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NEW PHOTOCLEAVABLE STRUCTURES I: SYTHESIS OF HYDROXYALKYLPHENONE ANALOGUES ELECTRON-RICH HETEROCYCLES

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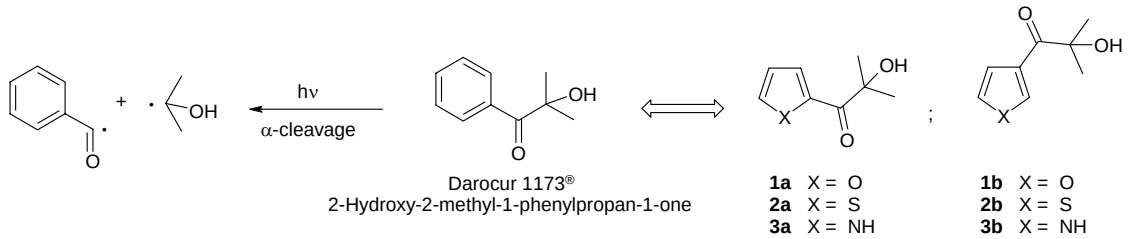
Abstract – A series of photoinitiating compounds with the general structure $ArCOCMe_2OH$, where Ar is 2-furyl (**1a**), 3-furyl (**1b**), 2-thienyl (**2a**), 3-thienyl (**2b**), 2-pyrrolyl (**3a**) and 3-pyrrolyl (**3b**), were prepared. The heterocyclic precursors were substituted by Friedel-Crafts type reaction with isobutyric acid derivatives. Subsequent bromination and hydrolysis gave **1a**, **2a** and **3b**. Derivatives (**1b**, **2b** and **3a**) were obtained by reaction of organometallic intermediates of heterocyclic precursors with suitable nitriles or esters.

INTRODUCTION

Among the large group of photoinitiator structures, hydroxyalkylphenones have gained much interest in the past decades due to their high reactivity and universal applicability.[1] 2-Hydroxy-2-methyl-1-phenyl-propan-1-one (Darocur 1173®) (Scheme 1) is an important derivative of these Type I photoinitiating systems. In these structures chromophoric groups are essential for the consumption of energy, which is introduced by UV-radiation. A conjugated system of an aromatic moiety and a carbonyl group leads to a $n \rightarrow \pi^*$ electron transition from which α-cleavage and formation of radicals can occur.



Scheme 1: α-Cleavage of hydroxyalkylphenones and products (**1**-**3**)

These radicals are formed by a monomolecular process and are able to initiate the polymerization of acrylates or methacrylates.[2] Formulations containing these monomers, polymerizable oligomers and, photoinitiators are used for coatings, printing inks, *etc.*[3] In the last decade, many modifications of this hydroxyalkylphenone structure have been investigated, since the chemical environment has an enormous

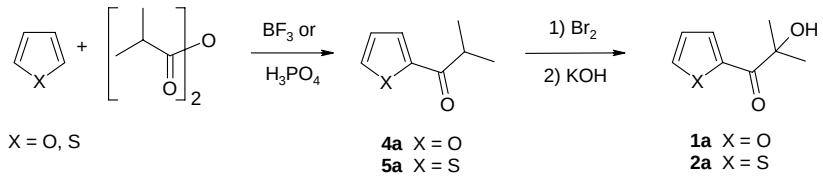
influence on the photochemistry of those systems. Triplet energy and life time, the quantum yield of α-cleavage, or the addition rate to double bonds is strongly influenced by different hetero-substituents.[2] Various electron donor substituents on the α-carbon atom lead to other well known photoinitiating systems such as benzoins, benzil ketals, aminoalkylphenones, or dialkoxyacetophenones.[4] On the other hand, substituents have been introduced at the *para*-position of the phenyl moiety, changing the photophysical and -chemical properties.[5] However, these modifications did not improve the photoinitiator performance.[6]

Replacement of the aromatic moiety has been described only for the 2-substituted furan (**1a**) and thiophene (**2a**) (Scheme 1).[7,8,9] Since photochemical data are currently unavailable, it was of interest to prepare various thiophene, furan and pyrrole derivatives. In this paper, we describe the synthesis of these heterocyclic hydroxyalkyl ketones. In contrast to published data,[9] preliminary tests revealed low photopolymerization activity.[10]

RESULTS AND DISCUSSION

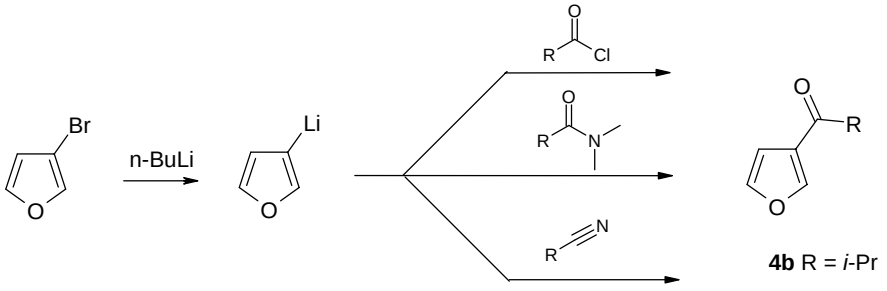
Furan analogues hydroxyalkylphenones

2-Acylfuran (**1a**) was synthesized according to the literature procedure by siteselective acylation[11] of furan with isobutyric anhydride, followed by bromination and alkaline hydrolysis (Scheme 2).[8]



Scheme 2: 2-Acylfurans and –thiophenes

In contrast to the 2-substituted species, it is known that 3-acylfurans are not easily accessible.[12] The siteselective introduction of a 3-acyl residue has been achieved by reaction of 3-lithiofuran with acid chlorides,[13,14] by acylation with amides,[15] or by reaction with nitriles[16-20] (Scheme 3, R = Alkyl).



Scheme 3: Synthetic pathways for 3-acylfurans

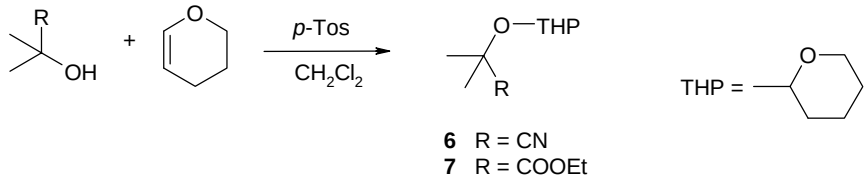
To evaluate the feasibility of these three synthetic routes, 2-lithiofuran,[22,23] which is more accessible than 3-lithiofuran,[13,21] was first used as a model.

The reaction pathway with isobutyric acid chloride and the *-ate* complex ($MnCl_2$;2LiCl),[14] which forms the manganese chloride-organolithium intermediate, was found to be less attractive because of the tedious separation of the catalyst iron(III) acetylacetonate. Additionally **4a** was obtained in low yields, which may be attributed to steric reasons since only the reactions of primary acid chlorides were described in the literature.[13]

The reaction of *N*,*N*-diethylisobutyric amide[24] with 2-lithiofuran gave the desired product (**4a**) in 82% yield. In the same manner, 3-lithiofuran reacted with the amide to afford the 3-acyl derivative (**4b**). Unfortunately, distillation of the crude product only gave 2-acylfuran (**4a**); this may be because the reaction temperature[25] is above the rearrangement temperature of 3-lithiofuran.[13]

The third model reaction of isobutyronitrile with 2-lithiofuran at low temperatures gave the desired product (**4a**) in less than 5% yield. The low yield of this product may be due to the acidity of the hydrogen at the α-carbon atom of the nitrile, which may lead to side reactions.[23] Therefore, other precursors without acidic hydrogens were synthesized.

Acetone cyanohydrin was reacted with 3,4-dihydropyran (Scheme 4), giving the protected acetone cyanohydrin[26] (**6**) in 91% yield. The protected 2-hydroxyisobutyric ethyl ester (**7**) formed in 91% yield is also a possible precursor for this type of reaction; however, it was used only for the pyrrole type derivatives due to unavoidable side reactions.[23]

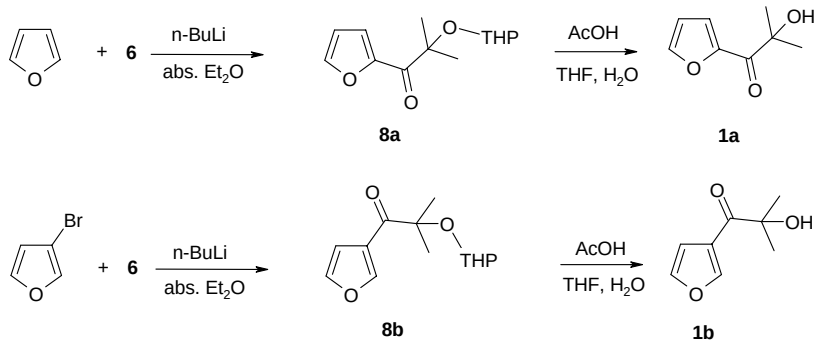


6 R = CN
7 R = COOEt

Scheme 4: THP-Protected precursors

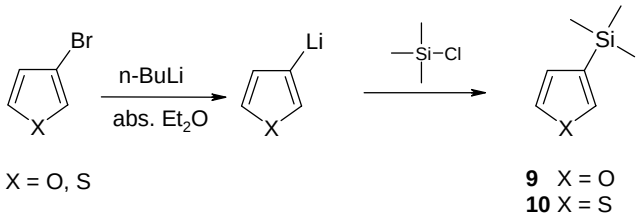
As a model reaction, the nitrile (**6**) was converted to the protected furan (**8a**) by reaction with 2-lithiofuran in ether at low temperatures[26] in 72% yield (Scheme 5). The imine intermediate was not isolated due to its instability.

With common cleavage methods for the THP group, such as the use *p*-toluenesulfonic acid[27] or Amberlyst H-15 resin[28] in methanol, no products were observed. However, cleavage of the protecting group occurred quantitatively in a mixture of AcOH/THF/H_2O (4:2:1) at 50°C within 4 h.[26] Thus **1a** was obtained without purification of the intermediate product (**8a**) in 65% overall yield.



Scheme 5: Synthetic pathway for acylfurans

Following these procedures, reaction of 3-lithiofuran with the protected acetone cyanohydrin (**6**) gave the desired product (**8b**) in only 0.8% yield, due to the unoptimized formation of 3-lithiofuran. The sequence of addition and halo-dance reactions at elevated temperatures are the main reasons for low yield. Estimation of optimum reaction conditions[23,29] for the metal halogen exchange was done by quenching 3-lithiofuran with the highly reactive trimethylchlorosilane giving **9** (Scheme 6) in 80% yield.



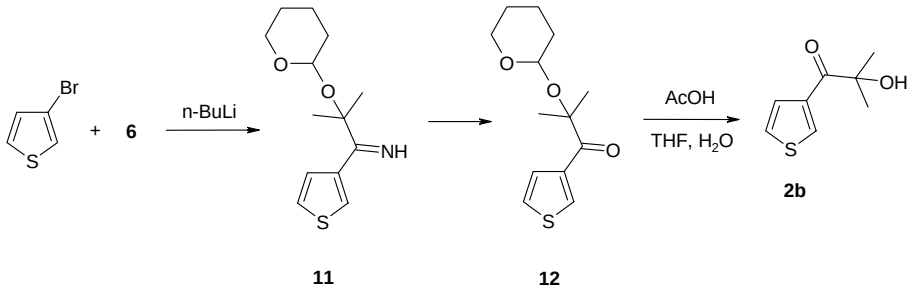
Scheme 6: Optimization of lithium halogen exchange

The best results were obtained by adding 3-bromothiophene to *n*-BuLi in ether at -80°C over 15 min. Complete metal halogen exchange was achieved in an additional 15 min, and **1b** was obtained under optimized reaction conditions by conversion of 3-lithiofuran[18] in 17% overall yield.

Thiophene analogues hydroxyalkylphenones

2-Acylthiophene (**2a**) was synthesized according to the literature procedure by siteselective acylation[30] of thiophene, bromination, and subsequent alkaline hydrolysis[9] (Scheme 2).

Since 3-lithiothiophene exhibits a much lower tendency for halo-dance reaction compared to the furan derivative, the pathway described above was adopted. 3-Bromothiophene was converted to 3-lithiothiophene and subsequently reacted with the appropriate nitrile. To revise the efficiency of metal halogen exchange, the formed 3-lithiothiophene was reacted with trimethylchlorosilane[29,31] (Scheme 6) using the parameters described for **9**. A total yield of 90% of **10** indicated optimum reaction conditions. Reaction with the protected acetone cyanohydrin (**6**) (Scheme 7) according to the procedure described for 3-acylfurans yielded **12** in 85 % yield.



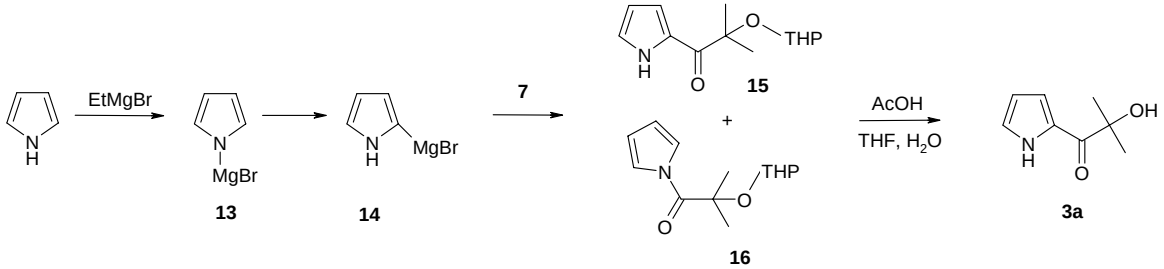
Scheme 7: Synthetic pathway for 3-acylthiophene

In contrast to furan, the imine intermediate (**11**) showed increased stability. But weak acidic conditions, such as those found with flash chromatography, converted the imine (**11**) to the corresponding ketone (**12**). Cleavage of the protective group with *p*-toluenesulfonic acid as catalyst, where the imine (**11**) could also be used without further purification, resulted in 64% overall yield after 4 days. In contrast, a solvent mixture of AcOH/THF/H_2O (4:2:1) allowed for complete cleavage after only 4 h, yielding **2b** in 84%.

Pyrrole analogues α-hydroxyalkylphenones

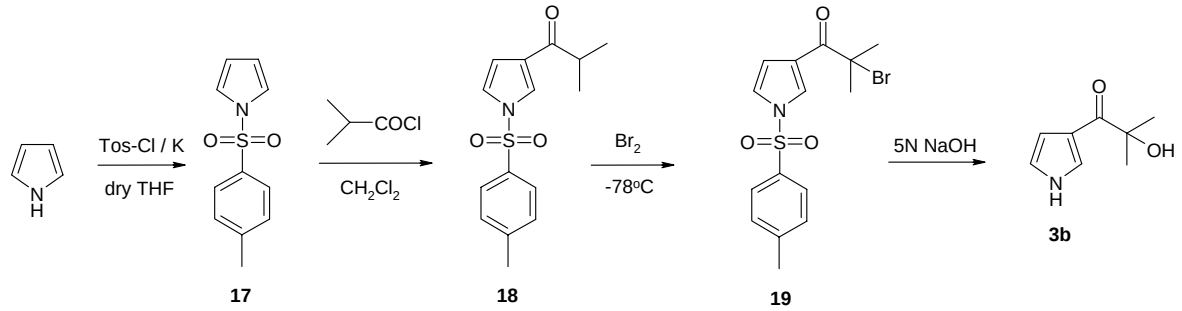
It is well known that siteselective α-acylation of pyrrole is not as easy as with furan and thiophene based electron rich heterocycles. By a proper choice of reaction conditions and directive substituents, site-specific substitution of pyrrole is possible.[32] The introduction of a 2-acyl substituent has been accomplished by direct electrophilic substitution of pyrroles,[33,34] or lithiation of pyrroles at C-2 followed by condensation with esters.[35,36] Additionally, pyrrole can be acylated by reaction of the organo-magnesium compound with nitriles or esters.[37]

The nitrogen substituted magnesium organic compound (**13**) (Scheme 8) was formed by reaction of ethylmagnesium bromide with pyrrole at low temperature. At ambient temperature, rearrangement reaction occurs[38] giving the desired, thermodynamic stable product (**14**). Since no product was obtained with **5**, the more reactive ester derivative (**7**) was used, which yielded the protected intermediate (**15**) in 85% yield. Though the 2-substituted derivative should be the more thermodynamically stable intermediate, the nitrogen substituted product (**16**) was also observed (8%). A side reaction to the 3-acylpyrrole, as reported by Castro[39] or Bean,[37] was not detected. The mixture of **15** and **16** was treated with AcOH/THF/H_2O (4:2:1) to cleave the protecting group and **3a** was obtained in 54% overall yield.



Scheme 8: Synthetic pathway for 2-acylpyrrole

In contrast to furan and thiophene derivatives, 3-acylpyrroles are more easily accessible. Bulky, electron withdrawing substituents at the nitrogen position direct acylation of the 3-position and additionally protect the nitrogen.[40] As suitable substituent, the tosyl protecting group was introduced (Scheme 9) by reaction of the potassium salt of pyrrole in THF with tosyl chloride.[41] Subsequent Friedel-Crafts acylation was carried out with isobutyric acid chloride in dichloromethane using anhydrous aluminum chloride as the catalyst[42] giving **18** in 73% yield.



Scheme 9: Synthetic pathway for 3-acylpyrrole

Pyrrole derivatives generally show an increased electrophilic reactivity compared to thiophene or furan heterocycles. Therefore, the tosyl protecting group was not cleaved to prevent any nuclear substitution in the next step. Bromination of **18** at the tertiary carbon atom was successful in dry dichloromethane at low temperatures yielding 71% 2-brom-2-methyl-1-(1*H*-pyrrol-3-yl)-1-propanone (**19**). Thus, simultaneous removal of the protecting group and hydrolysis of the bromo group under alkaline conditions are possible. The desired 2-hydroxy-2-methyl-1-(1*H*-pyrrol-3-yl)-1-propanone (**3b**) was obtained in 86% yield.

EXPERIMENTAL

Chemical reagents were obtained from Sigma Aldrich and Acros and used without further purification. The solvents were dried and purified by common methods. For column chromatography, Merck silica gel 60 was employed. Reaction mixtures and chromatography fractions were concentrated by using a rotary evaporator. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AC-E-200 FT-NMR-spectrometer and a Bruker Avance DRX 400 spectrometer. IR spectra using KBr-disks were recorded on a Biorad FTS 135 spectrophotometer. Melting points were measured by a Kofler hot-stage type microscope and are uncorrected. Elemental analysis was performed at the Microanalytical Laboratory of the Institute for Physical Chemistry at the University Vienna.

The following substances were prepared according to literature: **1-(2-Furanyl)-2-methyl-1-propanone** (**4a**)[11] (76%) with boron trifluoride etherate as catalyst followed by bromination to **2-bromo-1-(2-furanyl)-2-methyl-1-propanone,**[8] which was converted without further purification to **1-(2-furanyl)-2-hydroxy-2-methyl-1-propanone** (**1a**)[8] (82%) and **2-methyl-1-(2-thienyl)-1-propanone** (**5a**)[30] (86%). Subsequent bromination gave **2-bromo-2-methyl-1-(2-thienyl)-1-propanone**[7,9,43] (80 %), which was

converted without further purification to **2-hydroxy-2-methyl-1-(2-thienyl)-1-propanone** (**2a**)[7,9,43] (60%), ***N*,*N*-diethylisobutyric amide**[24] (68%), **1-(4-methylphenylsulfonyl)-1*H*-pyrrole** (**17**)[41] (72%), and **3-(2-methyl-1-oxopropyl)-1-(4-methylphenylsulfonyl)-1*H*-pyrrole** (**18**)[42] (73%). All spectral data were in agreement with the reported data.

1-(2-Furanyl)-2-methyl-1-propanone (**4a**) from *N*,*N*-diethylisobutyric amide[24]: Furan (2.5 g, 36.7 mmol) and dry ether (200 mL) were placed at –20°C under nitrogen in a round bottom flask with a reflux condenser. n-BuLi (23 mL, 1.6 M in hexane, 36.7 mmol) was added all at once by a syringe. The reaction mixture was allowed to warm to rt, while a white turbidity was formed. The mixture was refluxed for 15 min and afterwards cooled to -80°C. *N*,*N*-Diethylisobutyric amide (5.25 g, 36.7 mmol) was added and stirring was continued for 3 h at this temperature. The mixture was allowed to warm to rt over night and afterwards washed with 1N HCl (150 mL) and saturated sodium hydrogencarbonate solution (150 mL). The collected yellow colored aqueous layers were washed with ether, and the combined organic layers were washed once with brine and water, dried over sodium sulfate, filtered, and concentrated. The brown oil was distilled *in vacuum* giving **4a** (4.15 g, 82%) as a colorless oil. bp 86°C / 29 mbar (lit.,[11] 77.5-80°C / 26 mbar). ^{1}H-NMR ($CDCl_3$, 200 MHz) δ(ppm): 7.60 (s, 1H, H-3); 7.20 (d, J = 3.4 Hz, 1H, H-5); 6.50 (m, 1H, H-4); 3.35 (m, 1H, -CH); 1.20 (m, 6H, $-CH_3$).

2-Methyl-2-[(tetrahydro-2*H*-pyran-2-yl)oxy]propionitrile (**6**)[26] and **2-methyl-2-[(tetrahydro-2*H*-pyran-2-yl)oxy]propionic acid ethyl ester** (**7**)**:** *p*-Toluenesulfonic acid (30 mg, 0.174 mmol) was added to a mixture of 3,4-dihydro-2*H*-pyran (177.9 g, 2.12 mol) and acetone cyanohydrin (90.0 g, 1.06 mol) or 2-hydroxyisobutyric acid ethyl ester (133 g, 1.06 mmol) in dry CH_2Cl_2 (150 mL) at –20°C. After removal of the cooling bath, the reaction mixture was allowed to warm to rt and stirred overnight. The mixture was washed with saturated sodium bicarbonate solution (100 mL) and twice with water (100 mL). The organic layer was dried over sodium sulfate, filtered, evaporated, and the product distilled *in vacuum*. The nitrile (**6**) was obtained as a colorless oil (162 g, 91%), bp 58°C / 2.6 mbar, (lit.,[26] 106°C / 36 mbar). ^{1}H-NMR ($CDCl_3$, 200 MHz) δ(ppm): 5.00 (m, 1H, -CH); 4.00 (m, 1H, O-CH_2-); 3.60 (m, 1H, O-CH_2-); 1.90-1.50 (m, 12H, -CH_2, -CH_3). The ester (**7**) was obtained as colorless oil (196.8 g, 91%). bp 71°C / 0.2 mbar. ^{1}H-NMR ($CDCl_3$, 200 MHz) δ(ppm): 4.65 (m, 1H, C-H); 4.10 (m, 2H, -COOCH_2); 3.90 (m, 1H, O-CH_2-); 3.40 (m, 1H, O-CH_2-); 1.90-1.40 (m, 9H, C-H); 1.20 (t, J = 7,1 Hz, 3H, -CH_3). ^{13}C-NMR ($CDCl_3$, 50 MHz) δ(ppm): 174.71, 96.15, 63.35, 60.81, 31.42, 25.78, 25.20, 24.88, 20.34, 14.04; IR (KBr) ν_{max} (cm^{-1}): 2984, 2942, 2872, 1734, 1147, 1076; Anal. Calcd for $C_{11}H_{20}O_4$: C, 61.10; H, 9.32. Found: C, 61.72; H, 9.41.

1-(2-Furanyl)-2-methyl-2-[(tetrahydro-2*H*-pyran-2-yl)oxy]-1-propanone (**8a**)[26:] Furan (1.5 g, 22 mmol) was dissolved in dry ether (120 mL) under nitrogen, and n-BuLi (13.8 mL, 1.6 M in hexane, 22 mmol) was added at -40°C. The yellow solution was warmed to ambient temperature and refluxed for 30 min. After cooling to –80°C, the protected acetone cyanohydrin (**6**) (3.75 g, 22.2 mmol) was added, and the mixture stirred for 1 h at this temperature. The temperature was raised within 1 h to rt, and the

reaction mixture stirred for additional 3 h. A saturated solution of ammonium chloride (50 mL) was added slowly. The organic layer was washed twice with water (50 mL) and a saturated solution of sodium chloride (50 mL), dried over sodium sulfate, filtered, and distilled under reduced pressure to give **8a** (3.79 g, 72%) as a colorless oil. bp 90-95°C / 0.033 mbar. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ(ppm): 7.45 (d, J = 1.8 Hz, 1H, H-5); 6.97 (d, J = 3.3 Hz, 1H, H-3); 6.43 (dd, J = 1.8, 3.3 Hz, 1H, H-4); 4.57 (m, 1H, -CH); 3.87 (m, 1H, O-CH_2-); 3.40 (m, 1H, O-CH_2-); 1.90-1.40 (m, 12H, -CH_2, -CH_3). ^{13}C-NMR ($CDCl_3$, 100 MHz) δ(ppm): 170.78, 143.77, 113.83, 111.58, 95.45, 79.55, 63.25, 31.64, 27.60, 25.05, 20.38; IR (KBr) ν_{max} (cm^{-1}): 3140, 3117, 2942, 2868, 1603, 1564, 1122, 1050; Anal. Calcd for $C_{13}H_{18}O_4$: C, 65.53; H, 7.61. Found: C, 65.28; H, 8.06.

General Procedure for the cleavage of the THP protective group[26]**:** A solution of tetrahydropyranyl ether in the fifty equivalent of AcOH/THF/H_2O (4:2:1) was stirred at 50°C until the protecting group was cleaved (*ca*. 3 h, monitored by TLC). The solvent was evaporated, and the crude product dissolved in ether. After extraction with sodium bicarbonate, water, and a solution of sodium chloride the organic layer was dried over sodium sulfate, filtered, and concentrated.

1-(2-Furanyl)-2-hydroxy-2-methyl-1-propanone (**1a**) was obtained without purification of **8a** by the general procedure for the cleavage of the THP-protective group. Distillation *in vacuum* gave **1a** in 65% yield (2 steps) as a colorless oil. bp 122°C / 44 mbar: ^{1}H-NMR ($CDCl_3$, 400 MHz) δ (ppm): 7.62 (dd, J = 0.7, 1.6 Hz, 1H, H-3); 7.39 (dd, J = 0.7, 3.7 Hz, 1H, H-5); 6.56 (dd, J = 1.6, 3.7 Hz, 1H, H-4); 4.10 (s, 1H, O-H); 1.50 (s, 6H, CH_3). ^{13}C-NMR: ($CDCl_3$, 50 MHz) δ (ppm): 193.35, 149.33, 147.65, 121.97, 112.57, 75.99, 27.47; IR (KBr) ν_{max} (cm^{-1}): 3600-3200, 3138, 2981, 2942, 1661, 1564, 1157.

3-Furanyltrimethylsilane (**9**)[28,45] and **trimethyl-3-thienylsilane** (**10**)[29,31] : n-BuLi (11.9 mL, 1.6 M in hexane, 19 mmol) and dry ether (150 mL) were placed under nitrogen in a dried round bottom flask at -80°C, and 3-bromofuran (2.8 g, 19 mmol) or 3-bromothiophene (3.09 g 19 mmol) was added at this temperature over 15 min. The reaction mixture was stirred for 15 min, and distilled trimethylchlorosilane (2.24 g, 20.6 mmol) was added. Stirring was continued for an additional 20 min at -60°C, and the reaction mixture was quenched with a saturated solution of ammonium chloride (150 mL). The organic layer was separated, washed with brine, dried over sodium sulfate, filtered, and concentrated. Distillation produced **9** as colorless oil (2.16 g, 80%). bp 126°C. (lit.,[44] 126°C). ^{1}H-NMR ($CDCl_3$, 200 MHz) δ(ppm): 7.50 (m, 1H, H-5); 7.35 (m, 1H, H-2); 6.40 (m, 1H, H-4); 0.20 (s, 9H, Si-CH_3). **10** was obtained after distillation as yellow oil (2.65 g, 90%). bp 166-167°C (lit.,[31] 168°C). ^{1}H-NMR ($CDCl_3$, 200 MHz) δ(ppm): 7.50-7.40 (m, 2H, H-2, H-5); 7.20 (m, 1H, H-4); 0.30 (s, 9H, -CH_3).

1-(3-Furanyl)-2-methyl-2-[(tetrahydro-2*H*-pyran-2-yl)oxy]-1-propanone (**8b**)[18]: n-BuLi (85.1 mL, 1.6 M in hexane, 136 mmol) and dry ether (800 mL) were placed under nitrogen in a dried round bottom flask at –80°C and 3-bromofuran (20.0 g, 136 mmol) was added at this temperature over 15 min. The reaction mixture was stirred for 15 min and protected acetone cyanohydrin (**6**) (23.0 g, 136 mmol) was

added. Stirring was continued for an additional 20 min at –60°C, the mixture quenched with a saturated solution of ammonium chloride (250 mL) and the organic layer was washed with brine (250 mL), dried over sodium sulfate, filtered and concentrated. The residual oil was fractionated *in vacuum* giving **8b** as a yellow oil (5.6 g, 17.3%). bp 103-104°C / 9.3 mbar. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ(ppm): 8.23 (dd, J = 0.7, 1.3 Hz, 1H, H-2); 7.40 (m, J = 2.0, 3.3 Hz, 1H, H-5); 6.80 (m, 1H, H-4); 4.60 (m, 1H, CH); 3.95 (m, 1H, O-CH_2-); 3.45 (m, 1H, O-CH_2-); 1.90-1.45 (m, 12H, -CH_3, -CH_2). ^{13}C-NMR ($CDCl_3$, 50 MHz) δ(ppm): 198.28, 149.43, 144.30, 142.57, 116.97, 110.29, 108.94, 96.47, 96.32, 82.53, 81.23, 64.15, 63.95, 63.11, 31.68, 31.41, 31.06, 28.21, 27.51, 25.24, 25.05, 24.81, 24.09, 21.00, 20.73, 19.54; IR (KBr) ν_{max} (cm^{-1}): 3157, 3133, 2942, 2865, 1676, 1558, 1123, 1050; Anal. Calcd for $C_{13}H_{18}O_4$: C, 65.53; H, 7.61. Found: C, 65.11; H, 7.61.

1-(3-Furanyl)-2-hydroxy-2-methyl-1-propanone (**1b**) was obtained from **8b** following the general procedure for the cleavage of the THP protecting group. Purification by column chromatography (PE : EE 7:1) gave **1b** as a colorless oil in 44.8 % yield (7.8 % for both steps). **1b** was also obtained without purification of **8b** in 17% overall yield. bp 64-65°C / 0.1 mbar. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ(ppm): 8.22 (s, 1H, H-2); 7.41 (dd, J = 1.6 Hz, 1H, H-5); 6.81 (d, J = 1.6 Hz, 1H, H-4); 3.95 (bs, 1H, -OH); 1.49 (s, 6H, -CH_3). ^{13}C-NMR: ($CDCl_3$, 50 MHz) δ (ppm): 199.24, 148.81, 143.88, 122.42, 110.08, 76.50, 28.08; IR (KBr) ν_{max} (cm^{-1}): 3600-3200, 3138, 2981, 2942, 1661, 1564, 1157; Anal. Calcd for $C_8H_{10}O_3$: C, 62.33; H, 6.54. Found: C, 62.28; H, 6.37.

2-[(2-Imino-1,1-dimethyl-2-thienyl)ethoxy]tetrahydro-2*H*-pyran (**11**): n-BuLi (7.44 mL, 1.6 M in hexane, 11.9 mmol) and dry ether (40 mL) were placed under nitrogen in a dried round bottom flask at -80°C, and 3-bromothiophene (1.94 g, 11.9 mmol) was added at this temperature over 15 min. The reaction mixture was stirred for 15 min, and protected acetone cyanohydrin (**6**) (2.01 g, 11.9 mmol) was added. Stirring was continued for additional 20 min at –60°C, the mixture quenched with aqueous ammonium chloride (30 mL), and the organic layer was washed with brine (30 mL), dried over sodium sulfate, filtered, and concentrated. The crude product (**11**) (2.9 g, 96%) was used without further purification for the cleavage of the protecting group. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ(ppm): 9.80 (br s, 1H, C=N-H); 8.25 (d, J = 1.8 Hz, 1H, H-2), 7.60 (d, J = 5.1 Hz, 1H, H-4); 7.30 (dd, J = 2.9, 5.1 Hz, 1H, H-5); 4.91 (dd, J = 2.2, 4.7 Hz, 1H, C-H); 3.83 (m, 1H, O-CH_2); 3.47 (m, 1H, O-CH_2); 1.90-1.40 (m, 12H, CH_2, CH_3); ^{13}C-NMR ($CDCl_3$, 50 MHz) δ(ppm): 198.30, 136.85, 134.44, 128.73, 125.66, 94.48, 76.21, 62.82, 30.56, 28.17; 25,15; 20,24; IR (KBr) ν_{max} (cm^{-1}): 3498, 3112, 2939, 2871, 1676, 1507, 1465, 1255, 1124, 1075, 1016.

2-Methyl-2-[(tetrahydro-2*H*-pyran-2-yl)oxy]-1-(3-thienyl)-1-propanone (**12**)[31]: For elemental analysis the oil (**11**) (1.37 g) was purified by MPLC on silica gel (elution with 8% ethyl acetate in hexane) giving **12** (1.16 g, 85 %) as a yellow oil. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ(ppm): 8.25 (d, J = 1.8 Hz, 1H, H-2); 7.61 (d, J = 5.1 Hz, 1H, H-4); 7.30 (dd, J = 5.1, 2.9 Hz, 1H, H-5); 4.60 (m, 1H, C-H); 3.90 (m, 1H, O-CH_2); 3.40 (m, 1H, O-CH_2); 1.90-1.40 (m, 12H, CH_2, CH_3). ^{13}C-NMR ($CDCl_3$, 50 MHz) δ(ppm): 196.97,

138.29, 134.24, 129.53, 96.55, 82.51, 64.01, 31.59, 26.07; 25,39; 20,86; IR (KBr) ν_{max} (cm^{-1}): 3113, 2942, 2866, 1672, 1508, 1124, 1049; Anal. Calcd for $C_{13}H_{18}O_3S$: C, 61.39; H, 7.13; S, 12.61. Found: C, 62.06; H, 7.45; S, 12.08.

2-Hydroxy-2-methyl-1-(3-thienyl)-1-propanone (**2b**) was obtained from **11** following the general procedure for the cleavage of the THP protecting group. Purification by column chromatography (PE : EE 7:1) gave **2b** as a colorless oil in 84 % yield. bp 80°C / 0.03 mbar. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ(ppm): 8.25 (dd, J = 1.3, 2.9 Hz, 1H, H-2); 7.60 (dd, J = 1.3, 5.2 Hz, 1H, H-4); 7.29 (dd, J = 2.9, 5.2 Hz, 1H, H-5); 4.00 (br s, 1H, -OH); 1.55 (s, 6H, -CH_3). ^{13}C-NMR ($CDCl_3$, 50 MHz) δ (ppm): 198.41, 137.01, 134.71, 128.78, 125.48, 76.57, 27.98; IR (KBr) ν_{max} (cm^{-1}): 3600-3200, 3113, 2978, 2935, 2872, 1666, 1506, 1156; *Anal.* Calcd for $C_8H_{10}O_2S$: C, 56.45; H, 5.92; S, 18.84. Found: C, 56.47; H, 6.15; S, 18.50.

2-Methyl-2-[(tetrahydro-2*H*-pyran-2-yl)oxy]-1-(1*H*-pyrrol-2-yl)-1-propanone (**15**)[37,38]: A solution of ethylmagnesium bromide, prepared from dried magnesium (2.41 g, 99.2 mmol), distilled ethyl bromide (10.8 g, 99.2 mmol) and dry ether (50 mL), was cooled to –20°C under nitrogen and distilled pyrrole (6.65 g, 99.2 mmol) in dry ether (20 mL) was added. The suspension was refluxed for 15 min and then cooled to ambient temperature. The ester (**7**) (21.45 g, 99.2 mmol) was dissolved in dry ether (80 mL) and added to the reaction mixture over 10 min. A brown solid formed immediately in a green solution. The reaction mixture was stirred overnight and hydrolyzed with a saturated solution of ammonium chloride (100 mL). The organic layer was washed twice with brine (70 mL), dried over sodium sulfate, and concentrated. Unconverted ester (**7**) was evaporated (bp 71°C / 0.2 mbar), and the crude product (21.2 g, 90%) used without further purification for the removal of the protecting group. For elemental analysis, purification of the crude product (4.00 g) was carried out by column chromatography (eluted with hexane / ethyl acetate 15:1) giving **15** (3.4 g, 85%) as a colorless oil. ^{1}H-NMR ($CDCl_3$, 200 MHz) δ(ppm): 9.80 (m, 1H, N-H) 7.20 (m, 1H, H-3); 7.00 (m, 1H, H-5); 6.30 (m, 1H, H-4); 4.70 (m, 1H, C-H) 3.95 (m, 1H, O-CH_2-); 3.45 (m, 1H, O-CH_2-); 1.95-1.40 (m, 12H, C-H). ^{13}C-NMR ($CDCl_3$, 50 MHz) δ(ppm): 193.96, 193.04, 128.94, 127.25, 125.34, 124.13, 119.00, 118.60, 110.97, 110.35, 96.43, 94.49, 82.40, 75.10, 63.67, 62.81, 31.60, 30.58, 29.15, 26.97, 25.25, 25.10, 24.59, 20.62. Anal. Calcd for $C_{13}H_{19}NO_3$: C, 65.80; H, 8.07; N, 5.90. Found: C, 65.99; H, 7.90; N, 5.90 and **1-(2-methyl-2-[(tetrahydro-2*H*-pyran-2-yl)oxy]-1-oxopropyl)-1*H*-pyrrole** (**16**) (0.32 g, 8%) as a colorless oil. ^{1}H-NMR ($CDCl_3$, 200 MHz) δ(ppm): 7.15 (m, 2H, H-3,4); 6.25 (m, 2H, H-2,5); 4.70 (m, 1H, C-H); 3.95 (m, 1H, O-CH_2-); 3.45 (m, 1H, O-CH_2-); 1.95-1.40 (m, 12H, 3 x -CH_2, 2 x -CH_3).

2-Hydroxy-2-methyl-1-(1*H*-pyrrol-2-yl)-1-propanone (**3a**) was obtained from the crude tetrahydro-pyranyl ether (**15** + **16**) following the general procedure for the cleavage of the THP protecting group. Purification by column chromatography (elution with 6% ethyl acetate in hexane) gave **3a** in 63 % yield as white crystals. mp 66°C. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ(ppm): 9.90 (br s, 1H, N-H); 7.05 (dd, J = 1.0, 2.5 Hz, 1H, H-3); 7.00 (m, J = 1.0, 2.4 Hz, 1H, H-5); 6.30 (m, J = 2.4, 2.5 Hz, 1H, H-4); 4.26 (br s, 1H, O-H); 1.59 (s, 6H, -CH_3). ^{13}C-NMR: ($CDCl_3$, 50 MHz) δ (ppm): 194.04, 127.19, 125.50, 118.78, 111.09,

75.18, 29.18; IR (KBr) ν_{max} (cm^{-1}) 3600-3200, 3443, 3318, 3125, 2972, 2932, 2872, 1607, 1544, 1156 Anal. Calcd for $C_8H_{11}NO_2$: C, 62.73; H, 7.24; N, 9.14. Found: C, 63.01; H, 7.34; N, 8.99.

3-(2-Bromo-2-methyl-1-oxopropyl)-1-[(4-methylphenyl)sulfonyl]-1*H*-pyrrole (**19**)**:** A solution of 2-methyl-1-[1-((4-methylphenyl)sulfonyl)-1*H*-pyrrol-3-yl]propan-1-one (**18**) (10.20 g, 35.1 mmol) in dry dichloromethane (30 mL) was cooled to –80°C and a solution of bromine (5.61 g, 35.1 mmol) in dry dichloromethane (30 mL) was added dropwise over 15 min. The reaction mixture was stirred overnight at ambient temperature and, for completation, refluxed for 20 min. After washing with water, sodium bicarbonate, sodium thiosulfate and water, the organic layer was dried over sodium sulfate, filtered, and concentrated. The crude product was purified by MPLC (elution with 8% ethyl acetate in hexane) giving **19** (9.2 g, 71%) as a beige oil. ^{1}H-NMR ($CDCl_3$, 200 MHz) δ(ppm): 8.05 (s, 1H, H-2); 7.85 (d, J = 2.2 Hz, 2H, H-3', H-5') 7.40 (d, J = 2.2 Hz, 2H, H-2', H-6'); 7.15 (m, 1H, H-3); 6.90 (m, 1H, H-4); 2.50 (m, 3H, CH_3-Ar); 2.00 (s, 6H, 2 x CH_3). ^{13}C-NMR ($CDCl_3$, 50 MHz) δ(ppm): 190.32, 146.51, 133.85, 2 x 130.21, 129.26, 2 x 128.39, 122.62, 118.44, 101.09, 61.27, 31.13, 21,80; Anal. Calcd for $C_{15}H_{16}NO_3BrS$: C, 48.66; H, 4.36; N, 3.87; Br, 21.58; S, 8.66. Found: C, 48.55; H, 4.43; N, 3.73; Br, 21.70; S, 8.33.

2-Hydroxy-2-methyl-1-(1*H*-pyrrol-3-yl)propan-1-one (**3b**): The oil (**19**) (7.9 g, 21.3 mmol) was diluted with methanol (100 mL). A 10 wt% aqueous solution of potassium hydroxide (100 mL) was added, and the reaction mixture was refluxed for 4 h. After stirring overnight at ambient temperature, methanol was evaporated, and the solution extracted 4 times with ether (100 mL). The combined organic layers were dried and concentrated. The crude product was purified by reprecipitation (ethyl acetate / hexane) giving **3b** (2.8 g, 86%) as yellow crystals. mp 88°C. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ(ppm): 8.90 (br s, 1H, N-H); 7.56 (ddd, J = 1.5, 1.5, 3.0 Hz, 1H, H-2); 6.77 (dd, J = 4.8, 2.6 Hz, 1H, H-5); 6.69 (dd, J = 2.6, 4.1 Hz, 1H, H-4); 4.59 (s, 1H, -OH); 1.60 (s, 9H, CH_3). ^{13}C-NMR ($CDCl_3$, 50 MHz) δ (ppm): 199.64; 125.31; 119.81; 119.21; 110.50; 75.19; 29.76; IR (KBr) ν_{max} (cm^{-1}): 3600-3300, 3425, 3225, 3125, 2973, 2934, 2870, 1636, 1551, 1145; Anal. Calcd for $C_8H_{11}NO_2$: C, 62.73; H, 7.24; N, 9.14. Found: C, 62.60; H, 7.02; N, 9.06.

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REFERENCES

1. K. Dietliker, *Chemistry & Technology of UV & EB Formulation for Coatings, Inks & Paints,* Vol. 3, SITA Technology, 1999, 2nd ED.
2. J. P. Fouassier, *Photoinitiation, Photopolymerization and Photocuring*, Hanser Publishers, 1995.
3. C. Roffey, *Photogeneration of Reactive Species for UV Curing*, John Wiley & Sons, 1997.
4. H. F. Gruber, *Prog. Polym. Sci.*, 1992, **17**, 953.
5. D. Ruhlmann and J. P. Fouassier, *European Polymer J.*, 1992, **28**, 287.
6. J. P. Fouassier, *Radiation Curing in Polymer Science and Technology*, Vol. 2, Elsevier 1993.
7. E. Abele, *Chem. Heterocycl. Compd*., 1994, **30**, 275.

8. Y. L. Pascal, *Ann. Chim.*, 1968, **3,** 245.
9. L. Felder, R. Kirchmayr, and R. Hüsler, (Ciba-Geigy AG), *Eur. Pat. Appl. EP 3002* (Cl. C08F2/50), 11 Jul. 1979, 64pp (*Chem. Abstr.*, 1980, **92**, 94889w).
10. R. Liska, S. Knaus, and J. Wendrinsky, *Nucl. Instr. and Meth. in Phys. Res. B*, 1999, **151**, 290.
11. C. H. Rahn, D. M. Sand, Y. Wedmid, H. Schlenk, T. P. Krick, and R. L. Glass, *J. Org. Chem.*, 1979, **44**, 3420.
12. S. Clementi, F. Fringuelli, P. Linda, G. Marino, G. Savelli, and A. Taticchi, *J. Chem. Soc., Perkin Trans. 2*, 1973, 2097
13. G. Cahiez, P. Y. Chavant, and E. Metais, *Tetrahedron Lett.*, 1992, **33**, 5245.
14. G. Cahiez and M. Alami, *Tetrahedron*, 1989, **45**, 4163.
15. A. G. Myers and T. Yoon, *Tetrahedron Lett.*, 1995, **36**, 9429.
16. B. J. Barnes, P. J. Newcombe, and R. K. Norris, *Aust. J. Chem.*, 1983, **36**, 963.
17. T. Sugimura, A. Tai, and K. Koguro, *Tetrahedron*, 1994, **50**, 11647.
18. R. Baker, I. F. Cottrell, P. D. Ravenscroft, and C. J. Swain, *J. Chem. Soc., Perkin Trans. I*, 1985, 2463.
19. Y. Fukuyama, Y. Kawashima, T. Miwa, and T. Tokoroyama, *Synthesis*, 1974, 443.
20. T. Sugimura, K. Koguro, and A. Tai, *Tetrahedron Lett.*, 1993, **34**, 509.
21. Wm. W. Levis, (Pennsylvania Salt Mfg. Co), *US 2773882*, 11. Dec. 1956 (*Chem. Abstr*. 1957, **51**, 8803i).
22. W. E. Truce and E. Wellisch, *J. Am. Chem. Soc.*, 1952, **74**, 5177.
23. V. Ramanathan and R. Levine, *J. Org. Chem*., 1962, **27**, 1216.
24. J. Moens and G. Smets, *J. Polym. Sci.*, 1957, **23**, 931.
25. W. Leung and E. LeGoff, *Synth. Comm*., 1989, **19**, 787.
26. K. F. Bernady, M. B. Floyd, J. F. Poletto, and M. J. Weiss, *J. Org. Chem.*, 1979, **44**, 1438.
27. E. J. Corey, H. Niwa, and J. Knolle, *J. Am. Chem. Soc.*, 1978, **100**, 1942.
28. R. D. Johnston, C. R. Marston, P. E. Krieger, and G. L. Goe, *Synthesis*, 1988, 393.
29. L. Camici, P. Dembech, A. Ricci, G. Seconi, and M. Taddei, *Tetrahedron*, 1988, **44**, 4197.
30. E. Profft, *Chem. Ztg.*, 1958, **82**, 295.
31. S. Gronowitz, *Arkiv. Kemi*, 1954, **7**, 361 (*Chem. Abstr*., 1955, **49**, 13216b).
32. M. Kakushima, P. Hamel, R. Frenette, and J. Rokach, *J. Org. Chem.*, 1983, **48**, 3214 .
33. G. A. Olah, *Friedel-Crafts and Related Reactions*, Interscience, New York, 1964, Vol. 1-4.
34. G. H. Cooper, *J. Org. Chem.*, 1971, **36**, 2897.
35. K. C. Nicolaou, D. A. Claremon, and D. P. Papahatjis, *Tetrahedron Lett*., 1981, **22**, 4647.
36. G. R. Martinez, P. A. Grieco, and C. V. Srinivasan, *J. Org. Chem.*, 1981, **46**, 3760.
37. G. P. Bean, *J. Heterocycl. Chem.*, 1965, **2**, 473.
38. A. J. Castro, J. R. Lowell, J. P. Marsh, R. X. Xu, N. Le, N. J. Gogan, R. McDonald, and L. G. Edwards, *J. Heterocyc. Chem.*, 1964, **1**, 207.
39. W. Tschelinzeff and A. Terentjeff, *Ber.*, 1914, **47**, 2647.
40. H. J. Anderson and C. E. Loader, *Can. J. Chem.*, 1985, **63**, 896.
41. E. P. Papadopoulos and N. F. Haidar, *Tetrahedron Lett.*, 1968, 1721.
42. R. Settambolo, R. Lazzaroni, T. Messeri, M. Mazzetti, and P. Salvadori, *J. Org. Chem.*, 1993, **58**, 7899.
43. L. B. Volodarskii, I. A. Grigor'ev, L. N. Grigor'eva, I. A. Kirilyuk, and S. A. Amitina, *J. Org. Chem. USSR*, 1985, **21**, 401 (*Chem. Abstr*., 1985, **103**, 160440s), *Zh.Org.Chim.*, 1985, **21**, 443.
44. E. Lukevics, V. N. Gevorgyan, Y. S. Goldberg, and M. V. Shimanskaya, *J. Organometall. Chem.*, 1984, **263**, 283.