Scientific paper

A Novel Oxidative Rearrangement of *N*-Furanyl Carbamates Uncovered During a Planned Synthesis of a *Daphniphyllum* Alkaloid

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Dedicated to Professor Branko Stanovnik on the occasion of his 70th birthday

Abstract

E-Dimethyl 2-(2-oxycyclopentylidene)succinate was prepared by the $TiCl_4$ catalyzed [2+2]-cycloaddition of (trimethylsilyloxy)cyclopentene with DMAD followed by a base induced ring opening of the initially formed cycloadduct. It was necessary to protect the keto group as the 1,3-dithiane in order to prepare the corresponding *N*-furanyl carbamate **16**. Loss of the Boc group occurs on heating at 130 °C or upon treatment of **16** with $Mg(ClO_4)_2$. In an attempt to convert the 1,3-dithiane of the resulting NH-carbamate **17** to the corresponding carbonyl group, the compound was treated with iodine in a basic aqueous solution. Under these conditions, a rather unusual oxidative rearrangement occurred to produce a substituted 5-hydroxy-1*H*-pyrrol-2(5*H*)-one. Analogous oxidative rearrangements were found to occur with structurally related 2-amidofurans. The mechanism of the oxidative rearrangement is comparable to the aza-Achmatowicz reaction.

Keywords: Furanyl carbamate, oxidative rearrangement, aza-Achmatowicz, daphniphyllum, alkaloid

1. Introduction

Plants of the genus *Daphniphyllum* contain structurally diversified alkaloids possessing a highly complex polycyclic skeleton.[1,2] They were demonstrated to be derived from squalene-like intermediates by isotope tracer experiments[3] and biomimetic total synthesis.[4] Some of these alkaloids exhibit cytotoxin activities against several tumor cell lines.[5,6] Some years ago, Heathcock proposed a biogenetic pathway and developed biomimetic total syntheses of several members.[4] Recently many new alkaloids were isolated from the *daphniphyllum* species,[7] which have attracted interest as challenging targets for total synthesis[8] as well as biogenetic studies.[9–12] Members of this class of alkaloids generally possess an unprecedented hexacyclic ring framework containing a bridged ABC tricyclic 4-azatricyclo[5.2.2.$0^{4,8}$]undecane (Figure 1). Among these, we have focused our attention on longeracinphyllin A (**1**) which was isolated in 2006 from the leaves of *D. longeracemosum.* This particular alkaloid contains a daphnilongeranin B type skeleton with a rearranged α,β-unsaturated ketone group, and its structure was supported by X-ray crystal data.[13]

Our synthetic approach toward the hexacyclic core found in the *Daphniphyllum* alkaloids was guided by a long-standing interest in developing new applications of the intramolecular [4+2]-cycloaddition/rearrangement cascade of 2-amidofurans toward the synthesis of complex natural products.[14] Our recently completed syntheses of (±)-erysotramidine,[15] (±)-lycoricidine[16] and (±)-strychnine[17] nicely demonstrate the utility of this process for the construction of various alkaloids. On the basis of our earlier work, we felt that we could also use this methodology for the synthesis of longeracinphyllin A (**1**) and this is outlined in Scheme 1. As illustrated in this scheme, the final step of the planned synthesis would involve closure of the A-ring by a Bonjoch/Solé palladium-catalyzed intramolecular coupling of the amido-tethered vinyl iodide **2** with a keto-enolate generated anion.[18,19] Our retrosynthetic analysis envisions the pentacyclic amide **2** to be derived from an intramolecular Pauson-Khand reaction of alkyne **3**, which in turn, should be available in se-

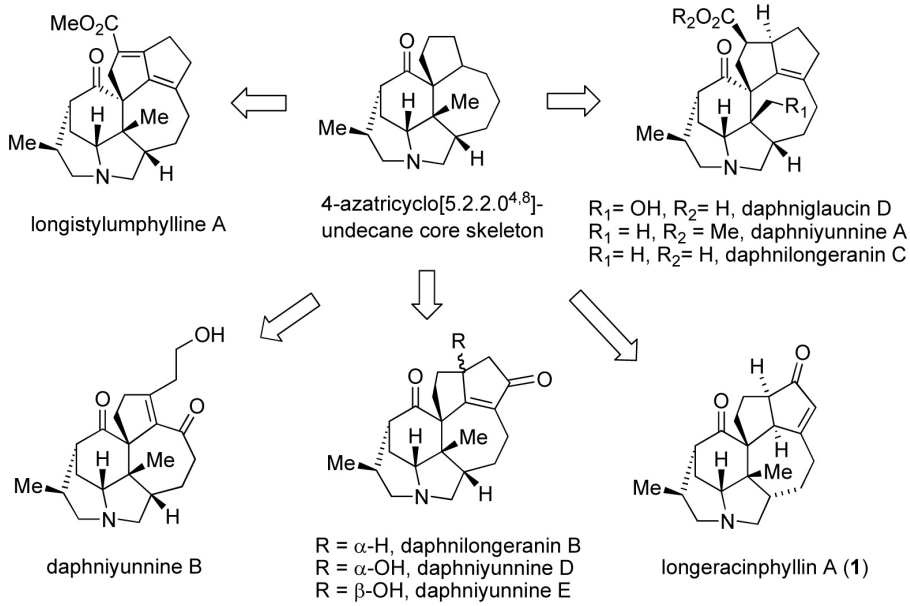
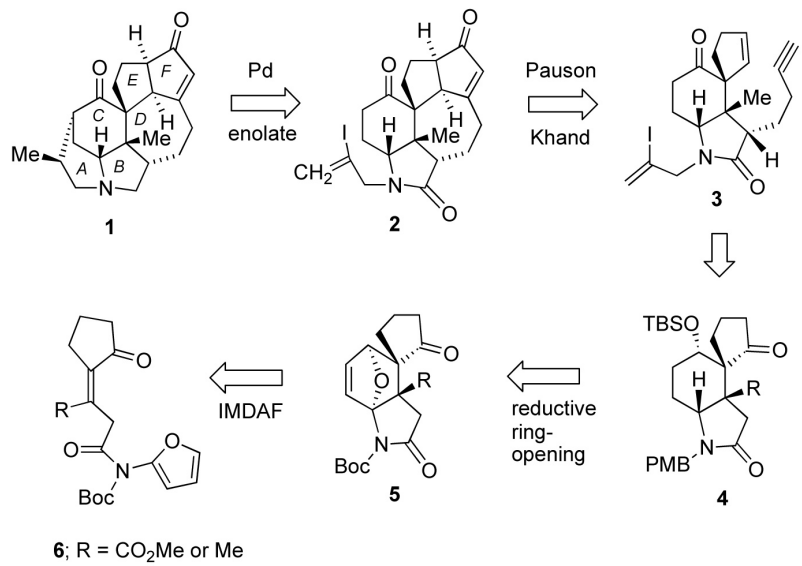


Figure 1. Structures of some *Daphniphyllum* Alkaloids



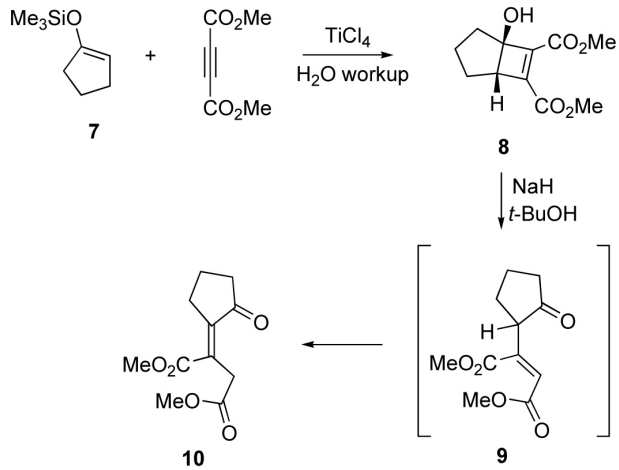
Scheme 1

veral straightforward steps from keto-amide **4**. A critical step of our synthetic plan relies upon the efficient construction of the oxa-bicyclic intermediate **5** by an intramolecular [4+2]-cycloaddition (IMDAF) of furanyl carbamate **6**. Reductive ring opening of cycloadduct **5** was expected to furnish **4**.

2. Results and Discussion

Following this approach, we first prepared *E*-dimethyl 2-(2-oxycyclopentylidene) succinate (**10**) by making use of a [2+2]-cycloaddition of (trimethylsilyloxy)cyclopentene (**7**) with DMAD under titanium tetrachloride catalysis.[20] The resulting cyclobutene derivative **8** was then subjected to reaction with sodium hydride in *t*-butanol to furnish the ring cleavage product **9** as a transient intermediate. This material was readily isomerized under the basic conditions to give the thermodynamically more stable isomer **10** (Scheme 2).

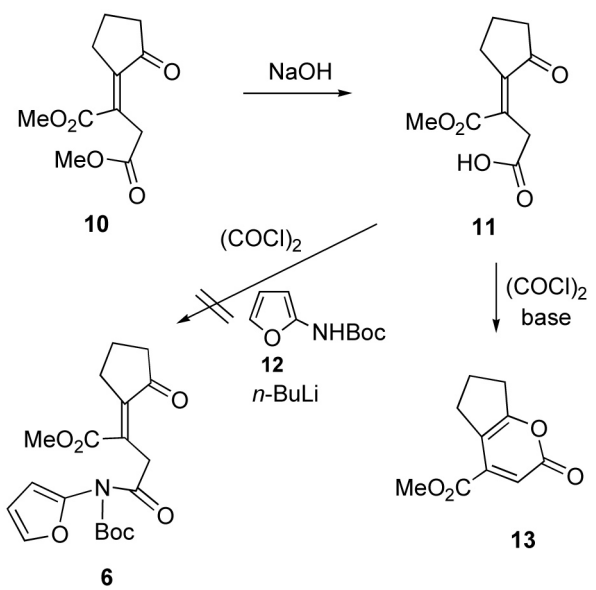
The base induced saponification of diester **10** proceeded smoothly with NaOH at 0 °C to give the expected mono-carboxylic acid **11** in excellent yield. However, all of our attempts to convert carboxylic acid **11** into furanyl carbamate **6** using either its acid chloride or mixed anhydride with the lithiated Boc-protected aminofuran **12** fai-



Scheme 2

led. Instead, the only product obtained corresponded to α-pyrone **13** (Scheme 3). Apparently, intramolecular cyclization of the activated carboxylic acid to α-pyrone **13** occurs at a much faster rate than bimolecular reaction with the lithiated amidofuran.

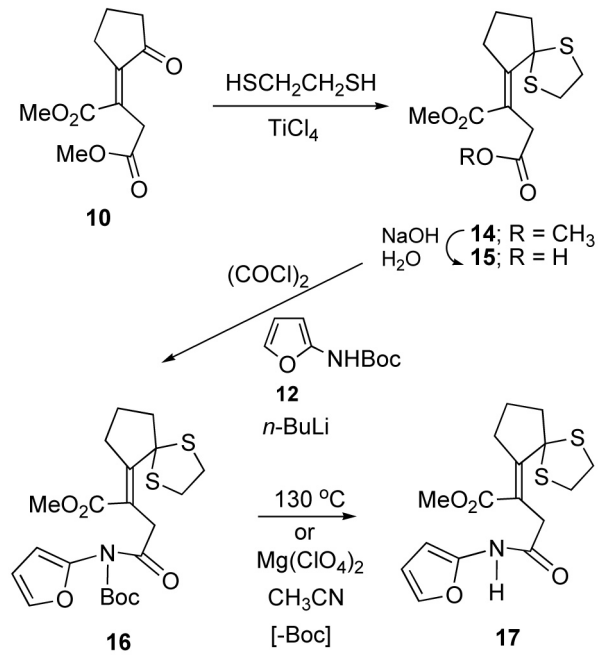
As a consequence of this ready cyclization, we decided to protect the keto group present in **10** so as to avoid α-pyrone formation in the coupling step. Thus, treatment of diester **10** with ethane-1,2-dithiol in the presence of 1 equiv of titanium tetrachloride furnished dithiane **14** in 85% yield. A subsequent base promoted saponification produced the expected carboxylic acid **15** which was smoothly converted to the corresponding furanyl carbamate **16** according to the reactions outlined in Scheme 4. Unfortunately, all of our attempts to induce the IMDAF reaction by heating **16** at 130 °C in toluene failed to give



Scheme 3

any cycloaddition product. Instead, the only product obtained corresponded to amide **17** derived by thermal loss of the Boc group. This same product could also be prepared by stirring a sample of **16** in CH_3CN at 50 °C in the presence of $Mg(ClO_4)_2$.

Our previous studies dealing with the bimolecular [4+2]-cycloaddition of 2-amino substituted furans have shown that the reaction rates and product of these thermolyses are markedly dependent upon the electronic properties of the alkenyl group.[21] Because electron-withdrawing substituents on the π-bond exhibit a powerful influence on the rate of HOMO-dienyl [4+2]-cycloadditions,[22] we reasoned that it might be possible to induce the desired thermal IMDAF reaction by converting the 1,3-



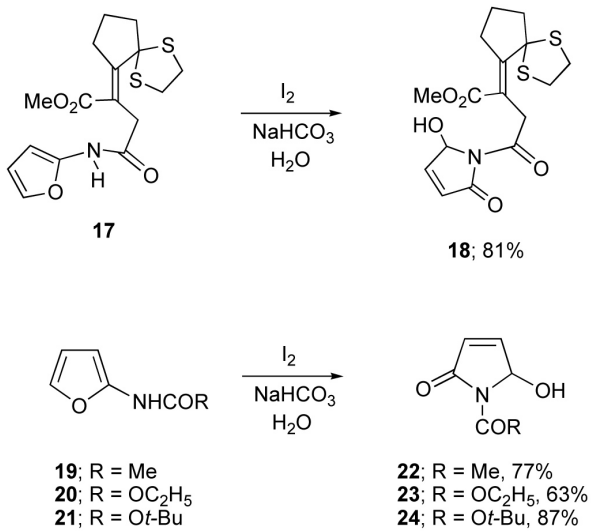
Scheme 4

dithiane functionality of **17** back to the corresponding carbonyl group. This would result in a lowering of the LUMO energy of the olefinic π-bond and should facilitate the HOMO/LUMO cycloaddition reaction of the resulting furanyl carbamate.

As a carbonyl protecting group, the S,S-ketal function has found wide use in organic synthesis due to its easy access and high stability towards both acidic and basic conditions.[23] 1,3-Dithianes are particularly important as intermediates for carbon-carbon bond formation reactions by way of temporary inversion of reactivity of electrophilic carbonyl carbon (umpolung) through metallation.[24] A large number of methods are available for deprotection of dithioketals to carbonyls.[25] However, the regeneration of the parent carbonyl compounds is not always a facile and straightforward process and therefore develop-

ment of dethioketalization protocols has engaged the attention of organic chemists over the years.[26] Many of the reported methods suffer from serious drawbacks such as the use of expensive catalysts,[27] toxic reagents[28] and in a few cases, more than stoichiometric amounts required of the reagents.[29]

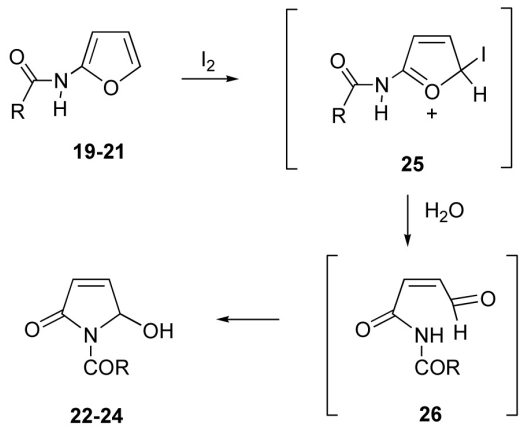
With this background in mind, we opted to adopt a simple and generally convenient method for the deprotection of dithianes[30] and this involved stirring a sample of **17** with iodine in a basic aqueous medium at 0 °C for 3 h. Rather than converting the 1,3-dithiane functionality in **17** into the corresponding keto group, a rather unusual oxidative rearrangement occurred. The major and unexpected product obtained from this reaction (81%) was identified as 5-hydroxy-1*H*-pyrrol-2(5*H*)-one **18** on the basis of its spectral data (Scheme 5). Related iodine induced oxidative rearrangements were also found to occur with amidofuran **19** as well as with furanyl carbamates **20** and **21**.



Scheme 5

It is well known that 2-furyl carbinols can be oxidatively rearranged to pyranones by a variety of reagents, such as bromine in methanol.[31] This transformation has become recognized as the Achmatowicz rearrangement in recognition of the pioneering work of O. Achmatowicz and his school in this area.[32] The aza-Achmatowicz oxidation corresponds to a related process which involves the conversion of furylamides into 1,6-dihydro-2*H*-pyridin-3-ones.[33] This novel oxidative rearrangement is often used for the synthesis of azasaccharides,[34] izidine structures, β-lactam intermediates, and unusual amino acids and has been shown to possess significant potential for the preparation of a variety of piperidine-based alkaloids.[35]

The oxidative process that we have uncovered and which is outlined in Scheme 5 is closely related to the aza-Achmatowicz reaction. The major difference is that the nitrogen atom is now attached directly to the furan ring rather than being separated from the heterocycle by a single carbon atom. More than likely the oxidative rearrangement proceeds by a mechanism related the aza-Achmatowicz reaction. This would involve electrophilic attack of iodine on the activated furan to sequentially provide intermediate **25** and then **26** which ultimately culminates in cyclization to furnish the 5-hydroxy-1*H*-pyrrol-2(5*H*)-one skeleton (Scheme 6). In the case of the dithianyl substituted carbamate **17**, the furan ring oxidation simply occurs at a faster rate than reaction at the S,S-ketal functionality.



Scheme 6

3. Conclusion

In conclusion, several 2-amidofurans were found to undergo a novel oxidative rearrangement when exposed to iodine to afford 5-hydroxy-1*H*-pyrrol-2(5*H*)-ones. The reaction proceeds by a mechanism similar to the aza-Achmatowicz oxidation. Electrophilic addition of iodine at the furan ring occurs at a faster rate than reaction at the 1,3-dithiane center with compound **17**, thereby preventing formation of the furanyl carbamate required for a synthesis of longeracinphyllin A. Application of other methods to generate the parent carbonyl compound from the 1,3-dithianyl substituted carbamate **17** is currently underway, the results of which will be disclosed in due course.

4. Experimental

(*E*)-Dimethyl 2-(2-oxocyclopentylidene)succinate (10). To a –78 °C solution containing 0.5 g (3.5 mmol) of dimethyl acetylenedicarboxylate and 0.96 g (5 mmol) of titanium tetrachloride in 10 mL of CH_2Cl_2 was added a solution of 0.55 g (3.5 mmol) of (trimethylsilyloxy)cyclopentene in 10 mL of CH_2Cl_2 dropwise over a period of 5 min. After stirring for an additional 20 min at –78 °C, ether was added and the organic layer was separated and

washed with water, brine, dried over $MgSO_4$, and evaporated under reduced pressure. The residue was subjected to silica gel chromatography to give dimethyl 1-hydroxybicyclo[3.2.0]hept-6-ene-6,7-dicarboxylate (**8**)[20] as a colorless oil in 20% yield: IR (film) 3400, 1710, 1640, 1280, and 1150 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.67 (m, 6H), 3.08 (m, 1H), and 3.82 (s, 6H); Anal. Calcd for $C_{11}H_{14}O_5$: C, 58.40; H. 6.24. Found: C, 58.27; H, 6.21.

A mixture containing 0.3 g (1.3 mmol) of the above alcohol **8** in 25 mL of *tert*-butyl alcohol was treated with sodium hydride (2 mmol) at 15 °C. After stirring for 10 min, several drops of acetic acid were added and the mixture was taken up in ether, washed with water, brine, dried over $MgSO_4$, and evaporated under reduced pressure. The residue was subjected to silica gel chromatography to give 0.18 g (60%) of **10** as a pale yellow oil; IR (film) 1735, 1700, 1620, 1200, and 990 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 41.95 (p, 2H, *J* = 7.6 Hz), 2.42 (t, 2H, *J* = 7.6 Hz), 3.12 (t, 2H, *J* = 7.6 Hz), 3.68 (s, 3H), 3.80 (s, 3H), and 4.06 (s, 2H); Anal. Calcd for $C_{11}H_{14}O_5$: C, 58.40; H, 6.24. Found: C, 58.32; H, 6.21.

(*E*)-Dimethyl 2-(1,4-dithiaspiro[4.4]nonan-6-ylidene)succinate (14). To a stirred solution containing 0.37 g (1.6 mmol) of the above diester **10** and 176 μL (2.1 mmol) of 1,2-ethanedithiol in 10 mL of CH_2Cl_2 at –78 °C was added 212 μL (1.9 mmol) of $TiCl_4$ dropwise. The reaction mixture was slowly stirred while warming to 0 °C over 2 h and then diluted with H_2O and extracted with Et_2O. The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by silica gel chromatography to give 0.42 g (85%) of **14** as a colorless oil; IR (thin film) 2951, 2870, 1732, 1434, 1333, 1278, 1197, 1166, and 1015 cm^{-1}; ^{1}H-NMR (400 MHz, CDCl3) δ 1.68 (p, 2H, *J* = 7.2 Hz), 2.17 (t, 2H, *J* = 7.2 Hz), 2.81 (t, 2H, *J* = 7.2 Hz), 3.24–3.31 (m, 2H), 3.35–3.41 (m, 2H), 3.59 (s, 3H), 3.66 (s, 3H), and 3.81 (s, 2H); ^{13}C-NMR (100 MHz, CDCl3) δ 24.5, 34.3, 35.1, 40.1, 50.2, 51.5, 51.6, 71.3, 123.5, 158.4, 167.7, and 171.7; HRMS Calcd. for [$C_{13}H_{18}S_2O_4$ + H^+]: 303.0725. Found: 303.0723.

1-Methyl 2-(1,4-dithiaspiro[4.4]non-6-ylidene)succinate (15). To a stirred solution containing 0.9 g (4.0 mmol) of diester **14** in 35 mL of a 10:1-mixture of THF/H_2O at 0 °C was added 26 mL of a 0.25 M NaOH solution (6.4 mmol) and the solution was stirred at rt for 4 h. The aqueous layer was acidified with 1 *N* HCl, extracted with EtOAc, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography to give 0.38 g (45%) of **15** as a white solid,[36] mp 144–145 °C; IR (thin film) 3184, 2953, 2922, 2730, 2636, 1704, 1636, 1434, 1289, 1192, 1165, 1093, 1063, 949, and 808 cm^{-1}; ^{1}H-NMR (400 MHz, CDCl3) δ 1.72–1.79 (m, 2H), 2.25 (t, 2H, *J* = 7.4 Hz), 2.88 (t, 2H, *J* = 7.4 Hz), 3.32–3.38 (m, 2H), 3.43–3.49 (m, 2H), 3.74 (s, 3H), and 3.93 (s, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 25.0, 35.0, 35.6, 40.6, 50.6, 52.0, 71.7, 123.4, 159.7, 168.1, and 177.4.

Methyl 4-(*tert*-Butoxycarbonyl-furan-2-yl-amino)-2-(1,4-dithiaspiro[4.4]non-6-ylidene)-4-oxo-butyrate(16). To a solution containing 0.4 g (2.2 mmol) of furan-2-yl carbamic acid *tert*-butyl ester (**12**) in 5 mL of THF at 0 °C was added dropwise 1.6 mL (2.2 mmol) of *n*-BuLi (2.5 M in hexane). The reaction mixture was stirred at 0 °C for 20 min. In a separate flask, 0.37 g (1.4 mmol) of 1-methyl 2-(1,4-dithiaspiro[4.4]non-6-ylidene)succinate (**15**) was dissolved in 5 mL of CH_2Cl_2 at –78 °C and 0.36 mL (4.0 mmol) of oxalyl chloride was added dropwise. After stirring for 25 min., the reaction mixture was warmed to 0 °C for 3 h and the solvent was removed under reduced pressure. The residue was taken up in 5 mL of THF and cooled to –78 °C and the above preformed lithiate was added dropwise *via* syringe. After stirring at –78 °C for 20 min and 0 °C for an additional 1 h, the reaction mixture was quenched with H_2O and extracted with EtOAc. The organic layer was washed with a saturated aqueous $NaHCO_3$ solution, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was subjected to flash silica gel chromatography to afford 0.28 g (36%) of the titled compound **16** as a pale yellow oil; IR (neat) 2956, 2928, 1714, 1435, 1394, 1202, 1154, and 1095 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.42 (s, 9H), 1.70–1.74 (m, 2H), 2.21 (t, 2H, *J* = 5.8 Hz), 2.85 (t, 2H, *J* = 5.8 Hz), 3.31–3.35 (m, 2H), 3.43–3.46 (m, 2H), 3.69 (s, 3H), 4.37 (s, 2H), 6.11 (dd, 1H, *J* = 2.4 and 0.8 Hz), 6.37 (dd, 1H, *J* = 1.6 and 1.2 Hz), and 7.28–7.29 (m, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 24.6, 27.7, 35.1, 38.0, 40.1, 50.2, 51.5, 71.5, 83.6, 105.7, 111.0, 124.2, 140.3, 143.6, 151.6, 157.4, 167.8 and 172.9; HRMS Calcd. for [$C_{21}H_{27}NO_6S_2$ + H^+]: 453.1280. Found: 453.1277.

Methyl 2-(1,4-Dithia-spiro[4.4]non-6-ylidene)-*N*-furan-2-yl-succinamate (17). To a solution containing 0.22 g (0.49 mmol) of methyl 4-(*tert*-butoxycarbonyl-furan-2-yl-amino)-2-(1,4-dithiaspiro[4.4]non-6-ylidene)-4-oxo-butyrate (**16**) in 5 mL of CH_3CN was added 0.14 g (0.6 mmol) of magnesium perchlorate. The solution was heated at 45 °C for 1.5 h, then cooled to room temperature and the solvent was removed under reduced pressure. The residue was subjected to flash silica gel chromatography to give 0.14 g (85% yield) of the titled compound **17** as a colorless oil; IR (neat) 3281, 2956, 2925, 1694, 1608, 1548, 1432, 1297, 1238, 1198, and 1145 cm^{-1}; ^{1}H-NMR (400 MHz, CDCl3) δ 1.74–1.83 (m, 2H), 2.25 (t, 2H, *J* = 6.4 Hz), 2.85 (t, 2H, *J* = 6.4 Hz), 3.32–3.37 (m, 2H), 3.46–3.51 (m, 2H), 3.73 (s, 3H), 3.91 (s, 2H), 6.25 (d, 1H, *J* = 3.2 Hz), 6.99 (s, 1H), and 8.16 (s, 1H); ^{13}C-NMR (100 MHz, CDCl3) δ 24.9, 35.7, 37.8, 40.8, 50.7, 52.3, 71.4, 95.1, 111.7, 124.2, 135.2, 145.8, 159.9, 167.1 and 168.4; HRMS Calcd. for [$C_{16}H_{19}NO_4S_2$ + H^+]: 354.0834. Found: 354.0833.

Methyl 2-(1,4-Dithiaspiro[4.4]non-6-ylidene)-4-(2-hydroxy-5-oxo-2,5-dihydropyrr-ol-1-yl)-4-oxo-butyrate (18). A mixture containing 0.036 g (0.43 mmol) of sodium bicarbonate and 0.054 mg (0.21 mmol) of iodine were successively added to 0.025 g (0.07 mmol) of methyl 2-(1,4-dithia-spiro[4.4]non-6-ylidene)-*N*-furan-2-yl-succinamate (**17**) in 5 mL of a 2:1-mixture of acetone/water at 0 °C. The reaction mixture was stirred for 3 h at 0 °C and then 15 mL of a saturated sodium thiosulfate solution was added. The solution was extracted with EtOAc and washed with brine, dried over magnesium sulfate, filtered, and concentrated under reduced pressure. The crude oil was purified by flash chromatography on silica gel to afford 0.021 g (81%) of the titled compound **18** as a pale yellow oil: IR (neat) 3441, 2926, 1731, 1434, 1361, 1232, and 1201 cm^{-1}; ^{1}H-NMR (400 MHz, CDCl3) δ 1.73–1.80 (m, 2H), 2.24 (t, 2H, *J* = 6.4 Hz), 2.92 (t, 2H, *J* = 6.8 Hz), 3.26–3.34 (m, 2H), 3.40–3.47 (m, 2H), 3.72 (s, 3H), 4.31 (brs, 1H), 4.49 (m, 1H), 6.14 (s, 1H), 6.20 (d, 1H, *J* = 6.4 Hz), and 7.16 (dd, 1H, *J* = 6.4 and 2.0 Hz); 13C-NMR (100 MHz, $CDCl_2$3) δ 24.7, 35.2, 37.2, 40.3, 50.4, 51.7, 71.5, 82.1, 123.2, 128.4, 147.5, 158.7, 167.8, 168.1 and 172.4.

1-Acetyl-5-hydroxy-1*H*-pyrrol-2(5*H*)-one (22). To a stirred solution containing 0.08 g (0.65 mmol) of *N*-(furan-2-yl)acetamide 37 in 50 mL of a 20:1-acetone/H_2O mixture at 0 °C was added 0.33 g (3.9 mmol) of $NaHCO_3$ and the reaction mixture was stirred for 10 min. A 0.49 g (1.9 mmol) sample of iodine was added in 3 portions and the mixture was stirred at 0 °C for 3 h, then quenched with a saturated aqueous sodium thiosulfate solution and extracted with EtOAc. The organic layer was washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by silica gel chromatography to give 0.05 g (77%) of **22** as a white solid, mp 86–87 °C (lit38 mp 90–91 °C); 1H-NMR (400 MHz, CDCl3) δ 2.54 (s, 3H), 4.48 (d, 1H, *J* = 4.0 Hz), 6.14–6.15 (m, 1H), 6.21 (dd, 1H, *J* = 6.0 and 1.2 Hz), and 7.16 (dd, 1H, *J* = 6.0 and 1.6 Hz); 13C-NMR (100 MHz, CDCl3) δ 24.3, 81.6, 128.2, 147.5, 167.8, and 171.3; Anal. Calcd. for $C_6H_7NO_3$: C, 51.06; H, 5.00; N, 9.92. Found: C, 50.87; H, 4.91; N, 9.89.

Ethyl 2-hydroxy-5-oxo-2,5-dihydro-1*H*-pyrrole-1-carboxylate (23). To a stirred solution of 6.1 g of furan-2-ylcarbamic acid ethyl ester (39 mmol) in 650 mL of a 10:1-acetone/H_2O mixture at 0 °C was added 19.8 g (236 mmol) of $NaHCO_3$ and the reaction mixture was stirred for 5 min. A 30 g sample (118.1 mmol) of iodine was added in 3 portions and the mixture was stirred at 0 °C for 3 h, then quenched with a saturated aqueous sodium thiosulfate solution and extracted with EtOAc. The organic layer was washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography to provide 4.2 g (63%) of **23** as a pale yellow oil; IR (thin film) 3424, 3103, 2985, 1775, 1726, 1532, 1427, 1374, 1305, 1207, 1172, 1098, and 1052 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.40 (t, 3H, *J* = 7.2 Hz), 4.11 (brs, 1H), 4.40 (q, 2H, *J* = 7.2 Hz), 6.05 (s, 1H), 6.19–6.21 (m, 1H), and 7.10 (dd, 1H, *J* = 6.0 and 2.0 Hz); 13C-NMR (100 MHz, CDCl3) δ 14.6, 63.5, 82.4, 128.9, 146.7, 151.9, and 166.0; HRMS Calcd. for [$C_7H_9NO_4$ + H+]: 172.0610. Found: 172.0609.

***tert*-Butyl 2-hydroxy-5-oxo-2,5-dihydro-1*H*-pyrrole-1-carboxylate (24).** To a stirred solution of 0.37 g of furan-2-ylcarbamic acid *tert*-butyl ester (**12**) (2.0 mmol) in 35 mL of a 10:1-acetone/H_2O mixture at 0 °C was added 1.0 g (12.0 mmol) of $NaHCO_3$ and the reaction mixture was stirred for 10 min. A 1.5 g (6.0 mmol) sample of iodine was added in 3 portions and the mixture was stirred at 0 °C for 3 h, then quenched with a saturated aqueous sodium thiosulfate solution and extracted with EtOAc. The organic layer was washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography to provide 0.35 g (87%) of **24** as a pale yellow solid, mp 80–81 °C; IR (thin film) 3428, 3102, 2981, 2935, 1766, 1368, 1314, 1258, 1160, 1106, and 1047 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.51 (s, 9H), 4.267–4.274 (m, 1H), 5.93 (d, 1H, *J* = 2.4 Hz), 6.09 (d, 1H, *J* = 4.4 Hz), and 7.00 (dd, 1H, *J* = 4.4 and 1.2 Hz); 13C-NMR (100 MHz, $CDCl_3$) δ 28.0, 82.1, 83.9, 128.4, 146.3, 149.9 and 166.4; HRMS Calcd. for [$C_9H1_3NO_4$ + H^+]: 200.0923 Found 200.0921.

5. Acknowledgement

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6. References

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Povzetek

E-Dimetil 2-(2-oksiciklopentilidenesuccinate je bil pripravljen s $TiCl_4$ kataliziranо [2+2]-cikloadicijo (trimetilsililoksi)ciklopentena z DMAD ter sledečim bazno induciranim odprtjem [2+2]-cikloadukta. Za nadaljnjo pretvorbo do *N*-furanil karbamata **16** je bilo potrebno keto skupino zaščititi kot 1,3-ditiane. Odstranitev Boc skupine z intermediata **16** in pretvorba v NH-karbamat je potekla v prisotnosti $Mg(ClO_4)_2$ pri 130 °C. Pri poskusu odstranitve Boc skupine z jodom pod bazičnimi pogoji pa je potekla precej nenavadna premestitev spojine **16** v substituiran 5-hidroksi-1*H*-pirol-2(5*H*)-on. Analogne oksidativne premestitev so potekle tudi s strukturno sorodnimi 2-amidofurani. Mehanizem omenjene oksidativne premestitve je primerljiv z aza-Achmatowiczevo reakcijo.