SYNTHETIC COMMUNICATIONS®
Vol. 34, No. 5, pp. 853–861, 2004

A Practical Two-Step Synthesis of 3-Alkyl-2,3-dihydro-1*H*-isoindolin-1-ones

Yuan-Ping Ruan, Ming-De Chen, Ming-Zhu He, Xiang Zhou, and Pei-Qiang Huang*

Department of Chemistry, Xiamen University, Xiamen, Fujian, China

ABSTRACT

A flexible approach to 3-alkyl-2,3-dihydro-1*H*-isoindolin-1-ones via the reductive-alkylation procedure is described. Present method is versatile in scope, allowing the easy introduction of various C-3 carbon-substituents by Grignard addition to phthalimide.

Key Words: Isoindolin-1-one; Grignard reaction; Reductive alkylation; Phthalimide.

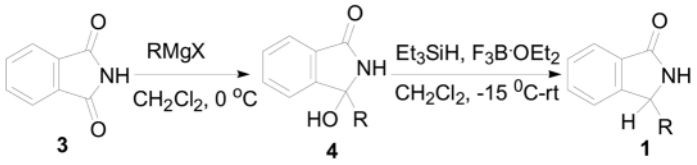
Due to the presence of 3-alkyl-2,3-dihydro-1*H*-isoindolin-1-ones (isoindolin-1-ones) as key structural units in a number of synthetic and natural bioactive molecules,[1] the chemistry of 3-alkyl-isoindolin-1-ones has attracted much current attention, and a number of valuable synthetic methods

*Correspondence: Pei-Qiang Huang, Department of Chemistry, Xiamen University, Xiamen, Fujian 361005, China; Fax: 86-592-2186400; E-mail: pqhuang@xmu.edu.cn.

DOI: 10.1081/SCC-120028358 0039-7911 (Print); 1532-2432 (Online)

have been developed.[2–5] Among them, the most flexible and straightforward ones are those where the 3-alkyl groups are introduced directly. This has been achieved either by the reaction of 3-metalated isoindolin-1-ones with electrophiles;[3] by the reaction of an *N*-acyliminium equivalent with nucleophiles;[4] by the reaction of methyl *o*-lithiobenzoate to imines,[5] or by organometallic reagents addition to phthalimide followed by reductive deoxygenation.[6] For the synthesis of *N*-unprotected 3-alkyl-2,3-dihydro-1*H*-isoindolin-1-ones,[6] recently reported two-step organolithiums addition-reductive deoxygenation procedure is the shortest route.[6a]

In connection with a program aimed at the development of asymmetric synthetic methodology based on the reductive alkylation of chiral nonracemic imides,[7] we have reported recently a versatile asymmetric approach to *N*-substituted 3-alkyl-isoindolin-1-ones,[8] we now wish to report herein that this two-steps approach is applicable to simple *N*-unprotected phthalimide.



Scheme 1.

Our method is displayed in Sch. 1. Treatment of commercially available phthalimide **3** with an excess of methyl magnesium iodide led to the desired α-hydroxylactam **4a** (Table 1, Entry 1) in a yield of 81%. Treatment of **4a** with

Table 1. Preparation of 3-alkyl-2,3-dihydro-1*H*-isoindolin-1-ones **1** via the reductive alkylation of phthalimide **3**.

Entry	RMgX (**2**)	Addition products (Yield, %)	Isoindolin-1-ones (Yield, %)
1	MeMgI	**4a** (81)	**1a** (65)
2	EtMgBr	**4b** (85)	**1b** (96)
3	*n*-PrMgBr	**4c** (92)	**1c** (75)
4	*n*-BuMgBr	**4d** (97)	**1d** (97)
5	*i*-BuMgBr	**4e** (77)	**1e** (55)
6	*n*-C_5H_{11}MgBr	**4f** (94)	**1f** (91)
7	*n*-C_7H_{15}MgBr	**4g** (96)	**1g** (96)
8	BnMgCl	**4h** (97)	**1h** (88)
9	PhMgBr	**4i** (88)	**1i** (90)

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016

triethylsilane[8] in the presence of boron trifluoride etherate afforded the desired deoxygenated product 3-methyl-2,3-dihydro-1*H*-isoindolin-1-one **1a** in 64% yield. Extension of the same procedure to other Grignard reagents led to the corresponding products **4b–h** and **1b–h** in good to excellent yields, except in the case of **1e**, where some dehydrated side-product was formed (40%). The successful preparation of 3-phenyl-2,3-dihydro-1*H*-isoindolin-1-one **1i** served to demonstrate that the present method can be extended to the preparation of 3-aryl-2,3-dihydro-1*H*-isoindolin-1-ones as well.

It is worth-mentioning that although the Grignard reagents addition to *N*-protected phthalimide[6a,10] is known for a long time, to the best of our knowledge, the direct Grignard reagents addition to *N*-unprotected phthalimide it-self and leading to the corresponding 3-alkyl-3-hydroxy-2,3-dihydro-1*H*-isoindolin-1-ones has not been reported (for Grignard addition to phthalimide see Ref.[11]). Comparing with an analogue method reported recently,[6b] the present method is more practical and versatile in view of the use of more easily available Grignard reagents instead of lithium reagents.[6b] In addition, the use of hazardous reagents such as HMPA and $NaBH_3CN$[6b] is avoided in the present method.

In summary, we have developed a flexible approach to 3-alkyl-2,3-dihydro-1*H*-isoindolin-1-ones via the reductive-alkylation procedure. This method is versatile in scope, since various C-3 carbon substituents can be introduced easily by Grignard reaction.

EXPERIMENTAL

Melting points were determined on a Yanaco M-500 micro melting point apparatus and the thermometer was uncorrected. IR spectra were obtained on a Nicholet Avatar 360 FT-IR spectrophotometer. ^{1}H NMR spectra were taken at a Varian Unity +500 spectrometer. Mass spectra were recorded on a Finnigan MAT-GCQ (direct injection, EI). Column chromatography was performed on silica gel H (Qingdao, 400 Mesh).

General Procedure for the Preparation of 3-Alkylisoindolin-1-ones and 3-Arylisoindolin-1-ones 1 by Reductive Alkylation of Phthalimide

To an ice-bath chilled solution of phthalimide (**3**) (1 mmol) in CH_2Cl_2 (10 mL) was added, under N_2, a Grignard reagent (3 mmol). After being stirred under the same temperature for 3 hr, the reaction was quenched by a saturated aqueous solution of NH_4Cl (6 mL). The resulting mixture was extracted with

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016

CH_2Cl_2 (3×10 mL). The combined organic phases were washed with brine, then dried (Na_2SO_4), filtered and concentrated. A short silica gel column filtration of the crude mixture [EtOAc-petroleum ether (60–90°C) = 2 : 1 as eluent] afforded **4**.

To a solution of **4** in dry CH_2Cl_2 (10 mL) was added successively triethylsilane (10.0 mmol) and trifluoroboron etherate (3.0 mmol) at −15°C under N_2. The mixture was allowed to stir at room temperature overnight. A saturated aqueous solution of $NaHCO_3$ (3 mL) was added, which was followed by CH_2Cl_2 extraction (3×6 mL). The combined organic layers were washed with brine, dried (Na_2SO_4), filtered and concentrated under reduced pressure. The crude was subjected to column chromatography purification on silica gel to afford **1**.

3-Methyl-2,3-dihydro-1*H*-isoindolin-1-one (1a)

Yield 65%. White crystal, mp 112–113°C (CH_2Cl_2) [Lit.[12] mp 112–114°C (DCM)]. R_f: 0.39 (AcOEt : PE = 1.5 : 1). IR (KBr, Pellet) ν_{max}: 3243, 2973, 2929, 1693, 1617, 1593, 1470, 1416, 1355, 1306, 1210, 1140, 1099 cm^{-1}. ^{1}HNMR (500 MHz, $CDCl_3$) δ: 1.51 (d, J = 6.7 Hz, 3H, CH_3), 4.54 (q, J = 6.7 Hz, 1H, CH_3CH), 6.90 (s, 1H, NH), 7.40–7.60 (m, 3H, Ar), 7.84 (d, 1H, Ar). MS (ESI, m/z): 148 ($M + H^+$, 100), 170 ($M + Na^+$, 77).

3-Ethyl-2,3-dihydro-1*H*-isoindolin-1-one (1b)

Yield 96%. White crystal, mp 105–106°C (CH_2Cl_2) [Lit.[13] mp 105°C]. R_f: 0.31 (AcOEt : PE = 1 : 1). IR (KBr, pellet) ν_{max}: 3208, 3081, 2968, 2929, 1689, 1615, 1593, 1468, 1423, 1361, 1305, 1206, 1140 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 0.96 (t, J = 7.4 Hz, 3H, CH_3), 1.66–1.78 (m, 1H, CH_2), 1.98–2.08 (m, 1H, CH_2), 4.61 (dd, J = 4.9, 6.9 Hz, 1H, NCH), 7.05 (s, 1H, NH), 7.42–7.60 (m, 3H, Ar), 7.84 (m, 1H, Ar). MS (ESI, m/z): 162 ($M + H^+$, 100), 163 [$(M + 2H)^+$, 11], 184 ($M + Na^+$, 7).

3-*n*-Propyl-2,3-dihydro-1*H*-isoindolin-1-one (1c)

Yield 75%. White crystal, mp 135–136°C (ether) [Lit.[14] mp 135–136°C (water)]. R_f: 0.48 (AcOEt : PE = 1 : 1). IR (KBr, pellet) ν_{max}: 3194, 3077, 2962, 2932, 2868, 1685, 1613, 1466, 1361, 1263, 1144 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 0.88 (t, J = 7.2 Hz, 3H, CH_3), 1.36–1.56 (m, 2H, CH_2CH_3), 1.60–1.98 (m, 2H, $CH_2CH_2CH_3$), 4.62–4.66 (dd, J = 4.4, 7.7 Hz,

Marcel Dekker, Inc.
270 Madison Avenue, New York, New York 10016

1H, NCH), 7.42–7.58 (m, 3H, Ar), 7.64–7.92 (brs, 1H, NH), 7.85 (m, 1H, Ar) ppm. MS (ESI, m/z): 176 ($M + H^+$, 100), 177 [$(M + 2H)^+$, 14], 198 ($M + Na^+$, 51), 351 [$(2M + H)^+$, 7], 373 [$(2M + Na)^+$, 17].

3-*n*-Butyl-2,3-dihydro-1*H*-isoindolin-1-one (1d)

Yield 97%. White crystal, mp 86–87°C (CH_2Cl_2) [Lit.[6a] mp 88–89°C]. R_f: 0.31 (AcOEt : PE = 1 : 1.5). IR (KBr, pellet) ν_{max}: 3226, 2956, 2931, 2861, 1696, 1616, 1468, 1418, 1359, 1310, 1141 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ: 0.90 (t, $J = 7.1$ Hz, 3H, CH_3), 1.22–1.50 (m, 4H, $2CH_2$), 1.60–1.70 (m, 1H, CH_2Pr), 1.92–2.00 (m, 1H, CH_2Pr), 4.61 (dd, 1H, $J = 4.6$, 7.7 Hz, NCH), 6.90 (s, 1H, NH), 7.40–7.62 (m, 3H, Ar), 7.85 (m, 1H, Ar) ppm. MS (ESI, m/z): 190 ($M + H^+$, 100), 191 [$(M + 2H)^+$, 12], 212 ($M + Na^+$, 4), 379 [$(2M + H)^+$, 8].

3-*iso*-Butyl-2,3-dihydro-1*H*-isoindolin-1-one (1e)

Yield 55%. White crystal, mp 176–177°C (CH_2Cl_2) [Lit.[15] mp 153°C (EtOH)]. R_f: 0.45 (AcOEt : PE = 1 : 1). IR (KBr, pellet) ν_{max}: 3192, 3074, 2957, 2922, 2863, 1683, 1613, 1469, 1363, 1268, 1209, 1142 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ: 1.00 (d, J = 6.5 Hz, 3H, CH_3), 1.06 (d, $J = 6.5$ Hz, 3H, CH_3), 1.46–1.53 (m, 1H, $CHCH_2$), 1.72–1.78 (m, 1H, $CHCH_2$), 1.79–1.88 (m, 1H, $CH(CH_3)_2$), 4.65 (dd, $J = 4.1$, 9.6 Hz, 1H, NCH), 6.64 (s, 1H, NH), 7.42–7.60 (m, 3H, Ar), 7.84 (m, 1H, Ar) ppm. MS (ESI, m/z): 190 ($M + H^+$, 100), 191 [$(M + 2H)^+$, 13], 212 ($M + Na^+$, 4).

3-*n*-Pentyl-2,3-dihydro-1*H*-isoindolin-1-one (1f)

Yield 91%. White crystal, mp 85–86°C (CH_2Cl_2). R_f: 0.48 (AcOEt : PE = 1 : 1). IR (KBr, pellet) ν_{max}: 3208, 3081, 2854, 2930, 1698, 1616, 1593, 1468, 1427, 1359, 1309, 1199, 1141 cm^{-1}. ^{1}HNMR (500 MHz, $CDCl_3$) δ: 0.88 (t, $J = 6.9$ Hz, 3H, CH_3), 1.24–1.38 (m, 5H, CH_2), 1.41–1.52 (m, 1H, CH_2), 1.58–1.70 (m, 1H, CH_2Bu), 1.90–1.98 (m, 1H, CH_2), 4.62 (dd, $J = 4.4$, 7.7 Hz, 1H, NCH), 7.01 (s, 1H, NH), 7.41–7.58 (m, 3H, Ar), 7.84 (m, 1H, Ar) ppm. MS (ESI, m/z): 204 ($M + H^+$, 100), 205 [$(M + 2H)^+$, 16], 407 [$(2M + H)^+$, 5].

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016

3-*n*-Heptyl-2,3-dihydro-1*H*-isoindolin-1-one (1g)

Yield 96%. White crystal, mp 71–72°C (ether). R_f: 0.52 (AcOEt : PE = 1.5 : 1). IR (KBr, pellet) ν_{max}: 3206, 3080, 2926, 2857, 1691, 1617, 1464, 1361, 1310, 1141 cm^{-1}. ^{1}HNMR (500 MHz, $CDCl_3$) δ: 0.86 (t, $J = 7.0$ Hz, 3H, CH_3), 1.22–1.34 (m, 9H, $(CH_2)_5$), 1.42–1.48 (m, 1H, CH_2), 1.60–1.68 (m, 1H, CH_2), 1.92–1.94 (m, 2H, CH_2), 4.60–4.64 (dd, $J = 4.6$, 7.5 Hz, 1H, NCH), 7.40–7.60 (m, 3H, Ar), 7.60–7.80 (brs, 1H, NH), 7.82 (m, 1H, Ar) ppm. MS (ESI, m/z): 232 ($M + H^+$, 100), 233 [$(M + 2H)^+$, 17], 463 [$(2M + H)^+$, 10], 485 [$(2M + Na)^+$, 3].

3-Benzyl-2,3-dihydro-1*H*-isoindolin-1-one (3h)

Yield 88%. White crystal, mp 134–135°C (CH_2Cl_2) [Lit.[16] mp 135–136°C (ether)]. R_f: 0.33 (AcOEt : PE = 1 : 1). IR (KBr, pellet) ν_{max}: 3202, 3079, 2917, 1693, 1615, 1557, 1359, 1274, 1141, 1074, 1022 cm^{-1}. ^{1}HNMR (500 MHz, $CDCl_3$) δ: 2.80 (dd, 1H, $J = 9.3$, 13.6 Hz, CH_2), 3.26 (dd, 1H, $J = 5.0$, 13.6 Hz, CH_2), 4.80 (dd, 1H, $J = 5.0$, 9.3 Hz, $CHCH_2$), 6.50 (s, 1H, NH), 7.20–7.38 (m, 6H, Ar), 7.44–7.60 (m, 2H, Ar), 7.84 (m, 1H, Ar) ppm. MS (ESI, m/z): 224 ($M + H^+$, 100), 225 [$(M + 2H)^+$, 17], 246 ($M + Na^+$, 3).

3-Phenyl-2,3-dihydro-1*H*-isoindolin-1-one (3i)

Yield 90%. White crystal, mp 206–208°C (CH_2Cl_2) [Lit.[17] mp 212°C (EtOH); Lit.[18] mp 218–220°C (EtOH)]. R_f: 0.53 (AcOEt : PE = 1.5 : 1). IR (KBr, pellet) ν_{max}: 3445, 3209, 3062, 2922, 2851, 1694, 1635, 1615, 1452, 1356, 1260, 1129, 1108, 1060, 1021 cm^{-1}. ^{1}HNMR (500 MHz, $CDCl_3$) δ: 5.62 (s, 1H, NCHPh), 6.72 (s, 1H, NH), 7.20–7.40 (m, 6H, Ar), 7.45–7.66 (m, 2H, Ar), 7.88 (m, 1H, Ar) ppm. MS (ESI, m/z): 210 ($M + H^+$, 100), 211 [$(M + 2H)^+$, 15], 232 ($M + Na^+$, 5).

ACKNOWLEDGMENT

We are grateful to the NNSC for financial support.

REFERENCES

1. (a) Belliotti, T.R.; Brink, W.A.; Kesten, S.R. Isoindolinone enantiomers having affinity for the dopamine D-4 receptor. Bioorg. Med. Chem. Lett. **1998**, *8*, 1499; (b) Wada, T.; Fukuda, N. Pharmacological profile of a new anxiolytic, DN-2327, effect of ro15-1788 and interaction with diazepam in rodents. Psychopharmacology **1991**, *103*, 314; (b) Fuchs, J.R.; Funk, R.L. Total synthesis of (+/−)-lennoxamine and (+/−)-aphanorphine by intramolecular electrophilic aroamatic substitution reaction of 2-amidoacroleins. Org. Lett. **2001**, *3*, 3923 (and references cited therein).
2. (a) Oppolzer, W.; Wills, M.; Kelly, M.J.; Signer, M.; Blagg, J. Chiral toulene-2, β-sultam auxiliaries: asymmetric Diels-Alder reactions of N-enoyl derivatives. Tetrahedron Lett. **1990**, *31*, 5015; (b) Luzzio, F.A.; Zacherl, D.P. Alkylation and annulation of 3-(phenylsulfonyl)-2-alkyl-2,3-dihydroisoindol-1-ones. Tetrahedron Lett. **1998**, *39*, 2285; (c) Koseki, Y.; Kusano, S.; Sakata, H.; Nagasaka, T. A new approach to isoindolobenzazepines via a ring-expansion of isoindolisoquinoline: synthesis of lennoxamine and chilenine. Tetrahedron Lett. **1999**, *40*, 2169; (d) Hunter, R.; Richards, P. Stereoselective tetrahydropyrido[2,1-*a*]isoindolone synthesis via carbaionic and radical intermediates: a model study for the Tacaman alkaloid D/E ring fusion. Tetrahedron Lett. **2000**, *41*, 3755; (e) Kundu, N.G.; Khan, M.W. Palladium-catalysed hetero-annulaion with terminal alkynes: a highly regio-and stereoselective synthesis of (*Z*)-3-aryl(alkyl)idene isoindolin-1-ones. Tetrahedron **2000**, *56*, 4777; (f) Epsztajn, J.; Jozwiak, A.; Koluda, P.; Sadokierska, I.; Wilkowska, I.D. Application of organolithium and related reagents in synthesis. Part 23: Synthetic strategies based on *ortho*-aromatic metallation. Synthesis of 4b-arylisondolo[2,1-*a*]quinoline derivatives. Tetrahedron **2000**, *56*, 4837; (g) Hoarau, C.; Couture, A.; Deniau, E.; Grandclaudon, P. A versatile synthesis of poly- and diversely substituted isoindolin-1-ones. Synthesis **2000**, 655.
3. (a) Couture, A.; Deniau, E.; Jonescu, D.; Grandclaudon, P. LDA-induced metalation of isoindolinones. An efficient route to 3-substituted isoindoline derivatives. Tetrahedron Lett. **1998**, *39*, 2319; (b) Deniau, E.; Enders, D. Synthesis of 3-alkyl-1-isoindolines by alkylation of a benzotriazolyl substituted *N*-dimethylamino-phthalimidine. Tetrahedron **2001**, *57*, 2581; (c) Pérard-Viret, J.; Prangé, T.; Tomas, A.; Royer, J. A simple and efficient aysmmetric synthesis of 3-alkyl-isoindolin-1-ones. Tetrahedron **2002**, *58*, 5103.

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016

4. Ukaji, Y.; Tsukamoto, K.; Nasada, Y.; Shimizu, M.; Fujisawa, T. Regulation of diastereofacial selection in the allylation reaction of *N*-acyliminium utilizing Lewis-acids. Chem. Lett. **1993**, 221.
5. (a) Campbell, J.B.; Dedinas, R.F.; Trumbower-Walsh, S.A. Addition of transiently-generated methyl *o*-lithiobenzanate to imines. An isoindolone annulation. J. Org. Chem. **1996**, *61*, 6205; (b) Enders, D.; Braig, V.; Raabe, G.A. Asymmetric synthesis of 3-aryl-substituted 2,3-dihydro-1H-isoindol-1-ones. Can. J. Chem. **2001**, *79*, 1528.
6. (a) Deniau, E.; Enders, D. A new simple and convenient synthesis of 3-substituted phthalimidines. Tetrahedron Lett. **2000**, *41*, 2347; (b) Wang, E.C.; Chen, H.F.; Feng, P.K.; Lin, Y.L.; Hsu, M.K. A new synthesis of 3-alkyl-isoindolinones. Tetrahedron Lett. **2002**, *43*, 9163.
7. (a) Huang, P.-Q.; Wang, S.-L.; Ye, J.-L.; Ruan, Y.-P.; Huang, Y.-Q.; Zheng, H. An easy access to protected (4S,5R)-5 alkyl-4-hydroxy-2-pyrrolidines and their use as versatile synthetic intermediates. Tetrahedron **1998**, *54*, 12547; (b) Huang, P.-Q.; Chen, Q.F.; Chen, C.-L.; Zhang, H.-K. Asymmetric synthesis of (−)-(*R*)-pyrrolam A starting from (*S*)-malic acid. Tetrahedron: Asymmetry **1999**, *10*, 3827.
8. Chen, M.-D.; He, M.-Z.; Ruan, Y.-P.; Huang, P.-Q. A versatile approach for the asymmetric synthesis of 3-alkyl-isoindolin-1-ones. Chin. J. Chem. **2002**, *20*, 1149.
9. Kursanov, D.N.; Parnes, Z.N.; Loim, N.M. Applications of ionic hydrogenation to organic synthesis. Synthesis **1974**, 633.
10. (a) Flitsch, von W. Zur umsetzung cyclischer imid mit allylmagnesium-bromid Liebigs 3-Formylmethylenepthalimidines. Ann. Chem. **1965**, *648*, 141; (b) Mueller, H.R.; Seefelder, M. Liebigs Ann. Chem. **1969**, *728*, 88; (c) Nishio, T.; Yamamoto, H. Preparation of 3-hydroxyisoindolin-1-ones and *O*-acylbenzamides, a study of ring–chain tautomerism. J. Heterocyclic Chem. **1995**, *32*, 883; (d) Pigeon, P.; Decroix, B. Benzothienoindolizidines via intramolecular aryl radical cyclization or palladium catalyzed cyclization. Tetrahedron Lett. **1996**, *37*, 7707.
11. (a) Beis, C. C. R. Acad. Sci., Paris **1904**, *138*, 988; (b) Beis, C. C. R. Acad. Sci., Paris **1904**, *139*, 62; (c) Kato, Y.; Takemoto, M.; Achiwa, K. Prostanoids and related-compounds 6. Synthesis of isoindolinone derivatives possesing inhibitory activity for thromboxane-A (2) analog (U-46619)-induced vasoconstriction. Chem. Pharm. Bull. **1993**, *41*, 2003.
12. Aeberli, P.; Houlihan, W.J. The lithuium aluminum hydride reduction products from heterocycles containing an isoindolone nucleus. J. Org. Chem. **1968**, *34*, 1720.
13. Helberger, von J.H.; Hevér, D.B. Uber die bildung von tetrabenzoporphin aus isoindolderivativaten. Justus Liebigs Ann. Chem. **1938**, *536*, 173.
14. Bromberg, B. Chem. Ber. **1896**, *29*, 1436.

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016

15. Wöelbling, B. Chem. Ber. **1905**, *38*, 3925.
16. Rosenthal, A.; Astbury, R.F.; Hubscher, A. Reaction of aromatic ketoximes with carbon monoxide hydrogen. J. Org. Chem. **1958**, *23*, 1037.
17. Bhatt, M.V.; Ravindranathan, M. Aspects of tautomerism 5. Solvent, substituents, and steric effects in their ring-chain tautomerism of ortho-benzoylbenzamides. J. Chem. Soc. Perkin Trans II **1973**, 1160.
18. Bartfeld, H.D.; Flitsch, W.; Gurke, K. Acyliminium 3. Reaction of acyliminium salts with Grignard-reagents. Chem. Ber. **1974**, *107*, 189.

Received in the USA August 21, 2003

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016