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Addition of hypobromous acid to 1-phenylcycloalkenes

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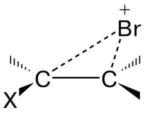
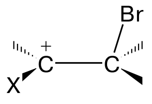
Reaction of 1-phenylcyclooctene and 1-phenylcycloheptene with *N*-bromosuccinimide (NBS) in aqueous DMSO gives the corresponding 3-bromo-2-phenylcycloalkenes and 2-phenylcycloalk-2-enols in a ratio of 3 : 1. Unlike them, 1-phenylcyclohexene gives a mixture of 3-bromo-2-phenylcyclohexene and 2-bromo-1-phenylcyclohexanol. The oxidation of allylic alcohols with pyridinium chlorochromate afforded the corresponding α,β-unsaturated ketones.

Key words: 1-phenylcycloalkenes, allylic bromides, allylic alcohols, *N*-bromosuccinimide, α,β-enones.

Nowadays the heterolytic bromination of the C=C bond is considered as a two-step process of *trans*-addition involving the bromonium ion as a key intermediate. However, the formation of the bromonium bridge is not general and mainly determined by the nature of substituents at the double bond. For instance, in the case of strong electron-donating substituents (X) capable of stabilizing the positive charge, along with bridge ions **1**, linear ions **2** are formed as intermediates.[1,2]



1



2

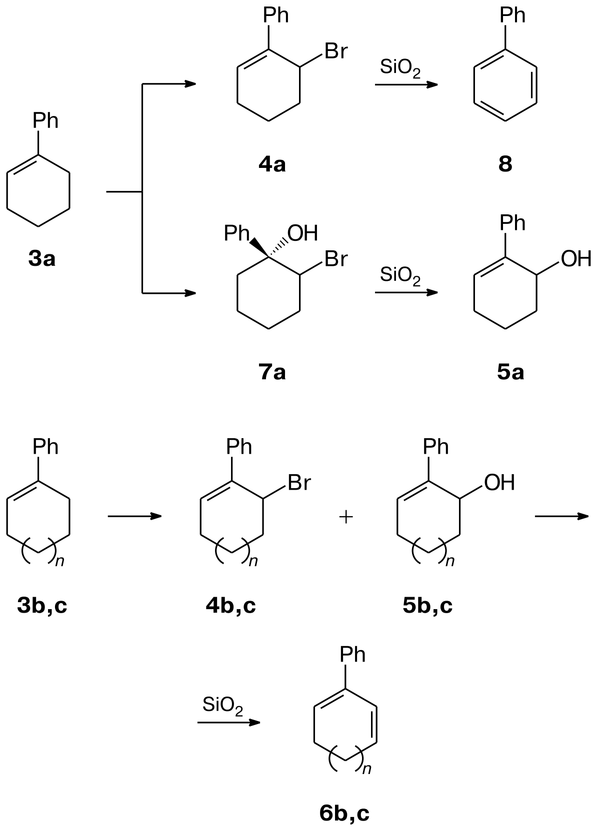
The addition of HOBr to alkene proceeds with the intermediate participation of the bromonium ion and affords bromohydrin according to the Markovnikov rule.[3]

In the present work, we studied the addition of HOBr (generated by hydrolysis of bromosuccinimide (NBS) in aqueous DMSO) to 1-phenyl-substituted cycloalkenes **3a—c** and the behavior of the products formed during chromatographic separation on SiO_2. The allylic alcohols obtained were also oxidized to the corresponding α,β-enones.

Results and Discussion

The addition of HOBr to 1-phenylcycloheptene (**3b**) and 1-phenylcyclooctene (**3c**) was accompanied by the

Scheme 1



n = 2 (**b**), 3 (**c**)

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evolution of water and hydrogen bromide and afforded allylic bromide **4b,c** and allylic alcohols **5b,c** in a ratio of 3 : 1 (Scheme 1). The products were isolated from the reaction mixture by chromatography on silica gel. In addition to bromides **4b,c** and alcohols **5b,c**, 1,3-dienes **6b,c** were obtained. Diene **6c** is poorly stable and was detected only by ^{1}H NMR in a mixture, therefore we failed to isolate it in a pure form. The reaction of 1-phenylcyclohexene (**3a**) under similar conditions gave **4a** bromohydrin **7a** along with the expected allylic bromide (4 : 3, overall yield 68%). The formation of bromohydrin **7a** has previously[2] been observed in the reaction of substrate **3a** with NBS in aqueous DMSO at 0 °C.

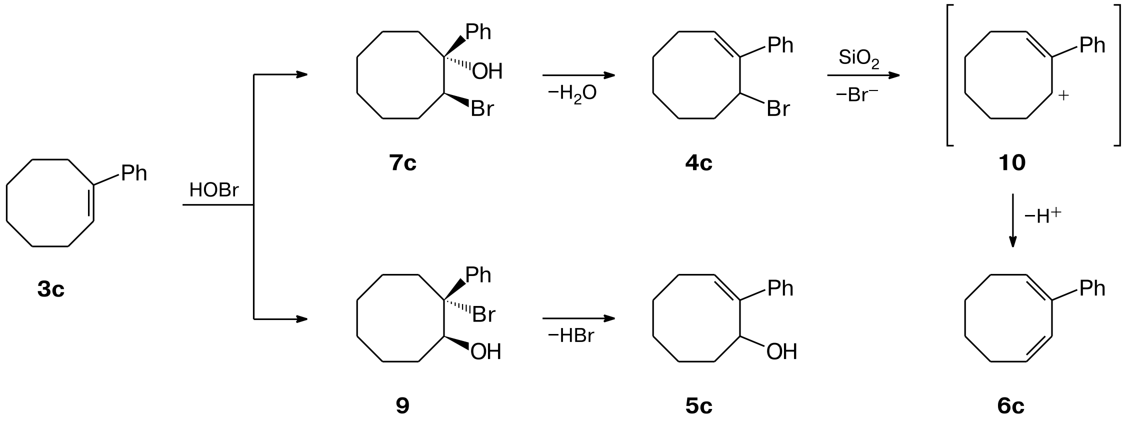
Bromide **4a** was isolated by chromatography of the reaction mixture using a short (5 cm) column with silica gel and hexane as an eluent. This bromide was also obtained by the reaction of alcohol **5a** with PBr_3 in benzene. Along with bromide **4a**, alcohol **5a**, bromohydrin **7a**, and biphenyl (**8**) were isolated from the reaction mixture by repeated column chromatography (see Scheme 1).

The formation of products **4c** and **5c** was due to the elimination of H_2O and HBr from bromohydrins **7c** and **9** formed at the initial step of the process. Diene **6c** is formed, probably, due to the SiO_2-assisted elimination of the bromide anion from bromo compound **4c** followed by proton elimination from allylic cation **10** (Scheme 2).

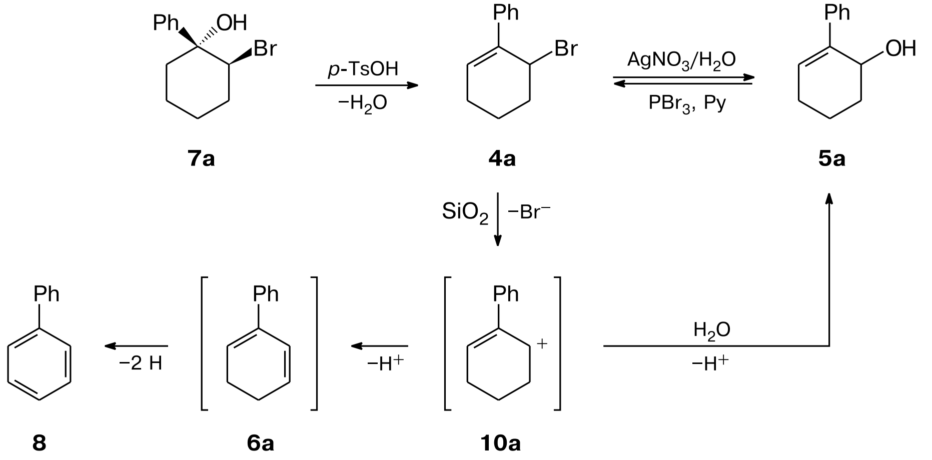
The structures of the products were determined by IR, ^{1}H and ^{13}C NMR spectroscopy, and by comparison with the published data.[4,5] The structures of products **4a**, **5a**, **7a**, and **8** were confirmed by their chemical transformations, in particular, by the *p*-TsOH-catalyzed dehydration of bromohydrin **7a** to allylic bromide **4a** and the transformation of the latter into allylic alcohol **5a** by the action of $AgNO_3$ and water and by the inverse transformation of alcohol **5a** into bromide **4a** on the treatment with PBr_3. Biphenyl (**8**) is formed from bromide **4a** due to the SiO_2-induced elimination of the bromide anion from the molecule of **4a** followed by proton elimination from allylic cation **10a** and diene **6a** aromatization (Scheme 3).

The synthesized allylic alcohols **5a—c** were converted to 2-phenylcycloalk-2-enones **11a—c** by the oxidation

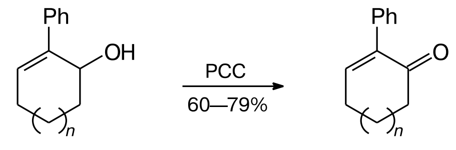
Scheme 2



Scheme 3



Scheme 4



5a—c **11a—c**

n = 1 (**a**), 2 (**b**), 3 (**c**)

with pyridinium chlorochromate (PCC) in dichloromethane at room temperature (3 h) (Scheme 4).

The X-ray study of crystals of ketone **11a** showed that its molecules form centrosymmetric space group *P*21/*c* ($Z = 4$) (Fig. 1). It contains the cyclohex-2-enone and phenyl moieties linked by the single C—C bond (C(6)—C(7), 1.489(3) Å). The cyclohexene ring has the half-chair conformation with the parameters $Q = 0.361(4)$ Å, $\theta = 53.9(5)°$, and $\phi = 192/1(6)°$ (see Ref. 6). The phenyl and cyclohexene moieties are considerably twisted relatively to each other about the C(6)—C(7) bond, and the dihedral angle formed by the phenyl and plane of the C(8)—C(7)—C(12) atoms is 49.7(1)°. Ketone **11a** exists in the strained conformation, which is facilitated by the participation of the carbonyl O atom in hydrogen bonding with the adjacent molecules. One of them (C(5)—H...O(1)) is directed along the *a* axis (C(5)—H, 0.93 E; C(5)...O(1)^i, 3.608(4) Å; C(5) H...O(1), 169°; *i*: $x + 1$, $+y$, $+z$), whereas another bond is directed along the *b* axis (C(9)—H, 0.97 Å; C(9)...O(1)^{ii}, 3.536(4) Å; the C(9)—H...O(1) angle is 156°; *ii*: $-x$, $+y - 1/2$, $-z + 1/2$). In addition the noncovalent interaction C(8)—H...π(phenyl) contributes, as a whole, to the stabilization of the structure of ketone **11a**. In this case, the hydrogen atom is stretched almost directly to the cyclic centroid (X) (C(8)...X, 3.701(4) Å; the C—H...X angle is 139°).

To sum up, the reaction of 1-phenyl-substituted cycloheptene and cyclooctene (**3b,c**) with NBS in aqueous DMSO affords allylic bromides **4b,c** and allylic alcohols **5b,c** in a ratio of 3 : 1. 1-Phenylcyclohexene (**3a**) forms bromohydrin **7a** along with allylic bromide. In addition, 2-phenylcycloalk-2-enones **11a—c** were synthesized in 60—79% yields by the oxidation of the obtained 2-phenylcycloalk-2-enols **5a—c** with chlorochromate.

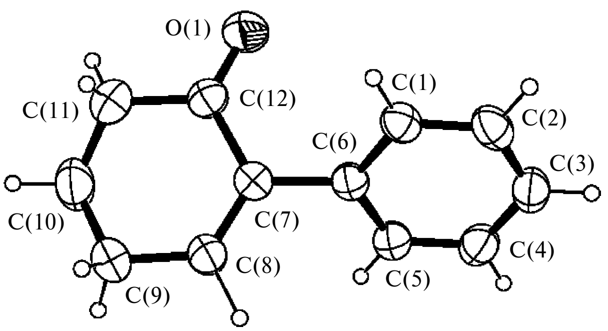


Fig. 1. Molecular structure of 2-phenylcyclohex-2-enone (**11a**).

Experimental

1-Phenylcyclohexene (**3a**),[4] 1-phenylcycloheptene (**3b**),[7] and 1-phenylcyclooctene (**3c**)[8] were synthesized using known procedures. The ^{1}H and ^{13}C NMR spectra of the solutions in $CDCl_3$ were recorded on Varian 200 and Varian Mercury 400 spectrometers using $SiMe_4$ and residual protons of $CDCl_3$ as references. IR spectra were recorded with a Jasco FT/IR-430 instrument (solutions in CCl_4). Elemental analysis was carried out on a Leco CHNS 932 analyzer. Melting points were measured on an Electrothermal 9100 apparatus. Column chromatography was carried out on silica gel (Merck, 60—230 mesh).

Reaction of 1-phenylcyclohexene (3a), 1-phenylcycloheptene (3b), and 1-phenylcyclooctene (3c) with NBS (general procedure). A mixture of NBS (2.4 g, 13.4 mmol), 1-phenylcycloalkene **3** (5.4 mmol), and water (0.2 g, 11 mmol) in DMSO (25 mL) was stirred at ~20 °C for 30 min, the solid materials formed were filtered off, the filtrate was extracted with ether (2×25 mL), and the combined ethereal extracts were washed with water, dried over Na_2SO_4, and evaporated. The obtained residue was chromatographed on silica gel (layer height 5 cm) using *n*-hexane as eluent. After one to two fractions were collected, the products were eluted with an *n*-hexane—$CHCl_3$ (7 : 3) mixture. 3-Bromo-2-phenylcycloalk-1-enes **4a—c** were isolated from the collected first fractions.

3-Bromo-2-phenylcyclohex-1-ene (4a). The yield was 28%, needle-like crystals, m.p. 49—51 °C (*cf.* Ref. 2: m.p. 50—52 °C). ^{1}H NMR, δ: 1.83—1.68 (m, 2 H); 2.46—2.12 (m, 4 H); 5.33—5.36 (m, 1 H); 6.19 (t, 1 H, $J = 3.6$ Hz); 7.25—7.63 (m, 5 H). ^{13}C NMR, δ: 141.47, 140.00, 129.00, 128.67, 127.41, 126.01, 50.70, 33.84, 25.99, 17.46. IR, ν/cm^{-1}: 3069, 3044, 3017, 2935, 2862, 1588, 1496, 1448, 1244, 1224, 758, 694, 536. Found (%): C, 60.48; H, 5.22. $C_{12}H_{13}Br$. Calculated (%): C, 60.78; H, 5.53.

(*Z*)-3-Bromo-2-phenylcyclohept-1-ene (4b). The yield was 36%, colorless oil. ^{1}H NMR, δ: 1.70—1.67 (m, 1 H); 2.08—1.95 (m, 3 H); 2.32—2.19 (m, 2 H); 2.49—2.41 (m, 2 H); 5.31—5.27 (m, 1 H); 6.17 (t, 1 H, $J = 7.2$ Hz); 7.43—7.26 (m, 5 H). ^{13}C NMR, δ: 143.95, 143.33, 136.31, 128.37, 127.11, 126.11, 57.36, 35.51, 28.53, 27.14, 26.69. IR, ν/cm^{-1}: 3062, 3029, 2937, 2883, 1602, 1455, 1448, 1303, 1016, 752, 702. Found (%): C, 62.97; H, 5.88. $C_{13}H_{15}Br$. Calculated (%): C, 62.77; H, 6.02.

(*Z*)-3-Bromo-2-phenylcyclooct-1-ene (4c). The yield was 31%, colorless oil. ^{1}H NMR, δ: 1.46—1.39 (m, 2 H); 1.60—1.49 (m, 1 H); 1.95—1.63 (m, 3 H); 2.47—2.28 (m, 2 H); 2.59—2.48 (m, 2 H); 5.50—5.46 (dd, 1 H, $J = 5.5$ Hz, $J = 11.7$ Hz); 5.94 (t, 1 H, $J = 8.6$ Hz); 7.39—7.32 (m, 5 H). ^{13}C NMR, δ: 142.20, 140.78, 132.35, 128.11, 127.86, 127.32, 51.19, 41.41, 29.54, 27.89, 27.28, 26.62. IR, ν/cm^{-1}: 3079, 3054, 3019, 2925, 2852, 1598, 1492, 1446, 1249, 1222, 763, 698, 534. Found (%): C, 63.22; H, 6.68. $C_{14}H_{17}Br$. Calculated (%): C, 63.41; H, 6.46.

2-Phenylcycloalk-2-enols **5a—c**, biphenyl (**8**), and 2-bromo-1-phenylcyclohexanol (**7a**) were isolated from the second and third fractions obtained by the elution of the reaction products of substrates **3a—c** with NBS with an *n*-hexane—$CHCl_3$ (7 : 3) mixture.

2-Phenylcyclohex-2-enol (5a). The yield was 14%, colorless solid substance, m.p. 55—57 °C (*cf.* Ref. 9: m.p. 58—59 °C). ^{1}H NMR, δ: 1.89—1.75 (m, 2 H); 2.05—1.93 (m, 2 H); 2.32—2.28 (m, 2 H); 4.79—4.77 (m, 1 H); 6.24 (t, 1 H, J = 3.9 Hz); 7.45—7.32 (m, 5 H). ^{13}C NMR, δ: 143.08, 142.02, 130.67, 130.53, 129.09, 128.01, 67.51, 33.57, 28.06, 19.36. IR, ν/cm^{-1}: 3419 3056, 3023, 295, 2863, 1683, 1494, 1446, 1220, 1058, 937, 758, 698. Found (%): C, 82.43; H, 8.45. $C_{12}H_{14}O$. Calculated (%): C, 82.72; H, 8.10.

(*Z*)-2-Phenylcyclohept-2-enol (5b). The yield was 16%, viscous oil. ^{1}H NMR, δ: 2.86—1.57 (m, 9 H); 4.83—4.77 (dd, 1 H, J = 2.2 Hz, J = 7.3 Hz); 6.03 (t, 1 H, J = 6.7 Hz); 7.37—7.25 (m, 5 H). ^{13}C NMR, δ: 146.51, 143.11, 132.14, 128.3, 126.84, 126.79, 72.81, 33.85, 27.73, 26.79, 25.06. IR, ν/cm^{-1}: 3428, 3058, 3025, 2929, 2856, 1683, 1598, 1492, 1446, 1274, 1078, 757, 700. Found (%): C, 82.74; H, 5.74. $C_{13}H_{16}O$. Calculated (%): C, 82.94; H, 5.57.

(*Z*)-2-Phenylcyclooct-2-enol (5c). The yield was 19%, viscous oil. ^{1}H NMR, δ: 1.48—1.39 (m, 2 H); 1.59—1.50 (m, 1 H); 1.89—1.66 (m, 4 H); 2.08—1.99 (m, 1 H); 2.32—2.27 (m, 2 H); 5.05—5.02 (dd, 1 H, J = 5.4 Hz, J = 9.2 Hz); 5.79 (t, 1 H, J = 8.9 Hz); 7.32—7.25 (m, 5 H). ^{13}C NMR, δ: 143.26, 140.27, 130.07, 128.44, 128.33, 127.19, 70.36, 39.17, 30.26, 27.41, 27.05, 24.54. IR, ν/cm^{-1}: 3390, 3080, 3060, 2923, 2852, 1652, 1558, 1448, 1218, 1052, 979, 771, 698. Found (%): C, 82.96; H, 9.18. $C_{14}H_{18}O$. Calculated (%): C, 83.12; H, 8.97.

Biphenyl (8). The yield was 25%, needle-like crystals.

(1*R,2*S**)-2-Bromo-1-phenylcyclohexanol (7a).** The yield was 27%, colorless solid, m.p. 52 °C (*cf.* Ref. 2: m.p. 48—49 °C). ^{1}H NMR, δ: 1.94—1.64 (m, 5 H); 2.19—2.11 (m, 1 H); 2.61—2.48 (m, 1 H); 2.77—2.65 (m, 1 H); 4.53—4.51 (m, 1 H); 7.48—7.32 (m, 3 H); 7.61—7.55 (m, 2 H). ^{13}C NMR, δ: 148.33, 130.14, 129.78, 127.59, 76.36, 62.02, 33.42, 33.23, 22.93, 22.38. IR, ν/cm^{-1}: 3421, 3089, 3058, 3027, 2939, 2862, 1496, 1446, 1213, 1145, 1033, 1008, 966, 761, 698, 559. Found (%): C, 56.22; H, 5.74. $C_{12}H_{15}BrO$. Calculated (%): C, 56.49; H, 5.93.

Diene **6c** was isolated from the second fraction obtained by the elution with *n*-hexane of the reaction products of substrate **3c** with NBS.

(1*E*,3*Z*)-2-Phenylcycloocta-1,3-diene (6c). The yield was 21%, colorless oil. ^{1}H NMR, δ: 1.54—1.43 (m, 4 H); 2.26—2.16 (m, 2 H); 2.32—2.27 (m, 2 H); 6.03—5.93 (m, 2 H); 6.11 (t, 1 H, J = 8.1 Hz); 7.24—7.18 (m, 1 H); 7.36—7.25 (m, 2 H); 7.42—7.37 (m, 2 H). ^{13}C NMR, δ: 141.29, 137.83, 133.73, 128.86, 128.39, 127.05, 126.72, 126.63, 28.70, 28.60, 24.37, 22.62. IR, ν/cm^{-1}: 3054, 2923, 2852, 1652, 1635, 1558, 1488, 1457, 750, 696. Found (%): C, 91.46; H, 8.98. $C_{14}H_{16}$. Calculated (%): C, 91.25; H, 8.75.

Oxidation of 2-phenylcycloalk-2-enols 5a—c with pyridinium chlorochromate (PCC) (general procedure). A solution of alcohol **5** (0.54 mmol) in CH_2Cl_2 (5 mL) was added to a stirred solution of PCC (0.12 g, 0.56 mmol) in CH_2Cl_2 (10 mL) at 0 °C for 30 min. The reaction mixture was stirred at ~20 °C for 3 h and then filtered. The organic layer was washed water (30 mL), and dried (Na_2SO_4), and the solvent was evaporated. Ketones **11a—c** were obtained in the residue.

2-Phenylcyclohex-2-enone (11a). The yield was 73%, colorless crystals, m.p. 78 °C (*cf.* Ref. 10: m.p. 67—69 °C). ^{1}H NMR, δ: 2.11 (t, 2 H, J = 6.2 Hz); 2.54 (m, 2 H); 2.59 (t, 2 H, J = 6.6 Hz); 7.06 (t, 1 H, J = 4.3 Hz); 7.25—7.36 (m, 5 H). ^{13}C NMR, δ: 198.22, 148.22, 140.65, 136.78,128.86, 128.23, 127.80, 39.30, 26.84, 23.17. IR, ν/cm^{-1}: 3054, 3023, 2938, 2865, 1680, 1628, 1610, 1502, 1460, 1430, 1390, 1160, 1130, 850, 702. Found (%): C, 83.98; H, 7.37. $C_{12}H_{12}O$. Calculated (%): C, 83.69; H, 7.02.

(*Z*)-2-Phenylcyclohept-2-enone (11b). The yield was 79%, viscous oil (*cf.* Ref. 11: m.p. 6—7 °C). ^{1}H NMR, δ: 1.96—1.75 (m, 4 H); 2.57—2.48 (m, 2 H); 2.77—2.71 (m, 2 H); 6.76 (t, 1 H, J = 6.43 Hz); 7.36—7.25 (m, 5 H). ^{13}C NMR, δ: 206.11, 144.71, 141.77, 138.90, 128.14, 128.10, 127.44, 43.19, 28.07, 24.86, 22.16. IR, ν/cm^{-1}: 3060, 3025, 2935, 2861, 1704, 1598, 1494, 1448, 1278, 1070, 939, 756, 698, 578. Found (%): C, 83.44; H, 7.69. $C_{13}H_{14}O$. Calculated (%): C, 83.83; H, 7.58.

(*Z*)-2-Phenylcyclooct-2-enone (11c). The yield was 60%, colorless crystals, m.p. 91—93 °C. ^{1}H NMR, δ: 1.73—1.67 (m, 4 H); 1.98—1.93 (m, 2 H); 2.41—2.36 (m, 2 H); 2.58—2.55 (m, 2 H); 6.24 (t, 1 H, J = 5.8 Hz); 7.32—7.30 (m, 5 H). ^{13}C NMR, δ: 212,94, 142.46, 140.22, 131.47, 128.75, 127.76, 126.27, 45.63, 29.75, 29.10, 23.55, 22.89. IR, ν/cm^{-1}: 3058, 3020, 2929, 2856, 1714, 1455, 1216, 1062, 1037, 771, 698. Found (%): C, 83.72; H, 8.38. $C_{14}H_{16}O$. Calculated (%): C, 83.96; H, 8.05.

X-ray diffraction study was carried out on a Rigaku R-AXIS RAPID-S diffractometer equipped with a two-dimensional area IP detector at 293 K (λ(Mo-Kα) radiation, graphite monochromator) using monoclinic crystals of compound **11a**, $C_{12}H_{12}O$, space group $P21/c$; unit cell parameters: a = 6.089(2) Å, b = 12.369(5) Å, c = 12.745(5) Å, β = 101.89(2)°; V = 939.3(2) Å^3; Z = 4; d_{calc} = 1.22 mg m^{-3}; absorption coefficient 0.076 mm^{-1}; F(000): 368; θ = 2.3—30.6°; θ range from 30.6° to 99.7%. The reflections of the substrate under study were obtained by the variation of the ω parameter with three sets of various χ and ϕ values. In each of six experiments performed, 108 reflections were obtained, which cover ~99.7% of the crystal surface of compound **11c**. The lattice parameters were determined taking into account reflections with $F^2 > 2\sigma(F^2)$. The calculations were performed using the CristalClear software.[12] The structure was solved by a direct method using the SHELXS-97 program[13] and refined in the anisotropic approximation. The final R factors are

Table 1. Selected bond lengths, bond angles, and torsion angles for structure **11c**

Parameter	Value
Bond	d/Å
O(1)—C(12)	1.213(3)
C(7)—C(8)	1.342(3)
C(7)—C(12)	1.485(3)
C(7)—C(6)	1.489(3)
C(12)—C(11)	1.505(4)
Bond angle	ω/deg
C(8)—C(7)—C(12)	119.7(2)
C(8)—C(7)—C(6)	121.1(2)
C(12)—C(7)—C(6)	119.20(19)
Torsion angle	θ/deg
C(8)—C(7)—C(6)—C(5)	48.6(3)
C(12)—C(7)—C(6)—C(5)	−130.9(2)
C(8)—C(9)—C(10)—C(11)	−40.5(4)

$R_1 = 0.076$ with $I > 2\sigma(I)$, $wR_2 = 0.226$ for 2874 reflections with $F^2 = 1.058$. The obtained bond lengths and selected bond and torsion angles are listed in Table 1.

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