85%). The time-consuming steam distillation purification method by Fieser was eliminated and replaced with Hinkel sodium bisulfite product purification procedure without loss of yield. Recrystallizations from ethanol–water gave pale yellow crystals: mp 87–88° (lit.[10] mp 87–88°); infrared $\lambda_{max}^{KBr}$ 6.0 (CO), 6.3 (aromatic C=C), 6.7, 8.3, 8.7, 10.9, 12.0, and 12.9 $\mu$; mass spectrum (70 eV) *m/e* (relative intensity) 153 (1000), 182 (943), 152 (585), 181 (413), 76 (366).

**5-Styrylacenaphthene (III).**—A Grignard reagent was prepared from 1.75 ml (0.015 mol) of benzyl chloride in 25 ml of anhydrous ether. A mixture of 1.85 g (0.01 mol) of II and 500 ml of anhydrous benzene was added and the resulting mixture was refluxed 2 hr. This mixture was decomposed with 1 *N* $H_2SO_4$. The organic layer was separated, concentrated (2.5 g) and combined with 0.17 g of potassium hydrogen sulfate. The mixture was heated 10 min at 200°. The residue was dissolved in an excess of benzene and passed through a 15 × 2 cm alumina column using hexane as the eluting solvent. Fractions (100 ml) yielded 0.40 g (30%) of III from fractions 3, 4 and 5: mp 96° (MeOH) [lit.[3] mp 94° (MeOH)]; infrared $\lambda_{max}^{KBr}$ 6.3 (aromatic C=C), 6.7, 10.4 (*trans* HC=CH), 12.0, 12.3, 13.0 (shoulder), 13.5 and 14.6 $\mu$; mass spectrum (70 eV) *m/e* (relative intensity) 256 (1000), 255 (321), 257 (279), 128 (217), 119.5 (192).

**6,7-Acechrysene (I).**—Eastman Spectro Grade cyclohexane (400 ml), 0.0292 g ($1.2 \times 10^{-4}$ mol) of iodine and 0.2054 g ($8 \times 10^{-4}$ mol) of III were placed in a 2 l. round-bottomed flask fitted with a 3 in. Vycor filter disk and reflux condenser. This mixture was irradiated with a 140-W Hanovia Quartz lamp for 4 hr. The solvent was evaporated and the residue eluted through a 15 × 2 cm basic alumina column with benzene. Recrystallization of the residue from ethanol–benzene (1:1) gave 0.15 g (74%) of I: mp 185° (*Anal.* Calcd for $C_{20}H_{14}$: C, 94.45; H, 5.55. Found: C, 94.63; H, 5.52); ultraviolet $\lambda_{max}^{cyclohexane}$ 272 m$\mu$ ($\epsilon$ $2.09 \times 10^5$), 262.5 ($1.06 \times 10^5$), 329 ($2.01 \times 10^4$), 314.5 ($1.98 \times 10^4$), 302 ($1.60 \times 10^4$); infrared $\lambda_{max}^{KBr}$ 6.2, 6.3 (aromatic C=C), 11.6, 12.4, 13.2, 13.4 $\mu$; mass spectrum (70 eV) *m/e* (relative intensity) 126 (1000), 254 (906), 113 (612), 127 (580), 125 (540); nmr ($C_6D_6$) $\delta$ 3.04 ($CH_2$), 8.39 (H-$\beta$, m), 7.75 (H-$\alpha$, m), and 7.46 (H-$\alpha$3, m).

**Registry No.**—I, 4766-40-9.

**Acknowledgment.**—We would like to thank Dr. Morton Jacobs of International Flavor and Fragrances, Inc., for obtaining the nmr spectrum.

(9) Melting points were determined in a capillary and were uncorrected. Infrared, ultraviolet, nmr and mass spectra were taken on a Perkin-Elmer 521 spectrophotometer, Beckman DK-2 spectrophotometer, Varian HA-100 spectrometer and CEC 104 mass spectrometer. The alumina used for chromatography was basic alumina from Arthur H. Thomas. Elemental analyses were performed by Galbraith Laboratories.

(10) L. E. Hinkel, E. E. Ayling, and J. H. Beynon, *J. Chem. Soc.*, 339 (1936).

(11) L. F. Fieser and J. E. Jones, *J. Amer. Chem. Soc.*, **64**, 1666 (1942).

## Organolithium Compounds and Acetylenes. VI. *p*-Chlorodiphenylacetylene[1]

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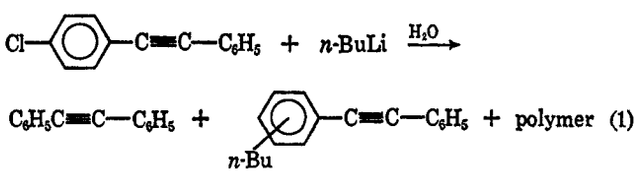
To determine the effect of substituents on addition, metalation, and electron-transfer reaction of organolithium compounds and acetylenes, *p*-chlorodiphenylacetylene was prepared and its reaction with *n*-butyllithium was studied.[2]

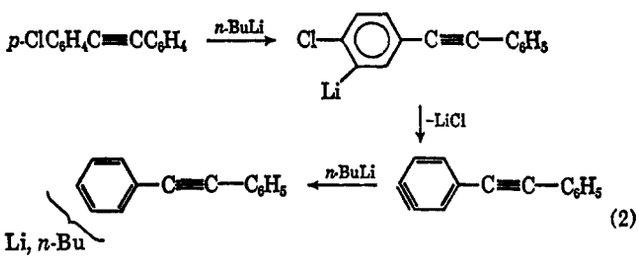
The reaction of *o*-chlorodiphenylacetylene and *n*-butyllithium has recently been reported to give an 80% yield of 1-(*o*-chlorophenyl)-2-phenyl-1-hexene after hydrolysis.[3]

Our results with *p*-chlorodiphenylacetylene are markedly different. When 2.2 mol of *n*-butyllithium in ethyl ether were treated with 1.0 mol of *p*-chlorodiphenylacetylene, there was obtained after hydrolysis 14% diphenylacetylene, 27% an equimolar mixture of *n*-butyldiphenylacetylenes, 3% starting material, and a moderate amount of polymeric material (eq 1).



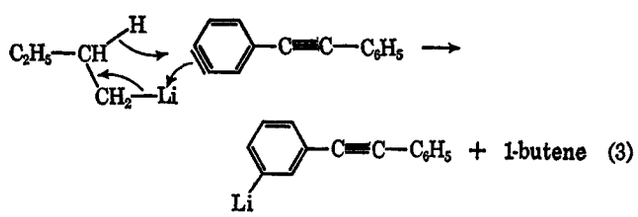

The polymeric material had a molecular weight of 2400, contained only a trace of chlorine, and had aromatic and aliphatic protons in approximately a 3:1 ratio. This mixture was not further identified.

There is no precedent for direct nucleophilic substitution of chlorine by *n*-butyllithium under these conditions. It is most likely that the *n*-butyldiphenylacetylenes arise *via* a benzyne intermediate (eq 2).




This would yield two *n*-butyl derivatives in equal amounts as is observed. Although chloroaromatics do not generally yield benzyne intermediates under these conditions the electron-withdrawing effect of the acetylenic bond would be expected to facilitate metalation of the hydrogen *ortho* to the chlorine.

Diphenylacetylene could arise by direct halogen–metal interconversion but it could also arise from the benzyne as indicated in eq 3. This kind of phenomenon




(1) (a) Research supported by AFOSR(SRC)-OAR, U. S. Air Force Grant No. 720-65. (b) For paper V, see J. E. Mulvaney, S. Groen, L. T. Carr, Z. G. Gardlund and S. L. Gardlund, *J. Amer. Chem., Soc.* **91**, 388 (1969).

(2) Unlike bromides and iodides an aromatic chloride does not generally undergo halogen–metal interconversion or induce *ortho* metalation when treated with organolithium compounds. H. Gilman and R. G. Jones, *Org. Reactions*, **6**, 342 (1951). H. Gilman and J. W. Morton, *ibid.*, **7**, 267 (1954).

(3) R. E. Dessy and S. A. Kandil, *J. Amer. Chem. Soc.*, **88**, 3027 (1966).

was first suggested by Franzen and Joschek[4] to explain the formation of benzoic acid from the reaction of *o*-bromochlorobenzene with *n*-butyllithium.

Although diphenylacetylene reacts with lithium in ethyl ether to give *cis,cis*-1,2,3,4-tetraphenylbutadiene,[5] the reaction of *p*-chlorodiphenylacetylene with lithium gave only 5% diphenylacetylene and 94% starting material.

### Experimental Section

*p*-Chlorodiphenylacetylene was prepared from *α*-*p*-chloroacetophenone.[6,7]

***n*-Butyllithium and *p*-Chlorodiphenylacetylene.**—*p*-Chlorodiphenylacetylene (25.0 g, 0.118 mol) in 250 ml of anhydrous ethyl ether was added dropwise over a period of 1 hr to a stirred solution under a helium atmosphere of *n*-butyllithium (0.260 mol) in 182 ml of ethyl ether. After stirring for 17 hr at room temperature, the dark solution, which contained a considerable amount of precipitate, was cooled (0°), and 50 ml of ice water was added slowly. An additional 100 ml of water was added and the layers separated. The ethereal solution was dried and concentrated to yield 23.5 g of a dark viscous oil. This oil was dissolved in 50 ml of 2-butanone and poured slowly into 250 ml of rapidly stirring methanol. Filtration gave 3.63 g of a tan polymer: softening point 175–183°; nmr (15% in $CDCl_3$), two broad multiplets at $\tau$ 2.25–3.09 and 8.53–9.62 (relative areas 3:1); $\nu_{max}^{CHCl_3}$ 1605 cm$^{-1}$.

*Anal.* Found: C, 91.39; H, 6.09; residue, 1.85; mol wt, 2420.

The methanolic filtrate was concentrated and distilled through a small column to give 10.91 g of pale yellow oil, bp 90–135° (0.10 mm.). Vapor phase chromatography (5-ft GE-SF-96, 200°) indicated the presence of diphenylacetylene (27%), *p*-chlorodiphenylacetylene (7%), and *m*- and *p*-*n*-butyldiphenylacetylenes (66%). Redistillation through a spinning-band column yielded 7.0 g (26%) of *m*- and *p*-*n*-butyldiphenylacetylenes: bp 160–161° (0.70 mm.); $n^{26.8}$D 1.6079; $\lambda_{max}$ 300 m$\mu$ ($\epsilon$ 33,000), 291 (28,000), 282 (39,000), 275 (31,000), and 267 (27,000); $\nu_{max}^{CHCl_3}$ 2225 cm$^{-1}$; nmr (20% in $CCl_4$), $\tau$ 2.44–3.04 (9, multiplet), 7.47 (2, triplet, $J$ = 7 cps), 8.33–8.92 (4, multiplet), and 9.10 (3, triplet, $J$ = 6 cps). Vapor phase chromatography showed two overlapping peaks of equal intensity.

*Anal.* Calcd for $C_{18}H_{18}$: C, 92.26; H, 7.74. Found: C, 91.96; H, 7.93.

**Lithium Metal and *p*-Chlorodiphenylacetylene.**—The reaction was run in the manner described by Smith and Hoehn.[5] To lithium wire (0.70 g, 0.10 g-atom) suspended in 130 ml of anhydrous ethyl ether under a helium atmosphere, there was added *p*-chlorodiphenylacetylene (21.25 g, 0.1000 mol). After stirring at room temperature for 12 hr, the mixture was heated under reflux for 13 hr. After the mixture cooled to 0°, 75 ml of 95% ethanol was added dropwise and the solution was stirred until all of the lithium metal had reacted. Water (100 ml) was added and the layers separated. The ethereal solution was dried and concentrated to give 20.9 g of solid. Vapor phase chromatography (5-ft GE-SF-96, 200°) indicated that this solid consisted of 94% starting material, 5% diphenylacetylene, and <1% an unidentified compound which had the lowest retention time of the three components.

**Registry No.**—*p*-Chlorodiphenylacetylene, 5172-02-1; *n*-butyllithium, 109-72-8; *m*-*n*-butyldiphenylacetylene, 19165-50-5; *p*-*n*-butyldiphenylacetylene, 19165-51-6.

(4) V. Franzen and H. Joschek, *Angew. Chem.*, **72**, 564 (1960).

(5) L. E. Smith and H. H. Hoehn, *J. Amer. Chem. Soc.*, **63**, 1184 (1941); H. H. Freedman, G. A. Doorakian and V. R. Sandel, *ibid.*, **87**, 3019 (1965).

(6) D. Y. Curtin and M. C. Crew, *ibid.*, **76**, 3719 (1954).

(7) M. S. Newman and D. E. Reid, *J. Org. Chem.*, **23**, 665 (1958).



## The 4-(Methylthio)phenyl and 4-(Methylsulfonyl)phenyl Esters in the Preparation of Peptides and Polypeptides.[1] Synthesis of a Linear O-Depsipeptide

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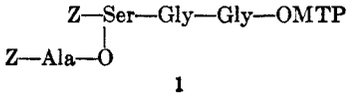
The synthesis of O-depsipeptides requires the condensation of the free carboxyl of a N-protected peptide with a free hydroxyl group. Attempts to form O-depsipeptides with such a terminal hydroxyl group have usually been unsuccessful.[2] For this and other reasons[3] the first bond formed in the synthesis of O-depsipeptides has been the O-peptide ester linkage, such that subsequent condensations then involve the easier amide bond formation. However, using this approach, the use of C-terminal protecting groups which are removed by alkaline treatment, *e.g.*, methyl and ethyl esters, are precluded because the O-peptide ester linkage is even more easily hydrolyzable.

In order to overcome this difficulty inherent in the synthesis of O-depsipeptides we have found that the 4-(methylthio)phenyl (MTP) protective[4] ester and the 4-(methylsulfonyl)phenyl ($MSO_2P$)[5] activated ester are particularly useful for extending the peptide chain in the presence of an O-peptide ester linkage. For this purpose the synthesis of N-carbobenzoxy-L-seryl-O-(N-carbobenzoxy-L-alanyl)glycylglycine 4-(methylthio)phenyl ester (**1**) is described as an illustration of this approach to the preparation of O-depsipeptides.




**1**

The synthesis commenced with the formation of N-carbobenzoxy-L-serylglycine 4-(methylthio)phenyl ester (**2**) by condensation of N-carbobenzoxy-L-serine and glycine 4-(methylthio)phenyl ester hydrochloride[3] using dicyclohexylcarbodiimide and triethylamine. The mixed-anhydride method was found to be the best procedure to form the O-peptide ester bond. Thus, the anhydride formed from N-carbobenzoxy-L-alanine and ethyl chloroformate was treated with the protected dipeptide MTP ester **2** to give the protected O-depsipeptide MTP ester, N-carbobenzoxy-L-seryl-O-(N-carbobenzoxy-L-alanyl)glycine 4-(methylthio)phenyl ester (**3**). In order to extend the peptide chain it was necessary to convert the protective MTP ester of **3** to its activated $MSO_2P$ counterpart. This activation was achieved by the use oxidative conditions which are more

(1) This is the fourth article in this series; see B. J. Johnson and P. M. Jacobs, *J. Org. Chem.*, **33**, 4524 (1968), for the previous paper.

(2) D. W. Russell, *Quart. Rev.* (London), **20**, 559 (1966).

(3) M. M. Shemyakin, E. I. Vinogradova, M. Yu. Feigina, N. A. Aldonova, Yu. A. Ovchinnikov, and A. A. Kiryushkin, *J. Gen. Chem. USSR*, **34**, 1796 (1964).

(4) B. J. Johnson and P. M. Jacobs, *Chem. Commun.*, 73 (1968).

(5) R. Schwyzer and P. Sieber, *Helv. Chim. Acta*, **41**, 2190 (1958), have reported a few 4-(methylsulfonyl)phenyl esters prepared from 4-(methylsulfonyl)phenol through the diaryl sulfite method.