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Photoreactions of Benzonitrile with Cyclic Enol Ethers[a,b]

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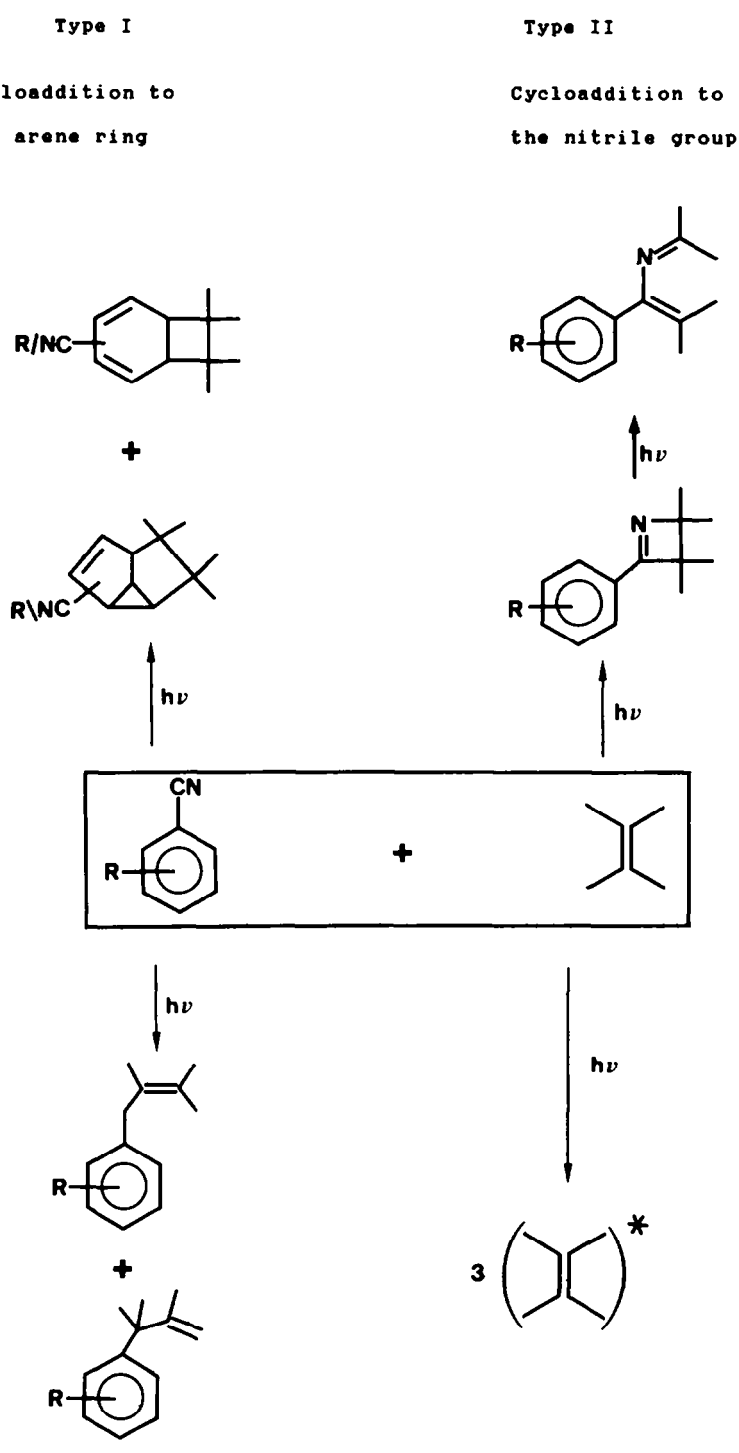
Abstract - Upon irradiation, cyclic enol ethers such as 1-methoxycyclopentene (4) mainly add across the cyano group of benzonitrile (1), under formation of 2-azabutadienes of an imidoester type. This is in agreement with the so-called ΔG-correlation which was reported earlier (ref. 5 and 6). 4-Phenyloxazole (9) is formed from 1 and 1,3-dioxole (5) probably by a similar photochemical process followed by electrocyclic ring opening and hydrolysis. The low yield of the latter photoreaction and the almost exergonic electron transfer between 5 and 1 may point to back electron transfer as the main energy wasting process. From 1 and 2,3-dihydrido-furan (2) only the ortho cycloadduct 6 has been isolated in low yields.

Since the early report of Büchi [1)] about the ortho cycloaddition of alkenes to benzonitrile different modes of photoreactions of cyano arenes with olefins, such as substitution at the arene ring [2)], cycloaddition to the nitrile group [3)] and more recently meta cycloaddition [4)], have been discovered. In addition triplet formation is sometimes observed [5)] (Scheme 1).

The first evidence for the involvement of polar factors in photoreactions of type I and II was already provided by Cantrell [3)], whereas Arnold's work [2)] was focussed more on the electron transfer aspects of the substitution reactions (type III). Recently all these features have been summarized by one of us resulting in a correlation between the free enthalpies of electron transfer and the selectivities of these reactions [5,6)]. Besides the usefulness of type I reactions with benzene derivatives, which lead e.g. to the synthesis of polycyclic natural products via the meta cycloaddition reported by

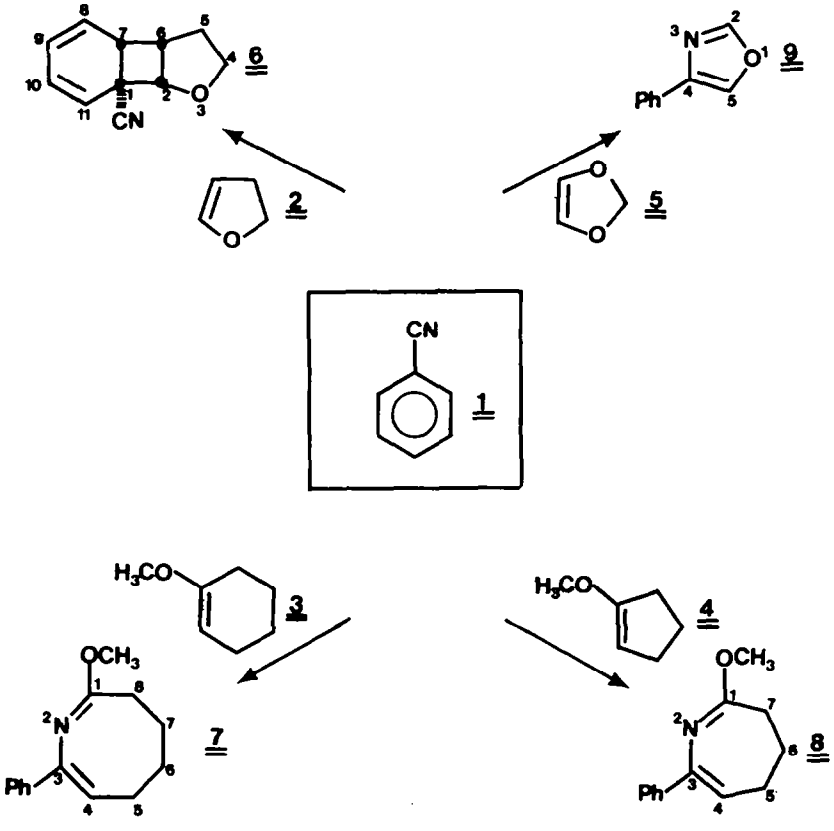


Scheme 1 : Modes of photoreactions of cyano arenes with alkenes.

Wender [7], the formation of azetines and 2-azabutadienes (type II) is of synthetic interest [8-10]. In order to obtain further information particularly about the type II cycloaddition we have investigated the photoreactions of benzonitrile with cyclic enol ethers which yielded new results with regard to the regioselectivity of the 2-azabutadiene formation.

Results

Irradiations of cyclohexane solutions of benzonitrile (1) (0.2 M) and one of the enol ethers 2-5 (0.2 - 1.0 M), at 254 nm, resulted in the products 6-10. While the yields of 7 and 8 were relatively high, i.e. 40-45% after chromatographic isolation based on starting materials consumed (in general the conversion did not exceed 50%), 6 and 9 could only be isolated in low yields up to 20%.



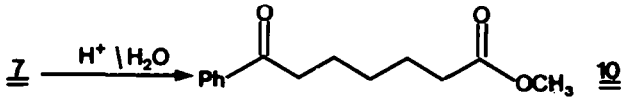
Scheme 2 : Main adducts of photoreactions of benzonitrile with cyclic enol ethers.

The ^{1}H- and ^{13}C-NMR spectroscopic data of 6 show the typical chemical shifts and coupling constants which are expected for 1-substituted ortho adducts [11]. Especially the coupling constant $J_{4,7}$ = 6.0 Hz points to the endo configuration of 6 (for a more detailed argumentation compare ref. 11).

The 2-azabutadiene derivative 7 exhibits similar ^{1}H-NMR data as already reported by Cantrell [3] who, however, assigned it to the 4-methoxy-2-aza-butadiene structure. Contrary to this, the ^{13}C-NMR data, which were obviously not accessible at that time, support the structure shown in formula 7. Finally this assignment has been proven by hydrolysis of 7 to methyl 7-phenyl-7-oxo-heptanoate (10). 8 has been assigned as the 1-methoxy-2-azabutadiene by its similar spectral properties in comparison to 7.

The product of the photoreaction of benzonitrile with 1,3-dioxole 5 was now identified as 4-phenyloxazole (9) by comparison with an authentic sample [12] contrary to a previous report [3].

In all cases the formation of some side products have been detected by means of GC or HPLC. Only the dimer 11 and the meta adduct 12 could be isolated from the reaction mixture of the (1+5) photoreaction. 11 was already identified earlier [5,13] and 12 shows the typical NMR data of cycloadducts especially with small coupling constants between H-5/H-6 and H-7/H-8 (see also refs. 11,14 : exo - $J_{5,6}$ and $J_{7,8}$ = 1 Hz, endo - $J_{5,6}$ and $J_{7,8}$ ca. 6 Hz) supporting the exo-configuration. The side products from 7 and 8 escaped our identification due to their small yields. However, azetines may be ruled out due to GC-Ms-analysis, which show mole peaks of higher molecular weight compared to 7 and 8, respectively. On the other hand a side product from 1 and 2 obviosusly is an isomer of 6 according to its similar MS data.



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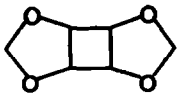

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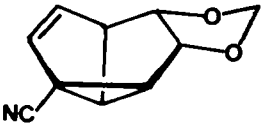

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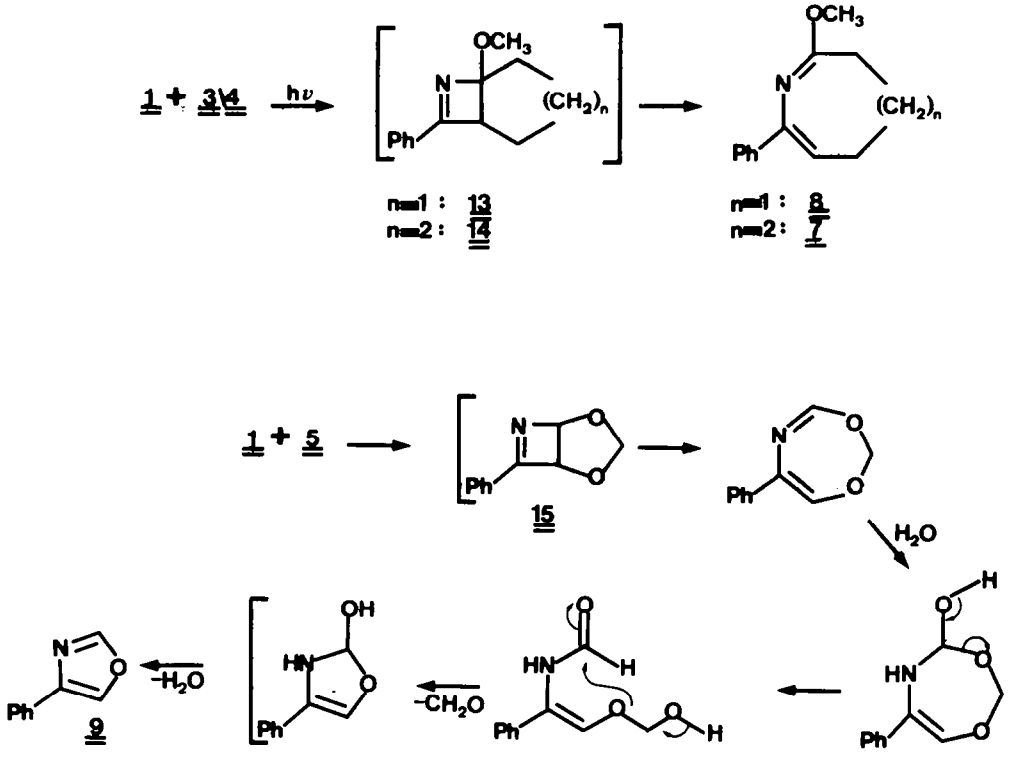
Discussion

Both methoxy-cyclohexene (3) and methoxy-cyclopentene(4) show a preference for type II cycloaddition. This is in agreement with a previous report [3] since the free enthalpy of electron transfer is slightly positive (with

$E_{1/2}^{ox}(3) = 0.95$ V and $E_{1/2}^{ox}(4) = 0.94$ V one can calculate $\Delta G(1+3) = 0.11$ eV and $\Delta G(1+4) = 0.10$ eV in cyclohexane; for a more detailed description see ref. 5). The photoreaction of 1 and 2 should also yield mainly products resulting from cycloaddition at the nitrile group since $E_{1/2}^{ox}(2) = 0.97$ V. However, we only have isolated the ortho cycloadduct 6 - even though in small yields indicating important unidentified reaction pathways. The photoreaction of 1 and 5 exhibits a $\Delta G = -0.08$ eV in cyclohexane ($E_{1/2}^{ox}(5) = 0.76$ V). Electron transfer should be the preferred reaction channel. Obviously back electron transfer mainly causes energy dissipation and therefore limitates the yields of the side reactions leading to 9, 11 and 12.

Although we have not been able to isolate or to scavenge intermediates we propose a mechanism for the formation of 7 - 9 as shown in Scheme 3.



Scheme 3: Proposed reaction mechanism for type II photoproducts 7 - 9.

It should be remarked that the intermediate azetines have so far only been isolated from simple alkenes such as tetramethyl ethene and 1,2-dimethyl

cyclohexene [3] (see also Tsuchiya and coworkers [15]). Alkoxy-substitution at the 4-position of 2-phenyl-1-azetine seems to destabilize the heterocyclic ring and support the formation of 2-azabutadienes of an imidoester type.

Whether the ring opening occurs via a secondary photochemical event as proposed by Cantrell [3] or simply thermally is not yet known for the systems which have been studied here. It should be emphasized that there is no change in product formation even at molar ratios of 1 : 3(4) = 5 : 1. Under these conditions most of the light is absorbed by 1 and even photochemically reactive intermediates should be detectable at low conversions. In the case of the cycloadduct 15 we assume that its valence isomer - a seven-membered imidoester - is very susceptible to hydrolysis. Traces of water suffice to induce a process (see Scheme 3), which results in the net loss of formaldehyde generating 4-phenyloxazole (9).

In summary certain electron-rich alkenes may add across the nitrile group of benzonitrile if the free enthalpy of electron transfer is slightly positive [5]. However, the primarily formed azetines can only be isolated with simple alkenes [3,16]. Furthermore unsymmetrical enol ethers preferentially yield 2-azabutadienes of an imidoester type contrary to an earlier report [3]. It is shown that 5 forms 4-phenyloxazole (9) rather than 2-phenyl-1-azetine-3-one as proposed earlier [5].

EXPERIMENTAL

The equipment, the synthetic and chromatographic procedures for product isolation, the measurement of the electrochemical oxidation potentials by means of cyclic voltametry versus $Ag/AgNO_3$ electrode, and the spectroscopic analyses have been described in detail elsewhere (see preceding parts of this series, e.g. refs. 5 and 11). Commercially available benzonitrile (1), 2,3-dihydro-furan (2), and the solvents which were used for synthesis, for cyclic voltametry measurements, and for working-up procedures were purified according to standard methods [5,11]. The 1-methoxy-cycloalkenes 3 and 4 and 1,3-dioxole 5 were synthesized according to Wohl [17] and Field [18], respectively.

Irradiation conditions and product isolation

Preparative irradiations were carried out by using a 70W low-pressure mercury lamp from Gräntzel (immersion lamp, quartz filter). In general 100 ml of a solution of benzonitrile (0.2 M) and one of the enol ethers 2-5 (0.2-1.0 M) were irradiated under nitrogen atmosphere. The reaction mixtures were checked by analytical g.c. . After max. 50% conversion the reaction was stopped and the products were isolated first by distilling the solvents at room temperature and then by means of HPLC (Si60).

Photoreaction of 1 + 2

1-Cyano-3-oxatricyclo[5.4.0.0^{2,6}]undeca-8,10-diene (6) : Colourless oil (after HPLC-isolation with ethyl acetate/ cyclohexane (5/95) as eluate).- IR($CDCl_3$) 3040(=CH), 2230(CN).- ^{1}H-NMR($CDCl_3$) δ= 1.87(m, 2H, H-5); 2.87(dd, $J_{7,6}$= 6.0Hz, $J_{7,8}$= 5.4Hz, 1H, H-7); 3.09(ddm, $J_{6,7}$= 6.0Hz, $J_{6,2}$= 5.6Hz, $J_{6,5}$= 8.5Hz, 1H, H-6); 4.26(m, 2H, H-4); 4.47(d, $J_{2,6}$= 5.6Hz, 1H, H-2); 5.56(dm, $J_{11,10}$= 9.2Hz, 1H, H-11); 5.82 (m, 2H, H-8 and H-9); 6.06(m, ΣJ= 18Hz, 1H, H-10).- ^{13}C-NMR($CDCl_3$) δ= 30.66(C-5); 37.10(C-1); 38.57(C-6); 50.84(C-7); 69.06(C-4); 86.98(C-2); 118.94, 120.43, 124.79 and 124.93(C-8 - C-11); nitrile-C hidden by signals of impurities.- MS: m/e= 173(1.4, M$^+$); 145(1.3); 143(4.1, M$^+$-CH_2O); 142(2.8); 130(1.6); 117(3.9); 116(7.2); 115(5.1); 103(11.1, 1$^+$); 70(100.2$^+$); 42(80.9, CH_2CO). - Anal. calcd for $C_{11}H_{11}NO$ (173.2): C, 76.28; H, 6.85. Found: C, 76.60; H, 6.54.

Photoreaction of 1 + 3

1-Methoxy-3-phenyl-2-azacycloocta-1,3-diene (7) : Colourless oil (after HPLC-isolation with ethyl acetate/ cyclohexane (5/95) as eluate or by destillation at 98 - 106°C/ 0.06mm Hg).- IR($CDCl_3$) 3080, 3060 and 3020(=CH); 1655(C=N).- ^{1}H-NMR($CDCl_3$) δ= 1.5-2.5(m, 8H, CH_2); 3.78(s, 3H, OCH_3); 5.57(t, J= 8 Hz, 1H, =CH); 7.15-7.3 (m, 3H, C_6H_5); 7.4-7.6(m, 2H, C_6H_5).- ^{13}C-NMR($CDCl_3$) δ= 22.72, 25.73, 25.85 and 29.91(CH_2, ^{1}J= 128 - 132Hz); 53.34 (OCH_3, ^{1}J= 146Hz); 110.92(=CH, ^{1}J= 154Hz); 125.16(ortho-C, ^{1}J= 160Hz); 127.25 (para-C, ^{1}J= 162Hz); 128.12(meta-C, ^{1}J= 161Hz); 138.55 and 145.28(quart. C); 164.04(C=N).- MS: m/e= 216(15.4, M$^+$+1); 215(100, M$^+$); 200(60.2, M$^+$-CH_3); 186(57.6); 185(13.4); 184(43.6); 173(13.4); 172(29.0); 146(16.2); 129(14.1); 117(11.2); 115(46.8); 112(23.9); 91(16.7); 84(11.1); 77(15.5); 69(24.3); 51(10.2); 43(10.6); 41(37.2). - Anal. calcd for $C_{14}H_{17}NO$ (215.3): C, 78.10; H, 7.96. Found: C, 78.14; H, 7.99.

Photoreaction of 1 + 4

1-Methoxy-3-phenyl-2-azacyclohepta-1,3-diene (8) : Colourless oil (after HPLC-isolation with ethyl acetate/ cyclohexane (5/95) as eluate).- IR($CDCl_3$) 3080, 3060 and 3020(=CH); 1640 and 1665(C=N).- ^{1}H-NMR($CDCl_3$) δ= 1.9-2.4 (m, 6H, CH_2); 3.80(s, 3H, OCH_3); 6.00(t, J= 7Hz, 1H, =CH); 7.1-7.35(m, 3H, C_6H_5); 7.5-7.8(m, 2H, C_6H_5).- ^{13}C-NMR($CDCl_3$) δ= 24.26(C-6); 29.70 and 33.66(C-5 and C-7 or reversed); 53.01(OCH_3); 111.44(C-4); 125.03(ortho-C); 127.27(para-C); 128.09(meta-C); 138.79 and 147.08(quart. C); 169.41(C-1).- MS: m/e= 202(13.7, M$^+$+1); 201(100, M$^+$); 200(42.7, M$^+$-1); 186(40.4); 173(27.0); 158(25.3); 128(11.3); 115(34.1); 103(10.2); 98(69.4); 97(34.2); 91(12.4); 77(15.9); 57(10.0); 55(23.9); 51(10.3). - Anal. calcd for $C_{13}H_{15}NO$ (201.3): C, 77.58; H, 7.51. Found: C, 77.02; H, 7.44.

Photoreaction of 1 + 5

Besides the dimer 11 several products have been formed according to chromatographic analyses. The main product and one side product could be isolated by means of HPLC with ethyl acetate/cyclohexane (15/85) as eluate. The main product was identified as 4-phenyloxazole (9) by comparison with an authentic sample [12] : b.p. 116 - 119°C/10mm Hg.- IR(neat) 3140, 3090, 3065, 3040 and 3020(=CH); 1610, 1600, 1590 and 1585(C_6H_5 and oxazole); 1510, 1445, 1105, 1062, 912, 747, 692, 680 and 610.- ^{1}H-NMR($CDCl_3$) δ= 7.25-7.45 (m, 3H, C_6H_5); 7.73-

7.78(m, 2H, C_6H_5); 7.95(s, 2H, oxazole). - ^{13}C-NMR($CDCl_3$) δ= 125.60(dt, ^{1}J=158Hz, ^{3}J=7.5Hz, C-2'); 128.23(dt, ^{1}J=168.3Hz, ^{3}J=7.7Hz, C-4'); 128.81(dd, ^{1}J=159.3Hz, ^{3}J=7.4Hz, C-3'); 130.68(t, J=7.6Hz, C-1'); 133.72(dd, ^{1}J=206.7Hz, ^{3}J=3.9Hz, C_5); 140.41(m, ΣJ=32Hz, C-4); 151.36(dd, ^{1}J=229.8Hz, ^{3}J=8.5Hz, C_2). - MS: m/e= 146(15, M$^+$+1); 145(100, M$^+$); 144(10); 117(72); 90(100); 89(88); 77(10); 73(14); 64(12); 63(58); 62(14); 59(18); 51(15); 50(14); 39(38). - Anal. calcd for C_9H_7NO (145.2): C, 74.47; H, 4.86. Found: C, 75.08; H, 5.30.

6,7-exo-Methylenedioxy-2-cyanotricyclo[3.3.0.0^{2,8}]oct-3-ene (12) : Colourless oil. - ^{1}H-NMR($CDCl_3$) δ= 2.48(d, $J_{8,1}$= 6.6Hz, 1H, H-8); 3.20(dd, $J_{1,8}$= 6.6Hz, $J_{1,5}$= 5.4Hz, 1H, H-1); 3.58(dd, $J_{5,1}$= 5.4Hz, $J_{5,4}$= 2Hz, 1H, H-5); 4.07(d, $J_{6,7}$= 3.6Hz, 1H, H-6); 4.47(d, $J_{7,6}$= 3.6Hz, 1H, H-7); 4.83 and 5.16(s, 2H, H-9); 5.60(br s, 2H, H-3 and H-4). - MS: no M$^+$; m/e= 145(7, M$^+$-CH_2O); 144(7); 129(36, M$^+$-CH_2O_2); 117(40); 116(60); 91(23); 90(48); 89(34); 72(100, 5$^+$); 71(26); 64(18); 63(32); 51(18); 50(14); 39(36); 29(32); 27(20).
At least another (1:1) adduct from 1 and 5 is formed according to MS analysis: m/e= 175(0.7, M$^+$); 72(100, 5$^+$); and similar signals as observed from 12.

Hydrolysis of 7 : A pure sample of 7 (isolated by means of HPLC) was dissolved in dioxane/H_2O (ca. 4:1). Some drops of diluted aqueous HCl were added and the mixture was kept at room temperature for one day. Only one product was formed in ca. 80 - 90% conversion according to GC-analysis. This product was isolated by means of HPLC (10% ethyl acetate in cyclohexane) and identified as **methyl 7-phenyl-7-oxo-heptanoate (10)** : Colourless oil. - IR($CDCl_3$) 1735($COOCH_3$); 1682(PhCO). - ^{1}H-NMR($CDCl_3$) δ= 1.42(m, 2H, CH_2); 1.72(m, 4H, CH_2); 2.34 (t, J= 7.5Hz, 2H, CH_2COOCH_3); 2.98(t, J=7.4Hz, 2H, $PhCOCH_2$); 3.67(s, 3H, OCH_3); 7.47(m, 2H); 7.51(m, 1H) and 7.95(m, 2H) of C_6H_5. - ^{13}C-NMR($CDCl_3$) δ= 23.87, 24.79 and 28.82(C-3 - C-5); 33.91(C-2); 38.30(C-7); 51.49(OCH_3); 128.04 and 128.58 (ortho- and meta-C); 132.95(para-C); 137.03(C-1 of C_6H_5); 174.12(C-1); 200.17(C-7). - MS: m/e= 234(1.0, M$^+$); 216(2.8); 203(1.0, M$^+$-OCH_3); 174(0.8); 157(5.3, M$^+$-C_6H_5); 120(62, $PhCOCH_3^+$); 105(100, $PhCO^+$); 77(42, $C_6H_5^+$); 55(10); 51(13). - Anal. calcd for $C_{14}H_{18}O_3$ (234.3): C, 71.77; H, 7.74. Found: C, 72.10; H, 8.01.

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