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Cycloadditions of Metal Oxyallyl Cations Generated from $\alpha\alpha'$-Dibromoketones to Furan and Pyrrole

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Summary. Furan (**1**) and 2,5-dimethylfuran (**2**) were added to tetrabromoacetone (**4**), 2,4-dibromopentan-3-one (**5**), and tribrombutanones **6a**,**b** under different reaction conditions to give the corresponding cycloadducts **7**–**10**, **11a**,**b**, and **12a**,**b** in moderate yields. Reductive debromination of **12a**,**b** with Zn/CuCl/NH_4Cl in methanol gave the debrominated cycloadduct **13** in good yield. The α,α'-dibromoketone **5** was added to 1-(2′-acetoxyethyl)pyrrole (**3**) to yield the corresponding cycloadduct **14** using the Na/Cu method. Upon attempted cycloaddition of **5** to the pyrrole derivative **3** using the $(EtO)_3B$/Zn method, the 2-substituted pyrrole derivatives **15a**–**d** were obtained. Almost all reactions resulted in the formation of a single isomer which by molecular mechanics calculations (MM3) also appeared to be the energetically most favored one.

Keywords. Cycloaddition; Oxyallyl cations; Stereoselectivity; MM3 calculations.

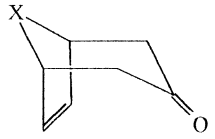
Cycloadditionen von Metalloxyallylkationen aus $\alpha\alpha'$-Dibromketonen an Furan und Pyrrol

Zusammenfassung. Furan (**1**) und 2,5-Dimethylfuran (**2**) wurden unter verschiedenen Reaktionsbedingungen an Tetrabromaceton (**4**), 2,4-Dibrompentan-3-on (**5**) und die Tribrombutanone **6a**,**b** addiert. Es entstehen die entsprechenden Cycloaddukte **7**–**10**, **11a**,**b** und **12a**,**b** in bescheidenen Ausbeuten. Reduktive Debromierung von **12a**,**b** mit Zn/CuCl/NH_4Cl in Methanol führt in guter Ausbeute zum debromierten Cycloaddukt **13**. Das α,α'-Dibromketon **5** konnte mittels der Na/Cu-Methode mit 1-(2′-Acetoxyethyl)-pyrrol (**3**) zum entsprechenden Addukt **14** umgesetzt werden. Der Versuch, diese Cycloaddition mit der $(EtO_3)B$/Zn-Methode durchzuführen, resultierte in den 2-substituierten Pyrrolderivaten **15a**–**d**. Fast alle Reaktionen ergaben einheitliche Produkte, die sich nach molekülmechanischen Berechnungen (MM3) als die energetisch günstigsten herausstellten.

Introduction

Seven-membered carbocycles are an important class of organic compounds that are of practical and theoretical interest. [4+3]-Cycloaddition of reactive three-carbon species with dienes is a convenient and straightforward method for the synthesis of a wide range of seven-membered rings [1] which cannot easily be prepared by other routes. The [4+3]-cycloaddition reaction of allyl cations with 1,3-dienes is an efficient and easy method for the stereoselective synthesis of seven-membered ring compounds [2].

Cycloaddition of metal oxyallyl cations to furan or pyrrole have been extensively studied for the preparation of 8-oxabicyclo[3.2.1]oct-6-en-3-ones (**a**) and 8-azabicyclo[3.2.1]oct-6-en-3-ones (**b**) which have served as starting materials for the synthesis of a number of natural products and tropane alkaloids [1, 2]. The reactivity and structure of oxyallyl cations towards [4+3]-cycloaddition reactions plays an active role with respect to yield and formation of the cycloadducts and will thus be investigated.



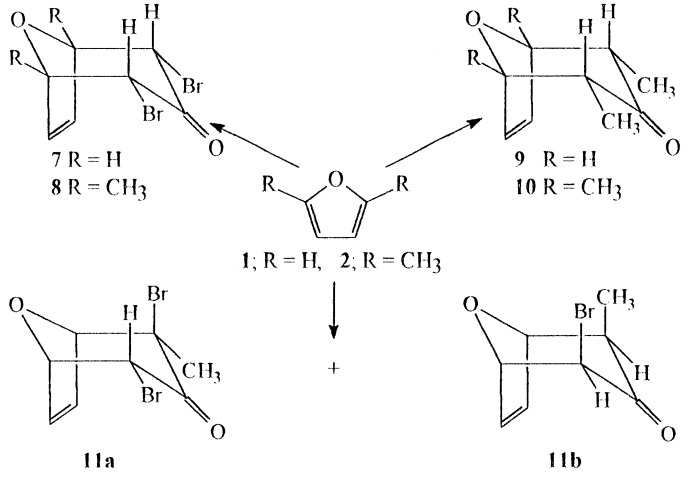
a: X = O
b: X = NR

Molecular mechanics calculations (MM3) [3] on the structures of the title compounds should provide insight into the stereochemistry of the various cycloadditions.

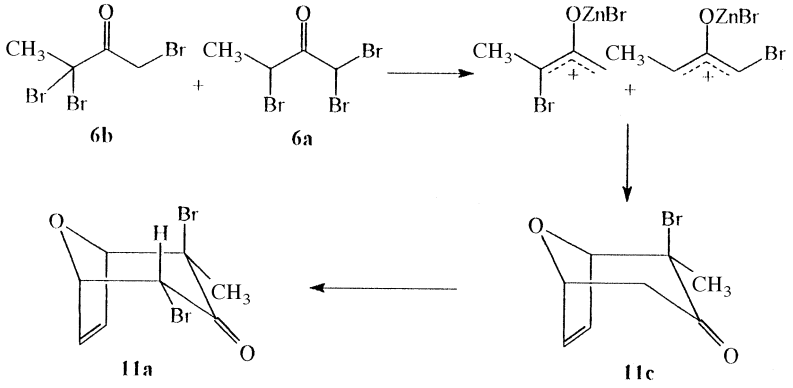
Results and Discussion

It is known that cycloadditions of tetrabromoacetone (**4**) to furan (**1**) and 2,5-dimethylfuran (**2**) employing the Zn-Cu couple in dioxane and sonication at 0–20°C afford the *cis*-diequatorial *ee* adducts **7** and **8** stereoselectively [2]. Therefore it seemed to be of interest if this reaction would also proceed with a less activated adduct. Accordingly, 2,4-dibromopentan-3-one (**5**) was allowed to cycloadd to furan (**1**) and 2,5-dimethylfuran (**2**) in the presence of NaI/Cu in acetonitrile at 50°C to give the corresponding isomers **9** (48%) [2g] and **10** (56%) stereoselectively [1f] (Scheme 1).

Moreover, tribromobutanones **6a**,**b** were prepared and allowed to cycloadd to furan (**1**) using the Zn-Cu/dioxane/ultrasonic method at 0–20°C for 4 h to give the



Scheme 1



Scheme 2

cycloadducts **11a**,**b**. Formation of the cycloadduct **11a** is believed to arise from bromination of the cycloadduct **11c** by $ZnBr_2$ [4] formed *in situ* during the generation of the allyl cations from both **6a** and **6b**. The monobromo cycloadduct **11c** could not be isolated from the reaction mixture. Formation of the isomer **11c** is suggested to proceed as shown in Scheme 2.

The reactivity of the allyl cation generated from **6a** towards the cycloaddition reaction is higher than that formed from **6b**. This is probably a consequence of steric hindrance caused by the methyl group and bromine atom on the same carbon atom.

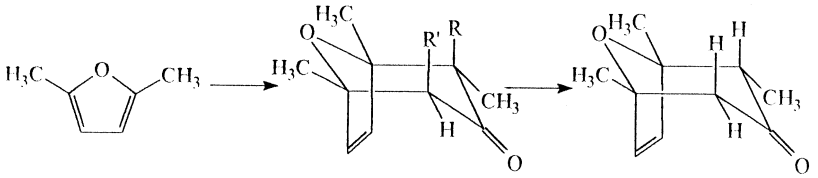
In the isomer **11a** the two bromine atoms are shown to be oriented *cis-trans* with an *e*,*a*-conformation. This conformation was confirmed by molecular mechanics calculations (MM3) which support the formation of an *e*,*a* arrangement rather than that of an *e*,*e* or *a*,*a* assembly. In the isomer **11b**, H-2 and H-4 occupy *cis*-diequatorial positions.

A spectroscopic discrimination of this type of stereoisomers is often quite difficult to achieve [5]. However, it should be noted that the cycloadduct **11b** shows a long-range coupling, in contrast to the coupling usually found in planar H–C–C–C–H chains. The ^{1}H NMR spectrum of **11b** revealed a J^4 coupling of H-2 and H-4 ($J^4 = 0.5$ Hz). This can only be the case if H-2 and H-4 are oriented *cis*-diequatorially (e,e).

The isomers **12a**,**b** were prepared in good yields by the cycloaddition of tribromobutanones **6a**,**b** to 2,5-dimethylfuran (**2**) using the Zn–Cu couple in dioxane by the ultrasonic method [5]. Reductive debromination of the bromocycloadducts **12a**,**b** by the Zn–Cu/NH_4Cl/MeOH method [6] gave the corresponding 1,2,5-trimethyl-8-oxabicyclo[3.2.1]oct-6-en-3-one (**13**) in 78% yield (Scheme 3).

Tetrabromoacetone (**4**), 2,4-dibromo-pentan-3-one (**5**), and tribromobutanones **6a**,**b** were prepared according to methods reported in the literature [2g, 7].

The tribromobutanones **6a**,**b** were not separated and used as a mixture in further reactions. The percentage of 1,1,3-tribromobutan-2-one (**6a**, 38%) and 1,3,3-tribromobutan-2-one (**6b**, 62%) in the mixture was in accordance with the ^{1}H NMR and ^{13}C NMR data [8]. Compounds **6a**,**b** were used as a mixture to find



2 **12a:** R = H, R' = Br **12b:** R = Br, R' = H 13

Scheme 3

out whether the oxyallyl cation of **6a** or **6b** is more reactive towards the cycloaddition with both furan and 2,5-dimethylfuran.

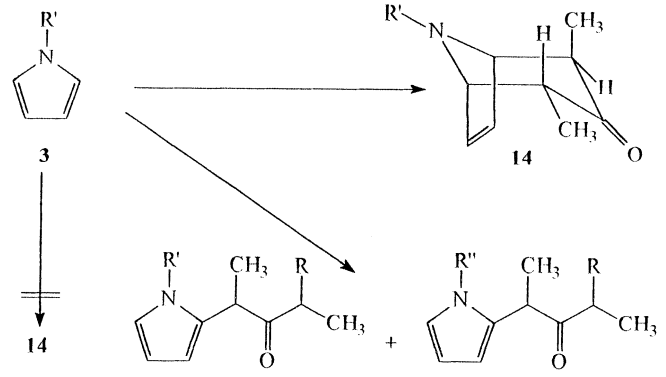
In accordance with the percentage of **6a** and **6b** in the reaction mixture and the yield of the cycloadducts **12a**,**b**, the oxyallyl cation from **6a** is more reactive than that from **6b** (Scheme 4). The cycloaddition of **6a**,**b** to 2,5-dimethylfuran was accomplished stereoselectively. Stereochemical relationships with respect to the carbons C-2 and C-4 are based on molecular mechanics calculations (MM3).

On the other hand, the cycloaddition of 2,4-dibromopentan-3-one (**5**) to pyrrole derivative **3** using the NaI/Cu method [2g] in acetonitrile at 50°C gave the corresponding cycloadduct **14** in 76% yield. The product was confirmed to be the *cis-trans* isomer with the two methyl groups in equatorial-axial positions. The isomer **14** showed also no long-range coupling in contrast to interactions usually observed in planar H–C–C–C–H chains. In contrast, the cycloaddition of dibromoketone **5** to pyrrole derivative **3** using the triethylborate/zinc method $(EtO)_3B/Zn/THF$, RT, 4 h) [9] afforded a mixture of the substituted pyrrole derivatives **15a–d** in 61% overall yield rather than the cycloadduct **14** which was formed only using the NaI/Cu method.

The first isomer (**15a**) was identified as 1-(2-acetoxyethyl)-2-(3′-bromo-1′-methyl-2′-oxobutyl)-pyrrole, the second isomer (**15b**) as a debrominated derivative of **15a**. The third isomer is 1-(2-hydroxyethyl)-2-(3′-bromo-1′-methyl-2′-oxobutyl)-pyrrole (**15c**), and the fourth one 1-(2-hydroxyethyl)-2-(1′-methyl-2′-oxobutyl)-pyrrole (**15d**) (Scheme 5).

It is known that the cycloaddition of an allyl cation to a conjugated diene may proceed *via* the compact transition state **16** and or the extended one **17**. The W-configured acyclic allyl cation, when added to the conjugated diene, leads to the initial conformation **19** containing a six-membered boat moiety that is thermodynamically unfavorable; therefore, ring flipping occurs to give the more stable conformer **20** [1b].

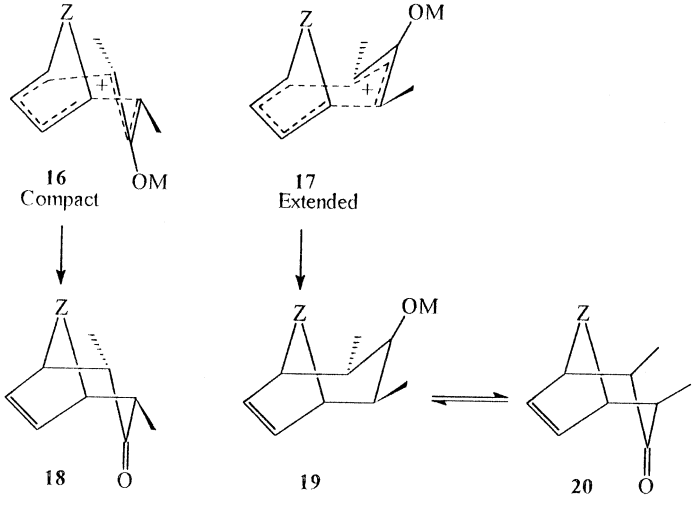
Scheme 4



15a,**b**: $R' = CH_2CH_2OCOCH_3$ **15c**,**d**: $R'' = CH_2CH_2OH$
15a: $R = Br$ (15%), **15b**: $R = H$ (12%), **15c**: $R = Br$ (14%), **15d**: $R = H$ (20%)

Scheme 5

From semiempirical molecular orbital calculations (CNDO/2) it was concluded that the compact conformation of cycloadducts like **18** is preferred over the extended one (**20**) [1b, 10]. Therefore, the conformation of such systems and that of the nitrogen analogue **14** was investigated by means of MM3 calculations [3] (Scheme 6). It was found that the minimized heats of formation ($kJ \cdot mol^{-1}$) decrease in the following order: **7** e^{Me} e^{Me} (−245.0) > **11b** a^{Me} a^{Br} (−251.6) > **9** e^{Me} e^{Me} (−271.4) > **11a** e^{Br} a^{Br} (−274.1) > **13** e^{Me} e^{M} (−325.3) > **8** e^{Me} e^{Me} (−328.0) > **12b** e^{Me} a^{Br} (−333.5) > **12a** e^{Me} a^{Br} (−334.8) > **10** e^{Me} e^{Me} (−349.7) > **14** e^{Me} e^{Me} (−469.2). As an example, the minimum energy conformation of **14** (e^{Me}, a^{Me}) is shown in Fig. 1.



Scheme 6

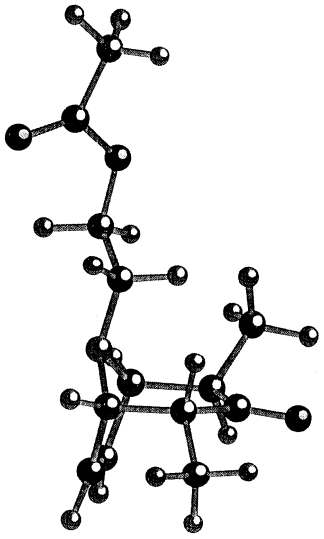


Fig. 1. Ball & Stick model of the most stable *trans* **14** (e^{Me},a^{Me}) conformation according to the MM3 calculations

Experimental

Column chromatography (silica gel, 0.02–0.63 mm, Merck) was carried out under weak positive pressure. TLC: precoated plates, Macherey-Nagel, Merck; IR spectra: Electrophotometer 580 and FT spectrometer 1710, Perkin-Elmer; ^{1}H NMR: WP 200 SY and AM 300, Bruker; ^{13}C NMR: WP 200 SY, AM 300, Bruker, APT (attached proton test); MS: Spectrometer MAT 312, Finnigan company, Spectral Unit, Department of Organic Chemistry (Hannover University, D-30167 Hannover, Germany). Elemental analyses were in satisfactory agreement with the calculated values. Cycloadduct **7** was prepared according to Refs. [1f–g, 2c], cycloadduct **8** according to Ref. [2c], cycloadduct **9** according to Ref. [2g]. Cycloadduct **10** has also been prepared by *Noyori et al* [1f] as colorless crystals, mp.: 66–67°C.

2,4-Dibromo-2-methyl-8-oxabicyclo[3.2.1]oct-6-en-3-one (**11a**; $C_8H_8Br_2O_2$) and *2-Bromo-4-methyl-8-oxabicyclo[3.2.1]oct-6-en-3-one* (**11b**; $C_8H_9BrO_2$)

A mixture of Zn powder (4 mmol), Cu(I)Cl (0.4 mmol), and furan (**1**, 5 ml) in 20 ml absolute dioxane in a three-necked flask was sonicated under nitrogen in an ultrasonic bath, and a solution of tribromobutanones **6a**,**b** (2 mmol) in 10 ml dry dioxane was added dropwise over a period of 0.5 h. The bath temperature was maintained below 20°C, and the reaction mixture was sonicated for 4 h. Afterwards, the reaction mixture was filtered, and the solvent was removed under vacuum. The residue was washed with H_2O and extracted with CH_2Cl_2. The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated under vaccum. The crude product was chromatographed on silica gel 60 (Macherey and Nagel, 0.05–0.2 mm, 100:1) to give **11a** as a colorless oil (yield: 32%, needles upon standing; m.p.: 92°C) followed by **11b** (yield: 20% m.p.: 62°C). **11a**: RF (*E*/*PE* 1:5) = 0.62; IR ($CHCl_3$) ν = 2964w, 2928w, 2856w, 1736s, 1448w, 1136s, 1104s, 820s cm^{-1}; NMR (200 MHz, δ, $CDCl_3$): 2.05 (s, 3H, CH_3-2), 4.9 (d, J = 2 Hz, 1H-4), 4.94 (d, J = 5 Hz, 1H-1), 5.1 (dd, J = 2 Hz, J = 6 Hz, 1H-5), 6.55 (dd, J = 2 Hz, J = 6 Hz, 1H-6 (7)), 6.65 (dd, J = 2 Hz, J = 6 Hz, 1H-7 (6)) ppm; MS: *m*/*z* (%) = 295 [M^+] (3), 280 (2), 217 (99), 215 (100), 200 (2), 189 (3), 171 (8), 159 (9), 136 (28), 121 (4), 108 (49), 95 (44), 81 (45), 79 (35), 67 (11), 65 (14), 55 (9), 51 (26), 45 (1).

11b: RF (*E/PE* 1:5) = 0.54; IR (thin film): $\nu = 2970$m, 1732s, 1593m, 1441m, 1134s, 1060s, 819m, 717s cm^{-1}; ^1H NMR (200 MHz, δ, $CDCl_3$): 1.07 (d, $J = 7$ Hz, 3H, CH_3-4), 3.05 (ddq, $^4J = 0.5$ Hz, $J = 7$ Hz, $J = 7$ Hz, 1H-4), 4.75 (dd, $^4J = 0.5$ Hz, $J = 5$ Hz, 1H-2), 4.87 (dd, $J = 2$ Hz, $J = 5$ Hz, 1H-5), 5.15 (dd, $J = 2$ Hz, $J = 5$ Hz, 1H-1), 6.41 (dd, $J = 2$ Hz, $J = 7$ Hz, 1H-6 (7)), 6.50 (dd, $J = 2$ Hz, $J = 7$ Hz, 1H-7 (6)) ppm; MS: *m/z* (%) = 217 [M^+] (1), 216 [M^{-1}] (3), 203 (8), 201 (8), 169 (1), 161 (2), 159 (2), 143 (3), 137 (95), 122 (6), 109 (20), 96 (35), 91 (10), 81 (100), 79 (17), 73 (7), 67 (14), 65 (14), 53 (5), 51 (2).

2-Bromo-1,4,5-trimethyl-8-oxabicyclo[3.2.1]oct-6-en-3-one (**12a**; $C_{10}H_{13}BrO_2$) *and* *2-Bromo-1,2,5-tri-methyl-8-oxa-bicyclo[3.2.1]oct-6-en–3-one* (**12b**; $C_{10}H_{13}BrO_2$)

According to the general procedure used above, 2,5-dimethylfuran (**2**, 1 mmol) and tribromobutanones **6a**,**b** (2 mmol) were allowed to react. Chromatography (ether/pet.ether 1:5) afforded **12a** (38%) in the first fraction followed by **12b** (31%).

12a: RF (ether/cyclohexane 1:6) = 0.42; IR (KBr): $\nu = 2979$m, 2935m, 2873m, 1727s, 1605w, 1449m, 1378m, 1167s, 1140s, 1049m, 819m, 739s cm^{-1}; ^1H NMR (200 MHz, δ, $CDCl_3$): 1.1 (d, $J = 7$ Hz, 3H, CH_3-4), 1.5, (s, 3H, CH_3-5), 1.7 (s, 3H, CH_3-1), 2.72 (q, $J = 7$ Hz, 1H-4), 4.55 (s, 1H-2), 6.1 (d, $J = 7$ Hz, 1H-6(7)) 6.18 (d, $J = 7$ Hz, 1H-6(7)) ppm; ^{13}C NMR (50.3 MHz, δ, $CDCl_3$): 10.89 (CH_3-4), 21.35, 22.60 (2 CH_3-1,5), 57.31, 62.86 (2 CH-2,4), 87.92, 88.01 (2 C-1,5), 135.51, 136.80 (2 CH-6,7), 199.59 (C = O) ppm; MS: *m/z* (%) = 247 [M^{+2}] (7), 245 [M^+] (7), 229 (3), 210 (3), 187 (5), 178 (4), 165 (70), 149 (4), 137 (13), 135 (13), 123 (38), 109 (100), 95 (20), 85 (18), 83 (30), 77 (9), 65 (8), 56 (12), 51 (6), 45 (2).

12b: RF (ether/cyclohexane 1:6) = 0.34; IR ($CHCl_3$): $\nu = 2928$m, 2852w, 1712s, 1612s, 1400s, 1380s, 1096s, 1008w, 840w cm^{-1}; ^1H NMR (200 MHz, δ, $CDCl_3$): 1.47 (s, 3H, CH_3-2), 1.65 (s, 3H, CH_3-1(5)), 1.9 (s, 3H, CH_3-5(1)), 2.56 (d, $J = 15$ Hz, 1H, (CH_2-4, AB-system), 2.83 (d, $J = 15$ Hz, 1H, CH_2-4, AB-system), 6.03 (d, $J = 5$ Hz, 1H-6(7)), 6.27 (d, $J = 5$ Hz, 1H-7(6)) ppm; ^{13}C NMR (50.3 MHz, δ, $CDCl_3$): 18.16 (CH_3, C-2), 22.50, 24.33 (2CH_3, C-1,5), 47.26 (C-2), 51.26 (CH_2, C-4), 84.55, 84.72 (2C, C-1,5), 136.93, 139.07 (2CH, C-6,7), 202.17 (CO) ppm; MS: *m/z* (%) = 246 [M^{+1}] (10), 245 [M^+] (10), 229 (10), 215 (2), 201 (5), 189 (21), 187 (43), 185 (24), 173 (15), 165 (33), 149 (7), 137 (97), 135 (100), 123 (81), 121 (88), 110 (62), 109 (68), 107 (76), 95 (53), 82 (15), 79 (11), 77 (9), 69 (10), 65 (5), 56 (57), 51 (9), 45 (2).

1,2,5-Trimethyl-8-oxabicyclo[3.2.1]oct-6-en-3-one (**13**; $C_{10}H_{14}O_2$)

A mixture of zinc powder (100 mmol), Cu(I)Cl (10 mmol), and 2 g NH_4Cl was stirred in 20 ml absolute CH_3OH at room temperature. The bromocycloadducts **12a**,**b** (10 mmol) dissolved in 20 ml absolute CH_3OH were added dropwise at room temperature. After stirring at room temperature for further 3.5 h, the reaction mixture was filtered through silica. The residue was washed with ether, the combined filtrates were extracted with water, dried ($CaCl_2$), and evaporated. The crude product was chromatographed (ether/petrol ether 2:5) to give adduct **13** in 78% yield.

M.p.: 34°C; RF (ether/petrol ether 3:5) = 0.5; IR (thin film): $\nu = 2976$s, 2933s, 2874m, 1714s, 1447s, 1407s, 1340s, 1177s, 1096s, 1039s, 819m, 748s cm^{-1}; ^1H NMR (200 MHz, δ, $CDCl_3$): 1.03 (d, $J = 7$ Hz, 3H, CH_3-2), 1.47 (s, 3H, CH_3-1(5)), 1.52 (s, 3H, CH_3-5(1)), 2.47 (q, $J = 7$ Hz, 1H-2), 2.37 (d, $J = 15$ Hz, 1H, CH_2-4, AB-system), 2.56 (d, $J = 15$ Hz, 1H, CH_2-4, AB-system), 6.0 (s, 2H-6,7) ppm; MS: *m/z* (%) = 167 [M^{+1}] (8), 166 [M^+] (46), 151 (7), 138 (2), 133 (2), 124 (16), 123 (52), 109 (97), 105 (3), 95 (100), 91 (4), 81 (9), 79 (7), 77 (5), 67 (14), 56 (10), 51 (5), 45 (2).

8-(2-Acetoxyethyl)-2,4-dimethyl-8-azabicyclo[3.2.1]oct-6-en-3-one (**14**; $C_{13}H_{19}NO_3$)

To a well-stirred mixture of 1.21 g NaI (8 mmol), 0.385 g Cu powder (6 mmol), and **3** (2 mmol) in 20 ml CH_3CN under N_2 a solution of **5** (3 mmol) in 20 ml CH_3CN was added dropwise over a period

of 30 min at room temperature. The temperature of the reaction mixture raised to 50°C. The mixture was stirred for further 5 h. Work-up was affected by pouring it into a mixture of aqueous NH_3 and anhydrous diethyl ether contained in a separating funnel after cooling. The combined etheral solutions were washed with dilute NH_3 and then with water until neutral. After washing with saturated brine, the etheral solution was dried ($MgSO_4$). The ether was removed under reduced pressure, and the residue was chromatographed on silica (ether/petrol ether 2:5) to give cycloadduct **14** in 76% yield as a colorless oil.

RF (ether/petrol ether 3:5) = 0.49; IR (thin film): $\nu = 3068$w, 2968s, 2936s, 2875m, 1741s, 1708s, 1375s cm^{-1}; ^{1}H NMR (200 MHz, δ, $CDCl_3$): 0.98 (d, 6H, $J = 7$ Hz, 2 CH_3-2,4), 2.08 (s, 3H, CH_3CO), 2.69 (t, $J = 6$ Hz, 2H, NCH_2), 2.71 (dq, $J = 7$ Hz, $J = 2$ Hz, 2H, H-2,4), 3.69 (d, $J = 4$ Hz, 2H-1,5), 4.22 (t, $J = 6$ Hz, 2H, OCH_2), 6.19 (s, 2H-6,7) ppm; ^{13}C NMR (50.3 MHz, δ, $CDCl_3$): 12.09 (2 CH_3-2,4), 20.95 (CH_3CO), 50.25 (C-2, C-4), 51.69 (NCH_2), 63.20 (OCH_2), 70.45 (C-1, C-5), 133.34 (C-6, C-7), 170.89 ($COOCH_3$), 210.85 (CO-3) ppm; MS: *m/z* (%) = 238 [M^{+1}] (4), 237 [M^+] (17), 222 (6), 181 (50), 180 (62), 94 (28), 93 (24), 87 (100), 80 (29).

Application of the triethylborate/Zn method for the preparation of cycloadduct **14**; *synthesis of 2-substituted N-acetoxyethylpyrroles* **15a–d**

A mixture of 1.15 g N-acetoxyethylpyrrole **3** (7.5 mmol) and 0.735 g Zn powder (11.25 mmol) was sonicated in 20 ml *THF* under a stream of N_2 at room temperature. While the mixture was sonicated in an ultrasonic bath, a solution of 2.745 g **5** (11.25 mmol) and 1.6 g $(EtO)_3B$ (11.25 mmol) in 20 ml *THF* was added dropwise over a period of 30 min at room temperature. The reaction mixture was further sonicated below 20°C for another 4 h. The reaction mixture was worked up by filtration, and the *THF* was removed under vacuum. The residue was dissolved in CH_2Cl_2, washed with water several times, and separated. The combined organic layer was dried ($CaCl_2$), filtered off, and the filtrate was concentrated under vacuum till dryness. The residue was chromatographed on silica (ether/petrol ether 1:5) to give a mixture of isomers **15a–d** as a colorles oil in 61% overall yield.

1-(2-Acetoxyethyl)-2-(1-methyl-3-bromo-2-oxobutyl)pyrrole (**15a**; $C_{13}H_{18}BrNO_3$)

Yield: 15%; RF (ether/petrol ether 2:5) = 0.61; IR (thin film); $\nu = 2976$s, 2934s, 1743s, 1719s, 1503s, 1445s, 1339s, 1235s, 1050s, 771s cm^{-1}; ^{1}H NMR (200 MHz, δ, $CDCl_3$): 1.4 (d, $J = 7$ Hz, 3H, CH_3-1′), 1.62 (d, $J = 7$ Hz, 3H, CH_3-4′), 2.05 (s, 3H, CH_3CO), 4.03–4.35 (m, 5H, NCH_2CH_2O, 1H, CH-1′), 4.6 (q, $J = 7$ Hz, 1H, CH-3′), 6.0 (m, 1H, H-4), 6.4–6.5 (m, 2H, H-4,5) ppm; ^{13}C-NMR (50.3 MHz, δ, $CDCl_3$): 17.736, 19.829, 20.80 (3 CH_3), 41.83, 44.99 (2 CH-1′,3′), 48.35 (NCH_2), 63.76 (OCH_2), 107.88, 118.94, 121.57 (3 CH-3, 4,5), 122.16 (C-2), 170.53 (*C*OO), 203.83 (C=O-2′) ppm; MS: *m/z* (%) = 316 [M^+] (2), 314 (2), 237 (2), 207 (1), 181 (10), 180 (79), 178 (1), 167 (1), 164 (2), 153 (3), 138 (9), 120 (16), 113 (7), 107 (10), 94 (23), 87 (100), 80 (10), 79 (8), 73 (6), 67 (9), 65 (7).

1-(2-Acetoxyethyl)-2-(1-methyl-2-oxobutyl)pyrrole (**15b**; $C_{13}H_{19}NO_3$)

Yield: 12%; RF (ether/petrol ether 2:5) = 0.5; IR (thin film): $\nu = 2977$s, 2938s, 1743s, 1717s, 1481s, 1455s, 1371s, 1235s, 1049s, 715s cm^{-1}; ^{1}H NMR (200 MHz, δ, $CDCl_3$): 0.95 (t, $J = 7$ Hz, 3H, CH_3-4′), 1.47 (d, $J = 7$ Hz, 3H, CH_3-1′), 2.05 (s, 3H, CH_3CO), 2.2–2.45 (m, 2H, CH_2-3′), 3.8 (q, $J = 7$ Hz, 1H, CH-1′) 4.03 (m, 2H, NCH_2CH_2O-), 4.25 (m, 2H, NCH_2CH_2O-), 6.0 (m, 1H, H-3), 6.13 (m, 1H, H-4), 6.5 (m, 1H, H-5) ppm; ^{13}C-NMR (50.3 MHz, δ, $CDCl_3$): 7.95, 16.58, 20.77 (3 CH_3), 31.77 (CH_2-3′), 44.91 (N CH_2), 45.05 (CH-1′), 63.70 (OCH_2), 106.88, 108. 121.61 (3 CH-3, 4, 5), 131.30 (C-2), 170.54 (*C*OO), 211.34 (CO-2′) ppm; MS: *m/z* (%) = 237 [M+1] (2), 236 [M^+] (2), 182

(2), 180 (83), 164 (1), 150 (1), 148 (2), 138 (9), 120 (14), 106 (11), 94 (23), 87 (100), 77 (7), 67 (5), 65 (6).

1-(2-Hydroxyethyl)-2-(1-methyl-3-bromo-2-oxobutyl)pyrrole (**15c**; $C_{11}H_{16}BrNO_2$)

Yield: 14%; IR (thin film): $\nu = 3442$s, 2977s, 2935s, 2878s, 1719s, 1478s, 1445s, 1375s, 1235s, 1122s, 1054s, 1026s, 718s cm^{-1}; ^1H NMR (200 MHz, δ, $CDCl_3$): 1.4 (d, $J = 7$ Hz, 3H, CH_3-1′), 1.6 (d, $J = 7$ Hz, d, 3H, CH_3-4′), 3.8–4.1 (m, 5H, NCH_2CH_2OH), 4.2 (q, $J = 7$ Hz, 1H, CH-1′), 4.65 (q, $J = 7$ Hz, 1H, CH-3′), 6.0–6.75 (m, 3H, arom-H) ppm; MS: *m/z* (%) = 275 [M+1] (2), 273 [M−1] (2), 195 (1), 180 (5), 170 (6), 153 (2), 141 (3), 138 (100), 123 (4), 113 (31), 110 (11), 106 (6), 94 (11), 87 (7), 86 (24), 77 (7), 67 (13), 65 (7).

1-(2-Hydroxyethyl)-2-(1-methyl-2-oxobutyl)pyrrole (**15d**; $C_{11}H_{17}NO_2$)

Yield: 20%; IR (thin film); $\nu = 3421$s, 2976s, 2936s, 2879s, 1714s, 1502s, 1481s, 1451s, 1292s, 1164s, 1055s, 866m, 715s cm^{-1}; ^1H NMR (200 MHz, δ, $CDCl_3$): 0.95 (t, $J = 7$ Hz, 3H, CH_3-4′), 1.4 (d, $J = 7$ Hz, 3H, CH_3-1′), 2.4 (q, $J = 7$ Hz, 2H, CH_2-3′), 2.7 (b, 1H, OH), 3.7–3.95 (m, 5H, NCH_2CH_2O, 1H, CH-1′), 5.97 (m, 1H, H-4), 6.1 (m, 1H, H-3), 6.7 (m, 1H, H-5) ppm; MS: *m/z* (%) = 196 [M^{+1}] (6), 180 (1), 139 (11), 138 (100), 125 (4), 120 (7), 110 (22), 106 (7), 103 (3), 94 (17), 91 (6), 87 (1), 81 (4), 77 (9), 67 (9), 65 (7).

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[8] ^{1}H NMR of **6a**,**b** ($CDCl_3$): **6a**: $\delta = 1.9$ (d, $J = 7$ Hz, 3H, CH_3), 5.0 (q, $J = 7$ Hz, 1H-3), 6.38 (s, 1H-1) ppm; **6b**: $\delta = 1.42$ (s, 3H, CH_3), 4.77 (s, 2H, CH_2-1) ppm; ^{13}C NMR (APT, $CDCl_3$) of **6a**,**b**: **6a**: $\delta = 20.89$ (CH_3), 39.21 (CH-3), 40.22 (CH-1), 189.63 (C=O) ppm; **6b**: $\delta = 26.91$ (CH_2), 28.71 (C-3), 35.13 (CH_3), 190.12 (C=O) ppm. The tribromobutanone **6a** has been prepared recently according to Ref. [7c] in 73% yield

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