after crystallization from dry $Me_2CO$ it showed mp 138–139 °C. The free base had $[\alpha]^{20}D$ −28° (c 3, MeOH/HCl 10:1).

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**Registry No.**—Ia, 91-03-2; Ib, 5400-92-0; Ic, 59434-10-5; IIa, 22563-99-1; IIb, 25287-79-0; IIc, 59434-11-6; IIIa, 2891-50-1; IIIb, 59434-12-7; (±)-IVa, 59461-64-2; (−)-IVa, 24190-15-6; (−)-IVa (−)-dibenzoyl tartrate, 24190-14-5; (±)-Va, 59434-13-8; (+)-Va, 59434-14-9; (+)-Va (−)-dibenzoyl tartrate, 59434-15-0; (+)-Vb, 59434-16-1; VIa, 27702-56-3; (−)-VIIa, 59434-17-2; (±)-VIIa, 59461-65-3; (−)-VIIa (−)-dibenzoyl tartrate, 59434-18-3; (−)-dibenzoyltartaric acid, 2743-38-6.

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# Carbonyl–Alkyne Exchange of 2*H*-Pyrans. A New Aryl Annelation Method

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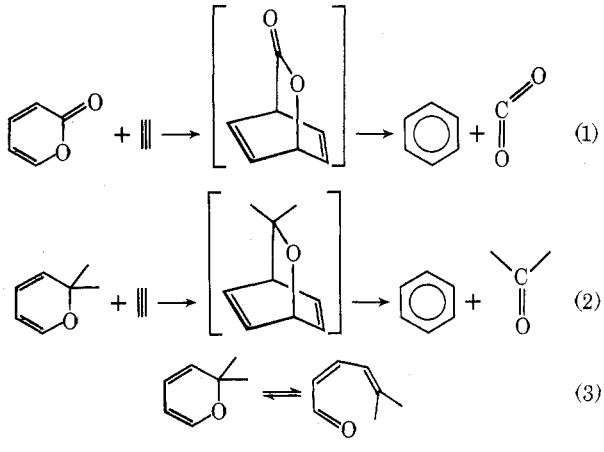
A synthesis of aryl derivatives is described which involves cycloelimination of ketones or aldehydes from the adducts obtained by cycloaddition of 2*H*-pyrans with acetylenic dienophiles. This carbonyl–alkyne exchange process is highly regiospecific. Even a 2*H*-pyran which constitutes only 20% of an equilibrium mixture with the corresponding dienone valence tautomer is shown to give good yields of the corresponding aryl derivatives upon reaction with methyl propiolate or dimethyl acetylenedicarboxylate.

Derivatives of α-pyrone react with alkynes to yield aryl derivatives and carbon dioxide (eq 1).[1] The intermediate Diels–Alder cycloadducts are generally unstable under the conditions of their formation. The analogous reaction of 2*H*-pyrans with alkynes to yield aryl derivatives and aldehydes or ketones (eq 2) has not been reported. One potential



(1)

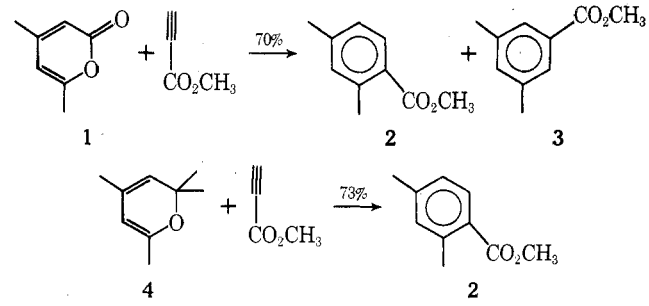
(2)

(3)

complication for such a carbonyl–alkyne exchange reaction is the fact that 2*H*-pyrans are in dynamic equilibrium with acyclic dienones (eq 3)[2] which might yield alternative products by Diels–Alder reactions. However, since 2*H*-pyrans are readily available by a variety of different synthetic routes,[3–16] it seemed worthwhile to examine the feasibility of carbonyl–alkyne exchange reactions with 2*H*-pyrans. We now report the first examples of the synthesis of aryl derivatives by the reaction of 2*H*-pyrans with acetylenic dienophiles.

## Results and Discussion

In order to compare the carbonyl–alkyne exchange of α-pyrones and 2*H*-pyrans we examined the reactions of methyl propiolate with 4,6-dimethyl-α-pyrone (1) and with 2,2,4,6-tetramethyl-2*H*-pyran (4). Both reactions give good yields of




1 2 3

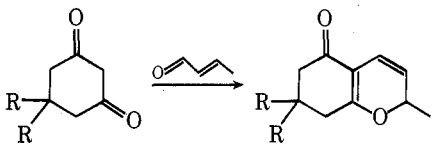



4 2

aryl derivatives. The α-pyrone (1) gives both methyl 2,4-dimethylbenzoate (2) and methyl 3,5-dimethyl benzoate (3) in a 4:1 ratio, respectively. The 2*H*-pyran (4) gives only **2**. The carbonyl group in **1** is expected to direct[17] the initial Diels–Alder addition to favor product **3**, while the ring oxygen and methyl groups in 1 direct the addition to favor product **2**. For 4 the exclusive formation of **2**, therefore, might be ascribed to the absence of the carbonyl group in the 2 position. However,

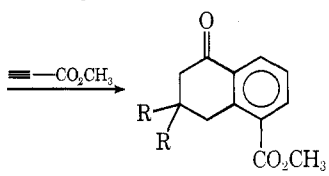
the regioselective reaction of **4** may also be due, at least in part, to steric hindrance by the substituents in the 2 position. Whatever the reason, all carbonyl–alkyne exchange reactions of 2*H*-pyrans examined are highly regiospecific.

β-Dicarbonyl compounds react with α,β-unsaturated aldehydes giving good to excellent yields of 2*H*-pyrans in a single step.[15,16] This synthesis in conjunction with the carbonyl–alkyne exchange reaction constitutes an effective new aryl annelation method. For example, 1,3-cyclohexanedione (**5a**) and its 5,5-dimethyl derivative (**5b**) give **6a** and **6b**, respectively, by reaction with crotonaldehyde.[16] These pyrans react regiospecifically with methyl propiolate to give methyl 5-oxo-5,6,7,8-tetrahydro-1-naphthoate (**7a**) and the 7,7-



**5a**, R = H
**b**, R = $CH_3$

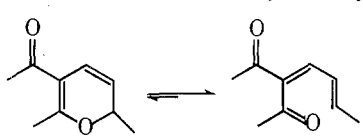
**6a**, R = H
**b**, R = $CH_3$



**7a**, R = H
**b**, R = $CH_3$

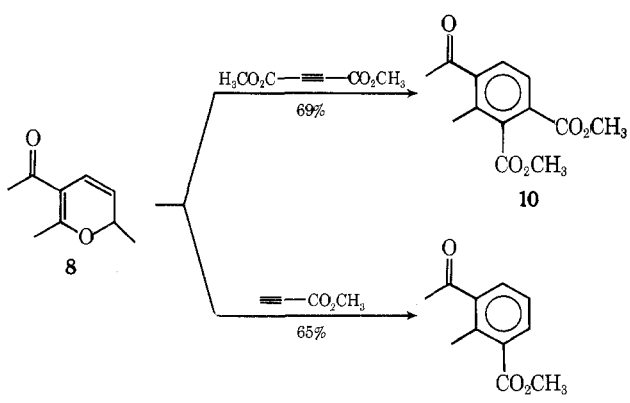
dimethyl derivative (**7b**), respectively. The assignment of the 1 position instead of the 2 position for the carbomethoxy substituent rests on an analysis of the $^1H$ NMR spectra of **7a** and **7b**. All of the aryl proton resonances in the NMR spectra of these compounds exhibit large (8 Hz) vicinal coupling. The $^1H$ NMR absorption due to the proton in the 1 position of the alternative 2-naphthoates would be a singlet or would exhibit only small long-range coupling.

Though the 2*H*-pyran **8** constitutes only 20% of an equilibrium mixture[16] with the dienone **9**, carbonyl–alkyne ex-



**8** **9**

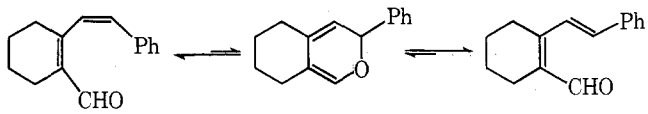
change reactions proceed normally to give good yields of aryl derivatives. Thus, the equilibrium mixture of **8** and **9** gives **10** by reaction with dimethyl acetylenedicarboxylate and gives **11** by regiospecific reaction with methyl propiolate. Whether the regiospecificity of the reactions of **4**, **5a**, **5b**, and **8** with



**8** **10** **11**

methyl propiolate is due to the electronic effect of the pyran oxygen or the steric effect of the substituents in the 2 position, it is noteworthy that both of these groups are not retained in the aryl products of these reactions. That is, the functionality which directs the initial alkyne cycloaddition is lost in the subsequent carbonyl cycloelimination.

Not all 2*H*-pyrans are present in the equilibrium mixture with dienones in sufficient concentrations to undergo carbonyl–alkyne exchange. Thus, the 2*H*-pyran **12** is not detectable in the $^1H$ NMR spectrum of the dienal **13c**.[18] When **13c** was heated with methyl propiolate under the usual con-



**13c** **12** **13t**

ditions, no trace of carbonyl–alkyne exchange was detected. However, **13c** isomerized to **13t** presumably via the 2*H*-pyran **12**.[18]

## Conclusions

The reaction of alkynes with 2*H*-pyrans is useful for the synthesis of certain aryl derivatives. The reaction is regiospecific with methyl propiolate. The ester group in the aryl product is exclusively ortho to the carbon derived from the 6 position of the pyran precursor. The functionality which directs the initial cycloaddition, the pyran oxygen or the substituents in the 2 position, is lost in the subsequent cycloelimination. In conjunction with a one-step conversion of 1,3-dicarbonyl compounds into 2*H*-pyrans, the carbonyl–alkyne exchange reaction constitutes an effective new aryl annelation method.

## Experimental Section

**General.** Reported procedures were utilized for the preparation of 4,6-dimethyl-α-pyrone (**1**),[19] 2,2,4,6-tetramethyl-2*H*-pyran (**4**),[7] 2-methyl-5-oxo-5,6,7,8-tetrahydro-2*H*-1-benzopyran (**6a**),[16] 5-oxo-5,6,7,8-tetrahydro-2,7,7-trimethyl-2*H*-1-benzopyran (**6b**),[16] 5-acetyl-2,6-dimethyl-2*H*-pyran (**8**),[16] and *cis*-2-(2-phenylvinyl)cyclohex-1-enecarboxaldehyde (**13c**).[18] NMR spectra were obtained on a Varian A-60A instrument. Preparative and analytical gas–liquid phase chromatography was performed with a Varian Aerograph 202B instrument. Elemental analyses were performed by Chemalytics, Inc., Tempe, Ariz.

**Carbonyl–Alkyne Exchange of 4,6-Dimethyl-α-pyrone (1) with Methyl Propiolate.** A mixture of pyrone **1** (2.5 g, 20 mmol) and methyl propiolate (10 g, 0.12 mol) was boiled under reflux under nitrogen for 160 h. Fractional distillation with a short-path distilling head (Kontes) gave an isomeric mixture of methyl dimethylbenzoates, bp 100–112 °C (8 mm) (70%). The mixture was shown to consist of methyl 2,4-dimethylbenzoate (**2**, 78%) and methyl 3,5-dimethylbenzoate (**3**, 22%) by gas–liquid phase chromatography (GLC) on a 10 ft × 0.25 in. column packed with 5% Bentone 34 and 5% diisodecyl phthalate on 60/80 Chromosorb W at 120 °C. Relative retention times were **2**, 1.0; **3**, 1.2. Pure samples of the isomeric products were obtained by preparative GLC and identified by NMR spectral comparison with authentic samples.

**Carbonyl–Alkyne Exchange of 2,2,4,6-Tetramethyl-2*H*-pyran (4) with Methyl Propiolate.** A mixture of pyran **4** (2.5 g, 18 mmol) and methyl propiolate (2.1 g, 25 mmol) was boiled under reflux under nitrogen for 100 h. Fractional distillation with a short-path distilling head gave methyl 2,4-dimethylbenzoate, bp 106–109 °C (10 mm) (73%).

**Methyl 5-Oxo-5,6,7,8-tetrahydro-1-naphthoate (7a).** A mixture of the pyran **6a**[16] (3.2 g, 19 mmol) and methyl propiolate (10 g, 0.12 mol) was boiled under reflux under nitrogen for 60 h. Excess methyl propiolate was recovered by distillation and the residual oil was distilled under reduced pressure through a short-path distillation head to give **7a** which crystallized in the receiver, bp 125–128 °C (0.1 mm) (70%). Recrystallization from cold methanol gave white crystals: mp 53–55 °C; NMR ($CCl_4$) δ 2.15 (2 H, m, $J$ = 6 Hz, C7), 2.60 (2 H, t, $J_{7,8}$ = 6 Hz, C8), 3.28 (2 H, t, $J_{5,6}$ = 6 Hz, C6), 3.87 (3 H, s, $CO_2CH_3$), 7.28 (1 H, apparent t, $J_{2,3} = J_{3,4}$ = 8 Hz, C3), 7.95 (1 H, dd, $J$ = 8, $J_{2,4}$ = 1.5 Hz), 8.15 (1 H, dd, $J$ = 8, $J_{2,4}$ = 1.5 Hz).

Anal. Calcd for $C_{12}H_{12}O_3$: C, 70.58; H, 5.92. Found: C, 70.40; H, 5.45.

**Methyl 7,7-Dimethyl-5-oxo-5,6,7,8-tetrahydro-1-naphthoate (7b).** A mixture of the pyran **6b**[16] (4.3 g) and methyl propiolate (10 g) was treated as above for **7a**. The ester **7b** was obtained: bp 118–121 °C (0.05 mm) (60%); NMR ($CDCl_3$) δ 1.08 (6 H, s, C7 methyls), 2.53 (2 H, s, C8), 3.22 (2 H, s, C6), 3.92 (3 H, s, $CO_2CH_3$), 7.36 (1 H, apparent t, $J_{2,3} = J_{3,4} = 8$ Hz, C3), 8.09 (1 H, dd, $J = 8$, $J_{2,4} = 1.5$ Hz), 8.16 (1 H, dd, $J = 8$, $J_{2,4} = 1.5$ Hz).

Anal. Calcd for $C_{14}H_{16}O_3$: C, 72.39; H, 6.94. Found: C, 72.23; H, 7.05.

**Dimethyl 4-Acetyl-3-methylphthalate (10).** An equilibrium mixture of the pyran **8** and the dienedione **9**[16] (0.91 g, 6 mmol) and dimethyl acetylenedicarboxylate (0.84 g, 6 mmol) was combined and heated under a reflux condenser under nitrogen at 110 °C for 10 h. The crude product was dissolved in $CCl_4$ (3 ml). The solution deposited white crystals at 0 °C which were collected by filtration at 0 °C with pressure: mp 75–76 °C (69%); NMR ($CDCl_3$) δ 2.39 (3 H, s), 2.56 (3 H, s), 3.90 (3 H, s, $CO_2CH_3$), 3.95 (3 H, s, $CO_2CH_3$), 7.57 (1 H, d, $J_{5,6}$ = 8.5 Hz), 7.91 (1 H, d, $J_{5,6}$ = 8.5 Hz); ($CCl_4$) δ 2.30 (3 H, s,), 2.50 (3 H, s), 3.86 (6 H, s, $CO_2CH_3$), 7.55 (1 H, d, $J_{5,6}$ = 8 Hz), 7.77 (1 H, d, $J_{5,6}$ = 8 Hz).

Anal. Calcd for $C_{13}H_{14}O_5$: C, 62.39; H, 5.64. Found: C, 62.20; H, 5.63.

**Methyl 3-Acetyl-2-methylbenzoate (11).** An equilibrium mixture of the pyran **8** and the dienedione **9**[16] (2.7 g, 18 mmol) and methyl propiolate (10 g) were treated as above for **7a**. The ester **11** was obtained: bp 117–119 °C (0.1 mm) (65%); NMR ($CDCl_3$) δ 2.54 (3 H, s, $CH_3$), 2.58 (3 H, s, $CH_3$), 3.90 (3 H, s, $CO_2CH_3$), 7.0–8.0 (3 H, multiplets, C4,5,6).

Anal. Calcd for $C_{11}H_{12}O_3$: C, 68.74; H, 6.29. Found: C, 68.31; H, 6.27.

**Isomerization of 13c in the Presence of Methyl Propiolate.** A mixture of the dienal **13c**[18] (0.38 g, 1.8 mmol) and methyl propiolate (1 g, 12 mmol) was boiled under reflux under nitrogen for 60 h. Excess methyl propiolate was distilled into a cold trap (−78 °C) under reduced pressure (0.1 mm). The NMR spectrum of the residual oil ($CCl_4$) was identical with that reported[18] for the trans isomer(**13t**).

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**Registry No.**—**1**, 675-09-2; **4**, 5526-16-9; **6a**, 58133-98-5; **6b**, 58134-01-3; **7a**, 59599-49-4; **7b**, 59599-50-7; **8**, 58134-11-5; **9**, 17448-92-9; **10**, 59599-51-8; **11**, 59599-52-9; **13c**, 21451-41-2; methyl propiolate, 922-67-8; dimethyl acetylenedicarboxylate, 762-42-5.

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# Electron Spin Resonance Studies of Structure and Conformation in Anion Radicals Formed during the Autoxidation of Hydroxylated Coumarins

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Coumarins containing hydroxyl groups in the aromatic ring are autoxidized in alkaline solution with the formation of semiquinone radicals, which have been studied by means of ESR spectroscopy. The hyperfine splitting data are consistent with some of these radicals possessing a closed pyrone ring, and others being cinnamic acid semiquinones formed as a result of pyrone ring opening. The cinnamic acid semiquinones are apparently observed in the trans configuration, and the effect of the side chain on the aromatic ring splittings is similar to those of alkyl and aryl groups. A qualitative model, considering delocalization of spin density from the aromatic nucleus into the side chain by both π overlap and hyperconjugation, is successful in relating conformational changes resulting from substitution, and the resultant extranuclear hyperfine splittings.

The coumarins form a group of natural products of considerable importance, being widely distributed throughout the plant kingdom.[1] Much of the interest in the chemistry of this group has arisen from their physiological activity, which manifests itself particularly in the hydroxylated derivatives.

One of the most valuable methods of structure determination for coumarins[1] is furnished by the alkaline degradation reaction, which invariably involves opening of the pyrone ring. In the course of our work on oxidation processes of some groups of natural products, we have studied the autoxidation, in alkaline solution, of coumarins containing hydroxyl groups in the aromatic ring. Under our conditions oxidation accompanies the alkaline degradation, and the intermediate semiquinone anion radicals involved in the combined process are conveniently studied by ESR spectroscopy.[2] We report here the useful relationships between the structures of the initial coumarins and the information gained from an ESR study of the radicals formed during these autoxidation reactions.

## Experimental Section

**Materials.** Caffeic acid (3,4-dihydroxycinnamic acid), chlorogenic acid [3-(3,4-dihydroxycinnamoyl)quinic acid], 7-hydroxycoumarin, 7-hydroxy-4-methylcoumarin, esculetin (6,7-dihydroxycoumarin),