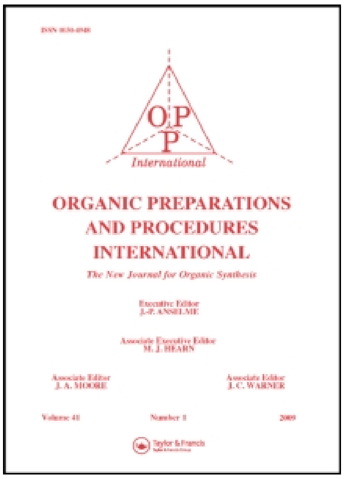

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PHENYLACETYLENE-1-^{13}C

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PHENYLACETYLENE-1-^{13}C

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$$^{13}CO_2 + C_6H_5MgBr \longrightarrow C_6H_5{}^{13}CO_2H$$

$$C_6H_5{}^{13}CO_2H + SOCl_2 \longrightarrow C_6H_5{}^{13}COCl$$

$$C_6H_5{}^{13}COCl + Cd(CH_3)_2 \longrightarrow C_6H_5{}^{13}COCH_3$$

$$C_6H_5{}^{13}COCH_3 + PCl_5 \longrightarrow C_6H_5{}^{13}CCl_2CH_3 + C_6H_5{}^{13}CCl{=}CH_2$$

$$C_6H_5{}^{13}CCl_2CH_3 + C_6H_5{}^{13}CCl{=}CH_2 + NaNH_2 \longrightarrow C_6H_5{}^{13}C{\equiv}CH$$

The preparation of phenylacetylene-1-^{13}C from benzoic acid-carboxyl-^{13}C required sufficient experimentation to optimize yields, particularly in the last two steps, that the present procedure is recorded. With adaptations for safety, ^{14}C labelled compounds along the synthetic route may be prepared. Phenylacetylene has been prepared from styrene dibromide with sodium amide[1a,b] or with methanolic potassium hydroxide[1c], from β-bromostyrene with potassium hydroxide[1d], and by reduction of phenylchloroacetylene[1e]. None of these procedures were suitable for the preparation of specifically labelled material. In the present case an overall yield of 15.5% of phenylacetylene, based on barium carbonate, was achieved.

Experimental[2]

Benzoic Acid-Carboxyl-^{13}C[3,4a,b]. Barium carbonate-^{13}C[5] (4.63 g, 23.4 mmole) gave 2.37 g (19.6 mmole, 84%) of benzoic acid-carboxyl-^{13}C, mp 120-121° (from water) $\tilde{\nu}$ 1695 cm^{-1} ($^{12}C{=}O$), 1656 cm^{-1} ($^{13}C{=}O$)[6], lit[3] yield 94%.

Benzoyl Chloride-Carbonyl-$^{13}C^{3,7}$. Benzoic acid-carboxyl-^{13}C (3.02 g, 25.0 mmoles) gave 3.08 g (22.0 mmole, 88%) of benzoyl chloride-carbonyl-^{13}C, bp 100° (25 mm), $\tilde{\nu}$ 1705 cm^{-1} ($^{12}C{=}O$), 1658 ($^{13}C{=}O$)^{6}.

Acetophenone-Carbonyl-$^{13}C^{3,7}$. A grignard reagent was prepared from 6.08 g of methyl iodide (42.8 mmoles) and 1.02 g of Grignard magnesium in 20 ml of sodium-dried ether and was cooled in an ice bath. Anhydrous cadmium chloride^{8} (4.03 g, 22.0 mmoles) was added over 7 minutes, and the mixture was stirred mechanically. The mixture was stirred and refluxed for 1 1/2 hours, then cooled in an ice bath while 2.74 g (19.5 mmoles) of benzoyl chloride-carbonyl-^{13}C is added, through a dropping funnel. After 3 hours of refluxing and stirring the mixture was cooled and treated with 50 ml of ice cold 6M sulfuric acid. The organic layer was separated and the aqueous layer extracted with ether. The combined ether extracts were washed with water, 5% sodium carbonate^{9}, and again with water. The ether was dried and distilled using a short Vigreaux column and the residue distilled in vacuum. The product, collected in a cold receiver, weighed 1.20 g (10.0 mmole, 51%) bp 40° (0.5 mm) $\tilde{\nu}$ 1698 cm^{-1} ($^{12}C{=}O$), 1653 cm^{-1} ($^{13}C{=}O$)^{6}.

1,1-Dichloro-1-phenylethane and 1-Chloro-1-phenylethylene-1-$^{13}C^{10,11}$. A solution of 1.20 g (10 mmoles) of acetophenone-carbonyl-^{13}C and 2.75 g (12.8 mmoles) of phosphorus pentachloride in 50.0 ml of sodium-dried benzene was refluxed for 1 1/2 hours. The ice-cooled solution was hydrolyzed by careful addition of 20 g of crushed ice. The phases were separated and the cold benzene solution quickly extracted with an additional 2X10 ml portions of water. The organic layer was dried immediately with calcium chloride, then filtered. The benzene was distilled under aspirator vacuum without heating.^{12} The residual oil was distilled at 32-44° (0.2 mm) to give 1.11 g of a mixture whose composition could be deduced from the proton resonance spectrum: 1,1-dichloro-1-phenylethane-1-^{13}C, $\delta_{CH_3} = 2.33$ ppm,

$^{2}J_{^{13}CCH}$ = 3.96 Hz^{13} (15%); 1-chloro-1-phenylethlene-1-^{13}C, $\delta_{\mathrm{vinyl}\ H_B}$ = 5.58 ppm, $^{2}J_{H_AH_B}$ = 1.60 Hz, $J_{^{13}CCH_B}$ = 5.62 Hz (85%). The α-^{13}C content was 56% calculated from $J_{^{13}CCH}$ coupling[14].

Phenylacetylene-1-^{13}C[14]. Sodium amide, prepared from 0.40 g (0.017 g atom) of sodium and 15 ml of anhydrous liquid ammonia with 100 mg of hydrated ferric chloride, was cooled in dry ice-acetone and treated with a solution of 1.00 g of the mixture of 1,1-dichloro-1-phenylethane and 1-chloro-1-phenylethylene (*vide infra*) in 25 ml of anhydrous ether. The reaction was strongly exothermic. The ammonia was permitted to evaporate and replaced by 20 ml of dry ether. The brown precipitate was stirred for one hour, cooled and treated with 3N hydrochloric acid until the reaction was slightly acidic. The ether layer was separated and the aqueous portion extracted with another portion of ether. The combined ether extracts were washed with water, dried and concentrated using a short Vigreaux column. The residue was distilled, bp 70-80° (35 mm). The phenylacetylene thus obtained (0.41 g) was 85% pure (glc) and was further purified as a silver salt. The sample was dissolved in 10 ml. of 1:1 ethanol: water. To this solution was added saturated alcoholic silver nitrate until a white precipitate just ceased to form. The precipitate was filtered, washed with small quantities of water, alcohol and ether. The solid was dried and transferred to 6 ml of 3N hydrochloric acid. Steam distillation of this mixture, using good stirring, gave phenylacetylene in the first milliter of distillate[16]. Pure phenylacetylene-1-^{13}C was obtained by separation, drying and vacuum transfer at 25° (0.0005 mm) of the water insoluble portion of the steam distillate. The sample (0.34 g) showed an infrared spectrum characteristic of phenylacetylene, ν 2130 cm^{-1} ($-{}^{12}C{\equiv}{}^{12}C-$), 2102 cm^{-1} ($-{}^{13}C{\equiv}{}^{12}C-$). The proton resonance spectrum δ_{CH} = 2.92 ppm, $^{2}J_{^{13}CCH}$ = 50.0 Hz[17] (CCl_4). The α-^{13}C content was 56%. The yield was 41% in two steps from acetophenone-carbonyl-^{13}C.

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12. At temperatures in excess of 80-90° the products will begin to decompose.

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16. If any transfers preceding this point are carried out using a high vacuum line, great care should be taken to avoid contamination of the sample by mercury. The presence of mercury during steam distillation catalyzes hydration of the acetylene to acetophenone.

17. A value of 44 Hz has been previously reported for $^{2}J_{^{13}C\equiv CH}$. (P. C. Lauterbur, "Determination of Organic Structures by Physical Methods", Vol. 2, (F. C. Nachod and W. D. Phillips, edit) Ch 7, Academic Press, New York, 1962)

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