crystallization from cyclohexane gave 1.6 g (10% yield) of **7**, mp 157–159°, identical by mixture melting point and infrared spectrum with **7** prepared from **12** or **13**.

Anal. Calcd for $C_{14}H_{13}BrN_2O_2$: C, 52.36; H, 4.08; N, 8.73. Found: C, 52.43; H, 4.06; N, 8.74.

Saponification of 7 to 3.—Compound **7**, 5.1 g (0.016 mol) in 75 ml of 2-PrOH and 20 ml of 50% aqueous NaOH formed a two-phase system. The mixture was stirred and heated under reflux for 1 hr and cooled, the lower aqueous solution separated, the 2-PrOH solution washed with 10 ml of saturated aqueous NaCl and filtered, and the filtrate concentrated to dryness *in vacuo* to give 3.2 g (91% yield) of **3**, mp 105–107°; a mixture melting point with **3** prepared *via* **8** was 106–107.5°, and their infrared spectra were identical.

Acetylation of 3 to Give 7.—When **3**, 0.50 g (0.018 mol), was mixed with 5 ml of Ac₂O, a clear solution formed after 0.5 hr. On keeping overnight at room temperature a crystalline mass separated. This was filtered to give 0.58 g (quantitative yield) of **7**, mp 157–158°; a mixture melting point with **7** prepared above was 157–159°, and their infrared spectra were identical.

Registry No.—**2**, 26372-71-4; **3**, 26419-18-1; **3** (HCl), 26372-55-4; **4**, 26372-72-5; **4** (HCl), 26372-73-6; **5**, 26372-74-7; **6**, 26372-75-8; **7**, 26372-76-9; **9**, 26372-77-0; **10**, 26372-53-2; **11**, 26372-54-3.

## Deuterated Olefins from the Wittig Reaction

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The usefulness of the Wittig reaction[2] for the preparation of deuterated olefins has been severely limited by the occurrence of large amounts of scrambling and exchange of label with the medium. Previous workers have used the anion of dimethyl sulfoxide[3] to generate ylides for this purpose. However, scrambling and loss of label make material so prepared unsuitable for use in mechanistic and spectroscopic studies. These problems are much less severe when alkyllithium reagents in ether[3,4] are used, but the yields in this case are low, and the procedures required for decomposition of the ylide are not convenient.

We have found that some α-deuterated olefins can be efficiently and conveniently prepared, using sodium hydride as the base, simply by changing the solvent to one not susceptible to hydrogen exchange. We have synthesized methylenecyclopentane-2,2,5,5-d_4 (1) and methylene-d_2-cyclopentane-2,2,5,5-d_4 (2). Our results
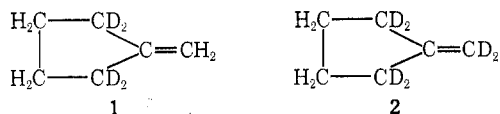
also suggest that the intramolecular scrambling of the label is a function of the base, rather than a solvent effect. The procedure we describe is operationally sim-

ple and gives good yields of material of high isotopic purity.

The d_6 material **2** was prepared from methyl-d_3-triphenylphosphonium bromide and cyclopentanone-2,2,-5,5-d_4. The deuterium exchange reaction involving phosphonium salts has been previously described by Schlosser[5] and the deuterium exchange reaction of cyclopentanone in basic solution has been cited by several workers.[6] The exchange reactions were carried out in two steps and the final starting materials for the Wittig reaction were greater than 98 at. % D, in the appropriate positions, as estimated from integrated nuclear magnetic resonance (nmr) spectra.

Attempts to prepare the tetradeuterio compound **1** by a similar procedure with unlabeled phosphonium bromide gave a mixture of isotopic derivatives. This product retained virtually all the deuterium present in the starting material, but 20% of it wound up in the exocyclic position. However, when *n*-butyllithium was used as the base in place of sodium hydride, a good yield of specifically labeled product was obtained.

The use of ethers of ethylene glycol as solvents for the Wittig reaction effectively eliminates exchange of hydrogen with the medium. When sodium hydride is used as a base, intramolecular scrambling across the incipient double bond occurs, but with no noticeable loss of deuterium from the molecule. The use of an alkyllithium leads to specifically labeled product without scrambling. This modification of the Wittig reaction should make the synthesis of α-deuterated olefins, particularly where both the carbonyl and ylide precursors are α-deuterated, accessible, and convenient (Table I).

TABLE I
LABEL DISTRIBUTION IN WITTIG PRODUCTS FROM
CYCLOPENTANONE-2,2,5,5-d_4 IN BIS(2-ETHOXYETHYL) ETHER

| | | | At. % D | |
Ylide	Base	Product	2,5 ring position	Exocyclic methylene
$Ph_3P=CH_2$	NaH	1	80	40
$Ph_3P=CH_2$	BuLi	1	98	0
$Ph_3P=CD_2$	NaH	2	98	97

Experimental Section

All of the products exhibited ir and nmr spectra which differed from those of authentic unlabeled analogs only in those respects expected as a result of deuterium incorporation. The use of undeuterated reagents gave materials identical in all respects measured with authentic samples.

Methyltriphenylphosphonium bromide was prepared by the method of Trippett.[7]

Methyl-d_3-triphenylphosphonium Bromide.—Methyltriphenylphosphonium bromide (25 g, 0.070 mol) was dissolved in 50 ml of heavy water (99.89 at. % D) and then 0.07 ml of 40% sodium deuterioxide in heavy water was added with stirring. The solution was stirred for 10 min and then immediately extracted with four 30-ml portions of methylene chloride. The combined methylene chloride layers were dried over sodium sulfate, filtered, concentrated under reduced pressure, and crystallized by addition of ether. This process was repeated with another 50-ml portion of heavy water; the crystals were dried in a vacuum oven overnight, to give 22.6 g (90%) of product which was estimated from the integrated nmr spectrum to have greater than 98 at. % D on the methyl group.

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Cyclopentanone-2,2,5,5-d_4.—Ten grams (0.119 mol) of freshly distilled, dry cyclopentanone was added to 40 ml of heavy water. Stirring was begun and 0.05 ml of 40% sodium deuterioxide in deuterium oxide was added. After 5 min, the solution was extracted with three 20-ml portions of methylene chloride. The combined methylene chloride layers were dried over sodium sulfate, filtered, and concentrated under reduced pressure. The process was repeated with a fresh 40-ml portion of heavy water and the product (6.80 g, 65%) distilled, that portion boiling from 126–129° being retained. Analysis by nmr indicated greater than 98 at. % D on the α positions.

Methylene-d_2-cyclopentane-2,2,5,5-d_4.—To 2.439 g (0.0546 mol) of sodium hydride (53.6%) dispersed in mineral oil and 20.0 g (0.0555 mol) of methyl-d_3-triphenylphosphonium bromide, was added approximately 250 ml of freshly distilled bis(2-ethoxyethyl) ether while the system was swept with dry nitrogen. The nitrogen sweep was passed through three traps, the first cooled with ice and the remaining two cooled with Dry Ice. After addition of the solvent, the temperature of the mixture was raised, over the period of 1 hr, to 60–70° and maintained at this level for 3 hr. The formation of the intermediate methylene-d_2-triphenylphosphorane was evidenced by the appearance of a yellow color shortly after stirring was begun. The mixture was then cooled to 30° and 4.81 g (0.0545 mol) of cyclopentanone-2,2,5,5-d_4 was added dropwise. The mixture was then heated to 85–90° over the period of 1 hr and maintained at this temperature overnight while the system was swept slowly with nitrogen. The crude product was recovered from the first Dry Ice trap. The nmr spectrum showed that ~10–15% benzene had been produced. The isotopic purity, determined from the integrated nmr spectrum was ~98 at. % D on the exocyclic methylene group. The product was purified by gas chromatography, using a 6 ft × 0.25 in. o.d. column of 15% di(2-ethylhexyl) sebacate on diatomaceous earth at room temperature. Although 2–3% of the mixture consisted of impurities other than benzene, no attempt was made to isolate or identify these components. Benzene was identified by its nmr signal and its retention time on the chromatographic column compared to the retention time of an authentic sample. This procedure yielded 3.05 g (64%) of product.

Methylenecyclopentane-2,2,5,5-d_4.—The methylenetriphenylphosphorane was formed by adding 12.8 ml of a 2.96 N solution of butyllithium in benzene to a slurry of 12.5 g (0.0352 mol) of methyltriphenylphosphonium bromide in approximately 150 ml of bis(2-methoxyethyl) ether. The procedure above was then followed. A yield of 1.18 g (39%) was obtained from 3.05 g of cyclopentanone-2,2,5,5-d_4. Analysis of the product by nmr showed greater than 98 at. % D on the 2,5 positions and less than 1 at. % D on the exocyclic methylene.

Registry No.—Methyl-d_3-triphenylphosphonium bromide, 1787-44-6; cyclopentonane-2,2,5,5-d_4, 3997-89-5; methylene-d_2-cyclopentane-2,2,5,5-d_4, 25966-75-0; methylenecyclopentane-2,2,5,5-d_4, 25966-76-1.

Friedel–Crafts Acetylation of Monoalkylbenzenes in Refluxing Carbon Disulfide

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Nightingale, Hucker, and Wright[1] reported that Friedel–Crafts acetylation of primary and secondary

monoalkylbenzenes in refluxing carbon disulfide (40°) gave acetophenone and a dialkylacetophenone along with the corresponding p-alkylacetophenone. This abnormal behavior was attributed to an initial disproportionation of the primary or secondary monoalkylbenzene, competitive with the acetylation reaction. Tertiary monoalkylbenzenes however gave low yields of the normal product with an apparent absence of the corresponding dialkylacetophenone and acetophenone, a result which appears incongruous in terms of the mechanism suggested by Nightingale, *et al.*, for the disproportionation of the primary and secondary alkylbenzenes.

Disproportionations associated with the acetylation of secondary and tertiary alkylbenzenes at 0° have been accounted for in terms of an intermolecular transfer of an alkyl group as an essentially free cation generated from the α complexed hydrocarbon,[2,3] whereas disproportionation of primary alkylbenzenes with essentially no rearrangement of the alkyl group has been attributed to a different mechanism.[4]

Barring the operation of an alternate mechanism, it is difficult to reconcile the products and mechanism suggested for acetylations carried out at 40° in carbon disulfide with those established for the same reaction at 0°. In order to account for these anomalies and to correlate the acetylations at 40° with those run at 0° a re-examination of the reaction has been undertaken.

Experimental Section

The acetylations in refluxing carbon disulfide were carried out as directed by Nightingale, Hucker, and Wright,[1] with particular attention being paid to the sequence and mode of addition of reagents. Thus the monoalkylbenzene was quickly added to the stirred mixture of aluminum chloride in carbon disulfide and immediately followed by addition of the acetyl chloride. The latter was added as rapidly as permitted by the exothermic reaction. Following a 3-hr reflux and subsequent work-up, the ether was removed by means of a spinning-band column. Samples (1 μl) of the residual liquid were fractionated on a Model 817 Packard dual column gas chromatograph fitted with a thermal detector. Quantitative analysis was accomplished on a 6 ft × 0.25 in. column of 10% Apiezon L on 70–80 mesh Anakron A programmed at 5°/min from 100 to 250°, using p-methylacetophenone as an internal standard. Samples of the individual components of the reaction mixture were isolated by means of a Wilkens Autoprep gas chromatograph equipped with a 20 ft × ³/₈ in. silicone gum rubber column. These samples were utilized for elemental analysis, ir examination, and preparation of phenylhydrazone derivatives.

These reactions were rerun under identical conditions with the exception that the reaction mixture was maintained at 0° throughout. Acetylations were also carried out at 40° by employing the inverse addition of the hydrocarbon to the acetyl chloride–aluminum chloride complex.

Results and Discussion

The identity of the products following gas chromatographic separation was checked by means of carbon and hydrogen analysis, ir spectra, and the preparation of 2,4-dinitrophenylhydrazones. Agreement to ±0.1% for carbon and hydrogen analysis and 1° in melting point was observed. Quantitative gas chromatographic analysis of the product mixture showed the presence of trace amounts of aromatic hydrocarbons. The yields of the major components are listed in Table I.

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