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A UNIQUE AND CONVENIENT ONE-STEP PREPARATION OF SPIRO[4.5]DECA-6,9-DIENE-2,8-DIONE

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Abstract:: A facile one-step synthesis of spiro[4.5]deca-6,9-diene-2,8-dione(**1**) from p-methoxyphenylacetyl chloride via a Friedel-Crafts acylation followed by ring closure is reported.

During the course of our research, we found the need to prepare large amounts of 6-methoxy-β-tetralone. The standard procedure[1] for the synthesis of 6-methoxy-β-tetralone involves the Friedel-Crafts acylation of ethylene with p-methoxyphenylacetyl chloride at -78 °C, followed by ring closure at room temperature over several hours. This procedure gives only a modest yield of about 60% of the 6-methoxy-β-tetralone and we therefore attempted to increase the efficiency of the reaction by modifying the reaction conditions. When the reaction was run at -30 °C, a second product, which was identified as the known spiro[4.5]deca-6,9-diene-2,8-dione (**1**), was found.

The synthesis of spiro [4.5] deca-6,9-diene-2,8-dione is of interest because of its potential use in the preparation of spirocyclic sesqui- and diterpenes.[2-3] There are several literature procedures for the preparation of spirodienones.[4-7] The most common method involves the preparation of a p-hydroxybenzyl diazomethylketone followed by reaction with boron trifluoride (Scheme 1).[5] However, this synthesis

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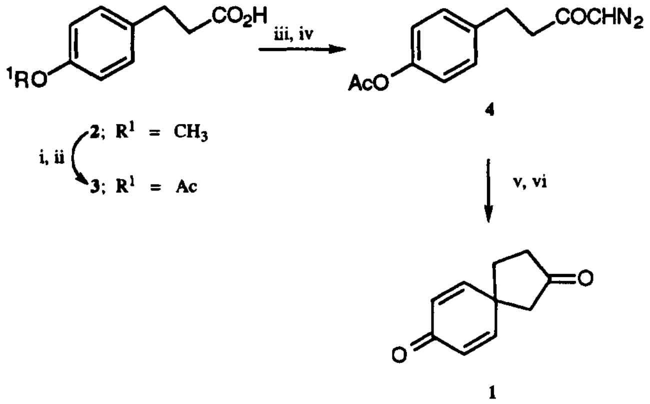
*To whom correspondence should be addressed requires the use of diazomethane, a potentially dangerous material, involves four steps, and the overall yield is low (<25%).

Scheme 1[a]



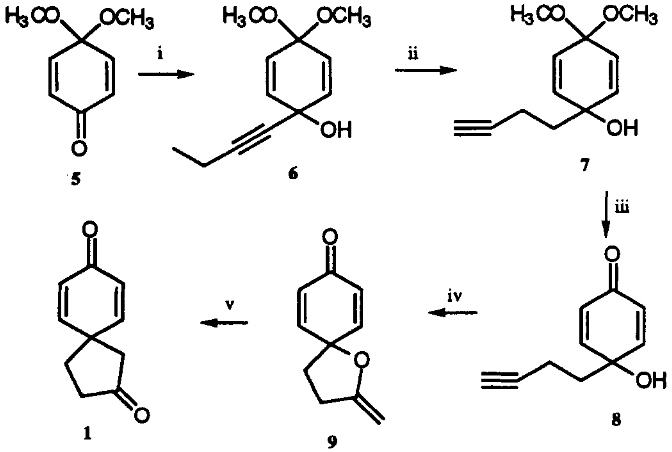
[a]Reagents: (i) py HCl, 210 °C; (ii) Ac_2O, NaOAc; (iii) py, $(COCl)_2$; (iv) CH_2N_2; (v) Na_2CO_3, $NaHCO_3$, H_2O, MeOH; (vi) BF_3

A second method involves the preparation of 2-methylene-1-oxaspiro[4.5]deca-6,9-dien-8-one (**9**) via a mercury (II) catalyzed cyclization of 4-(3-butynyl)-4-hydroxycylohexa-2,5-dienone (**8**), which can be synthesized fairly readily from 3,3,6,6-tetramethoxycylohexa-1,4-diene (**5**). The 2-methylene-1-oxaspiro[4.5]deca-6,9-dien-8-one is then pyrolyzed at 130°C in a sealed tube to give the required spirodienone (Scheme 2).[7] Again, this reaction sequence is unsatisfactory since it requires six steps and the overall yield is low (<25%).

Our synthetic method also gives a low yield (23%), however, the sequence only requires a single step which can be accomplished in several hours and is readily amenable to scale-up. This represents a considerable advantage over the previous methods of preparation.

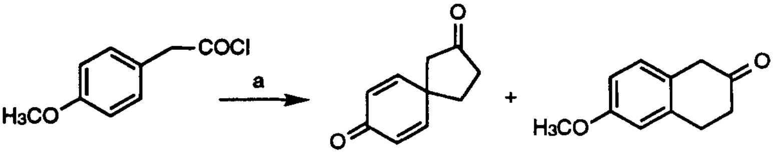
A cursory examination of our reaction conditions in an attempt to optimize the yield of the spirodienone (**1**) has not achieved the desired results. Table I indicates the

Scheme 2[b]



[b]Reagents: (i) 1-butyne, ethyl ether, BuLi, - 78 °C ; (ii) KAPA; (iii) HOAc, H_2O; (iv) Hg(II)Cl_2, Et $_3$N, benzene, reflux; (v) 130 °C

Table I



Rx Temp °C	Equiv. $AlCl_3$	Ratio T/S[b]	area % tetralone[c]	area % cmpd 1[c]
-78 °C	2		100%	
-30 °C	2	2.1	66.0%	31.4%
-5 °C	2	4.15	71.0%	17.1%
25 °C	2	5.22	47.0%	9.0%
-30 °C	3	1.58	52.3%	33.0%
-30 °C	6	3.12	72.0%	23.1%

a) ethylene gas, 2-6 eq. $AlCl_3$, -78 - 25 °C, methylene chloride.

b) % area of tetralone over % area of spirodienone

c) % area under the curve from GC traces of crude reaction mixture. These do not indicate isolated yields.

results of our examination. The yields shown are based on area under the curve from the gas chromatograph traces. We believe that this is mainly a result of the non-linear relationship between temperature and solubility effects: ie. when the temperature is raised, the solubility of ethylene gas decreases, the solubility of aluminum chloride increases, and the rates of formation of both the tetralone and the spirodienone change. In addition, at room temperature or higher, side reactions became significant. Increasing the amount of aluminum chloride while keeping the temperature constant changes the amounts of tetralone and spirodienone produced only slightly. The best reaction conditions examined for the formation of the spirodienone (**1**) appear to be 2-2.5 equivalents of aluminum chloride at -30 °C.

Conclusion

Spiro[4.5]deca-6,9-diene-2,8-dione can be prepared from p-methoxyphenylacetyl chloride via a Friedel-Crafts acylation followed by ring closure in a single step which can be accomplished in several hours. This is a distinct advantage over previously reported syntheses of the spirodienone which require multiple steps to achieve similar yields. Work is currently ongoing in order to determine whether this reaction can be expanded to include the formation of larger-sized spirodienones and whether changing the Lewis acid catalyst can affect the rate of spirodienone formation.

Experimental Section

The melting point was determined with a Thomas Hoover melting point apparatus and is uncorrected. The NMR spectra were recorded using a Varian XL-300 spectrometer. Elemental microanalysis was determined by Atlantic Microlabs (Atlanta, GA) and gave combustion values for C, and H within 0.4% of theoretical values. GC traces were determined using a 10% OV 101 column (1/8" x 6'), using a flame ionization detector. Preparative column chromatography was done using the flash chromatography technique[8] on Silica Gel 60 (40-63 m, E. Merck No. 9385). Solvents were evaporated by rotary evaporation (Buchi flash evaporator) using a temperature-controlled water bath.

Spiro[4.5]deca-6,9-diene-2,8-dione (1).

A solution of aluminum chloride (14.44g, 0.108mol) in 250mL of dry methylene chloride was cooled to -30 °C under a nitrogen atmosphere. Ethylene gas was bubbled in for five minutes and then 4-methoxy-phenylacetyl chloride (10.0g, 0.054mol) in 25mL of dry methylene chloride was dripped in simultaneously with more ethylene gas, keeping the temperature less than -27 °C. After addition of the acid chloride was complete, ethylene gas was bubbled in for an additional thirty minutes. Then the temperature was allowed to rise to -10 °C and the reaction mixture was stirred for another hour. The mixture was poured over ice and stirred for one hour. The organic layer was washed with bicarbonate, dried over magnesium sulfate and concentrated *in vacuo*. The crude material was flash chromatographed on silica gel with 80% ethyl acetate/hexane to give 1.96g (22.4%) of **1**, mp 72-74°C (lit.[7] mp 72-74°C). ^{1}H-NMR (DMSO-d_6): 7.19 (AA', J_{AB}= 10.9Hz, 2H), 6.19 (BB', 2H), 2.4-2.6 (m, 2H), 2.45 (s, 2H), 2.1-2.2 (t, 2H).

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References

(1) Sims, J.J., Selman, L.H., and Cadogan, M. *Org. Syn.* **1971**, *51*, 109.

(2) Iwata, C., Yamada, M., Ida, Y., Imau, T., Miyagawa, H., and Miyashita, K. *Chem. Pharm. Bull.* **1988**, *36*, 2864.

(3) Iwata, C., Yamada, M., Fusaka, T., Miyashita, K., Nakamura, A., Tanaka, T., Fujiwara, T., and Tomita, K. *Chem. Pharm. Bull.* **1987**, *35*, 544.

(4) Iwata, C, Miyashita, K., Imao, T., Masuda, K., Kondo, N., and Uchida, S. *Chem. Pharm. Bull.* **1985**, *33*, 853.

(5) Beames, D.J. and Mander, L.N. *Aust. J. Chem.* **1974**, *27*, 1257.

(6) Dorling, S., and Harley-Mason, J. *Chem. and Ind.* **1959**, 1551.

(7) Swenton, J.,Bradin, D., and Gates, B. *J. Org. Chem.* **1991**, *56*, 6156.

(8) Still, W.C., Kahn, M. and Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

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