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Base-catalyzed cascade dimerization of γ-aryl-β,γ-enones into acylated terphenyls

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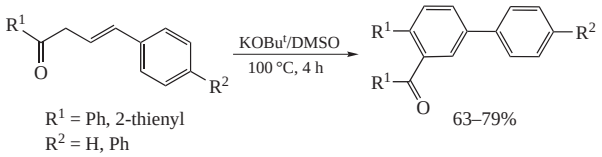
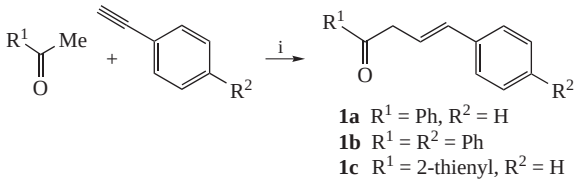
4-Aryl-1-(het)arylbut-3-en-1-ones dimerize smoothly in the Bu^{t}OK/DMSO superbase system at 100 °C for 4 h to afford acylated terphenyls in up to 79% yield. The dimerization is accompanied by elimination of the methylarene molecule.



β,γ-Enones readily available from the recently discovered base-catalyzed addition of ketones to acetylenes,[1] are now rapidly gaining attraction as a new family of versatile building blocks for organic synthesis. They have already been successfully employed for the expedient preparation of furans,[1(a),2] isoxazolines,[3] pyrazolines,[4] 3-styrylpyrroles,[5] keto phosphine chalcogenides,[6] and benzoxepines.[7]

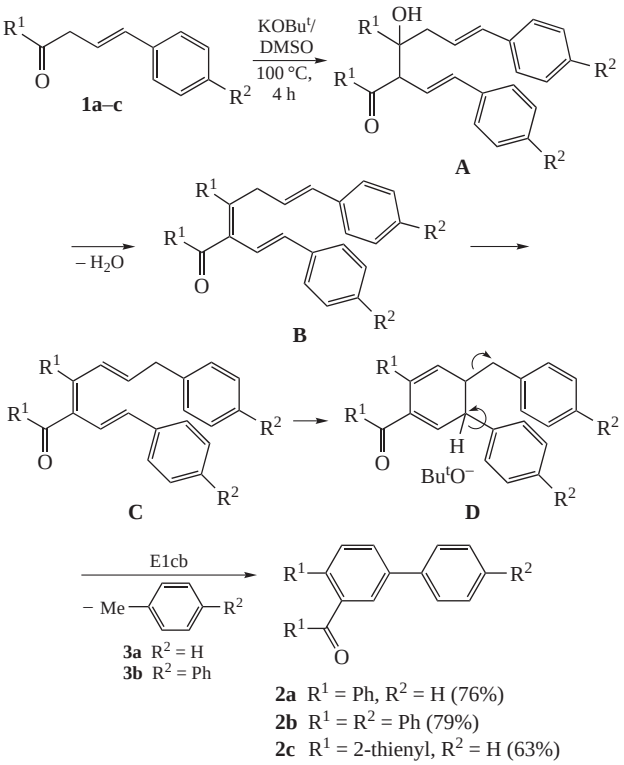
This communication is a concise report on a novel unexpected feature in the chemical behavior of the β,γ-enones **1a**–**c**, namely 4-aryl-1-(het)arylbut-3-en-1-ones, which are readily obtained by the addition of acetophenone or 2-acetylthiophene to arylacetylenes in the presence of superbase (Scheme 1).



Scheme 1 *Reagents and conditions*: i, KOH/DMSO (100 °C, 1 h), KOBu^t/DMSO (100 °C, 0.5 h).

Surprisingly, it turns out that ketones **1a**–**c**, when heating at 100 °C for 4 h, are smoothly converted to acylated terphenyls **2a**–**c** in up to 79% yields, which are actually dimers lacking a substituted benzene moiety (Scheme 2).†

Structure of the compounds synthesized was proved by the 1D and 2D NMR technique. In the ^{1}H NMR spectrum of compound **2c**, the signals of thiophene cycles (doublets of doublets) were assigned using 2D COSY data (Figure 1). The ^{13}C signals



Scheme 2

† The IR spectra were recorded on a Bruker IFS25 spectrophotometer. Mass spectra were recorded on an Agilent 5975C spectrometer. NMR spectra were recorded on Bruker DPX-400 and AV-400 spectrometers (400.1 MHz for ^{1}H and 100.6 MHz for ^{13}C) in $CDCl_3$ using HMDSO as internal standard. Basic aluminum oxide was used for column chromatography.

Dimerization of β,γ-enones **1a**–**c**. A mixture of enone **1** (5 mmol) and KOBu^t (1.5 mmol, 0.17 g) in DMSO (15 ml) was heated to 100 °C and stirred at this temperature for 4 h. After cooling, it was diluted with H_2O (15 ml), neutralized with NH_4Cl and extracted with Et_2O (4×10 ml). The organic extract was washed with H_2O (3×5 ml) and dried ($MgSO_4$). The solvent was evaporated in a vacuum and the residue was purified by column chromatography (Al_2O_3, eluent hexane–Et_2O with gradient from 1:0 to 10:1).

Phenyl([1,1';4',1'']terphenyl-2'-yl)methanone **2a**: yield 0.64 g (76%); white powder, mp 124–126 °C (lit.,[10] yellow solid, mp 135 °C). IR (film, ν/cm^{-1}): 3436, 1665, 1594, 1475, 1448, 1339, 1240, 761, 748, 723, 699. ^{1}H NMR ($CDCl_3$) δ: 7.10–7.23 (m, 4H), 7.25–7.30 (m, 3H), 7.33–7.39 (m, 2H), 7.36–7.40 (m, 2H), 7.54 (d, 1H, *J* 8.0 Hz), 7.60–7.63 (m, 2H), 7.64–7.70 (m, 2H), 7.71 (d, 1H, *J* 1.6 Hz), 7.78 (dd, 1H, *J* 8.0 and 1.6 Hz). ^{13}C NMR ($CDCl_3$) δ: 127.3, 127.5, 127.6, 128.0, 128.4, 128.5, 129.0, 129.1, 129.2, 130.2, 130.8, 133.1, 137.6, 139.7, 140.0, 140.3, 198.9. MS (EI), *m*/*z*: 334 [M]$^+$.

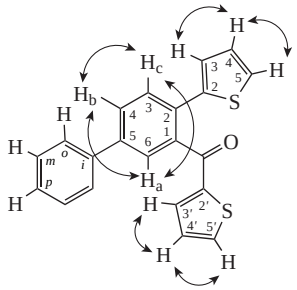


Figure 1 Characteristic COSY correlations of compound **2c**.

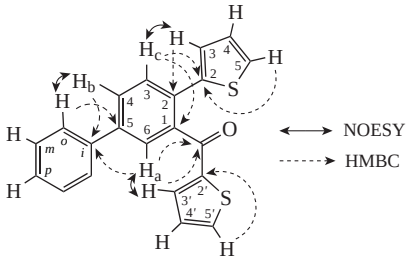


Figure 2 Characteristic NOESY and HMBS correlations of compound **2c**.

were unambiguously determined according to the 2D ^{1}H-^{13}C HSQC and HMBC spectra (Figure 2). Additional information related to structural establishment and signal assignments in the ^{1}H NMR spectrum was obtained from the 2D NOESY data (Figure 2).

Obviously, the reaction represents an auto-condensation of ketones **1a–c** that starts from the formation of aldol intermediates **A** giving further trienes **B** and then (after prototropic isomerization) fully conjugated trienes **C** (see Scheme 2). The latter undergo base-promoted or concerted cyclization to dihydrobenzene **D**. Elimination of methylarenes **3** from the dihydrobenzene moiety (apparently by E1cb mechanism with participation of base) leads to its aromatization being a driving force of this elimination.

In the reaction mixtures, eliminated toluene **3a** was detected by GLC. Likewise, in the case of ketone **1b**, 4-methyl-1,1′-biphenyl **3b**, the product of the same elimination process, was isolated thus proving this aromatization mode to be a general one.

Terphenyls and their derivatives find application in design of Hi-Tech materials,[8] *e.g.* for optoelectronics and IT-technologies, heat-resistant polymers, or heat transfer agents. Some of them possess cytotoxic, immunosuppressant, neuroprotective, antithrombotic and anticoagulant activities.[9]

In conclusion, the reaction found opens an unprecedentedly easy access to diverse terphenyl derivatives, in which the acyl functionality additionally increases the potential for their application. It is understood that no essential limitations exist for extending the substrate scope of this synthesis and its scaling up. This is warranted by the transition metal free experimental procedure, inexpensive available starting materials and catalyst.

Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.mencom.2016.09.003.

Phenyl([1,1′;4′,1″;4″,1‴]quarterphenyl-2′-yl)methanone **2b**: yield 0.81 g (79%); white crystals, mp 179–181 °C. IR (film, ν/cm^{-1}): 3059, 3028, 2925, 2854, 1662, 1597, 1580, 1546, 1476, 1448, 1410, 1389, 1318, 1296, 1261, 1241, 1178, 1157, 1118, 1075, 1020, 1007, 947, 830, 765, 733, 698, 648, 616, 534, 503. ^{1}H NMR ($CDCl_3$) δ: 7.12–7.25 (m, 8H), 7.29–7.35 (m, 2H), 7.37–7.42 (m, 2H), 7.43–7.55 (m, 6H), 7.77 (dd, 1H, *J* 8.0 and 1.8 Hz), 7.82–7.90 (m, 3H). ^{13}C NMR ($CDCl_3$) δ: 126.8, 127.0, 127.1, 127.3, 127.5, 127.7, 128.2, 128.4, 128.7, 128.8, 128.9, 129.1, 129.8, 130.0, 130.3, 130.7, 132.3, 133.0, 139.6, 140.6, 198.7. MS (EI), *m*/*z*: 410 $[M]^+$.

(Thiophen-2-yl)[4-(thiophen-2-yl)biphenyl-3-yl]methanone **2c**: yield 0.55 g (63%); white powder, mp 122–124 °C. IR (film, ν/cm^{-1}): 3103, 3087, 3073, 3030, 2917, 2850, 1646, 1600, 1581, 1552, 1530, 1514, 1479, 1448, 1430, 1411, 1390, 1354, 1314, 1285, 1253, 1231, 1208, 1180, 1154, 1112, 1077, 1047, 1024, 959, 908, 891, 857, 849, 829, 788, 763, 728, 698, 671, 665, 654, 612, 582, 565, 513, 487, 464. ^{1}H NMR ($CDCl_3$) δ: 6.89 (dd, 1H, H-4, *J* 5.1 and 3.6 Hz), 6.94 (dd, 1H, H-4′, *J* 4.9 and 3.9 Hz), 7.03 (dd, 1H, H-3, *J* 3.6 and 1.2 Hz), 7.21 (dd, 1H, H-5, *J* 5.1 and 1.2 Hz), 7.30 (dd, 1H, H-3′, *J* 3.9 and 1.2 Hz), 7.33–7.37 (m, 1H, *p*-H), 7.42–7.46 (m, 2H, *m*-H), 7.59 (dd, 1H, H-5′, *J* 4.9 and 1.2 Hz), 7.59–7.63 (m, 2H, *o*-H), 7.63 (dd, 1H, H_c, *J* 8.1 and 0.4 Hz), 7.70 (dd, 1H, H_a, *J* 2.0 and 0.4 Hz), 7.73 (dd, 1H, H_b, *J* 8.1 and 2.0 Hz). ^{13}C NMR ($CDCl_3$) δ: 126.4 (C-5), 126.8 (C^6_{Ar}), 127.1 (*o*-C), 127.4 (C-3), 127.8 (C-4), 128.0 (*p*-C), 128.1 (C-4′), 128.8 (C^4_{Ar}), 129.0 (*m*-C), 130.8 (C^3_{Ar}), 131.6 (C^2_{Ar}), 134.9 (C-5′), 135.4 (C-3′), 139.3 (C^1_{Ar}), 139.6 (*i*-C), 140.4 (C^5_{Ar}), 141.2 (C-2), 144.6 (C-2′), 190.5 (C=O). MS (EI), *m*/*z*: 346 $[M]^+$.

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