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A SIMPLE ORGANOCOBALT MEDIATED SYNTHESIS OF SUBSTITUTED 3-OXABICYCLO[3.3.0]OCT-6-EN-7-ONES

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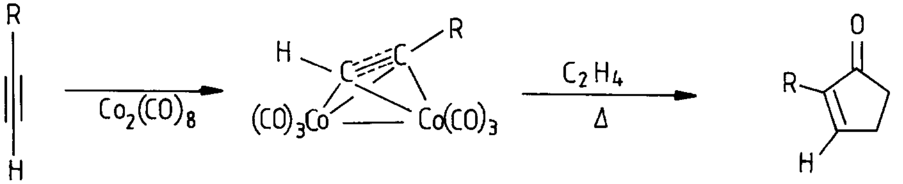
ABSTRACT:

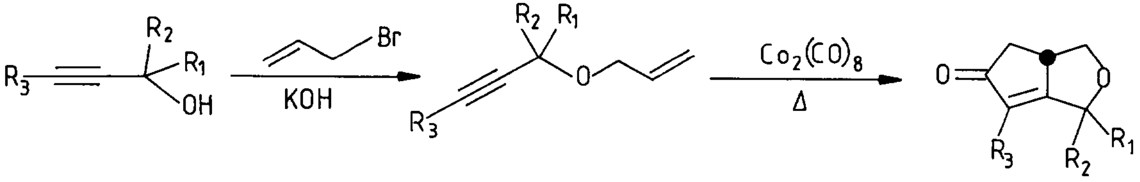
A range of substituted propargyl alcohols form ethers with allyl bromide in good yields; conversion of these ethers to the alkyne hexacarbonyl dicobalt complexes using $Co_2(CO)_8$, followed by intramolecular cyclisation gives substituted 3-oxabicyclo[3.3.0]oct-6-en-7-ones (**4a**-**4e**) in fair to moderate yields.

3-Oxabicyclo[3.3.0]octenones (e.g. **4a**-**4e**) are a class of compounds which are not easily accessible by conventional routes. A convenient, general synthesis of this skeleton would be valuable, as the compounds have been useful intermediates in both natural[1] and unnatural product[2] syntheses, and have considerable potential as intermediates for the preparation of iridoid monoterpenes.

Most alkynes react with $Co_2(CO)_8$ under mild conditions, giving alkyne hexacarbonyl dicobalt complexes in excellent yields.[3] The complexes are relatively stable, and react with alkenes at elevated temperatures, giving cyclopentenones.[4,5]



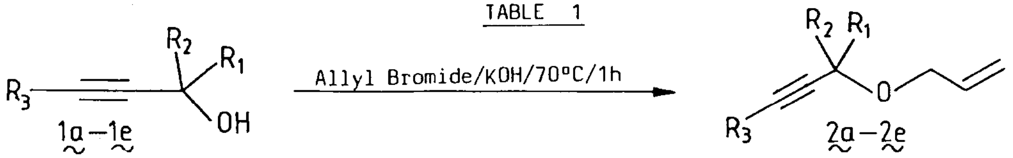
Intramolecular reaction giving bicyclic systems is also possible.[6] We report here the synthesis of a series of substituted allyl-propargyl ethers (**2a**-**2e**), and their cyclisation via the derived hexacarbonyl dicobalt complexes (**3a**-**3e**), giving 3-oxabicyclo[3.3.0]oct-6-en-7-ones (**4a**-**4e**). The overall synthetic approach is outlined below. This represents the first synthesis of heterocyclic systems by this method,[7] and allows ready access to the title compounds.



Preparation of ethers, **2a**-**2e**

Alcohols **1a**-**1d** are all commercially available. Alcohol **1e** was prepared from THP protected 2-bromoethanol and the dianion of propargyl alcohol by the method of Brandsma.[8] Treatment of the alcohols **1a**-**1e** with allyl bromide in the presence of potassium hydroxide gave the desired ethers **2a**-**2e**, which were isolated by fractional distillation, in yields ranging from 42-80%[9] Table 1.

TABLE 1

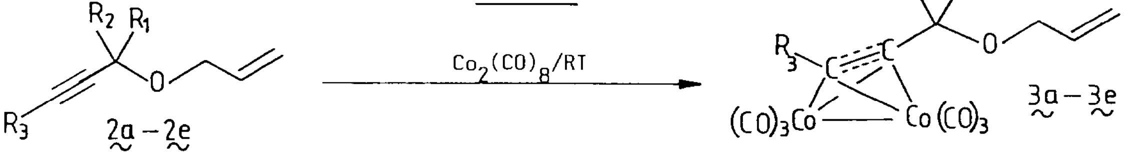


Alcohol		Product		Yield		b.p.
1a, $R_1=R_2=R_3=H$	→	**2a**	—	62%	—	50-62°C/100 mm
1b, $R_1=CH_3$; $R_2=R_3=H$	→	**2b**	—	54%	—	24°C/10 mm
1c, $R_1=R_2=CH_3$; $R_3=H$	→	**2c**	—	42%	—	26-33°C/20 mm
1d, $R_1=R_2=H$; $R_3=CH_3$	→	**2d**	—	72%	—	47-50°C/10 mm
1e, $R_1=R_2=H$; $R_3=CH_2CH_2OTHP$	→	**2e**	—	80%	—	90-100/0.02 mm

Preparation of Hexacarbonyl Dicobalt Complexes, **3a**-**3e**.

Addition of the ethers **2a**-**2e** to a solution of $Co_2(CO)_8$ in petroleum ether over 2-4 h at 25°C, followed by stirring until evolution of CO had ceased, gave solutions of the crude complexes **3a**-**3e**. The crude complexes were purified by chromatography on neutral alumina to give the pure complexes **3a**-**3e** in 69-92% isolated yields, Table 2.

TABLE 2

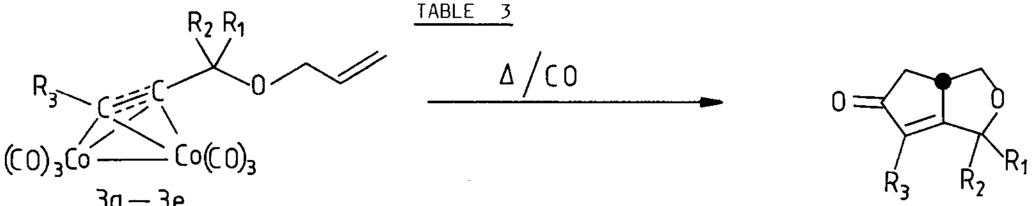


Ether		Product		Isolated Yield
2a, $R_1=R_2=R_3=H$	→	**3a**	—	90%
2b, $R_1=CH_3$; $R_2=R_3=H$	→	**3b**	—	86%
2c, $R_1=R_2=CH_3$; $R_3=H$	→	**3c**	—	69%
2d, $R_1=R_2=H$; $R_3=CH_3$	→	**3d**	—	87%
2e, $R_1=R_2=H$; $R_3=CH_2CH_2OTHP$	→	**3e**	—	92%

Preparation of 3-Oxabicyclo[3.3.0]oct-6-en-7-ones, **4a**-**4e**.

The complexes **3a**-**3e** were heated at 60° in isooctane under an atmosphere of CO for 24 h. Isolation by filtration from cobalt metal followed by chromatography on neutral alumina (petroleum ether followed by chloroform) gave the desired products, contaminated with traces of organometallic impurities. Subsequent purification by "flash-chromatography"[10] gave the 3-oxabicyclo[3.3.0]oct-6-en-7-ones, **4a**-**4e** in the yields given in Table 3.[9] The low yield of the parent compound, **4a**, could not be improved, despite a wide range of reaction conditions being employed.[11]

TABLE 3



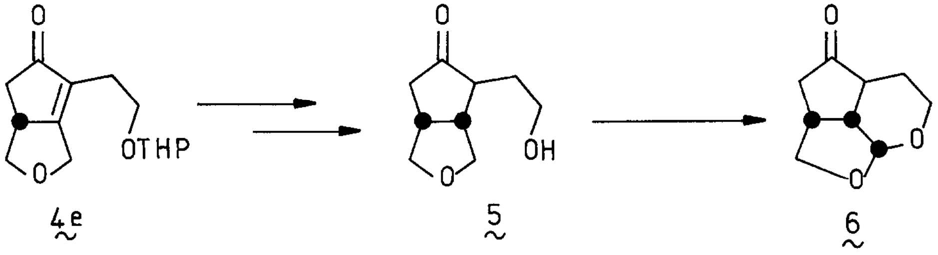
3a—**3e**

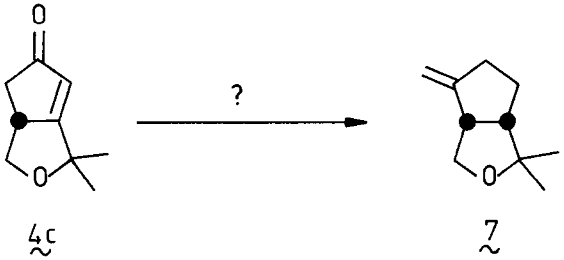
4a–**4e**

Complex	Product	Isolated Yield
3a	**4a**, $R_1=R_2=R_3=H$	14%
3b	**4b**, $R_1=CH_3$; $R_2=R_3=H$	29%
3c	**4c**, $R_1=R_2=CH_3$; $R_3=H$	29%
3d	**4d**, $R_1=R_2=H$; $R_3=CH_3$	41%
3e	**4e**, $R_1=R_2=H$; $R_3=CH_2CH_2OTHP$	41%

Enone **4e** was converted by hydrogenation and deprotection,[12] into **5**, the penultimate intermediate in the recent synthesis of (±)-tetrahydroanhydroaucubigenone **6** reported by Obara _et al._[1] We are currently exploring the use of enone **4c** as an intermediate for the synthesis of the Japanese hop ether **7**,[4b,13] and the use of this general class of compounds for the synthesis of iridoid monoterpenes.

The synthetic approach outlined above allows preparation of substituted 3-oxabicyclo [3.3.0]oct-6-en-7-ones on a gram scale, in only three steps from commercially available materials. The ready availability of these enones should make them much more attractive in the future as synthetic intermediates





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