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A unique rhodium-catalyzed rearrangement process: isomerization of an alkyne to a 1,3-diene with concomitant migration of a formyl group. An expeditious route to dienals from readily available 4-alkynals†

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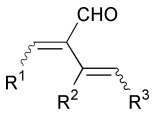
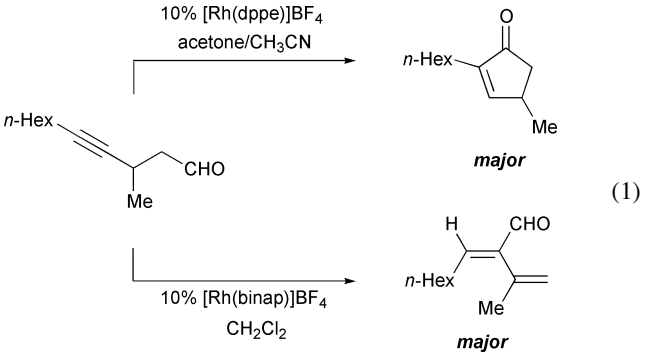
In CH_2Cl_2, [Rh(BINAP)]BF_4 catalyzes the isomerization of 4-alkynals to dienals with excellent regio- and stereoselectivity; this new process compares favorably with previously reported methods for the synthesis of this class of compounds; a possible pathway for this unusual rearrangement is provided.

Dienals such as **1** represent interesting targets for synthesis, due in part to their use in perfumes and flavorings.[1] Of the existing approaches to the generation of these dienals, the hydroformylation of enynes is perhaps the most straightforward. Unfortunately, this process typically furnishes a mixture of regioisomeric aldehydes, as well as products arising from over-reduction (hydrogenation).[2]



1

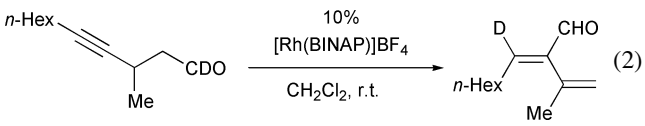
During a recent study of rhodium-catalyzed intramolecular hydroacylations of 4-alkynals to provide cyclopentenones [eqn. (1)],[3] we surveyed a variety of reaction conditions. Interestingly, the fate of the 4-alkynal is very dependent on the choice of conditions—in the presence of Rh/BINAP and in CH_2Cl_2, we instead observe an intriguing isomerization of the alkyne to a diene, with concomitant migration of the formyl group [eqn. (1)]. As we describe in this Communication, this unique rearrangement process has proved to have significant generality.



(1)

We have established that a variety of 4-alkynals can be rearranged in moderate to good yield by 5–10% [Rh(BINAP)]BF_4 in CH_2Cl_2 (Table 1).[4,5] The 5 position of the alkyne can be substituted with an alkyl (entry 1), benzyl (entry 2), alkenyl (entry 3), aryl (entry 4), or silyl group (entry 5), and the 3 position can bear either an alkyl (entries 1–4) or an aryl (entry 5) substituent. In no instance have we detected any regioisomers or *E*/*Z* olefin isomers. Since 4-alkynals are easily accessed through 1,4-addition of alkynylmetals to α,β-unsaturated aldehydes,[6] this new rhodium-catalyzed rearrangement provides an expeditious, completely regio- and stereoselective two-step synthesis of dienals from readily available starting materials.

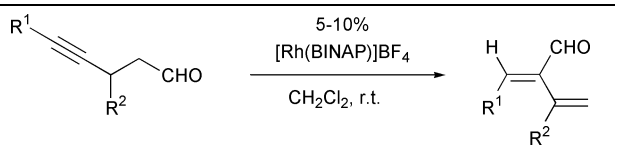
A possible mechanism for this intriguing rearrangement is outlined in Fig. 1.[7,8] In the first step, the rhodium catalyst oxidatively inserts into the aldehyde C–H bond, affording rhodium acyl hydride **A**. *Cis* hydrometalation of the pendant alkyne furnishes metalacyclopentane **B**, which undergoes a de-insertion reaction to produce metalacyclobutane **C**. α-Migratory insertion then leads to ring-expanded, conjugated metalacycle **D**. β-Hydride elimination, followed by reductive elimination, then generates the dienal. The result of the deuterium labeling study illustrated in eqn. (2) is consistent with the proposed pathway.

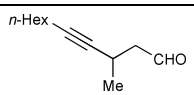
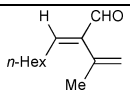
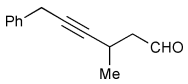
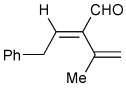
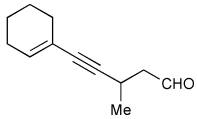
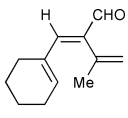
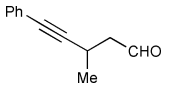
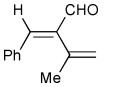
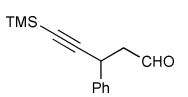
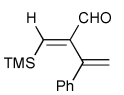


(2)

In conclusion, we have discovered a novel rhodium-catalyzed rearrangement of 4-alkynals to dienals, a process that simulta-

Table 1 [Rh(BINAP)]BF_4-catalyzed rearrangement of 4-alkynals to dienals



Entry	Substrate	Product	Yield (%)[a]
1			50
2			57
3			72
4			58
5[b]			87

[a] Isolated yields, average of two runs. [b] Solvent: acetone; temperature: 60 °C.

† Electronic supplementary information (ESI) available: experimental details. See http://www.rsc.org/suppdata/cc/b2/b200208f/

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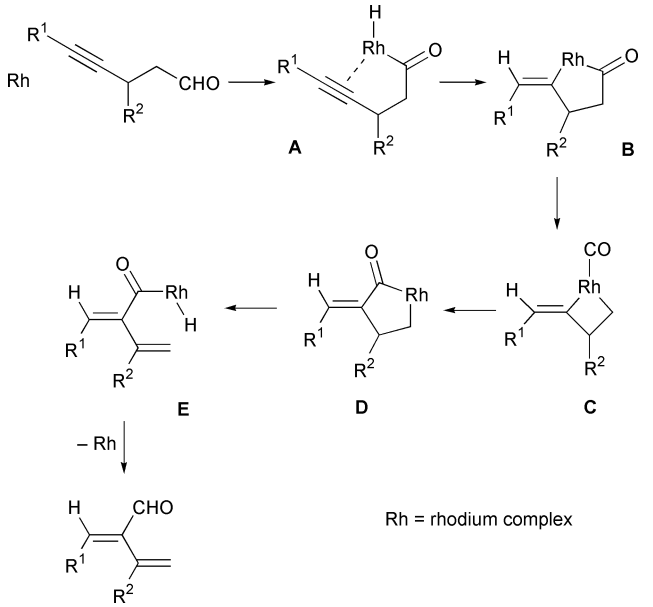

Fig. 1 A possible mechanism for the [Rh(BINAP)]BF_4-catalyzed rearrangement of 4-alkynals to dienals.

neously effects isomerization of an alkyne to a 1,3-diene and migration of a formyl group. Relative to previous approaches to the synthesis of dienals, this new method compares favorably with respect to brevity, regioselectivity, and stereoselectivity.

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Notes and references

1 For example, see: (*a*) A. Sanderson, W. L. Schreiber, M. Van Praag, A. O. Pittet, W. J. Evers and H. H. Heinsohn, Jr., DE 2433199, February 20, 1975; *Chem. Abstr.*, 1975, **83**, 42826t; (*b*) W. L. Schreiber and A. O. Pittet, US 3920755, November 18, 1975; *Chem. Abstr.*, 1976, **84**, 58641k; (*c*) W. L. Schreiber and A. O. Pittet, US 3922309, November 25, 1975; *Chem. Abstr.*, 1976, **84**, 58642m; (*d*) W. L. Schreiber and A. O. Pittet, US 4045497, August 30, 1977; *Chem. Abstr.*, 1978, **88**, 22140q.

2 For example, see: (*a*) K. Doyama, T. Joh, T. Shiohara and S. Takahashi, *Bull. Chem. Soc. Jpn.*, 1988, **61**, 4353–4360; (*b*) E. M. Campi and W. R. Jackson, *Aust. J. Chem.*, 1989, **42**, 471–478; (*c*) Y. Ishii, K. Miyashita, K. Kamita and M. Hidai, *J. Am. Chem. Soc.*, 1997, **119**, 6448–6449; (*d*) B. G. Van den Hoven and H. Alper, *J. Org. Chem.*, 1999, **64**, 3964–3968.

3 K. Tanaka and G. C. Fu, *J. Am. Chem. Soc.*, 2001, **123**, 11492–11493.

4 Sample experimental (Table 1, entry 1): in the air, [Rh(cod)(BINAP)]BF_4 (51 mg, 0.055 mmol) was placed into a Schlenk tube, which was then filled with argon. Under a positive pressure of argon, CH_2Cl_2 (3 mL) was added. H_2 was then introduced to the Schlenk tube, and the mixture was stirred at room temperature for 0.5 h. The flask was then purged with argon, and a solution of 3-methylundec-4-ynal (100 mg, 0.555 mmol) in CH_2Cl_2 (2 mL) was added to the dark-red reaction mixture. The mixture was stirred at room temperature for 24 h. The resulting solution was concentrated and purified by column chromatography (pentane : Et_2O = 10 : 1), which furnished (*E*)-isopropen-2-ylnon-2-enal (48.8 mg, 0.271 mmol; 49%).

5 The predominant side-product is the cyclopentenone (ref. 3). If there is no substituent in the 3 position, the cyclopentenone and other side-products are generated, rather than the dienal.

6 M. Eriksson, T. Iliefski, M. Nilsson and T. Olsson, *J. Org. Chem.*, 1997, **62**, 182–187.

7 In Fig. 1, for the sake of simplicity, the elementary steps are drawn as irreversible.

8 For mechanistic studies of rhodium-catalyzed cyclizations of 4-alkenals to cyclopentanones, see: (*a*) R. E. Campbell, Jr. and R. G. Miller, *J. Organomet. Chem.*, 1980, **186**, C27–C31; R. E. Campbell, Jr., C. F. Lochow, K. P. Vora and R. G. Miller, *J. Am. Chem. Soc.*, 1980, **102**, 5824–5830; (*b*) D. P. Fairlie and B. Bosnich, *Organometallics*, 1988, **7**, 946–954; B. Bosnich, *Acc. Chem. Res.*, 1998, **31**, 667–674.