The Reaction of Arylmagnesium Bromides with *N*-(ω-Bromoalkyl)phthalimides

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The reaction of the *N*-(ω-bromoalkyl)phthalimides, **1** and **2**, with a series of arylmagnesium bromides in tetrahydrofuran yielded the corresponding oxazoloisoindoles **4a-4h** and oxazinoisoindoles **5a-5f**. At low temperatures, phenylmagnesium bromide, on treatment with **1** and **2**, yielded the open-chain alcohols, **7** and **8**. With **3**, phenylmagnesium bromide yielded the corresponding alcohol **9** under any conditions utilized.

In several cases, the products isolated from the reaction of **1** with arylmagnesium bromides were shown to depend on the order of addition, with monoarylated oxazoloisoindoles **4c** and **4d** being formed when the Grignard reagent was added to **1**, and triarylated products **10a** and **10b** formed when the order of addition was reversed. A further triarylated product **10c** was also obtained by the latter method.

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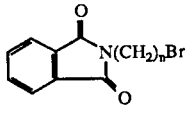
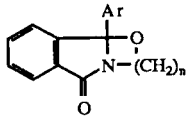
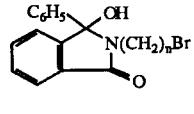
It has been shown that phenyllithium reacts with the *N*-(ω-bromoalkyl)phthalimides **1**, **2**, and **3**, to yield respectively the oxazoloisindole, **4a**, the oxazinoisoindole, **5a**, and the oxazepinoisoindole, **6a** [1]. In view of the reported anticonvulsant and antiinflammatory activity of these heterocycles [2], we decided to investigate the reaction of arylmagnesium bromides with **1**, **2**, and **3** as a more convenient means of effecting cyclization and as a method of preparing a variety of arylated derivatives in the **4**, **5** and **6** series.



1, n = 2
2, n = 3
3, n = 4



4a, n = 2, Ar = C_6H_5
4b, n = 2, Ar = *p*-FC_6H_4
4c, n = 2, Ar = *p*-$CH_3C_6H_4$
4d, n = 2, Ar = *m*-$CH_3C_6H_4$
4e, n = 2, Ar = *m*-ClC_6H_4
4f, n = 2, Ar = 3,5-$Cl_2C_6H_3$
4g, n = 2, Ar = *p*-$C_6H_5C_6H_4$
4h, n = 2, Ar = *p*-*t*-BuC_6H_4
5a, n = 3, Ar = C_6H_5
5b, n = 3, Ar = *p*-FC_6H_4
5c, n = 3, Ar = *p*-$CH_3C_6H_4$
5d, n = 3, Ar = *m*-$CH_3C_6H_4$
5e, n = 3, Ar = *p*-*t*-BuC_6H_4
5f, n = 3, Ar = *p*-$CH_3OC_6H_4$
6a, n = 4, Ar = C_6H_5



7, n = 2
8, n = 3
9, n = 4

When *N*-(2-bromoethyl)phthalimide (**1**) is added to phenylmagnesium bromide in tetrahydrofuran, formation of the tricyclic product (**4a**) occurs readily. Yields of up to 69% of isolated product were obtained when addition occurred at −10° and the mixture was allowed to rise to room temperature slowly before work-up. The yield was somewhat less (60%) when addition occured at room temperature and was followed by a one-hour reflux period. The yield rose to 75%, however, when the room temperature addition was followed by a two-hour reflux period, and to 82% with a four-hour reflux.

When **1** was added to phenylmagnesium bromide at −78° and the mixture allowed to rise slowly to room temperature, the only product which could be isolated was the corresponding alcohol, **7**, (36% yield).

Treatment of phenylmagnesium bromide with *N*-(3-bromopropyl)phthalimide (**2**) at room temperature followed by a reflux period of four hours gave a 43% yield of the tricylic product, **5a**. Reversing the order of addition did not increase the yield significantly (45%). If the reflux period was omitted, mixtures of products were obtained from which no pure substance could be isolated. Addition at −20° with no subsequent reflux gave a 62% yield of **8**.

The alcohols **7** and **8** have been previously prepare by Kohn and Lakner [3] by treatment of **1** and **2** respectively with phenylmagnesium bromide in ether solution. They subsequently obtained **4a** and **5a** in a separate step by cyclization of **7** and **8** with sodium ethoxide in ethanol. Our procedure is a one-step alternative for the preparation of the tricyclic products.

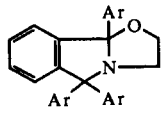
When *N*-(4-bromobutyl)phthalimide (**3**) was added to phenylmagnesium bromide, the only product which could be isolated, regardless of temperature of addition or length of subsequent reflux period, was **9**. The best yield (59%) of **9** was obtained when addition occurred at −10° with no subsequent reflux period.

In contrast, according to Torian and Braun [1], **3**, when treated with phenyllithium yields the cyclized product, **6a**.

The formation of **4a** and **5a** in moderate to good yields encouraged us to study further cyclizations of **1** and **2** utilizing a series of arylmagnesium bromides under similar conditions.

Addition of **1** to *p*-fluorophenylmagnesium bromide (room temperature addition, 4 hour reflux) resulted in a

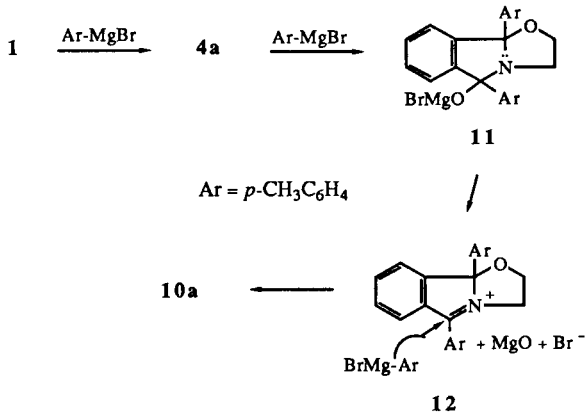
42% yield of **4b**. However, when **1** was added to *p*-tolylmagnesium bromide, a triarylated oxazoloisoindole, **10a**, was the only product which could be isolated (28%).



10a, Ar = *p*-$CH_3C_6H_4$
10b, Ar = *m*-$CH_3C_6H_4$
10c, Ar = *p*-$CH_3OC_6H_4$

The yield of **10a** was increased to 73% when a 3:1 ratio of *p*-tolylmagnesium bromide to the phthalimide **1** was utilized. A probable mechanism for the formation of **10a** is indicated in Scheme I. The initial cyclization to **4a** is followed by an attack of the Grignard reagent on the remaining carbonyl group to form a magnesium salt, **11**, which loses an oxygen atom to form the iminium salt, **12**, as an intermediate. An attack by **12** on another molecule of the arylmagnesium halide yields the product, **10a**.

Scheme I



Similarly, **10b** and **10c** were formed in 59% and 32% yields respectively when **1** was added to tetrahydrofuran solutions of *m*-tolylmagnesium bromide and *p*-methoxyphenylmagnesium bromide.

To avoid triarylation, the order of addition was reversed. The addition of each of a series of arylmagnesium bromides to the phthalimide, **1**, led to the formation of the corresponding oxazoloisoindoles **4c** through **4h** in moderate yields.

In the same manner, a sequence of oxazinoisoindoles **5b** through **5f** was obtained by the addition of the corresponding arylmagnesium bromides to **2**.

Attempts to prepare triarylated oxazinoisoindoles corresponding to the oxazoloisoindoles **10a**, **10b**, and **10c** were unsuccessful.

EXPERIMENTAL

Melting points were determined in capillary tubes using either a Thomas-Hoover or Mel-Temp apparatus. Elemental analyses were performed by Desert Analytics, Tucson, Arizona and Galbraith Laboratories, Inc., Knoxville, Tennessee. The ^{13}C-nmr spectra were recorded on a Varian XL300 spectrometer (Department of Chemistry and Biochemistry, Utah State University, Logan, Utah). The ^{1}H-nmr spectra were recorded as specified on a Varian XL300 spectrometer (300 MHz) or a Varian EM360L spectrometer (60 MHz). All nmr spectra were determined in deuteriochloroform solution unless otherwise indicated and are reported in parts per million (δ) downfield from internal TMS. Infrared spectra were recorded on a Perkin-Elmer 283B spectrometer and were obtained from potassium bromide pellets unless otherwise specified. A mass spectrum was obtained on a Hewlett Packard 5995 Gas Chromatograph Mass Spectrometer (American Microsystems, Inc., Pocatello, Idaho). Dry tetrahydrofuran was obtained by distillation from sodium benzophenone ketyl.

2,3-Dihydro-9b-phenyloxazolo[2,3-*a*]isoindol-5(9b*H*)-one (**4a**).

A solution of phenylmagnesium bromide was prepared under dry nitrogen by the addition of 3.86 g (24.5 mmoles) of bromobenzene to 583 mg (24 mmoles) of magnesium and 15 ml of supernatant tetrahydrofuran. The resulting Grignard reagent was kept at room temperature by means of a water bath and stirred as a solution of 5.6 g (22 mmoles) of *N*-(2-bromoethyl)phthalimide (**1**) was added *via* syringe over a period of 20 minutes. The color on addition first became blue-green, changing to brownish-green as addition was completed. The mixture was heated under reflux for four hours and allowed to stand overnight. The mixture, containing a white solid, was added to 250 ml of 1 *M* ammonium chloride. It was extracted with 150 ml of methylene chloride. After dilution with 150 ml more solvent, the methylene chloride solution was washed with water and dried over magnesium sulfate and the solvent removed. The remaining white solid was recrystallized from 95% ethanol, yield 4.5 g (82%), mp 146-147°, lit [4] mp 147-149°. An ir spectrum was consistent with that reported in the literature [4].

2,3-Dihydro-9b-(*p*-fluorophenyl)oxazolo[2,3-*a*]isoindol-5(9b*H*)-one (**4b**).

This was prepared under the same conditions as **4a**. The reaction mixture obtained on treatment of the Grignard reagent prepared from 5.6 g (25 mmoles) of *p*-bromofluorobenzene and 4.2 g (22 mmoles) of **1** was poured into 1 *M* ammonium chloride. The mixture was extracted with ether. After drying (magnesium sulfate) the ether was removed and the residue recrystallized from 95% ethanol. The yield was 2.50 g (42%); ir: 1730 (C=O), 1044 (C-O) cm^{-1}; ^{1}H-nmr: (60 MHz) δ 2.94-3.60 (m, 1H, NCH_A), 3.80-4.60 (m, 3H, CH_2O and NCH_B) [4], 6.90-8.10 (m, 8H, ArH).

Anal. Calcd. for $C_{16}H_{12}FNO_2$: C, 71.37; H, 4.49; N, 5.20. Found: C, 71.40; H, 4.44; N, 5.11.

3,4-Dihydro-10b-phenyl-2*H*-[1,3]oxazino[2,3-*a*]isoindol-6-(10b*H*)-one (**5a**).

This was prepared in the same manner as **4a** except that ether rather than methylene chloride was used for extraction. From the Grignard reagent (prepared from 0.58 g, 24 mmoles, of magnesium and 3.9 g, 24 mmoles, of bromobenzene) and 5.9 g (22 mmoles) of **2** was obtained 2.0 g (43%) of product, mp 127-128°

(recrystallized from 95% ethanol), lit [4], 128-130°. The ir and ^{1}H-nmr spectra were also consistent with that reported in the literature [4].

2-(2-Bromoethyl)-2,3-dihydro-3-hydroxy-3-phenyl-1*H*-isoindol-1-one (**7**).

Phenylmagnesium bromide, prepared as above from 0.73 g (30 mmoles) of magnesium and 4.8 g (30 mmoles) of bromobenzene, was cooled in a dry ice-acetone bath and treated with a solution of 7.1 g (28 mmoles) of **1** in 50 ml of tetrahydrofuran with stirring under dry nitrogen. The mixture was allowed to reach room temperature overnight. It was poured into 1 *M* ammonium chloride and extracted several times with ether. The ether portions were combined and dried over magnesium sulfate. The solvent was removed and the remaining oil crystallized from 95% ethanol, yield 3.32 g, 36%, mp 187-190°, lit [3] 189-191°; ir: 3180 (OH), 1680 (C=O), 1485, 1462, 1408, 1230, 1201, 1062, 939, 772, 762, 702 cm^{-1}; ^{1}H-nmr (hexadeuteriodimethyl sulfoxide + deuteriochloroform): (60 MHz) δ 3.2-4.1 (m, 5H, CH_2CH_2, OH), 7.2-8.0 (m, 9H, ArH).

2-(3-Bromopropyl)-2,3-dihydro-3-hydroxy-3-phenyl-1*H*-isoindol-1-one (**8**).

Phenylmagnesium bromide, prepared from 0.73 g (30 mmoles) of magnesium and 4.8 g (30 mmoles) of bromobenzene was cooled in an ice-methanol bath to −20°. To the mixture, stirred under dry nitrogen, was added (over a period of 20 minutes) a solution of 7.5 g (28 mmoles) of **2** dissolved in 50 ml of dry tetrahydrofuran. Stirring and cooling (−20° to −11°) was continued for *ca.* 7 hours. It was then stirred overnight as the mixture was allowed to reach room temperature. Work-up and isolation as described for **7** yielded 6.0 g (62%) of white crystals, mp 168-171°, lit [3], 169-171°; ir: 3230 (OH), 1680 (C=O), 1485, 1450, 1418, 1270, 1200, 1060, 940, 865, 778, 762, 709 cm^{-1}; ^{1}H-nmr (hexadeuteriodimethyl sulfoxide + deuteriochloroform): (60 MHz) δ 2.05 (quintet, 2H, $CH_2CH_2CH_2$), 2.8-3.8 (m, 5H, CH_2Br, CH_2N, OH), 7.1-7.9 (m, 9H, ArH).

2-(4-Bromobutyl)-2,3-dihydro-3-hydroxy-3-phenyl-1*H*-isoindol-1-one (**9**).

Phenylmagnesium bromide, prepared from 0.32 g (13 mmoles) of magnesium and 2.0 g (13 mmoles) of bromobenzene, was cooled to −10° in an ice-acetone bath under dry nitrogen. To the stirred mixture was added over a period of 10 minutes a solution of 3.0 g (11 mmoles) of **4** in 25 ml of tetrahydrofuran. After stirring and cooling for 10 hours, the mixture was allowed to reach room temperature. The product was isolated in the same manner as was **7**. There was obtained 2.34 g (59%) of white crystals mp 118-119° (recrystallized from 95% ethanol); ir: 3240 (OH), 1684 (C=O), 1471, 1450, 1418, 1196, 1061, 770, 759, 705, cm^{-1}; ^{1}H-nmr (hexadeuteriodimethyl sulfoxide + deuteriochloroform): (60 MHz) δ 1.4-2.0 (m, 4H, $CH_2CH_2CH_2CH_2$), 2.9-3.7 (m, 5H, CH_2Br, CH_2N, OH), 7.1-8.0 (m, 9H, ArH).

Anal. Calcd. for $C_{18}H_{18}BrNO_2$: C, 60.01; H, 5.04; N, 3.89. Found: C, 60.18; H, 4.72; N, 3.87.

2,3-Dihydro-5,5,9b-tri(*p*-methylphenyl)oxazolo[2,3-*a*] (9b*H*)isoindole (**10a**).

A solution of **1** (1.85 g, 7.3 mmoles) in tetrahydrofuran (50 ml) was added to a solution of *p*-tolymagnesium bromide (prepared from 4.2 g, 25 mmoles, of *p*-bromotoluene and 0.68 g, 28 mmoles, of magnesium) in tetrahydrofuran (*ca.* 20 ml) dropwise at room temperature under dry nitrogen. The mixture was heated under reflux for 4 hours and allowed to cool with overnight stirring. It was poured into 1 *M* ammonium chloride (250 ml), extracted with ether, dried with magnesium sulfate and the solvent removed. The residue was recrystallized from 95% ethanol (difficultly soluble) to yield 2.30 g, (73%) of product mp 179-181°. The ir shows no carbonyl band; ^{1}H-nmr: (300 MHz) δ 2.31 (s, 3H, CH_3 on *p*-tolyl ring attached to C-9b), 2.37 and 2.38 (overlapping singlets, 6H, CH_3 groups on *p*-tolyl rings attached to C-5), 2.71 (m, 1H), 3.11 (m, 2H) and 3.48 (m, 1H) all from OCH_2CH_2N, 6.8-7.9 (m, 16H, ArH); ^{13}C-nmr: δ 20.98 (overlapping CH_3 groups of *p*-tolyl rings attached to C-5), 21.14 (CH_3 of *p*-tolyl ring attached to C-9b), 45.77 (CH_2N), 66.14 (CH_2O), 78.40 (C-5), 107.21 (C-9b); 123.74, 124.10, 126.99, 127.83, 127.91, 128.58, 128.66, 129.22, 130.56, 136.39, 136.94, 137.13, 140.72, 141.42, 142.18, 143.77, 147.02 (aromatic).

Anal. Calcd. for $C_{31}H_{29}NO$: C, 86.27; H, 6.77; N, 3.25. Found: C, 85.94; H, 6.85; N, 3.16.

2,3-Dihydro-5,5,9b-tri(*m*-methylphenyl)oxazolo[2,3-*a*] (9b*H*)isoindole (**10b**).

This compound was prepared in the same manner as **10a**. Addition of 7.3 mmoles of **1** to the Grignard reagent prepared from 25 mmoles of *m*-bromotoluene yielded 1.86 g (59%) of product, mp 161-162° (from 95% ethanol in which it was difficultly soluble). The ir lacked a carbonyl band; ^{1}H-nmr (60 MHz) δ 2.20 (s, 3H, CH_3 of *p*-tolyl ring attached to C-9b), 2.33 and 2.37 (overlapping singlets, 6H, CH_3 groups of *p*-tolyl rings attached to C-5), 2.60-3.90 (m, 4H, OCH_2CH_2N), 6.7-8.1 (m, 16H, ArH); ^{13}C-nmr:δ 21.50 and 21.60 (CH_3 groups of *p*-tolyl rings attached to C-5), 21.82 (CH_3 group of *p*-tolyl ring attached to C-9b), 45.82 (CH_2N), 66.19 (CH_2O), 78.85 (C-5), 107.25 (C-9b), 123.76, 124.15, 124.28, 125.24, 127.14, 127.59, 127.73, 127.83, 127.91, 128.04, 128.29, 128.64, 129.23, 131.22, 136.71, 137.33, 141.46, 143.66, 145.00, 146.65, 146.78 (aromatic); ms: for all peaks of m/e >100 (70 eV) 431 (6, M^+), 401 (13, $M^+ - CH_2O$), 400 (21), 341 (25), 340 (100, $M^+ - C_7H_7$), 178 (6), 119 (15).

Anal. Calcd. for $C_{31}H_{29}NO$: C, 86.27; H, 6.77; N, 3.25. Found: C, 86.10; H, 6.92; N, 3.15.

2,3-Dihydro-5,5,9b-tri(*p*-methoxyphenyl)oxazolo[2,3-*a*] (9b*H*)isoindole (**10c**).

This compound was prepared in the same manner as **10a**. From 7.3 mmoles of **1** and the Grignard reagent prepared from 25 mmole of *p*-bromoanisole, there was obtained 1.12 g (32%) of product, mp 198.5-201.5° recrystallized from ethyl acetate. The ir showed strong bands at 1251 and 1035 cm^{-1} (C-O) but no carbonyl band; ^{1}H-nmr: (300 MHz) δ 2.68 (m, 1H), 3.12 (m, 2H) and 3.50 (m, 1H) all three signals from OCH_2CH_2N, 3.78 (s, 3H, OCH_3 of the *p*-anisyl ring attached to C-9b), 3.80 and 3.81 (overlapping singlets, 6H, OCH_3 groups attached to C-5), 6.65-9.30 (m, 16H, ArH); ^{13}C-nmr: δ 45.77 (CH_2N), 55.16, 55.21 and 55.26 (all three signals from OCH_3 groups), 66.09 (CH_2O), 77.8 (C-5), 107.04 (C-9b), 112.48, 113.19, 113.28, 123.74, 124.02, 127.81, 128.20, 129.01, 129.23, 131.79, 135.72, 137.26, 138.85, 141.27, 147.18, 158.52, 158.63, 159.08 (aromatic).

Anal. Calcd. for $C_{31}H_{29}NO_4$: C, 77.64; H, 6.09; N, 2.92. Found: C, 77.30; H, 6.11; N, 2.80.

2,3-Dihydro-9b(*p*-methylphenyl)oxazolo[2,3-*a*]isoindol-5(9b*H*)-one (**4c**).

A Grignard reagent was prepared under dry nitrogen by the

addition of 4.2 g (25 mmoles) of *p*-bromotoluene to 0.68 g (28 mmoles) of magnesium and *ca.* 15 ml of supernatant tetrahydrofuran. The solution of Grignard reagent was then added with stirring under dry nitrogen over a 20 minute period to a solution of *N*-(2-bromoethyl)phthalimide (5.6 g, 22 mmoles) in *ca.* 25 ml of tetrahydrofuran held at room temperature by means of a water bath. After addition was complete, the mixture was heated under reflux for four hours and then stirred at room temperature overnight. It was poured into 1 *M* ammonium chloride and extracted with ether. The ether solution was washed with water, dried over magnesium sulfate, and the solvent removed. The residue was recrystallized from 95% ethanol to yield 2.60 g (45%) of white crystals, mp 84-85°; ir: 1730 (C=O), 1023 (C-O); ^{1}H-nmr: (300 MHz) δ 2.33 (s, 3H, CH_3), 3.21 (m, 1H), 4.07 (m, 2H), 4.33 (m, 1H) all three signals from OCH_2CH_2N, [4], 7.10-8.79 (m, 8H, ArH). ^{13}C-nmr: δ 20.83 (CH_3), 41.10 (CH_2N), 69.71 (CH_2O), 99.97 (C-9b), 122.98, 123.73, 125.18, 128.00, 129.50, 130.66, 132.64, 134.42, 138.12, 146.37 (all aromatic), 173.32 (C=O).

Anal. Calcd. for $C_{17}H_{15}NO_2$: C, 76.96; H, 5.70; N, 5.28. Found: C, 76.77; H, 5.68; N, 5.20.

The following compounds were prepared similarly except where noted.

2,3-Dihydro-9b-(*m*-methylphenyl)oxazolo[2,3-*a*]isoindol-5(9b*H*)-one (**4d**).

Treatment of 22 mmoles of **1** with the Grignard reagent prepared from 25 mmoles of *m*-bromotoluene yielded an oil. Upon distillation, there was obtained 4.65 g (80%) of **4d** collected at 174-176°/30 μ Hg; ir (neat): 1720 (C=O), 1044 (C-O), cm^{-1}; ^{1}H-nmr: (300 MHz) δ 2.36 (s, 3H, CH_3), 2.65 (m, 1H), 4.10 (m, 2H), 4.38 (m, 1H) all three signals from OCH_2CH_2N, 7.10-7.85 (m, 8H, ArH); ^{13}C-nmr: δ 21.15 (CH_3), 41.52 (CH_2N), 70.10 (CH_2O), 100.32 (C-9b), 122.67, 123.41, 124.13, 126.16, 128.55, 129.41, 129.89, 131.02, 133.00, 137.73, 138.36, 146.67 (aromatic), 173.68 (C=O).

Anal. Calcd. for $C_{17}H_{15}NO_2$: C, 76.96; H, 5.70; N, 5.28. Found: C, 77.23; H, 5.66; N, 5.11.

2,3-Dihydro-9b-(*m*-chlorophenyl)oxazolo[2,3-*a*]isoindol-5(9b*H*)-one (**4e**).

Addition of the Grignard reagent prepared from 25 mmoles of *m*-chlorobromobenzene to 22 mmoles of **1** yielded 2.3 g (40%) of **4e**, mp 106-108° (from 95% ethanol); ir: 1710 (C=O), 1040 (C-O) cm^{-1}; ^{1}H-nmr: (60 MHz) δ 2.90-3.55 (m, 1H, NCH_A), 3.60-4.60 (m, 3H, CH_2O and NCH_B) [4]; ^{13}C-nmr: δ 41.23 (CH_2N), 69.87 (CH_2O), 99.36 (C-9b), 123.00, 123.52, 123.91, 125.50, 128.49, 129.66, 129.82, 130.53, 132.83, 134.29, 139.89, 145.70, (aromatic), 173.14 (C=O).

Anal. Calcd. for $C_{16}H_{12}ClNO_2$: C, 67.25; H, 4.23; N, 4.90. Found: C, 66.96; H, 4.32; N, 4.71.

2,3-Dihydro-9b-(3,5-dichlorophenyl)oxazolo[2,3-*a*]isoindol-5(9b*H*)-one (**4f**).

Addition of the Grignard reagent prepared from 25 mmoles of 1-bromo-3,5-dichlorobenzene to 22 mmoles of **1** yielded 3.20 g (45%) of **4f**, mp 161-162° (from 95% ethanol); ir: 1720 (C=O), 1050 (C-O) cm^{-1}; ^{1}H-nmr: (60 MHz) δ 2.90-3.70 (m, 1H, NCH_A), 3.75-4.60 (m, 3H, OCH_2 and NCH_B) [4], 7.10-8.10 (m, 7H, ArH).

Anal. Calcd. for $C_{16}H_{11}Cl_2NO_2$: C, 60.02; H, 3.46; N, 4.37. Found: C, 59.92; H, 3.39; N, 4.30.

2,3-Dihydro-9b-(*p*-biphenylyl)oxazolo[2,3-*a*]isoindol-5(9b*H*)-one (**4g**).

Addition of the Grignard reagent prepared from 24 mmoles of *p*-bromobiphenyl to 22 mmoles of **1** yielded 2.60 g (36%) of **4g**, mp 133-135° (from 95% ethanol); ir: 1720 (C=O), 1045 (C-O) cm^{-1}; ^{1}H-nmr: (60 MHz) δ 2.91-3.60 (m, 1H, NCH_A), 3.70-4.50 (m, 3H, OCH_2 and NCH_B) [4], 7.10-8.00 (m, 13H, ArH).

Anal. Calcd. for $C_{22}H_{17}NO_2$: C, 80.71; H, 5.23; N, 4.28. Found: C, 80.64; H, 5.17; N, 4.21.

2,3-Dihydro-9b-(*p*-*t*-butylphenyl)oxazolo[2,3-*a*]isoindol-5(9b*H*)-one (**4h**).

Addition of the Grignard reagent prepared from 24 mmoles of *p*-*t*-butylbromobenzene to 22 mmoles of **1** yielded an oil. On distillation the product was collected as a fraction boiling at 194-195°/85 μ Hg, yield 2.1 g (31%). On standing several weeks the substance became a waxy solid; ir (neat): 1730 (C=O), 1044 (C-O) cm^{-1}; ^{1}H-nmr (60 MHz) δ 1.30 (s, 9H, *t*-Bu), 2.90-3.50 (m, 1H, NCH_A), 3.70-4.60 (m, 3H, CH_2O and NCH_B) [4], 6.90-8.00 (m, 8, ArH).

Anal. Calcd. for $C_{20}H_{21}NO_2$: C, 78.15; H, 6.89; N, 4.55. Found: C, 77.82; H, 6.76; N, 4.39.

2,3-Dihydro-10b-(*p*-fluorophenyl)-2*H*-[1,3]oxazino[2,3-*a*]isoindol-6(10b*H*)-one (**5b**).

After addition of the Grignard reagent prepared from 12 mmoles of *p*-bromofluorobenzene to 11 mmoles of **2**, the mixture was heated under reflux for 5.5 hours (rather than the usual 4 hours). There was obtained 1.84 g (56%) of **5b**, mp 161-164° (from 95% ethanol); ir: 1705 (C=O), 1060 (C-O) cm^{-1}; ^{1}H-nmr: (60 MHz) δ 1.10-2.30, (m, 2H, CCH_2C), 2.75-4.80 (m, 4H, CH_2O and CH_2N), 6.70-8.30 (m, 8H, ArH).

Anal. Calcd. for $C_{17}H_{14}FNO_2$: C, 72.07; H, 4.98; N, 4.94. Found: C, 72.32; H, 4.89; N, 4.93.

3,4-Dihydro-10b-(*p*-methylphenyl)-2*H*-[1,3]oxazino[2,3-*a*]isoindol-6(10b*H*)-one (**5c**).

Addition of the Grignard reagent prepared from 12 mmoles of *p*-bromotoluene to 11 mmoles of **2** yielded 2.10 g (68%) of **5c**, mp 157-159° (from 95% ethanol); ir: 1700 (C=O), 1058 (C-O), cm^{-1}; ^{1}H-nmr: (60 MHz) δ 1.00-2.10 (m, 2H, CCH_2C), 2.25 (s, 3H, CH_3), 2.80-4.80 (m, 4H, NCH_2 and OCH_2), 7.10-8.10 (m, 8H, ArH).

Anal. Calcd. for $C_{18}H_{17}NO_2$: C, 77.40; H, 6.13; N, 5.01. Found: C, 77.48; H, 6.03; N, 5.01.

3,4-Dihydro-10b-(*m*-methylphenyl)-2*H*-[1,3]oxazino[2,3-*a*]isoindol-6(10b*H*)-one (**5d**).

Addition of the Grignard reagent prepared from 12 mmoles of *m*-bromotoluene to 11 mmoles of **2** yielded 1.43 g (46%) of **5d**, mp 108-111° (from ether); ir: 1710 (C=O), 1036 (C-O) cm^{-1}; ^{1}H-nmr: (60 MHz) 1.15-2.10 (m, 2H, CCH_2C), 2.30 (s, 3H, CH_3), 2.80-4.70 (m, 4H, CH_2O and CH_2N), 7.00-8.05 (m, 8H, ArH).

Anal. Calcd. for $C_{18}H_{17}NO_2$: C, 77.40; H, 6,13; N, 5.01. Found: C, 77.66; H, 6.06; N, 4.91.

3,4-Dihydro-10b-(*p*-*t*-butylphenyl)-2*H*-[1,3]oxazino[2,3-*a*]isoindol-6(10b*H*)-one (**5e**).

Addition of the Grignard reagent prepared from 12 mmoles of *p*-bromo-*t*-butylbenzene to 11 mmoles of **2** yielded 1.67 g (47%) of **5e**, mp 121.5-124° (from ether-pentane); ir: 1710 (C=O), 1055 (C-O), cm^{-1}; ^{1}H-nmr: (60 MHz) δ 1.05-2.32 (m, 11H, singlet at 1.30 superimposed on a broad multiplet, *t*-butyl and CCH_2C), 2.80-4.70 (m, 4H, CH_2O and CH_2N), 7.00-8.00 (m, 8H, ArH).

Anal. Calcd. for $C_{21}H_{15}NO_2$: C, 78.47; H, 7.21; N, 4.36. Found:

C, 78.21; H, 7.22; N, 4.42.

3,4-Dihydro-10b-(*p*-methoxyphenyl)-2*H*-[1,3]oxazino[2,3-*a*]isoindol-6(10b*H*)-one (**5f**).

Addition of the Grignard reagent prepared from 12 mmoles of *p*-bromoanisole to 11 mmoles of **2** yielded the product as a thick oil. Upon distillation there was obtained 1.95 g (60%) of **5f** collected at 228°/50 μ Hg. The product became a yellow gum on standing. Bremner and Thirasasana [5] reported the preparation of **5f** by another method. Their product is also described as a yellow gum; ir (neat): 1703 (C=O), 1248 and 1035 (C-O), cm^{-1}; ^{1}H-nmr (60 MHz) δ 1.20-2.20 (m, 2H, CCH_2C), 2.75-4.78 (m, 7H: singlet at 3.82, OCH_3 superimposed on a broad multiplet, from OCH_2 and NCH_2), 6.75-8.15 (m, 8H, ArH).

Anal. Calcd. for $C_{18}H_{17}NO_2$: C, 73.20; H, 5.80; N, 4.74. Found: C, 73.25; H, 5.82; N, 4.47.

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