*Anal.* Calcd. for $C_{15}H_{17}NO_4$: N, 5.09. Found: N, 4.93.

The compound when mixed with the material from procedure A failed to show any depression in the melting point. The ultraviolet absorption curves for both compounds were identical, exhibiting a maximum at 293 mμ (Fig. 1, A and B). The infrared absorption curves for both compounds were also identical (Fig. 2, A and B).

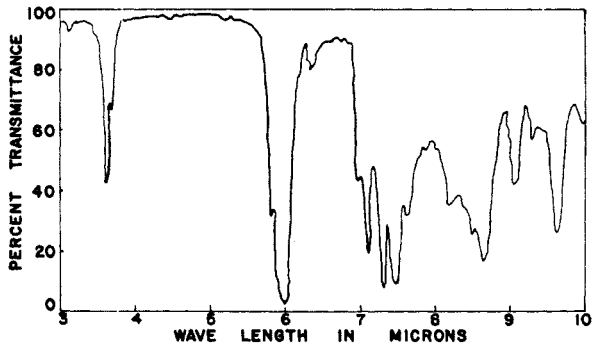


Fig. 2(A). Infrared absorption curve for methyl-ε-phthalimidocaproate prepared by procedure A

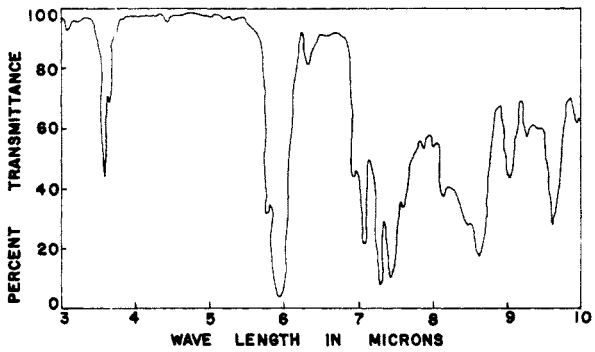


Fig. 2(B). Infrared absorption curve for methyl-ε-phthalimidocaproate prepared by procedure B

*Methyl hydrogen phthalate.* Methyl hydrogen phthalate was prepared following the procedure of Eliel and Burgstahler.[4] Thus, 74 g. (0.50 mol.) of phthalic anhydride and 50 ml. of methanol were refluxed for 2 hr. The excess methanol was distilled off, 25 ml. of benzene was added and the distillation continued to insure the complete removal of the excess alcohol. The residual oil was dissolved in 200 ml. of benzene following which 300 ml. of Skellysolve B was added. Upon cooling in an ice-salt bath, the product crystallized following which it was filtered, washed with more Skellysolve B and finally dried in vacuo. There was obtained 80 g. (89%) of methyl hydrogen phthalate; m.p. 80–82°; lit. val. 82°.[4]

*o-Carbomethoxybenzoyl chloride.* A mixture of 36 g. (0.2 mol.) of methyl hydrogen phthalate and 100 ml. of thionyl chloride was refluxed for 1 hr. on a steam bath. The excess thionyl chloride was removed under reduced pressure following which dry benzene (two 50-ml. portions) was added and distilled away from the acid chloride *in vacuo* two times, to complete the removal of unreacted thionyl chloride. The acid chloride, a pale yellow oily liquid was used as such in the following experiment without any further purification.

*N-(o-Carbomethoxybenzoyl)-ε-caprolactam.* Into a flask equipped with an agitator, thermometer, dropping funnel and reflux condenser was placed a solution of 22.6 g. (0.20 mol.) of caprolactam in 100 ml. of dry dioxane. While stirring, a solution of the *o*-carbomethoxybenzoyl chloride (from the previous experiment) in 100 ml. of dioxane was added dropwise over a period of 30 min. The mixture was next cooled to 10° and a solution of 20.2 g. (0.20 mol.) of triethylamine in 200 ml. of dioxane was added dropwise, maintaining the temperature below 20°. After the addition was complete, the mixture was refluxed for 3 hr., cooled to room temperature and filtered to remove the triethylamine hydrochloride.

The salt was washed with two 50-ml. portions of fresh dioxane following which the combined filtrates were subjected to a vacuum distillation to remove the dioxane. The residue was distilled at reduced pressures to yield 31 g. (57%) of *N*-(*o*-carbomethoxybenzoyl)-ε-caprolactam; b.p. 190–194°/0.8 mm. The compound crystallized on standing. After recrystallizing from Skellysolve B, the compound melted at 68–70°.

*Anal.* Calcd. for $C_{15}H_{17}NO_4$: C, 65.46; H, 6.18; N, 5.09. Found: C, 65.39; H, 5.51; N, 4.97.

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(4) E. L. Eliel and A. W. Burgstahler, *J. Am. Chem. Soc.*, **71**, 2251 (1949).

## Benzyllithium from Triphenylbenzyltin and Phenyllithium

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In a recent communication to this journal procedures were described for the direct preparation of benzyllithium by cleavage reactions.[1] An attempt was made to list all types of procedures that had been described for the synthesis of benzyllithium. However, a method involving a metal-metal interconversion or exchange was not included.[2] This involves the following reaction:

$$(C_6H_5)_3SnCH_2C_6H_5 + C_6H_5Li \longrightarrow C_6H_5CH_2Li + (C_6H_5)_4Sn$$

The yield of phenylacetic acid obtained subsequent to carbonation was 39%; and the yield of tetraphenyltin was as high as 91.8%. This exchange reaction between organotin and organolithium compounds is one which has been employed broadly for some time,[3] and a particularly effective use of it was described recently by Seyferth and Weiner[4] for a neat preparation of vinyllithium from tetravinyltin and phenyllithium.

(1) H. Gilman, H. A. McNinch, and D. Wittenberg, *J. Org. Chem.*, **23**, 2044 (1958).

(2) S. D. Rosenberg, Doctoral Dissertation, Iowa State College, 1952.

(3) H. Gilman, F. W. Moore, and R. G. Jones, *J. Am. Chem. Soc.*, **63**, 2482 (1941). See, also, R. G. Jones and H. Gilman, *Chem. Revs.*, **54**, 835 (1954) on the preparation of organometallic compounds.

(4) D. Seyferth and M. A. Weiner, *Chem. & Ind. (London)*, 402 (1959).

EXPERIMENTAL

To 5.0 g. (0.0113 mol.) of triphenylbenzyltin in 150 ml. of ether cooled to −35° (by a Dry Ice–acetone bath) was added 0.012 mol. of phenyllithium in 10 ml. of ether. The solution turned bright yellow immediately and then tetraphenyltin precipitated from the solution a few minutes later. After 1 hr. of stirring the mixture was allowed to stand a few minutes while the solid settled. The supernatant solution was decanted onto a Dry Ice–ether slurry with vigorous stirring, and the yellow color of benzyllithium was discharged. On working up the mixture by conventional procedures involving alkaline liquid–liquid extraction, acid liquid–liquid extraction, and crystallization there was obtained 0.6 g. (39%) of phenylacetic acid melting at 73–74° (mixed melting point). From this experiment, the yield of tetraphenyltin was 4.1 g. (88%). In two other experiments the yields of tetraphenyltin were 91.8% and 89%, respectively.

It might be mentioned that, under corresponding conditions, from reaction between triphenylethyltin and phenyllithium there was obtained a 9.4% yield of tetraphenyltin in addition to a 52.6% recovery of triphenylethyltin.

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## Studies on Synthetic Estrogens. I

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Following the observation that oxygen heterocyclic compounds such as coumarins,[1] isoflavens, isoflavones,[2] etc. have estrogenic activity, Buu-Hoï and co-workers[3] synthesized a number of benzofuran derivatives and some of these compounds showed estrogenic activity. In view of the physiological properties of the benzofuran derivatives[4] it was of considerable interest to synthesize additional derivatives.

2-*p*-Anisoylbenzofurans were prepared by refluxing an alcoholic solution of the potassium salt of *o*-hydroxyketones with *p*-methoxyphenacylbromide[5] according to Buu-Hoï.[3b] They have been characterized through their oximes.

The details of the *in vivo* biological activity of these compounds will be reported later.

EXPERIMENTAL[6]

*o-Hydroxyketones* were prepared by the method of Fries.[7]

*2-p-Anisoyl-3,5-dimethylbenzofuran.* A solution of 5-methyl-2-hydroxyacetophenone (0.1 mole) dissolved in caustic potash (0.125 mole) was added to *p*-methoxyphenacylbromide (0.1 mole) in ethanol. It was refluxed for 2 hr. on a water bath. The 2-*p*-anisoyl-3,5-dimethylbenzofuran formed was isolated and recrystallized from an acetic acid ethanol mixture. Similarly other benzofurans were prepared. The data concerning the new compounds are listed in Table I.

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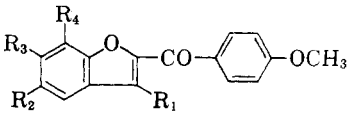
TABLE I

2-*p*-ANISOYLBENZOFURANS




| Sl. No. | $R_1$ | $R_2$ | $R_3$ | $R_4$ | Formula | Solvent for Recrystn. | M.P., °C. | | Analysis Calcd. | Analysis Found | Oxime M.P., °C. | | Oxime Analysis Calcd. | Oxime Analysis Found |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1. | $CH_3$ | $CH_3$ | H | H | $C_{18}H_{16}O_3$ | AcOH-EtOH | 118 | C: | 77.14 | 76.7 | 169 | C: | 73.23 | 72.9 |
| | | | | | | | | H: | 5.71 | 5.55 | | H: | 5.76 | 5.61 |
| 2. | $CH_3$ | Cl | H | H | $C_{17}H_{13}O_3Cl$ | AcOH-EtOH | 165 | Cl: | 11.81 | 11.6 | 110 | Cl: | 11.26 | 10.8 |
| 3. | $CH_3$ | Br | H | H | $C_{17}H_{13}O_3Br$ | AcOH-EtOH | 154 | Br: | 23.19 | 22.6 | 189 | Br: | 22.22 | 22.1 |
| 4. | $CH_3$ | $CH_3$ | H | Br | $C_{18}H_{15}O_3Br$ | AcOH-EtOH | 190 | Br: | 22.28 | 21.9 | | | | |
| 5. | $CH_3$ | Cl | Cl | H | $C_{17}H_{12}O_3Cl_2$ | AcOH-EtOH | 155 | Cl: | 21.19 | 20.8 | | | | |
| 6. | $C_2H_5$ | $CH_3$ | H | H | $C_{19}H_{18}O_3$ | EtOH | 148 | C: | 77.56 | 77.1 | 213 | C: | 73.77 | 73.4 |
| | | | | | | | | H: | 6.12 | 5.71 | | H: | 6.15 | 5.92 |
| 7. | $C_2H_5$ | Cl | H | H | $C_{18}H_{15}O_3Cl$ | EtOH | 103 | Cl: | 11.29 | 11.1 | 144 | Cl: | 10.77 | 10.5 |
| 8. | $C_2H_5$ | Br | H | H | $C_{18}H_{15}O_3Br$ | EtOH | 93 | Br: | 22.28 | 21.8 | 215 | Br: | 21.39 | 20.9 |

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(2) (a) R. B. Bradbury and D. E. White, *J. Chem. Soc.*, 3447 (1951); 871 (1953); (b) G. S. Pope, P. V. Elcoate, S. A. Simpson, and D. G. Andrews, *Chem. & Ind. (London)*, 1092 (1953); (c) G. S. Pope and H. G. Wright, *Chem. & Ind. (London)*, 1019 (1954); (d) J. L. Bose and K. Chandran, *J. Sci. Ind. Research (India)*, **13B**, 888 (1954).

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(5) J. B. Rather and E. M. Reid, *J. Am. Chem. Soc.*, **41**, 75 (1919).

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