which reacts with $Rh_2(pfb)_4$ as it is formed. When the metal carbene is produced in the presence of diazo compound, azine formation is predominant even when *n*-butyl vinyl ether is present in much higher concentrations. In contrast, when the metal carbene is formed in the presence of both the vinyl ether and diazirine, cyclopropanation of the vinyl ether is the preferred pathway. That **8** is formed exclusively from the metal carbene in $Rh_2(pfb)_4$ catalyzed reactions can be seen from its stereoisomer ratio which is constant (± 0.05) relative to the substantial variation in the isomer ratio for **8** that occurs under thermal and photochemical conditions in the absence of the rhodium(II) catalyst.

In contrast to 3-methyl-3-phenyldiazirine, for which 1,2-hydrogen migration to form styrene is a minor pathway, the carbene generated from phenyl-*n*-butyldiazirine (**9**) undergoes a facile 1,2-carbon-hydrogen migration which occurs to the exclusion of carbene dimer formation.[6,12] When the thermal decomposition is performed in refluxing toluene at 102°C, 1-phenyl-1-pentene (**11**) is formed together with the carbene dimer, azine, and variable amounts of valerophenone, and the olefin isomer ratio is 3.5 (trans/cis).[13] When this same reaction is performed in the presence of 20 mol % of rhodium(II) acetate, **11** is formed with a trans/cis ratio of only 0.45 together with only a minor amount of valerophenone (<5%). Neither the carbene dimer nor the azine are obtained from reactions performed in the presence of the rhodium(II) catalyst. Decreasing the mol % of $Rh_2(OAc)_4$ from 20 to 2.0 changes neither the product composition nor the isomer ratio for **11**. In refluxing benzene the trans/cis ratio for **11** is 2.1 in the absence of rhodium(II) carboxylate and 0.57 in the presence of 2.0 mol % of $Rh_2(pfb)_4$. These dramatic reversals in the olefin isomer ratio, especially as they occur in the direction of the less stable geometrical isomer, can be attributed to constraints by the face of the rhodium carboxylate on orientation of the alkyl chain for hydrogen migration in the metal carbene intermediate (Scheme I).[14,15] Obviously,

Scheme I



rhodium(II) carboxylates are very effective in their interception of the diazo compound formed by isomerization of the corresponding diazirine. However, 1,2-hydrogen migration, which is the principal reaciton pathway for the free carbene, is also preferred by the metal carbene. In the presence of 10 molar equivalents of *n*-butyl vinyl ether and 2.0 mol % of $Rh_2(pfb)_4$ in refluxing benzene, phenyl-*n*-butyldiazirine yielded only 10% of cyclopropane products with the remainder being **11**.

The data presented here further demonstrates that alkyl diazo compounds are generally unsuitable for catalytic metal carbene transformations. However, diazirines that undergo rate-limiting isomerization to their corresponding diazo compound can be effectively employed for cyclopropanation or for intramolecular transformations without undue competition from azine formation, which is dominant when the diazo compound is the reactant. Further investigations into the scope of this methodology are underway.

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