2-p-Methoxyphenoxy-5-chloromethyl-5-methyl-2-oxo-1,3,2-dioxaphosphorinan. A solution of phosphorochloridate (2.18 g, 0.01 mol) and lithium perchlorate (1.06 g, 0.01 mol) in 10 ml of dried, freshly distilled acetonitrile was added to a solution of *p*-methoxyphenol (1.24 g, 0.01 mol) and triethylamine (1.01 g, 0.01 mol) in 10 ml of the same solvent. The solution was stirred at room temperature for 2 h and added to 200 ml of H_2O. The crystalline solid was removed by suction filtration, washed well with water, and dried. The product was recrystallized from carbon tetrachloride without undergoing a change in isomers ratio, 2.65 g (92.7%), 96.1% cis, 3.9% trans.

Anal. Calcd for $C_{12}H_{16}ClO_5P$:[11] C, 50.35; H, 5.59; Cl, 12.24. Found: C, 50.46; H, 5.52; Cl, 12.38.

This procedure is typical of those used to obtain the ratios of Table I.

Registry No.—*cis*-2-*p*-Methoxyphenoxy-5-chloromethyl-5-methyl-2-oxo-1,3,2-dioxaphosphorinan, 36912-31-9; *trans*-2-*p*-methoxyphenoxy-5-chloromethyl-5-methyl-2-oxo-1,3,2-dioxaphosphorinan 36912-32-0; *trans*-2-chloro-5-(chloromethyl)-5-methyl-2-oxo-1,3,2-dioxaphosphorinan, 28097-07-6; *p*-methoxyphenol, 150-76-5; $LiClO_4$, 7791-03-9; $Mg(ClO_4)_2$, 13770-16-6; $KClO_4$, 7778-74-7; $(C_2H_5)_3N^+CH_2C_6H_5Cl^-$, 56-37-1; *trans*-2-thiophenyl-5-chloromethyl-5-methyl-2-oxo-1,3,2-dioxaphosphorinan, 36912-44-4; *trans*-2-methoxy-5-chloromethyl-5-methyl-2-oxo-1,3,2-dioxaphosphorinan, 36912-27-3; *cis*-2-methoxy-5-chloromethyl-5-methyl-2-oxo-1,3,2-dioxaphosphorinan, 28097-12-3.

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Addition of Lithium Iodide to a Strained Carbon–Carbon σ Bond. In Situ Protonation, Methylation, and Benzylation of the Adduct

Gerald F. Koser* and Attila G. Relenyi

Department of Chemistry, The University of Akron, Akron, Ohio 44325

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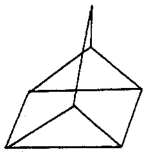
Tetracyclo$[3.2.0.0^{2,7}.0^{4,6}]$heptane (1) has emerged as a useful substrate for the study of nucleophilic additions to strained carbon–carbon σ bonds. When electrophilic substituents are attached at C-1, the 1–7 bond becomes vulnerable to nucleophilic cleavage, under mild reaction conditions.[1a,b,2,3] It seems likely that such reactions proceed through nortricyclyl anions of general structure 2, their ease of formation being determined by the ability of the attached group X to stabilize adjacent negative charge.[2] However, until now those anions have been intercepted only by protonation, even when acetonitrile was the sole proton source.[3] This research was initiated with the objective of trapping 2 with alkylating agents, and, to that end, the iodide opening of 1-carbomethoxyquadricyclene (3) was chosen as a model reaction.



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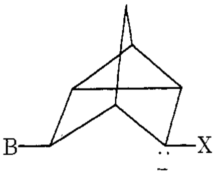

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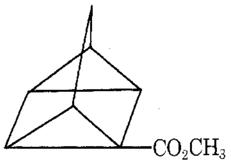

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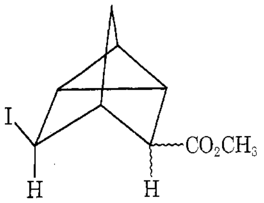

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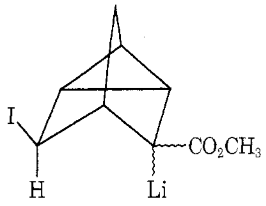

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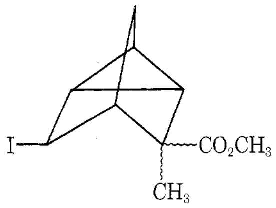
Our first task, then, was to demonstrate the feasibility of 1–7 bond cleavage in 3 by iodide ion, and, accordingly, 3 was allowed to react with lithium iodide in acetonitrile. Following work-up, a 43% yield of crude 3-carbomethoxy-5-iodonortricyclene (4), epimeric at C-3, was obtained.[4] The structure of 4 was inferred from its elemental composition and spectra (ir, near ir, NMR). Specifically, the 60-MHz ^{1}H NMR spectrum of 4 displays a complex 7 H multiplet at high field, a carbomethoxy singlet at δ 3.67, and a pair of broad singlets at δ 3.92 and 4.10 which we assign to H-5 of the individual epimers.

It seems likely that 3-lithio-3-carbomethoxy-5-iodonortricyclene (5) is an *intermediate* in the above reaction. Indeed, a successful in situ methylation of 5 has been achieved. When a solution of 3 in THF was added dropwise to a solution of lithium iodide in iodomethane–THF, a mild, exothermic reaction ensued. Following work-up, a 74% yield of *crude* 3-methyl-3-carbomethoxy-5-iodonortricyclene (6) was obtained as a yellow oil. Unfortunately, while 4 is stable in air, 6 rapidly turns green, and the precipitation of a black, amorphous solid follows. The 60-MHz ^{1}H NMR spectrum of 6 is similar to that of 4 except that it exhibits a carbon-bound methyl singlet at δ 1.23. However, we have been unable to obtain a *completely* satisfactory ^{1}H NMR spectrum of 6. The carbomethoxy singlet invariably



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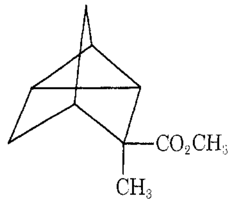

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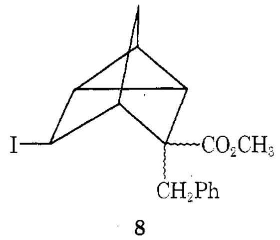

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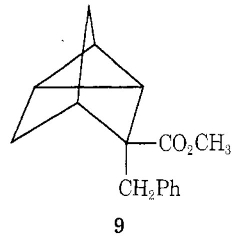

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appears to be 20–30% more intense than the methyl singlet. We think that this is due to the presence of an impurity (possibly 4) with a carbomethoxy group but not a carbon-bound methyl group which is not eliminated by our isolation techniques. In any event, we sought to substantiate our NMR assignments and subjected 6 to reductive deiodination with zinc in methanol. The reaction was not clean but 3-methyl-3-carbomethyoxynortricyclene (7) was a major product and was isolated in small quantity from an Apiezon L column. In the 60-MHz ^{1}H NMR spectrum of **7**, the carbomethoxy singlet appears to be a little more intense than the methyl singlet, but in the 300-MHz spectrum, they are clearly of equal intensity.

The lithium iodide adduct of 3 can also be benzylated. When a solution of 3 in THF was added to a solution of lithium iodide and benzyl iodide in THF, *crude* 3-carbomethoxy-3-benzyl-5-iodonortricyclene (8) was isolated in ~80% yield. When 8 was subjected to the action of zinc in methanol, reductive deiodination occurred, but the product mixture was extremely complex. Even so, the major product (~30–40%), 3-carbomethoxy-3-benzylnortricyclene (9), was purified by distillation and characterized by elemental, ir, and NMR analysis.

Finally, in control studies, it was shown that 3 does not react with either iodomethane or benzyl iodide in the absence of lithium iodide.

Experimental Section

General. ^{1}H NMR spectra (60 MHz) were recorded on a Varian Model A-60 NMR spectrometer (relative to internal Me_4Si), infrared spectra on a Perkin-Elmer Model 337 spectrophotometer, and near infrared spectra on a Cary 17 uv-visible–ir spectrophotometer. NMR spectra (300 MHz) were recorded on a Varian Model HR-300 NMR spectrometer at The University of Akron's NMR Center. GLC analyses and collections were conducted on a Hewlett-Packard F and M Model 700 Scientific gas chromatograph, a 6 ft × 0.25 in. column of Apiezon L being utilized. Elemental compositions were determined by Galbraith Laboratories, Inc., Knoxville, Tenn. The lithium iodide (99+% pure, anhydrous reagent) employed in these studies was purchased from Ventron and was pumped under vacuum just prior to use, a procedure which caused the salt to change in color from tan to off-white. Benzyl iodide was prepared by the action of sodium iodide in acetone on benzyl chloride and was distilled. Some of it was a gift from Mr. Gary Linden of this department. THF was distilled either from lithium aluminum hydride or lithium triphenylmethide just prior to use. Iodomethane was distilled from anhydrous magnesium sulfate and used directly.

Reaction of 3 with Lithium Iodide in Acetonitrile. A solution of 3 (1.50 g, 9.98 mmol) in CH_3CN (5 ml) was added dropwise to a solution of lithium iodide (2.0 g, 14.9 mmol) in CH_3CN (20 ml). The reaction mixture was allowed to stir for 2 h under nitrogen at room temperature and was then concentrated in vacuo to a dry white solid. The solid was treated with water (50 ml) and extracted with three 25-ml portions of CH_2Cl_2. The organic extracts were combined, dried ($MgSO_4$), and concentrated in vacuo and yielded 1.2 g (43%) of crude 3-carbomethoxy-5-iodonortricyclene (4) as a yellow oil. The crude oil was subjected to column chromatography (silica gel, CH_2Cl_2) followed by preparative TLC (silica gel, CH_2Cl_2) and reisolated as a clear, colorless oil.

Anal. Calcd for $C_9H_{11}IO_2$: C, 38.87; H, 3.99. Found: C, 39.00; H, 4.02.

Spectroscopic Data for 4. Ir (neat) 3.38 (CH), 3.26 (sh, cyclopropyl CH), 5.74 (C=O), 12.15 μ (nortricyclene skeleton);[5a–c] near ir (CH_2Cl_2) λ_{max} 1.653 μ (ϵ 1.143) (first C–H stretching vibration overtone characterisitic of nortricyclenes);[6] NMR ($CDCl_3$) δ 4.10 and 3.92 (broad singlets, H-5), 3.67 (s, O=COCH$_3$), 2.65–1.20 (complex multiplets, H-1, 2, 3, 4, 6, 7, 7′).

Alkylation of 3 with Iodomethane. A solution of 3 (1.83 g, 12.19 mmol) in THF (15 ml) was added dropwise to a solution of lithium iodode (1.82 g, 13.59 mmol) in iodomethane (10 ml) and THF (5 ml). The reaction mixture became turbid and warmed to ca. 45 °C. The reaction mixture was allowed to stir under nitrogen for 1 h at room temperature and was then concentrated under vacuum to a yellow slurry. The slurry was taken up in CH_2Cl_2, filtered through a fine porosity, sintered glass funnel (to remove LiI), dried ($MgSO_4$), and concentrated in vacuo to yield 2.62 g (74%) of crude 3-methyl-3-carbomethoxy-5-iodonortricyclene as a yellow oil which rapidly turned green upon exposure to light and air.

Purification of 6. A 1.98-g portion of the crude product was subjected to column chromatography on silica gel (50 g) with CH_2Cl_2, and 1.78 g of a yellow oil was obtained. A 0.48-g portion of the oil was subjected to preparative TLC (silica gel, CH_2Cl_2, fluoresceine indicator) which yielded 0.40 g of pure 6 as a pale yellow oil.

Anal. Calcd for $C_{10}H_{10}IO_2$: C, 41.09; H, 4.48. Found: C, 41.15; H, 4.49.

Spectroscopic Data for 6. Ir (neat) 3.40 (CH), 3.25 (sh, cyclopropyl CH), 5.79 (C=O), 12.15 μ (nortricyclene skeleton);[5a–c] near ir (CH_2Cl_2) λ_{max} 1.655 μ (ϵ 1.296);[6] NMR ($CDCl_3$) δ 3.92 (broad singlet, H-5), 3.68 (s, O=COCH$_3$), 1.23 (s, C–CH$_3$), 2.65–1.10 (complex multiplets, H-1, 2, 4, 6, 7, 7′).

Alkylation of 3 with Benzyl Iodide. A solution of 3 (1.02 g, 6.79 mmol) in THF (5 ml) was added dropwise to a solution of LiI (0.6 g, 4.5 mmol) and benzyl iodide (1.57 g, 7.2 mmol) in THF (10 ml). The reaction mixture was allowed to stir under nitrogen for 3 h at room temperature and was then concentrated in vacuo. The remaining slurry was treated with CH_2Cl_2 (10 ml) and extracted with three 25-ml portions of H_2O. The combined aqueous extracts were back extracted with three 25-ml portions of CH_2Cl_2. The organic solutions were combined, dried ($MgSO_4$), and concentrated and yielded 2.56 g of a thick yellow oil. A sample of analytically pure material was obtained by adsorption chromatography (column and preparative TLC).

Anal. Calcd for $C_{16}H_{17}IO_2$: C, 52.19; H, 4.65. Found: C, 52.03, 51.94; H, 4.67, 4.73.

Spectroscopic Data for 8. Ir (neat) 5.79 (C=O), 6.23 (C=C), 6.69 (C=C), 12.15 μ (nortricyclene skeleton);[5a–c] near ir (CH_2Cl_2) λ_{max} 1.656 μ (ϵ 1.155) (first CH stretching vibration overtone characteristic of nortricyclenes);[6] NMR ($CDCl_3$) δ 7.19 (m, 5 H), 3.90 (broad singlet, 1 H, H-5), 3.51 (s, 3 H, O=COCH$_3$), 2.85 (m, 2 H, –CH$_2$–), 2.5–1.2 (complex multiplets, 8 H).

Control: 3 and Iodomethane. A solution of 3 (0.254 g, 1.691 mmol) in THF (1.0 ml) was added to a solution of iodomethane (1.0 ml) in THF (1.0 ml). The reaction mixture was allowed to stir for 5 h at room temperature and was then concentrated in vacuo to 0.217 g of an oil identified by NMR analysis as unreacted 1-carbomethoxyquadricyclene (3).

Control: 3 and Benzyl Iodide. A solution of 3 (0.278 g, 1.85 mmol) in THF (1.0 ml) was added to a 2-ml solution of benzyl iodide (0.17 g, 0.78 mmol) in THF, and the resulting solution was allowed to stir for 5 h at room temperature in indirect light. The reaction mixture was then concentrated in vacuo and gave 0.370 g of an *oil*, determined by NMR analysis to be a 0.24:1.00 mol mixture of benzyl iodide and unreacted 1-carbomethoxyquadricyclene (3).

Reductive Deiodination of 6. A sample of crude 6 (2.73 g) was dissolved in methanol (20 ml) and heated in the presence of excess zinc dust for 4 days at 60 °C. The insoluble material was then removed by filtration, and the filtrate was concentrated at reduced pressure. The oil which remained was dissolved in ether (100 ml), washed with three 100-ml portions of dilute ammonium hydroxide, and reconcentrated to a light yellow oil (0.67 g). GLC analysis of the oil revealed at least eight components, the major component being 3-methyl-3-carbomethoxynortricyclene (7). A small quantity of 7 (0.049 g) was isolated by collection from the GLC column.

Anal. Calcd for $C_{10}H_{16}O_2$: C, 72.26; H, 8.49. Found: C, 72.17; H, 8.37.

Spectroscopic Data for 7. Ir (neat) 3.42 (CH), 3.27 (*weak* sh, cyclopropyl CH), 5.75 (ester C=O), 12.41 μ (nortricyclene skeleton); NMR ($CDCl_3$, 60 MHz) δ 3.65 (s, O=COCH$_3$), 1.12 (s, C–CH$_3$), 2.5–0.7 (complex multiplets fused into C–CH$_3$ singlet at high end); NMR ($CDCl_3$, 300 MHz) δ 3.67 (s, O=COCH$_3$), 1.15 (s, C–CH$_3$), 1.27 (~8-line multiplet, 6 H), 1.47, 1.65 (pair of doublets, ~1:4 relative intensity, $J \sim 2$ Hz, 1 H), 1.93, 2.22, 2.41 (three singlets, ~4:1:1 relative intensity, 1 H).

Reductive Deiodination of 8. A sample of crude 8 (7.27 g) was dissolved in methanol (35 ml) and heated in the presence of zinc dust (2 g) for 24 h at 60 °C. The cooled mixture was then filtered, and 1.0 g of gray solid was removed. The filtrate was concentrated to a viscous yellow oil which was redissolved in methanol. The resulting solution was cooled, and an off-white solid (presumably ZnI_2) precipitated which was then removed by filtration (yield 0.87 g). This procedure was repeated until precipitation was no longer significant. The final crude oil was treated with water (20 ml) and extracted once with ether (30 ml). The ether solution was isolated, dried, and concentrated and gave 2.10 g of a yellow oil, GLC analysis of which revealed at least 20 components, many of them minor. The major component (~30% relative peak area), 3-carbomethoxy-3-benzylnortricyclene (**9**), was collected in small quantity from the GLC column, and eventually it solidified (mp 38.0–39.5 °C). A sample of analytical purity was obtained by distillation of the crude product (~40 °C 0.05 mm) which yielded a white semisolid. The distilled material was vacuum pumped (room temperature, 0.05 mm) in a sublimator, and that semisolid which remained in the sublimator gave the correct CH analysis.

Anal. Calcd for $C_{16}H_{18}O_2$: C, 79.34; H, 7.43. Found: C, 79.01; H, 7.58.

Spectroscopic Data for 9. Ir (neat) 3.32 (sh, cyclopropyl CH), 3.44 (CH), 5.77 (C=O), 12.40 μ (nortricyclene skeleton); NMR ($CDCl_3$, 300 MHz) δ 1.07–1.43 (complex multiplet, 6 H), four sharp resonances at 1.85, 1.88, 2.05, 2.16 (2 H), 2.78 (AB quartet, $-CH_2-$ adjacent to an asymmetric center), 3.50 (s, $O{=}COCH_3$), 6.97–7.27 (complex aromatic multiplet, 5 H). Minor impurites were observed in the spectrum.

Registry No.—**3**, 24161-47-5; **4**, 57951-46-9; **6**, 57951-47-0; **7**, 57951-48-1; **8**, 57951-49-2; **9**, 57951-50-5; lithium iodide, 10377-51-2; iodomethane, 74-88-4; benzyl iodide, 620-05-3.

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Preparation of Aroylbenzoic Acid. Reaction of Aryllithium Reagents with Phthalic Anhydride[1]

William E. Parham* and R. M. Piccirilli

Paul M. Gross Chemical Laboratory, Duke University,
Durham, North Carolina 27706

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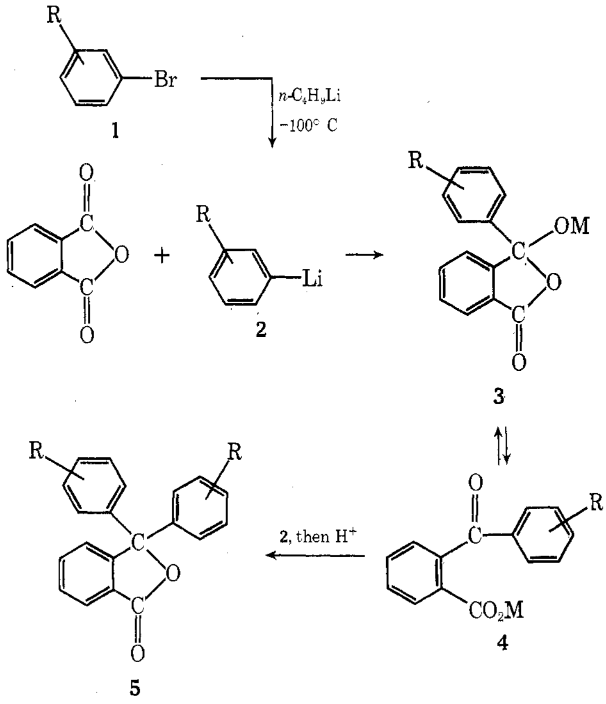
The preparation of a benzoylbenzoic acid by reaction of Grignard reagents with phthalic anhydride[2-4] offers advantages over the usual synthesis involving phthalic anhydride, aromatic hydrocarbons, and aluminum chloride in that isomers can be obviated when substituted aromatic compounds are employed. The method is limited, however, since Grignard reagents cannot be employed if the aromatic system contains functional groups that react with Grignard reagents. Since it has been shown[5-8] that organolithium reagents can be prepared at low temperature by halogen–metal exchange of aryl bromides substituted with groups normally reactive toward Grignard reagents (COO^-, CN, NO_2), the reaction of aryllithium reagents with phthalic anhydride has been examined as a route to *o*-benzoylbenzoic acids substituted with cyano functions. Previously, there has been little work related to the reaction of aryllithium with phthalic anhydride. Wittig and Leo report[9] that the reaction of phenyllithium with phthalic anhydride gives only a resinous compound and triphenylcarbinol, while Wilson reported an unworkable oil from which some diphenylphthalide[10] was isolated by distillation.

The reaction of organometallic reagents with phthalic anhydride is thought to proceed as shown in Scheme I. The products are generally *o*-benzoylbenzoic acids (**4**) and/or phthalides (**5**). Initially it was hoped that at low temperature, the equilibrium between the lithium salts **3** and **4** might favor **3**, which would obviate the necessity of employing inverse addition and/or an excess of phthalic anhydride to minimize phthalide (**5**) formation.[3] However, preliminary experiments using phenyllithium showed that this was not the case. When phthalic anhydride (1 equiv) was added to phenyllithium (1 equiv) at −78 °C the yield of phthalide **5a** was 78% base on phenyllithium. When the same ratios were maintained but the order of addition reversed, the yield of isolated phthalide **5a** was 9% while the yield of *o*-benzoylbenzoic acid was 35%. Furthermore, the yield of *o*-benzoylbenzoic acid was further increased (55%) when excess (2 equiv) of phthalic anhydride was employed.

Scheme I



a, R = H
b, R = OCH_3 (ortho)
c, R = CN (ortho)
d, R = CN (meta)
e, R = CN (para)
f, R = NO_2 (ortho)

In subsequent experiments, the aryllithium reagent was added rapidly to 2 equiv of phthalic anhydride in tetrahydrofuran at −100 °C. Reasonably good yields of substituted benzoylbenzoic acids were obtained; the results are summarized in Table I.

Table I. Reactions of Aryllithium Derivatives with Phthalic Anhydride

Aryl halide	Product[f]	Yield, %	Mp, °C
o-$CH_3OC_6H_4Br$ (**1b**)	**4b** (M = H)	70	142–144[a]
o-NCC_6H_4Br (**1c**)	**4c** (M = H)	87	146–147[b]
m-NCC_6H_4Br (**1d**)	**4d** (M = H)	60	175–176[c]
p-NCC_6H_4Br (**1e**)	**4e** (M = H)	71	179–186[d]
o-$O_2NC_6H_4Br$ (**1f**)	**4f** (M = H)	43	174–176[e]

[a] Lit.[4] 145–146 °C from CH_3COOH. [b] From H_2O. [c] From ethanol. [d] From ethanol-water. [e] From $CHCl_3$. [f] Satisfactory analytical data (±0.3% for C, H, N) for all new compounds were submitted for review.