formed free metal hydride cannot isomerize the olefin and decomposes rapidly in the presence of base.

A particularly interesting feature of the reaction with allyl alcohol, not observed with other allylic alcohols, is the formation of aldol condensation products **2** and **3** (eq 2, entry 1), a process that has been postulated to explain the low isolated yield of 3-phenylpropionaldehyde.[9] Apparently these products arise from 3-(3′-pyridyl)propionaldehyde and propionaldehyde, formed in situ by olefin migration. Furthermore the isolation of 2-methyl-2-(3′-pyridyl)pent-4-enal (**4**) suggests that under the present reaction conditions the π-allylpalladium complex, probably formed by the oxidative addition of Pd(0) to allyl alcohol, reacted with the enolate of 2-(3′-pyridyl)propionaldehyde.[10]

In conclusion, the present palladium-catalyzed reaction is a good method to prepare the 3-alkylpyridines, with the following advantages. (a) The manipulation is very easy (not rigorously sensitive to moisture) and applicable to a large scale reaction. (b) By the combination with an appropriate allylic alcohol, we can modify the alkyl substituent with a carbonyl group at the 3′ position, permitting further transformations.

Experimental Section

General Procedure for the Reactions of 3-Bromopyridine and Allylic Alcohols. The general procedure was exemplified by the reaction of 3-bromopyridine and α-methallyl alcohol (entry 4, Table I). Into an argon purged mixture of $Pd(OAc)_2$ (9 mg, 0.04 mmol), PPh_3 (31.5 mg, 0.12 mmol), and $NaHCO_3$ (404 mg, 4.8 mmol) were added 3-bromopyridine (632 mg, 4 mmol), α-methallyl alcohol (432 mg, 6 mmol), and 3 mL of HMPA by means of a syringe. The slurry mixture was stirred and heated at 120 °C for 5 h. The reaction was monitored by means of VPC (SiDC 550, He) by sampling 2 μL from the reaction mixture at an appropriate interval. The reaction mixture was poured into 20 mL of water and extracted with ether (30 + 20 + 20 mL). The combined ether extracts were washed with 10 mL of saturated NaCl and dried over $MgSO_4$. Evaporation of a solvent and the subsequent distillation (Kugelrohr 150 °C (15–5 mmHg)) gave a colorless oil (48% isolated yield), which consisted of 83% of 2-(3′-pyridyl)ethyl methyl ketone, 9% of 1-(3′-pyridyl)-1-buten-3-ol, and 8% of 1-(3′-pyridyl)-ethyl methyl ketone.

For the reaction in DMF (entry 8), the workup was undertaken as follows. The reaction mixture diluted with 20 mL of ether was filtered through a Florisil column (mesh 100–200, 1 cm length). Distillation of filtrate gave 545 mg of colorless oil (94% isolated yield, Kugelrohr 150 °C (13–10 mmHg)), consisting of 93% of methyl 2-(3′-pyridyl)-ethyl ketone and 7% of methyl 1-(3′-pyridyl)ethyl ketone.

Registry No.—**1**, 39976-56-2; **5** (R = H; R = Me), 66702-67-8; **5** (R = R′ = Me), 66702-68-9; **6** (R = H; R′ = Me), 66702-69-0; **6** (R = R′ = Me), 66702-70-3; **6** (R = H; R′ = Ph), 66702-71-4; 3-(3-pyridyl)-propanal, 1802-16-0; 2-methyl-3-(3-pyridyl)propanal, 66417-76-3; (*E*)-2-methyl-3-(3-pyridyl)propenal, 66702-72-5; 4-(3-pyridyl)-2-butanone, 55161-19-8; 4-(3-pyridyl)-3-penten-2-ol, 66702-73-6; 3-(3-pyridyl)-3-penten-2-ol, 66702-74-7.

Supplementary Material Available: ^{1}H NMR, IR, and mass spectra of 3- and 2-(3′-pyridyl)aldehydes and ketones and related compounds (5 pages). Ordering information is given on any current masthead page.

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(10) The mechanistic study and the examination of the scope of this anomalous reaction are currently under way. For a comprehensive review for the reaction of π-allylpalladium complexes and enolates, see B. M. Trost, *Tetrahedron*, **33**, 2615–2649 (1977).

Magnetic Equivalence and Nonequivalence of Methylene Groups Adjacent to an Asymmetric Center in a Series of γ-Phenyl-γ-butyrolactones[1]

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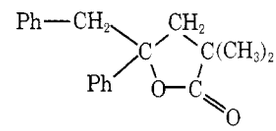
In recent studies, several γ-benzyl-γ-phenyl-γ-butyrolactones were prepared as intermediates in the synthesis of benzyltetralins and benzyltetralols.[2,3] The NMR spectrum of α,α-dimethyl-γ-phenyl-γ-butyrolactone (**1**) attracted our



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interest because it showed a clear AB pattern (centered at ca. δ 3.1) for one of the methylene groups and a sharp singlet (at δ 2.38) for the other. The ring methylene hydrogens would certainly be expected to be nonequivalent, and the benzyl methylene hydrogens might also be expected to be nonequivalent since they are adjacent to an asymmetric center. This spectrum was compared with those of the diastereomers of α-methyl-γ-benzyl-γ-phenyl-γ-butyrolactone[4,5] (*Z*-**2** and *E*-**2**); see Table I. The spectra of *Z*-**2** and *E*-**2** indicate that both the ring methylene and benzyl methylene hydrogens are nonequivalent in these lactones. This aroused our curiosity as to which pair of methylene hydrogens in lactone **1** were the NMR equivalent ones.

To determine this, we first prepared the dideuterio analogue of **1** in which the deuterium atoms were placed unequivocally in the benzyl position. As may be seen in Table I, this lactone (**1d**) had an NMR spectrum identical with that of lactone **1** except that the singlet at δ 2.38 was missing. This proved that this singlet comes from the benzyl methylene hydrogens of lactone **1** and not from the β hydrogens of the lactone ring. Hence the β hydrogens of lactone **1** are nonequivalent, as expected, but the benzyl methylene hydrogens are NMR equivalent.

The same test was applied to lactone *Z*-**2**. Its α,α-dideuteriobenzyl derivative was also synthesized. As may be seen in Table I, this lactone (*Z*-**2d**) had an NMR spectrum virtually identical with that of lactone *Z*-**2** except that the AB signal at δ_A 3.20, δ_B 3.09 was missing, confirming the analysis of the spectrum of lactone *Z*-**2** as presented in Table I. Comparing the assigned NMR signals of lactone **1** with those of *Z*-**2** and *E*-**2** (Table I) reveals the surprising fact that the chemical shifts of the benzyl and methylene hydrogens are virtually reversed in these compounds!

An attempt was made to sort out the ABC signal from the α- and β-hydrogens remaining in lactone *Z*-**2d**. It consisted of two separated multiplets at δ 1.74–2.22 and δ 2.62–3.03,

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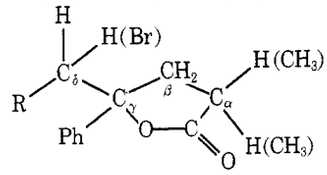
Table I. NMR Spectra of γ-Phenyl-γ-butyrolactones[a]



registry no.	lactone	δ	β	α	CH_3
60484-03-9	R = Ph, δ H_2, α-$(CH_3)_2$ (1)	s, 2.38	AB, $\delta A = 3.20$, $\delta_B = 3.00$, $J \approx 13$ Hz		s, 0.85 s, 0.95
66687-62-5	R = Ph, δ D_2, α-$(CH_3)_2$ (**1d**)		AB, $\delta_A = 3.19$, $\delta_B = 3.00$, $J \approx 13$ Hz		s, 0.85 s, 0.95
38436-24-7	R = Ph, δ H_2, α H, α-CH_3 (*Z*-**2**)[b]	AB, $\delta_A = 3.20$, $\delta_B = 3.09$, $J = 14$ Hz	ABC, 1.74–3.03, J(gem) = 11 Hz, J(vic) ≈ 8 Hz		d, 1.05 $J = 6.5$ Hz
66687-63-6	R = Ph, δ D_2, α-CH_3 (*Z*-**2d**)[b]		ABC, 1.74–3.03		d, 1.06 $J = 6$ Hz
38436-23-6	R = Ph, δ H_2, α H, α-CH_3 (*E*-**2**)[b]	AB, $\delta_A = 3.28$, $\delta_B = 3.10$, $J = 14$ Hz	ABC, 2.00–2.90		d. 1.06 $J = 6$ Hz
66719-16-2	R = Ph, δ H, Br, α-$(CH_3)_2$ (**3**)	s, 5.17	AB, $\delta_A = 2.86$, $\delta_B = 2.54$, $J \approx 13$ Hz		s, 0.87 s, 1.14
66687-64-7	R = Ph, δ H_2, α-H_2 (**4**)	AB, $\delta_A = 3.21$, $\delta_B = 3.05$, $J \approx 15$ Hz	AA′BB′, 1.85–2.65		
66687-65-8	R = CH_3, δ H_2, α-$(CH_3)_2$ (**5**)	q, 1.75–2.10, $J \approx 7$ Hz	AB, $\delta_A = 2.43$, $\delta_B = 2.27$, $J \approx 12$ Hz		s, 0.88 s, 1.24
66687-66-9	R = *n*-Pr, δ H_2, α-$(CH_3)_2$ (**6**)	m, ~1.68–2.20	AB, $\delta_A = 2.46$, $\delta_B = 2.26$, $J \approx 13$ Hz		s, 0.87 s, 1.26
894-15-5	R = Ph, α-$(CH_3)_2$ (**7**)		s, 2.82		s, 1.06
66687-67-0	R = *p*-$CH_3C_6H_4$, α-$(CH_3)_2$ (**8**)		s, 2.82		s, 1.05

[a] Spectra of lactones *Z*-**2**, *Z*-**2d**, *E*-**2**, **3**, and **4** were determined in $CDCl_3$ solution. Others were determined in CCl_4 solution. [b] Spectra of lactones *Z*-**2**, *Z*-**2d**, and *E*-**2** were recorded on a HA-100 spectrometer. Others were recorded on a 60 MHz spectrometer.

indicating that one of the three protons is chemically shifted away from the other two. A deuterium exchange of the α proton was attempted with the aim of ascertaining its contribution to the NMR spectrum. Although complete exchange with the α proton was not effected by two treatments with LiOD in D_2O and 1,2-dimethoxyethane, the following changes in the NMR spectrum were observed: (1) after the first treatment, the doublet of the α-methyl group became smaller and a small singlet peak appeared in the middle of the doublet; and (2) after the second treatment the doublet became a broad singlet and the relative area of the resonance in the region δ 1.74–2.22 became smaller and about equal to the area in the region δ 2.62–3.03. These observations imply that considerable deuterium exchange of the α-proton occurred and that this α proton is one of the two which produce the signal at δ 1.74–2.22. Thus, the α-proton and one of the two β-methylene protons must produce the signal at δ 2.62–3.03.

Bromination of lactone **1** with *N*-bromosuccinimide gave the bromo lactone **3**. Obviously, one the basis of the NMR spectrum of **3**, the bromine replaced one of the benzyl hydrogens, as expected. The remaining benzyl hydrogen signal was shifted far downfield to δ 5.17 and the AB signal of the ring methylene hydrogens was shifted slightly upfield.

For comparison of a γ-phenyl-γ-butyrolactone with no substituents in the α position, γ-benzyl-γ-phenyl-γ-butyrolactone (**4**) was synthesized and its NMR spectrum was recorded. The benzyl methylene hydrogens were nonequivalent, giving an AB signal in the same region as those of lactones *Z*-**2** and *E*-**2**. The α- and β-methylene hydrogens gave a typical AA′BB′ signal.

Two γ-phenyl-γ-butyrolactones with a γ-alkyl substituent were synthesized, in one case ethyl (**5**) and in the other *n*-butyl (**6**). Both showed the AB signal characteristic of the nonequivalent β-methylene ring hydrogens. The δ-methylene hydrogens of the γ-ethyl lactone (**5**) gave a quartet of broad peaks indicating an uncertain degree of nonequivalence, and those of the γ-butyl lactone (**6**) gave an unresolved multiplet.

Of the final two lactones which were synthesized, one has two phenyl groups in the γ position (**7**) and the other has one phenyl and one *p*-tolyl group (**8**). Lactone **7** was expected to show equivalent β-methylene hydrogens, and it did, with a singlet at δ 2.82. Lactone **8** was of some interest because it also showed equivalence of the β-methylene hydrogens with a singlet at the same place. Although in the strictest sense they are not equivalent owing to the difference between the phenyl and the *p*-tolyl groups in the γ position, apparently the site of difference, the para position of the *p*-tolyl group, is too far away to affect the resonance of the β-methylene hydrogens.

We are grateful to Dr. Ben Shoulders of this Department for help in interpreting the NMR spectra described.

Experimental Section

General Procedures. Melting points were determined with a Laboratory Devices Mel-Temp capillary apparatus and are uncorrected. Infrared spectra of all new compounds were recorded on a Beckmann Model IR-5A spectrometer and were compatible with the expected structures. Nuclear magnetic resonance spectra were recorded at 60 MHz on a Varian A-60 or a Perkin-Elmer R12A spectrometer and at 100 MHz on a Varian HA-100 spectrometer. The solvents used are specified in Table I. All chemical shifts are reported as δ values in ppm downfield from Me_4Si as the zero standard. Microanalyses of new compounds were performed by Galbraith Laboratories, Knoxville, Tenn. and were in satisfactory agreement (±0.4% for C and H) with described structures.[6]

Synthesis of the γ-Phenyl-γ-butyrolactones. The new lactones were synthesized by a procedure analogous to that described previously for the *Z* and *E* isomers of α-methyl-γ-benzyl-γ-phenyl-γ-butyrolactone (*Z*-**2** and *E*-**2**).[4] The appropriate Grignard reagents were added to the methyl esters of β-benzoylpropionic acid, α-methyl-β-benzoylpropionic acid, or α,α-dimethyl-β-benzoylpropionic acid. In the case of the dideuterio lactones (**1d** and *Z*-**2d**), the α,α-dideuteriobenzyl chloride required for the Grignard reagent was prepared by reduction of benzoyl chloride with lithium aluminum deuteride.

The physical constants of the lactones were as follows: 1, mp 97–99 °C; **1d**, mp 97–100 °C; *Z*-**2d**, mp 134–135 °C; **3**, mp 149–151 °C; **4**, mp 78–80 °C; **5**, bp 145–148 °C (0.3 mm); **6**, mp 69–72 °C; **7**, mp 110–112 °C; **8**, bp 180–185 °C (0.6 mm).

The NMR spectra of the lactones are presented in Table I.

Bromination of α,α-Dimethyl-γ-benzyl-γ-phenyl-γ-butyrolactone. To 2.80 g (0.01 mol) of the title lactone in 50 mL of CCl_4 was added 1.78 g (0.01 mol) of *N*-bromosuccinimide and 50 mg of benzoyl peroxide. The mixture was stirred and irradiated with a sunlamp for 3 h and then cooled. Succinimide was removed by filtration and the filtrate was washed with hot water, dried, and concentrated, yielding a white crystalline solid. Recrystallization from ether–chloroform (1:1 v/v) gave α,α-dimethyl-γ-(α-bromobenzyl)-γ-phenyl-γ-butyrolactone (**3**): 2.99 g (75%); mp 149–151 °C.

Anal. Calcd for $C_{19}H_{19}O_2Br$: C, 63.50; H, 5.29. Found: C, 63.56; H, 5.30.

Deuterium Exchange with (*Z*)-α-Methyl-γ-(α′,α′-dideuteriobenzyl)-γ-phenyl-γ-butyrolactone. (*Z*-2d). A small piece of lithium wire was dissolved in 5 g of D_2O. In a 10-mL flask was placed 0.5 g of the title lactone dissolved in a few milliliters of 1,2-dimethoxyethane. The lithium deuteroxide solution was added and then more 1,2-dimethoxyethane was added dropwise until the mixture became homogeneous. The solution was heated at 80 °C for 1 h and stirred at room temperature overnight. The solvent was evaporated and then D_2O was added, producing a cloudy solution from which white crystals soon separated. The crystals were washed with D_2O and recrystallized from methanol; 0.4 g of product was recovered, mp 134–135 °C. The NMR spectrum of the recovered lactone indicated partial exchange of hydrogen in the α position. The deuterium exchange procedure was repeated, giving the deuterated lactone whose NMR spectrum is described in the body of the paper.

Registry No.—Methyl β-benzoylpropionate, 25333-24-8; methyl α-methyl-β-benzoylpropionate, 36057-38-2; methyl α,α-dimethyl-β-benzoylpropionate, 15118-66-8.

References and Notes

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(3) C.-E. Low and R. M. Roberts, *J. Org. Chem.*, **38**, 1909 (1973).
(4) A. A. Khalaf and R. M. Roberts, *J. Org. Chem.*, **38**, 1388 (1973). Although the *Z,E* assignment of these isomers was tentative at the time this paper was published, a subsequent X-ray crystal structure analysis confirmed the assignment unequivocally as correct.[5]
(5) R. L. Harlow and S. H. Simonsen, *Acta Crystallogr., Sect. B*, **32**, 2137 (1976).
(6) The only exception to this statement is that the microanalysis for C, H of lactone **1** was inadvertently overlooked. However, reliable evidence of this structure has been provided by a published X-ray crystal structure determination.[5]

New Mild Conditions for the Synthesis of α,β-Unsaturated γ-Lactones. β-(2-Phthalimidoethyl)-$\Delta^{\alpha,\beta}$-butenolide

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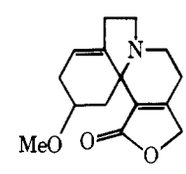
In connection with a synthetic approach to D ring lactone erythrina alkaloids,[2] particularly cocculolidine (**1**),[3] we needed an efficient route to β-(2-phthalimidoethyl)-$\Delta^{\alpha,\beta}$-butenolide (**2a**).

Despite the variety of methods that have been devised for the synthesis of the frequently encountered $\Delta^{\alpha,\beta}$-butenolide system[4] and the relatively simple structure of this particular example, such a route proved to be surprisingly difficult to develop. We did meet with some initial success in that the reaction between ethyl bromoacetate and 1-acetoxy-4-phthalimido-2-butanone (**3a**) under classic Reformatsky conditions gave[5] acetoxy lactone **4**, which we find eliminates HOAc on heating in *N,N*-diethylaniline to give **2a** cleanly and



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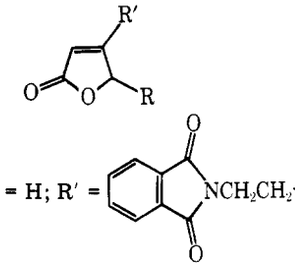
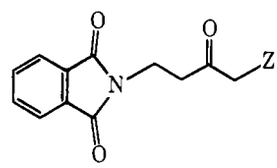


2a, R = H; R′ = NCH_2CH_2-

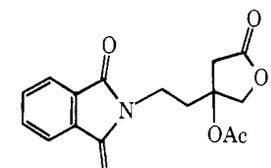
b, R = H; R′ = Ph
c, R = R′ = Ph
d, R = R′ = $-(CH_2)_4-$

in high yield. The Reformatsky reaction with α-acetoxy ketones has recently been stated[4] to be the method of choice for the preparation of $\Delta^{\alpha,\beta}$-butenolides. Unfortunately, in spite of considerable effort, the best yields that could be obtained in that step were low (20–21%) and even then somewhat variable with respect to product isolation, so that a better overall route to **2a** was needed.

More recent variations[6,7] in the Reformatsky procedure as well as other established methods[8–11] of introducing appropriate two carbon units as applied to 1-substituted 4-phthalimido-2-butanones (**3**), with the exception of BF_3-catalyzed addition of ethoxyacetylene[12] to α-chloro ketone **3b**,[5] were useless. The latter reaction gave in about 50% yield a product which appeared, as judged by the NMR spectrum, to be the expected α,β-unsaturated esters **5**, but without selectivity with respect to the required *Z* isomer and in any case as a very dark oil which resisted attempts at purification and complete characterization.



3a, Z = OAc
b, Z = Cl
c, Z = N_3
d, Z = $OCOCH_2Br$
e, Z = Br
f, Z = $OCOCH_2P^+Ph_3\ Br^-$
g, Z = $OCOCH{=}PPh_3$



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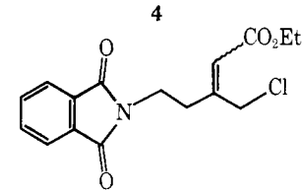

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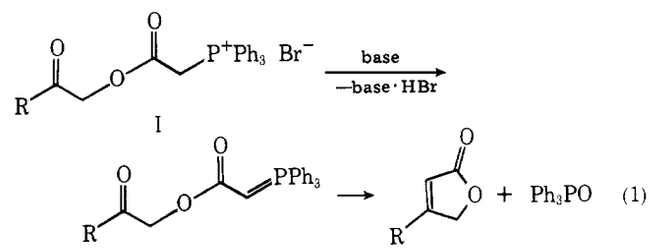
We then turned to an intramolecular approach to carbon–carbon bond formation, specifically via the Wittig reaction (eq 1).



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(1)

Compounds of type I have been cyclized to $\Delta^{\alpha,\beta}$-butenolides once before. In the two reported[13] examples (eq 1, R = steroidal), similar moderate yields were obtained using the rather diverse systems NaH/Me_2SO (100 °C for 4 h; 51%) and K_2CO_3/*t*-BuOH (reflux 8 h; 67%); apparently, the exact nature of the base is not critical, and thus it seemed that one more compatible with our system could be effective. It was further hoped that less drastic conditions (purification was by chromatography) would suffice.

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