which received the same amount of light.

The light intensity was modified by surrounding the source with wire netting, and the irradiation time was adjusted in order that all the tubes receive approximately the same amount of photons. The amount of **9a** formed was then determined as previously described. $\Phi$ remained equal to 0.33 ± 0.01 for 8.10 and 15 × $10^{-7}$ einstein/h light intensities.

Identical results were obtained when **2a** ($10^{-3}$ M) was irradiated similarly in methanol.

**UV-Visible Spectra at Low Temperature.** Thoroughly deoxygenated solutions of **1a** (see text for the concentrations) in pentane were placed in a UV cell which was immersed in a quartz Dewar containing ice-water and irradiated at 254 nm (condition 3).

After 3-min irradiation, absorption spectra were recorded immediately (see Figures 7 and 8).

**Attempted Trapping of the Intermediate.** A solution of **1a** (240 mg, 1.2 mmol) in acetonitrile (50 mL) was irradiated at −30 °C for 45 min at 254 nm (conditions 3). The solution turned deep yellow. Immediately, triethylamine (240 mg, 2.4 mmol) and trimethylchlorosilane (190 mg, 1.8 mmol) were added to the solution which was then allowed to warm to room temperature. After evaporation under vacuum, no silylated product was determined by $^1$H NMR.

**Quenching Experiments.** A $10^{-3}$ M solution of **1a** in pentane (3 mL) was irradiated in the presence of various concentrations of naphthalene ranging from 0 to 8 × $10^{-5}$ M. Determination of **9a** by HPLC showed that naphthalene had no effect on the quantum yield.

Similar results were obtained for **2a**, $10^{-3}$ M in methanol, with concentrations of naphthalene ranging from 0 to 3.33 × $10^{-4}$ mol $L^{-1}$.

**Sensitization Experiments.** **1a** (2 × $10^{-4}$ M) was irradiated in acetone (3 mL) as solvent and sensitizer at 254 nm (condition 3). Irradiation times ranged from 1 to 20 min. No trace of **9a** was detected by HPLC.

When a solution of **1a** ($10^{-4}$ M) and *p*-methoxyacetophenone (2 × $10^{-3}$ M) in pentane (3 mL) was irradiated under the same conditions, no trace of **9a** was detected by HPLC.

**2a** ($10^{-4}$ M) was irradiated in acetone (3 mL) as sensitizer at 254 nm (condition 3). No trace of **10a** was detected by HPLC.

When solutions of **2a** ($10^{-4}$ M) and *p*-methoxyacetophenone or benzophenone ($10^{-2}$ M) in methanol (3 mL) were irradiated in the same conditions, no trace of **10a** was detected by HPLC.

In all these experiments, the sensitizers absorbed more than 98% of the incident light.

**Influence of Oxygen and Iodine.** Calibrated quartz tubes containing the three solutions a, b, and c were irradiated for 90 min at 254 nm (condition 3) on a merry-go-round apparatus. The determinations of **2a** and **10a** were achieved by HPLC: **10a** by detection at 313 nm using xanthone as internal standard and **2a** by detection at 254 nm. Tube a: $10^{-3}$ M solution of **2a** in methanol (3 mL) previously deoxygenated. Tube b: $10^{-3}$ M solution of **2a** in methanol (3 mL) previously oxygenated by a 20-min oxygen stream. Tube c: $10^{-3}$ M solution of **2a** in methanol (3 mL) and $10^{-3}$ M in iodine, previously deoxygenated.

The UV spectra of the solutions a, b, and c were identical.

| tube | convn, % | yield in **10a**, % |
|---|---|---|
| a (argon) | 25 | 30 |
| b ($O_2$) | 42 | 23.5 |
| c ($I_2$) | 38 | 33 |

Similar results were obtained when **1a** ($10^{-3}$ M) in pentane (3 mL) was irradiated at 254 nm (condition 3).

**Registry No.** **1a**, 89114-50-1; **1b**, 89114-51-2; **1c**, 104214-12-2; **1d**, 89114-53-4; **1e**, 89114-54-5; **2a**, 89228-94-4; **2b**, 89228-95-5; **2c**, 89228-96-6; **2d**, 89228-97-7; **2e**, 104214-13-3; **5a**, 70871-45-3; **6a**, 30414-54-1; **6b**, 39815-78-6; **6c**, 22348-95-4; **6d**, 104214-14-4; **8a**, 5724-15-2; **8e**, 24252-43-5; **9a**, 89114-55-6; **9b**, 89114-56-7; **9c**, 104214-15-5; **9d**, 89114-58-9; **9e**, 89114-59-0; **10a**, 62264-34-0; **10b**, 89228-98-8; **10c**, 89228-99-9; **10d**, 89229-00-5; **10e**, 14427-61-3.

# 6-Endo-Dig vs. 5-Exo-Dig Ring Closure in *o*-Hydroxyaryl Phenylethynyl Ketones. A New Approach to the Synthesis of Flavones and Aurones

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*Received February 14, 1986*

The aryl phenylpropynoates **3a-c**, prepared by esterification of phenylpropynoic acid with the corresponding phenols, by means of *N,N'*-dicyclohexylcarbodiimide, give upon irradiation the *o*-hydroxyaryl phenylethynyl ketones **4a-c**. The cyclization of these compounds in basic media follows two alternative pathways: 6-endo-dig ring closure, to give the flavones **8a-c**, and/or 5-exo-dig ring closure, to give the aurones **9a-c**. The predominance of one or the other cyclization mode is strongly influenced by the reaction conditions. Thus, the use of potassium carbonate in acetone as cyclizing reagent favors the 6-endo-dig process, while the 5-exo-dig process becomes clearly enhanced when using sodium ethoxide or potassium carbonate in ethanol. The mechanistic implications of these facts are discussed within the framework of Baldwin's rules. From the preparative point of view, the above results disclose the synthetic possibilities of the key ketones **4** as precursors of flavones and aurones.

Less than 10 years ago, Baldwin described a set of simple rules to predict the relative facility of different ring forming reactions.[1] Since then, the general validity of these rules has been confirmed by an overwhelming number of publications, and the borderlines between favored and disfavored processes have been defined in a more precise way.[2]

Nonetheless, for cyclizations involving nucleophilic attacks at triple bonds, the situation remains less clear-cut than for the analogous ring closures in tetrahedral or trigonal systems. Thus, the original rules postulated an

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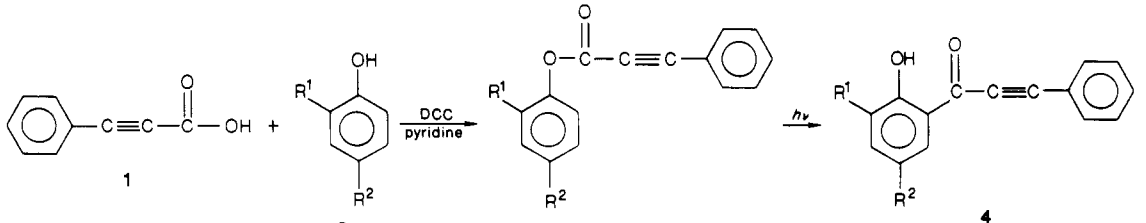
(2) A systhematic search through the Science Citation Index reveals that ref 1 has been cited by several hundreds of papers since the data of publication.

0022-3263/86/1951-4432$01.50/0 

**Scheme I**




1 2 3 4

| product | yield(%)[a] |
|---|---|
| 3a | 92 |
| 3b | 86 |
| 3c | 80 |

3: a: $R^1$ = H; $R^2$ = $OCH_3$; b: $R^1$ = H; $R^2$ = $CH_3$; c: $R^1$ = $CH_3$; $R^2$ = $CH_3$

| product | yield(%) |
|---|---|
| 4a | 30 |
| 4b | 25 |
| 4c | 20 |

[a] Procedure A.

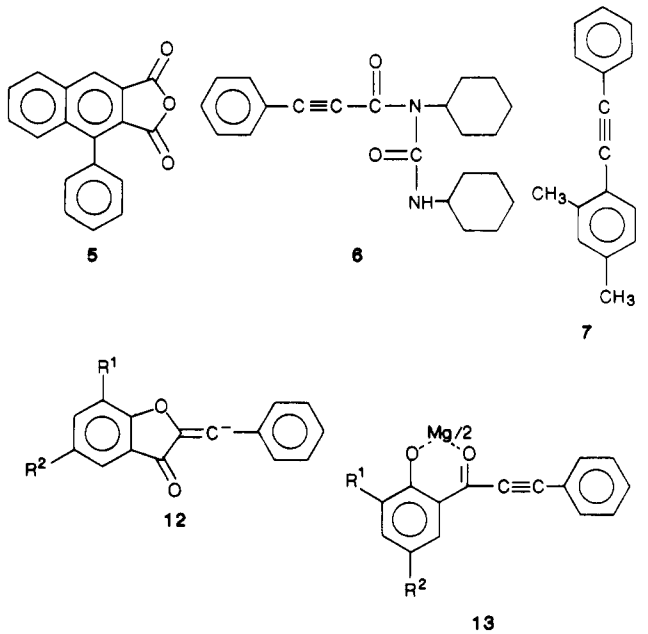
acute approach angle of about 60° in digonal systems and stated that the endo-dig closures are generally preferred, rather than the exo-dig ones, for the formation of five- and six-membered rings. However, subsequent experimental work suggests that, in the case of electronically unbiased acetylenes, exo-dig cyclizations are favored,[3,4] and there are recent ab initio calculations supporting the proposal of obtuse approach angles in digonal systems.[5-8]

The aim of the present work was to carry out an exploratory study on the cyclization of the *o*-hydroxyaryl phenylethynyl ketones **4**. As far as we know, this reaction has not yet been investigated, in spite of the ability of $\alpha,\beta$-acetylenic carbonyl compounds to readily undergo nucleophilic additions;[9-11] by contrast, the related cyclizations of *o*-hydroxychalcones and their derivatives have been extensively documented.[12]

Our results are relevant to the understanding of cyclizations involving nucleophilic attacks at triple bonds. They show that, in the case of the ketones **4**, it is possible to control to a certain degree the direction of the ring closure (6-endo-dig vs. 5-exo-dig type) by means of a suitable variation of the experimental conditions. From a preparative viewpoint, this finding may provide a new entry to the basic skeleton of the widely distributed flavones and aurones.

## Results and Discussion

The route followed for the preparation of the *o*-hydroxyaryl phenylethynyl ketones **4** is illustrated in Scheme I. In the first step, phenylpropynoic acid (**1**) was condensed with the respective phenol **2** by means of *N*,*N*′-dicyclohexylcarbodiimide,[13-15] using pyridine as solvent. The experimental procedure was fairly simple, and the aryl phenylpropynoates **3** were obtained in almost quantitative yields. The presence of pyridine was found to be of critical importance in order to avoid competitive processes leading to the formation of undesired products; thus, when pyridine was substituted by chloroform in an attempted synthesis of **3a**, the only products were the dimeric anhydride **5**,[16] arising from a self-condensation of phenylpropynoic acid, and the acylurea **6**.[16] Alternatively, the ester **3a** was obtained by reaction of phenylpropynoyl chloride with *p*-methoxyphenol. The yield, although reasonably good, was markedly lower than that obtained by the *N*,*N*′-dicyclohexylcarbodiimide method. Since, on the other hand, there is a certain risk associated with the use of phenylpropynoyl chloride, which has been reported to decompose when distilling,[17] this method was considered comparatively less advantageous and was not extended to the synthesis of **3b** and **3c**.



5 6 7 12 13

We have found no literature data concerning the preparation, characterization, or chemical properties of aryl esters of phenylpropynoic acid. This is surprising, since acetylenic esters are reagents widely used in organic synthesis, being recognized as valuable precursors to a number of heterocycles.[10,11]

The second step in the synthesis of the *o*-hydroxyaryl phenylethynyl ketones **4** was the photo-Fries rearrangement of the respective aryl phenylpropynoates **3**. Related processes have been reported in the literature, being especially relevant in terms of chemical analogy to those undergone by aryl cinnamates[18-23] and their dihydro de-

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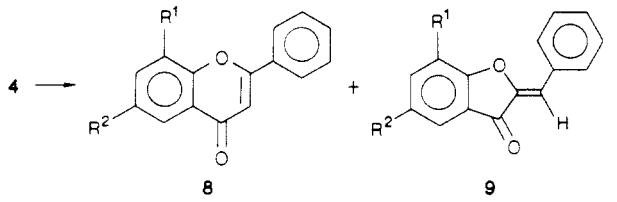
**Scheme II**



8 9

| substrate | $R^1$ | $R^2$ | reagent[a] | yield (%) 8 | yield (%) 9 | ratio 9/8 |
|---|---|---|---|---|---|---|
| **4a** | H | $OCH_3$ | A | 45 | 7 | 0.15 |
| | | | B | 15 | 65 | 4.33 |
| | | | C | 11 | 54 | 4.91 |
| **4a** | H | $CH_3$ | A | 85 | 8 | 0.09 |
| | | | B | 12 | 77 | 6.42 |
| | | | C | 15 | 79 | 5.27 |
| **4c** | $CH_3$ | $CH_3$ | A | 57 | 7 | 0.12 |
| | | | B | 4 | 66 | 16.50 |
| | | | C | 18 | 62 | 3.44 |

[a] A: $K_2CO_3$/acetone; B: NaOEt/ethanol; C: $K_2CO_3$/ethanol.

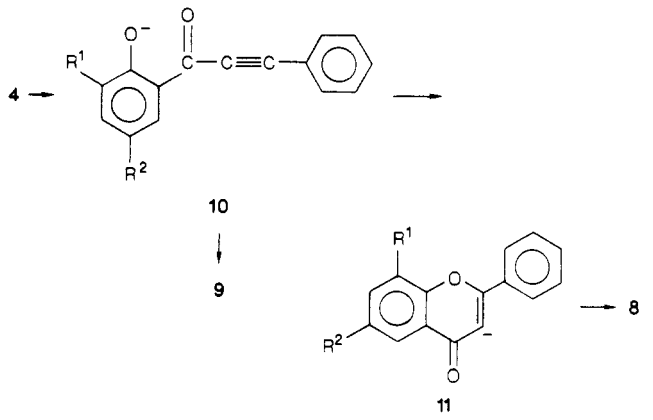
rivatives.[23,24] In general, the irradiation of **3** allowed the isolation of **4** as the only photoproducts; however, the sterically crowded dimethyl derivative **3c** also gave rise to a small amount of the hydrocarbon **7**, whose formation can be explained by way of a competitive photodecarboxylation.[25]

α,β-Acetylenic ketones are also highly valuable synthetic intermediates, because of their potential conversion to acetylenic alcohols, unsaturated ketones, and a variety of cycloaddition and Michael addition compounds.[11,26,27] Consequently, a considerable number of studies have been devoted to the development of simple and efficient synthetic methods leading to these substrates.[28-30] This is in sharp contrast with the fact that very few *o*-hydroxyaryl phenylethynyl ketones of the type **4** have been previously described,[31] especially taking into account that these compounds are the dehydrogenated equivalents of very common *o*-hydroxychalcones.[12]

The easy accesibility of the target ketones **4a**, **4b**, and **4c**, through the synthetic route shown in Scheme I, allowed us to carry out the necessary experiments in order to establish their behavior under different cyclization conditions. The results of these experiments are given in the Scheme II.

When a refluxing suspension of potassium carbonate in acetone was used to assay the cyclization, products of both 6-endo-dig and 5-exo-dig ring closure were isolated, although the 6-endo mode was decisively preferred, thus being obtained the flavones **8a**,[32] **8b**,[33] and **8c** as major products. This was to be expected according to the suggestions of the original Baldwin's rules and also in view of the usual reactivity of α,β-acetylenic carbonyl compounds, which are typically vulnerable to nucleophilic attack at the β-carbon.

**Scheme III**



However, rather different results were obtained when the cyclization was attempted by means of an ethanolic solution of sodium ethoxide, at room temperature. Under these conditions the reaction proceeded very fast, and the 5-exo-dig ring closure, to give the (*Z*)-aurones **9a**,[34] **9b**,[34] and **9c**, became clearly enhanced. A similar effect was observed when potassium carbonate in ethanol was used as cyclizing reagent.

A straightforward mechanism to account for the above results is outlined in Scheme III. The flavones **8** would be formed by stepwise conjugate intramolecular addition of the phenolate oxygen to the activated triple bond. In this case, the vinyl carbanion **11** would be stable enough to become a full intermediate. However, the vinyl carbanion **12**, probably arising from the kinetically controlled nucleophilic attack at the α-carbonyl carbon, would be less stable, and for that reason we presume that the predominance of aurones **9** in the cyclization with sodium ethoxide or potassium carbonate in ethanol is due to the capture of the anion by the protic solvent, avoiding the β-elimination process; the development of the unstable anion **12** could be substantially facilitated by assistance from the solvent. This effect would have a marked influence on the course of the reaction, even for a small degree of proton transfer in the transition state.

In connection with the above reasoning, it is noteworthy that flavones are immediately deprotonated by lithium diisopropylamide in tetrahydrofuran at −78 °C, giving a 3-lithio derivative which is stable at that temperature, while aurones react sluggishly with the same reagent, suffering ring opening to the phenolate **10** instead of becoming lithiated at the vinylic position.[35] These facts are compatible with our mechanistic proposals.

To complete our studies on the ring closure of the *o*-hydroxyaryl phenylethynyl ketones **4**, we carried out additional series of experiments, introducing further variations on the experimental conditions. Thus, the cyclization

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of 4 was attempted in ethanol at 150 °C (in a sealed reactor) and also in a refluxing solution of hydrogen chloride in ethanol, but in both cases the starting ketones were recovered unchanged after several hours, confirming our presumption that the actual cyclizing species is the phenolate anion instead of the free phenol. Finally, a singular result was obtained when ethanolic solutions of the ketones 4 were treated with ethylmagnesium bromide in ether. This reagent provoked the precipitation of a very characteristic orange solid, whose structure is presumably that of magnesium chelate 13. The formation of this complex would prevent rotation around the aryl–carbonyl bond, thus making it difficult to adopt the conformation from which ring closure must occur. Since the starting ketones 4 are easily regenerated upon addition of diluted acid, the whole process can be employed as a method for the purification of these compounds. In fact, we have found that it works satisfactorily to achieve the quantitative separation of 4 from the crude mixtures obtained after irradiation of the aryl phenylpropynoates 3.

In summary, it seems that the cyclization of the *o*-hydroxyaryl phenylethynyl ketones 4 in basic media lies close to the dividing line between the 6-endo-dig and the 5-exo-dig modes, since the direction of the ring closure is strongly influenced by changes in the experimental conditions. We feel that our results are also relevant in the context of the extensively studied cyclizations of chalcone derivatives,[12,36] especially dihalides (Emiliewicz–von Kostanecki reaction) and epoxides (Algar–Flynn–Oyamada reaction).[37] From the practical point of view, the most important contribution of our work is the disclosure of the synthetic possibilities of *o*-hdyroxyaryl phenylethynyl ketones as precursors of flavones and aurones.

## Experimental Section

The melting points were measured with a Büchi 510 apparatus and are uncorrected. IR spectra were obtained in $CCl_4$ solutions or Nujol suspensions with a Perkin-Elmer 781 spectrophotometer; absorptions ($\bar{\nu}$, $cm^{-1}$) are given only for the main bands. $^1H$ NMR spectra were recorded on a 60-MHz Varian EM 360A instrument in $CCl_4$ or $CDCl_3$ solutions; chemical shifts are reported as $\delta$ values (ppm) using $Me_4Si$ as internal standard. UV spectra were measured in hexane with a Varian 634 spectrophotometer; absorbed radiation is defined by its wavelength (nm) and log $\epsilon$. Mass spectra were determined on a VG ZAB-2F spectrometer; the ratio $m/e$ and the relative intensities are indicated for the significative peaks. Elemental analyses were performed at the Instituto de Química Bio-Orgánica of C.S.I.C. in Barcelona. Isolation and purification were done by flash column chromatography on silica gel Merck 60, 70–230 mesh, using a 5:1 mixture of hexane–ether as eluent and a Waters isocratic HPLC equipment with a semipreparative Microporasil column, using hexane–ethyl acetate as eluent. Analytical samples were obtained by recrystallization from hexane.

**Preparation of Aryl Phenylpropynoates 3. Procedure A.** To a solution of phenylpropynoic acid (1 g, 6.8 mmol) and the corresponding phenol (6.8 mmol) in pyridine (25 mL) was added dropwise *N,N'*-dicyclohexylcarbodiimide, DCC (1.4 g, 6.8 mmol), in pyridine (5 mL); the mixture was stirred for 15 min at room temperature, then poured into 5% aqueous HCl (100 mL), and filtered in vacuo. The solid residues were washed with cold water, dried, and extracted thoroughly with $CCl_4$. Solvent evaporation gave the aryl phenylpropynoates 3, which were used without further purification.

**Procedure B.** DCC (1.4 g, 6.8 mmol) in $CHCl_3$ (5 mL) was added slowly to a solution of phenylpropynoic acid (1 g, 6.8 mmol) and 4-methoxyphenol (0.85 g, 6.8 mmol) in $CHCl_3$. The reaction mixture was stirred 15 min at room temperature. The precipitated *N,N'*-dicyclohexylurea was removed by filtration and the resulting solution was concentrated and purified by chromatography to give 1-phenylnaphthalene-2,3-dicarboxylic anhydride (5) (0.52 g, 55%) and *N*-(phenylpropynoyl)-*N,N'*-dicyclohexylurea (6) (0.24 g, 10%). Samples of 5 and 6 were shown to be identical with those prepared as described in ref 16.

**Procedure C.** Phenylpropynoyl chloride was prepared treating 1 (1 g, 6.8 mmol) with freshly distilled thionyl chloride (0.8 g, 6.8 mmol) in $CHCl_3$ (100 mL) for 4 h at room temperature. Solvent was eliminated in vacuo to remove the unreacted $SOCl_2$ and the crude chloride was stirred overnight with 4-methoxyphenol (0.85 g, 6.8 mmol) in $CHCl_3$. The reaction mixture was concentrated and submitted to purification, giving the aryl ester 3a (0.83 g, 48%).

**Irradiation. General Procedure for Preparation of 2-Hydroxyaryl Phenylethynyl Ketones 4.** A solution of the aryl phenylpropynoate 3 (500 mg) in hexane (300 mL) was placed in a quartz immersion well photoreactor with a 125-W medium pressure mercury lamp and irradiated for 6 h under magnetic stirring. After this time, the resulting solution was concentrated in vacuo and the mixture submitted to chromatography. Alternatively, an ethereal solution of freshly prepared ethylmagnesium bromide (275 mg, 2.1 mmol) was added to the residue dissolved in ethanol (25 mL), appearing an orange solid, which was filtered in vacuo and washed with dry ethyl ether. Treatment of the magnesium complex with 5% aqueous HCl (25 mL) followed by extraction with ether gave the 2-hydroxyaryl phenylethynyl ketone 4 in pure form.

**Cyclizations of 2-Hydroxyaryl Phenylethynyl Ketones 4. Sodium Ethoxide Catalyzed Cyclization in Ethanol.** To 2-hydroxyaryl phenylethynyl ketone 4 (250 mg) in dry ethanol (10 mL) was added an ethanolic solution (1 mL) of sodium ethoxide, which was made by allowing sodium metal (20 mg, 0.87 mmol) to react with dry ethanol (10 mL). After 15 min, the reaction mixture was concentrated, then diluted with ethyl ether, and washed with water. The ethereal phase was dried over anhydrous $Na_2SO_4$, the solvent removed in vacuo, and the residue submitted to HPLC purification.

**Potassium Carbonate Catalyzed Cyclization in Ethanol at Room Temperature.** Anhydrous potassium carbonate (25 mg) was added to a solution of 4 (250 mg) in ethanol (10 mL). The resulting suspension was stirred 1 h and then filtered, the solvent removed, and the residue subjected to HPLC purification.

**Potassium Carbonate Catalyzed Cyclization in Acetone.** To a solution of 4 (250 mg) in dry acetone (10 mL) was added potassium carbonate (25 mg). The suspension was refluxed for 30 min and then filtered, and the resulting solution was concentrated and subjected to HPLC purification.

**Attempted Cyclization in Ethanol.** A solution of 4 (250 mg) in ethanol (10 mL) was placed in a sealed reactor and heated for 5 h at 110 °C. Removal of the solvent led to a total recovery of the starting material.

**Attempted Acid-Catalyzed Cyclization in Ethanol.** To a solution of 4 (250 mg) in ethanol (10 mL) was added concentrated chlorhydric acid (0.5 mL). Then, the mixture was refluxed for 1 h, concentrated, diluted with ether, and finally neutralized with 5% aqueous sodium hydrogen carbonate. The organic phase was dried over anhydrous $Na_2SO_4$ and the solvent removed, leading to a total recovery of the starting material.

**Attempted Ethylmagnesium Bromide Catalyzed Cyclization in Ethanol.** Magnesium (50 mg, 2.2 mmol) was allowed to react with ethyl bromide (260 mg, 2.2 mmol) in ethyl ether (20 mL) and, then, the resulting ethereal solution of ethylmagnesium bromide (1 mL) was added to a solution of 4 (250 mg) in ethanol (10 mL). The mixture became orange-red and a solid crystallized from the mixture. After 15 min, the suspension was neutralized with 5% aqueous HCl and extraction workup led to a total recovery of unchanged starting material.

**Analytical and Spectral Data of the New Compounds. 4-Methoxyphenyl phenylpropynoate (3a):** mp 67–69 °C; IR 2230 (C≡C), 1730 (C=O, ester); NMR 7.70–7.29 (m, 5 H, $C_6H_5$), 7.19–6.69 (m, 4 H, MeO-$C_6H_4$), 3.80 (s, 3 H, $OCH_3$); UV 258 (4.4); MS, 252 (52), 129 (100), 123 (26). Anal. Calcd for $C_{16}H_{12}O_3$: C, 76.18; H, 4.79. Found: C, 76.00; H, 4.73.

**4-Methylphenyl phenylpropynoate (3b):** mp 57–58 °C; IR 2230 (C≡C), 1730 (C=O, ester); NMR 8.00–6.90 (m, 9 H, Ar H),

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2.40 (s, 3 H, $CH_3$); UV 259 (4.2); MS, 236 (36), 129 (100), 107 (12). Anal. Calcd for $C_{16}H_{12}O_2$: C, 81.34; H, 5.12. Found: C, 81.60; H, 4.96.

**2,4-Dimethylphenyl phenylpropynoate (3c)**: mp 104–106 °C; IR 2230 (C≡C), 1730 (C=O, ester); NMR 7.90–7.21 (m, 5 H, $C_6H_5$), 7.18–6.83 (m, 3 H, $(CH_3)_2C_6H_3$), 2.25 (s, 3 H, $CH_3$), 2.19 (s, 3 H, $CH_3$); UV 260 (4.4); MS, 250 (7), 129 (100), 121 (7). Anal. Calcd for $C_{17}H_{14}O_2$: C, 81.58; H, 5.64. Found: C, 81.28; H, 5.65.

**1-(2-Hydroxy-5-methoxyphenyl)-3-phenylpropynone (4a)**: mp 85–86 °C; IR 2190 (C≡C), 1630 (C=O); NMR 11.30 (s, 1 H, OH), 7.80–6.68 (m, 8 H, Ar H), 3.83 (s, 3 H, $OCH_3$); UV 397 (3.8), 306 (4.4), 288 (4.3); MS, 252 (77), 251 (58), 150 (63), 129 (100), 105 (52). Anal. Calcd for $C_{16}H_{12}O_3$: C, 76.18; H, 4.79. Found: C, 76.06; H, 4.93.

**1-(2-Hydroxy-5-methylphenyl)-3-phenylpropynone (4b)**: mp 57–60 °C; IR 2210 (C≡C), 1630 (C=O); NMR 11.40 (s, 1 H, OH), 8.00–6.81 (m, 8 H, Ar H), 2.42 (s, 3 H, $CH_3$); UV 370 (3.7), 306 (4.3), 294 (4.2); MS, 236 (100), 235 (36), 134 (98), 129 (5), 105 (18). Anal. Calcd for $C_{16}H_{12}O_2$: C, 81.34; H, 5.12. Found: C, 80.87; H, 4.93.

**1-(3,5-Dimethyl-2-hydroxyphenyl)-3-phenylpropynone (4c)**: mp 79–80 °C; IR 2210 (C≡C), 1630 (C=O); NMR 11.80 (s, 1 H, OH), 8.00–7.01 (m, 7 H, Ar H), 2.30 (s, 3 H, $CH_3$), 2.20 (s, 3 H, $CH_3$); UV 380 (3.7), 309 (4.3), 295 (4.2); MS, 250 (94), 249 (32), 222 (16), 148 (100), 129 (84), 105 (14). Anal. Calcd for $C_{17}H_{14}O_2$: C, 81.58; H, 5.64. Found: C, 81.21; H, 5.93.

**1-(2,4-Dimethylphenyl)-2-phenylethyne (7)**: oil; IR 1580, 1490, 1440; NMR 7.73–6.80 (m, 8 H, Ar H), 2.45 (s, 3 H, $CH_3$), 2.33 (s, 3 H, $CH_3$); MS, 206 (84), 205 (21), 191 (100).

**6,8-Dimethylflavone (8c)**: mp 163–164 °C; IR 1650 (C=O); NMR 8.50–7.24 (m, 7 H, Ar H), 6.70 (s, 1 H, H at C-3), 2.55 (s, 3 H, $CH_3$), 2.40 (s, 3 H, $CH_3$); UV 300 (4.2), 211 (4.2), 263 (4.3); MS, 250 (100), 222 (20), 148 (92), 120 (52). Anal. Calcd for $C_{17}H_{14}O_2$: C, 81.58; H, 5.64. Found: C, 81.40; H, 5.69.

**(Z)-5,7-Dimethylaurone (9c)**: mp 114–115 °C; IR 1700 (C=O); NMR 8.22–7.10 (m, 7 H, Ar H), 6.92 (s, 1 H, Ph-CH), 2.48 (s, 3 H, $CH_3$), 2.39 (s, 3 H, $CH_3$); UV 380 (4.2), 323 (4.4), 308 (4.4), 290 (4.1); MS, 250 (100), 249 (100), 235 (15), 180 (34), 179 (20), 178 (29), 165 (18), 149 (16), 148 (46), 147 (14), 129 (12), 120 (82). Anal. Calcd for $C_{17}H_{14}O_2$: C, 81.58; H, 5.64. Found: C, 81.42; H, 5.66.

**Acknowledgment.** We thank the CAICYT for financial support (project 1303/83) and for a postgraduate fellowship to S.I.

**Registry No.** 1, 637-44-5; 1 (acid chloride), 7299-58-3; **2a**, 150-76-5; **2b**, 106-44-5; **2c**, 105-67-9; **3a**, 104213-86-7; **3b**, 20984-26-3; **3c**, 104213-87-8; **4a**, 104213-88-9; **4b**, 104213-89-0; **4c**, 104213-90-3; **5**, 1985-37-1; **6**, 40886-78-0; **7**, 78594-13-5; **8a**, 26964-24-9; **8b**, 29976-75-8; **8c**, 104213-91-4; **9a**, 38216-58-9; **9b**, 37542-10-2; **9c**, 104213-92-5.

# Synthesis of 2-(4′-Amino-4′-deoxy-β-D-ribofuranosyl)thiazole-4-carboxamide, a Carbon-Linked Nucleoside with a Free Pyrrolidine Sugar

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*Received March 5, 1986*

The first synthesis of a carbon-linked nucleoside containing a 4-amino-4-deoxy-β-D-ribofuranosyl moiety is reported. Methyl 2,3-*O*-isopropylidene-α-L-lyxopyranoside (**5**) was activated as its trifluoromethanesulfonate ester **6**. Displacement of **6** with azide ion led to methyl 4-azido-4-deoxy-2,3-*O*-isopropylidene-β-D-ribopyranoside (**7**). Catalytic reduction of **7** resulted in methyl 4-amino-4-deoxy-2,3-*O*-isopropylidene-β-D-ribopyranoside (**8**) which on treatment with trifluoroacetic anhydride gave the corresponding N-acetylated derivative, methyl 4-deoxy-2,3-*O*-isopropylidene-4-(trifluoroacetamido)-β-D-ribopyranoside (**9**). Acid hydrolysis of **9** with aqueous acetic acid followed by rearrangement and acetylation resulted in 1,2,3,5-tetra-*O*-acetyl-4-deoxy-4-(trifluoroacetamido)-D-ribofuranose (**10**). Lewis acid catalyzed cyanidation of **10** with trimethylsilyl cyanide gave the corresponding 1,2,3,5-tri-*O*-acetyl-4-deoxy-4-(trifluoroacetamido)-D-ribofuranosyl cyanide (**11**). Treatment of nitrile **11** with liquid hydrogen sulfide gave the corresponding thioamide, which was subsequently cyclized by reaction with ethyl bromopyruvate to yield ethyl 2-[2′,3′,5′-tri-*O*-acetyl-4′-deoxy-4′-(trifluoroacetamido)-D-ribofuranosyl]thiazole-4-carboxylate (**12**). Ammonolysis of **12** with methanolic ammonia led to 2-(4′-amino-4′-deoxy-β-D-ribofuranosyl)thiazole-4-carboxamide (**3**), the structure of which was confirmed by mass spectral and NMR studies.

We wish to report the first synthesis of a carbon-linked nucleoside containing a 4-amino-4-deoxy-β-D-ribofuranosyl moiety. Previous attempts to form nucleosides[1] or other glycosides[2] containing free pyrrolidine sugars (i.e., 4-amino-4-deoxyfuranose) have been unsuccessful due to the decomposition of the products immediately following deblocking of the amino function, presumably as a consequence of rapid elimination of the heterocyclic base or glycosyl function. The antibiotic anisomycin (**1**) was first isolated by Sobin and Tanner[3] and is active against protozoa and certain fungi and acts as an inhibitor of protein synthesis.[4,5] The structure of anisomycin has been elu-

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