Available online at www.sciencedirect.com

ScienceDirect

*Mendeleev Commun.*, 2012, **22**, 181–183

Mendeleev
Communications

# Unexpected formation of 4-arylcyclopentane-1,1,3,3-tetracarboxylates in $GaCl_3$-catalyzed reaction of 2-arylcyclopropane-1,1-dicarboxylates with tetrasubstituted 1-pyrazolines

**Roman A. Novikov, Yury V. Tomilov* and Oleg M. Nefedov**

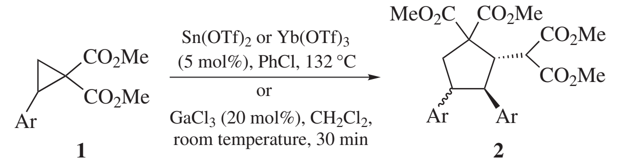
*N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, 119991 Moscow, Russian Federation.*
*Fax: +7 499 135 5328; e-mail: tom@ioc.ac.ru*

DOI: 10.1016/j.mencom.2012.06.002

Gallium trichloride-catalyzed reaction between 2-arylcyclopropane-1,1-dicarboxylates and 3,3,5,5-tetrasubstituted 1-pyrazolines affords 4-arylcyclopentane-1,1,3,3-tetracarboxylates, which originate from cycloaddition of the two molecules of the starting cyclopropane with the loss of one arylidene fragment subtracted by the 1-pyrazoline.

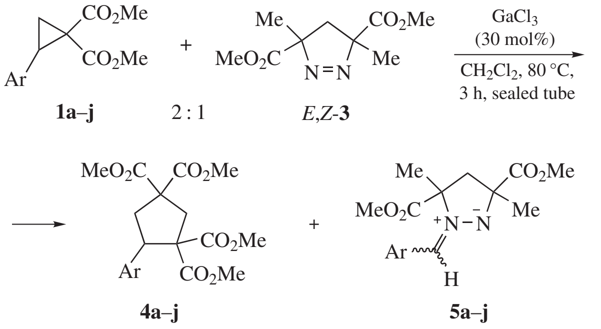
We have recently shown[1] that scandium or ytterbium triflate-catalyzed reactions between 2-arylcyclopropane-1,1-dicarboxylates (usually referred to as donor-acceptor cyclopropanes[2]) and 2-pyrazolines give 1,2-diazabicyclo[3.3.0]octanes as the major products. The similar reactions with 1-pyrazolines containing at least one hydrogen atom in 3- or 5-position mostly afford N-substituted 2-pyrazolines. The same products are also formed if an equimolar amount of $GaCl_3$ is used and the reaction is carried out at 0–5 °C.[1]

On the other hand, studies on the chemical behaviour of donor-acceptor cyclopropanes on contact with various Lewis acids revealed a few unusual pathways of their dimerization,[2–5] for instance, conversion of 2-arylcyclopropane-1,1-dicarboxylates **1** to polysubstituted cyclopentanes *E*,*E*- and *E*,*Z*-**2** in yields above 70% (Scheme 1).[3,4]



**Scheme 1**

Herein, we studied the Lewis acid-catalyzed reaction of 2-arylcyclopropane-1,1-dicarboxylates **1** in the presence of dialkyl 3,5-dimethyl-1-pyrazoline-3,5-dicarboxylates **3** containing no hydrogen atoms in 3- or 5-positions of the heterocycle. Such a substitution pattern in pyrazoline was found to be the crucial factor determining the new type of transformation of cyclopropanes **1**. In fact, heating of cyclopropane **1a** with pyrazoline *E*-**3** in the presence of 30 mol% anhydrous $GaCl_3$ in dichloromethane in a sealed tube at 80 °C gave 4-phenylcyclopentane-1,1,3,3-tetracarboxylate **4a** (Scheme 2, Ar = Ph) in up to 60% yields.† Unlike the dimerization products of donor-acceptor cyclopropanes described previously,[3–5] compound **4a** is not a true dimer, though it is formed from two cyclopropanedicarboxylate molecules. The transformation is accompanied by elimination of one CH–Ph moiety, which is trapped by a molecule of pyrazoline **3** to produce azomethineimine **5a**. No such reactions involving fragmentation of the cyclopropane ring on treatment with Lewis acids have been reported so far. Unfortunately, we failed to isolate the pure azomethineimine **5a**, since such attempts resulted in its fast hydrolysis to give benzaldehyde and the corresponding pyrazolidine.



**Scheme 2**

When other Lewis acids were applied, *e.g.* $EtAlCl_2$ or scandium or ytterbium triflates, the conversion of cyclopropane **1a** to products **4** and **5** did not occur at all. Similarly, they were not formed

---

† $^1H$ and $^{13}C$ NMR spectra were recorded on Bruker AMX-400 (400.1 and 100.6 MHz, respectively) and Bruker AVANCE II 300 (300 and 75 MHz, respectively) spectrometers in $CDCl_3$ containing 0.05% TMS as the internal standard. $^{19}F$ NMR spectra were recorded on Bruker AVANCE II 300 (282.4 MHz); standard, $CFCl_3$. Assignments of $^1H$ and $^{13}C$ signals were made with the aid of 1D DEPT-135 and 2D COSY, NOESY, HSQC and HMBC spectra.

*General procedure.* All operations were performed under a dry argon atmosphere. Solid $GaCl_3$ (0.3 mmol) in one portion was added to a solution of cyclopropane **1** (1 mmol) and pyrazoline **3** (0.5 mmol) in 5 ml of anhydrous dichloromethane at room temperature with vigorous stirring. The reaction mixture was heated at 80 °C under a slight pressure in a sealed tube and was stirred during 3 h. After that, an aqueous solution of HCl (5%) was added to the mixture at room temperature until pH 3 was achieved, and the reaction mixture was extracted with dichloromethane (3×10 ml). The extract was dried with $MgSO_4$ and the solvent was removed *in vacuo*. The residue was subjected to column chromatography on silica gel (benzene–EtOAc, 20 : 1) to afford pure cyclopentanes **4** as thick colourless oils in yields indicated in Table 1.

*Tetramethyl 4-phenylcyclopentane-1,1,3,3-tetracarboxylate* **4a**. Yield, 60%. $^1H$ NMR, $\delta$: 2.64 (ddd, 1H, $H_a$-5, $^2J$ 13.5 Hz, $^3J$ 6.8 Hz, $^4J$ 1.7 Hz), 2.88 (dd, 1H, $H_b$-5, $^2J$ 13.5 Hz, $^3J$ 13.0 Hz), 3.01 (dd, 1H, $H_a$-2, $^2J$ 14.5 Hz, $^4J$ 1.7 Hz), 3.17 (s, 3H, $C^3O_2Me$), 3.20 (d, 1H, $H_b$-2, $^2J$ 14.5 Hz), 3.78, 3.79 and 3.82 (all s, 3×3H, 3OMe), 4.16 (dd, 1H, H-4, $^3J$ 13.0 and 6.8 Hz), 7.23–7.37 (m, 5H, Ph). $^{13}C$ NMR, $\delta$: 38.8 ($C^5H_2$), 41.4 ($C^2H_2$), 49.2 ($C^4H$), 52.2, 52.7, 53.0 and 53.2 (4OMe), 58.8 ($C^1$), 64.6 ($C^3$), 127.4 (*p*-CH), 128.3 and 128.7 (2*o*-CH, 2*m*-CH), 138.1 (*i*-C), 170.4, 171.1, 171.9 and 172.0 (4COO). HRMS, *m/z*: 401.1202 (calc. for $C_{19}H_{22}O_8$, *m/z*: 401.1207 $[M+Na]^+$).

when other nitrogen-containing compounds (azobenzene, pyridine, or triethylamine) were used in place of pyrazoline **3**. The reaction using other 1-pyrazolines containing a hydrogen atom in the $\alpha$-position with respect to the N=N bond occurred by the pathways described previously[1] without fragmentation of the starting reactants. Thus, the system comprising 1-pyrazoline **3** and GaCl$_3$ proved to be specific, ensuring the formation of compounds **4** and **5**. Note that both the individual *E*- and *Z*-isomers of pyrazoline **3** or their mixture (~3.5 : 1) prepared by 1,3-dipolar cycloaddition of methyl diazopropionate to methyl methacrylate[6] were equally efficient in the reaction.

The discovered method for synthesizing cyclopentanetetracarboxylate **4a** from **1a** is well reproducible for other 2-arylcyclopropane-1,1-dicarboxylates **1b–j** (Table 1).[†] The reactions with cyclopropanes **1b–d** containing halogen atoms in the *ortho*- and *meta*-positions of the benzene ring occurred most readily. Similar reactions proceeded with naphthyl-substituted substrates **1i,j**. All the 4-arylcyclopentane-1,1,3,3-tetracarboxylates **4a–j** obtained manifest a characteristic upfield shift of protons of one of the methoxy groups ($\delta_H$ 3.13–3.27, and even higher, *viz.*, 2.83 and 3.03, for naphthyl-substituted derivatives **4i,j**). This arrangement of signals is typical of the *cis*-CO$_2$Me group at C$^3$, which is located above the plane of the adjacent benzene ring within its ‘negative cone’ of anisotropy.

**Table 1** Formation of 4-arylcyclopentane-1,1,3,3-tetracarboxylates **4** in the GaCl$_3$-catalyzed reaction of 2-arylcyclopropane-1,1-dicarboxylates **1** with pyrazoline *E*-**3**.[a]

| Entry | Reagent | Ar | Product | Yield (%)[b] |
|---|---|---|---|---|
| 1 | **1a** | Ph | **4a** | 60 |
| 2 | **1b** | 2-ClC$_6$H$_4$ | **4b** | 91 |
| 3 | **1c** | 3-ClC$_6$H$_4$ | **4c** | 86 |
| 4 | **1d** | 3-BrC$_6$H$_4$ | **4d** | 80 |
| 5 | **1e** | 4-MeC$_6$H$_4$ | **4e** | 57 |
| 6 | **1f** | 4-FC$_6$H$_4$ | **4f** | 68 |
| 7 | **1g** | 4-ClC$_6$H$_4$ | **4g** | 69 |
| 8 | **1h** | 4-BrC$_6$H$_4$ | **4h** | 65 |
| 9 | **1i** | 1-naphthyl | **4i** | 50 |
| 10 | **1j** | 2-naphthyl | **4j** | 48 |

[a] *Reaction conditions*: **1** : **3** : GaCl$_3$ = 1 : 0.5 : 0.3, CH$_2$Cl$_2$, sealed tube, 80 °C, 3 h. The optimum time and temperature were determined by NMR monitoring the reaction in an NMR tube. [b] Isolated yields.

The proposed mechanism of this process is outlined in Scheme 3. First, cyclopropanedicarboxylate **1** on contact with gallium trichloride is opened to give bipolar intermediate **I**, which adds to a molecule of pyrazoline **2** to produce intermediate **II**. No migration of substituents at the heterocycle can occur in intermediate **II**, so it adds a second molecule **1** to form bipolar intermediate **III**. Intramolecular S$_N$2 attack by a malonyl anion on the sterically free CH$_2$ group in **III** results in splitting of the latter to afford cyclopentane **4** and azomethineimine **5**. The nucleophilic attack occurs on the methylene group, whereas attack on the methine C atom appears unlike due to considerable steric hindrance. The resulting azomethine **5** is unstable under acidic conditions and is hydrolyzed during the workup of the reaction mixture to give pyrazolidine **6** and the corresponding benzaldehydes **7**.

Note that cyclopentanes **4** cannot be obtained by direct [2+3]-cycloaddition of cyclopropanedicarboxylates **1** to methylidenemalonate, since donor-acceptor cyclopropanes readily add to electron-rich double bonds,[7] but do not react with electron-deficient ones. In this study, we suggested a ‘bypass’ route for synthesizing cyclopentanes **4** by oxidative doubling of readily available cyclopropanedicarboxylates **1**. During the doubling of cyclopropanedicarboxylates, the second molecule of cyclopropane **1** is synthetically equivalent to methylidenemalonate.

In summary, we have discovered a new unusual reaction of 2-arylcyclopropane-1,1-dicarboxylates with a 3,3,5,5-tetrasubstituted 1-pyrazoline in the presence of catalytic amounts of GaCl$_3$ to give 4-arylcyclopentane-1,1,3,3-tetracarboxylates in high yields. In this case, 1-pyrazoline acts as the oxidant, causing

---

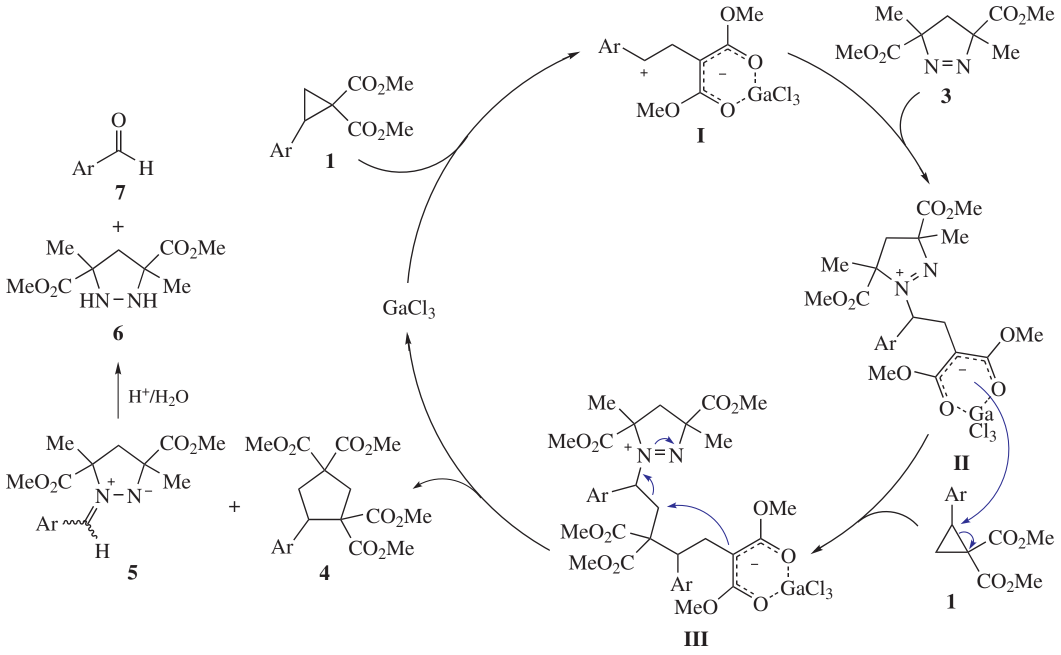
*Tetramethyl 4-(2-chlorophenyl)cyclopentane-1,1,3,3-tetracarboxylate* **4b**. Yield, 91%. IR (CHCl$_3$, $\nu$/cm$^{-1}$): 3020, 2976, 1956, 2896, 2846, 1734 (br., O=CO), 1521, 1479, 1436, 1393, 1256. $^1$H NMR, $\delta$: 2.67 (dd, 1H, H$_a$-5, $^2J$ 14.0 Hz, $^3J$ 10.4 Hz), 2.89 (ddd, 1H, H$_b$-5, $^2J$ 14.0 Hz, $^3J$ 8.1 Hz, $^4J$ 1.3 Hz), 3.05 (dd, 1H, H$_a$-2, $^2J$ 14.5 Hz, $^4J$ 1.3 Hz), 3.27 (s, 3H, C$^3$O$_2$Me), 3.28 (d, 1H, H$_b$-2, $^2J$ 14.5 Hz), 3.73, 3.76 and 3.78 (all s, 3×3H, 3OMe), 4.83 (dd, 1H, H-4, $^3J$ 10.4 and 8.1 Hz), 7.14 (ddd, 1H, C$_6$H$_4$, $^3J$ 7.8 and 7.6 Hz, $^4J$ 1.6 Hz), 7.19 (ddd, 1H, C$_6$H$_4$, $^3J$ 7.7 and 7.6 Hz, $^4J$ 1.5 Hz), 7.27 (dd, 1H, C$_6$H$_4$, $^3J$ 7.7 Hz, $^4J$ 1.6 Hz), 7.35 (dd, 1H, C$_6$H$_4$, $^3J$ 7.8 Hz, $^4J$ 1.5 Hz). $^{13}$C NMR, $\delta$: 40.9 (C$^5$H$_2$), 41.9 (C$^2$H$_2$), 45.0 (C$^4$H), 52.3, 53.1 and 53.2 (1C, 1C and 2C, 4OMe), 58.9 (C$^1$), 64.9 (C$^3$), 126.7, 128.4, 129.2 and 129.7 (4CH, C$_6$H$_4$), 135.3 (CCl), 137.5 (*i*-C), 169.9, 171.2, 171.4 and 171.6 (4COO). MS, *m/z* (%): 377 (11), 317 (24), 261 (11), 257 (10), 155 (13), 149 (11), 115 (20), 113 (24), 103 (7), 89 (7), 77 (8), 59 (100). HRMS, *m/z*: 435.0809 (calc. for C$_{19}$H$_{21}$$^{35}$ClO$_8$, *m/z*: 435.0817 [M+Na]$^+$).

*Tetramethyl 4-(3-chlorophenyl)cyclopentane-1,1,3,3-tetracarboxylate* **4c**. Yield, 86%. $^1$H NMR, $\delta$: 2.58 (ddd, 1H, H$_a$-5, $^2J$ 13.5 Hz, $^3J$ 6.8 Hz, $^4J$ 1.6 Hz), 2.80 (dd, 1H, H$_b$-5, $^2J$ 13.5 Hz, $^3J$ 13.1 Hz), 2.96 (dd, 1H, H$_a$-2, $^2J$ 14.5 Hz, $^4J$ 1.6 Hz), 3.13 (s, 3H, C$^3$O$_2$Me), 3.16 (d, 1H, H$_b$-2, $^2J$ 14.5 Hz), 3.75, 3.76 and 3.79 (all s, 3×3H, 3OMe), 4.07 (dd, 1H, H-4, $^3J$ 13.1 and 6.8 Hz), 7.17–7.24 (m, 3H, C$_6$H$_4$), 7.31 (m, 1H, H$^{2'}$, C$_6$H$_4$). $^{13}$C NMR, $\delta$: 38.7 (C$^5$H$_2$), 41.4 (C$^2$H$_2$), 48.9 (C$^4$H), 52.4, 53.0, 53.1 and 53.2 (4OMe), 58.6 (C$^1$), 64.5 (C$^3$), 127.0, 127.7, 128.8 and 129.3 (4CH, C$_6$H$_4$), 134.0 (CCl), 140.2 (*i*-C), 170.3, 170.9, 171.6 and 171.9 (4COO). MS, *m/z* (%): 414 (2) and 412 (5) [M]$^+$, 383 (1) and 381 (3) [M–OMe]$^+$, 354 (6) and 352 (16) [M–HCO$_2$Me]$^+$, 349 (7), 322 (18), 321 (11), 320 (54), 292 (19), 263 (18), 262 (11), 261 (64), 260 (8), 233 (24), 205 (12), 175 (17), 155 (17), 149 (18), 141 (16), 139 (32), 115 (27), 113 (30), 71 (25), 59 (100). HRMS, *m/z*: 435.0809 (calc. for C$_{19}$H$_{21}$$^{35}$ClO$_8$, *m/z*: 435.0817 [M+Na]$^+$).

*Tetramethyl 4-(4-fluorophenyl)cyclopentane-1,1,3,3-tetracarboxylate* **4f**. Yield, 68%. IR (CHCl$_3$, $\nu$/cm$^{-1}$): 3020, 2956, 2928, 2853, 1733 (br., O=CO), 1686, 1654, 1646, 1602, 1513, 1474, 1436, 1347, 1263, 1223. $^1$H NMR, $\delta$: 2.58 (ddd, 1H, H$_a$-5, $^2J$ 13.4 Hz, $^3J$ 6.7 Hz, $^4J$ 1.6 Hz), 2.81 (dd, 1H, H$_b$-5, $^2J$ 13.4 Hz, $^3J$ 13.2 Hz), 2.97 (dd, 1H, H$_a$-2, $^2J$ 14.5 Hz, $^4J$ 1.6 Hz), 3.15 (d, 1H, H$_b$-2, $^2J$ 14.5 Hz), 3.20, 3.75, 3.76 and 3.80 (all s, 4×3H, 4OMe), 4.10 (dd, 1H, H-4, $^3J$ 13.2 and 6.7 Hz), 6.95 (m, 2H, 2*m*-CH, $^3J_{HF}$ 8.7 Hz), 7.31 (m, 2H, 2*o*-CH, $^4J_{HF}$ 5.5 Hz). $^{13}$C NMR, $\delta$: 38.8 (C$^5$H$_2$), 41.4 (C$^2$H$_2$), 48.5 (C$^4$H), 52.3, 52.9, 53.1 and 53.2 (4OMe), 58.7 (C$^1$), 64.5 (C$^3$), 114.9 (2*m*-CH, $^2J_{CF}$ 21.2 Hz), 130.3 (2*o*-CH, $^3J_{CF}$ 7.9 Hz), 133.7 (*i*-C, $^4J_{CF}$ 3.3 Hz), 162.2 (*p*-CF, $^1J_{CF}$ 246 Hz), 170.4, 171.0, 171.8 and 172.0 (4COO). $^{19}$F NMR, $\delta$: –116.0 (tt, 1F, $^3J_{HF}$ 8.7 Hz, $^4J_{HF}$ 5.5 Hz). MS, *m/z* (%): 396 (0.2) [M]$^+$, 365 (0.2) [M–OMe]$^+$, 336 (6) [M–HCO$_2$Me]$^+$, 304 (18), 276 (8), 245 (25), 217 (19), 159 (15), 133 (25), 123 (35), 113 (14), 95 (14), 59 (100). HRMS, *m/z*: 419.1104, 435.0848 (calc. for C$_{19}$H$_{21}$FO$_8$, *m/z*: 419.1113 [M+Na]$^+$, 435.0852 [M+K]$^+$).

*Tetramethyl 4-(1-naphthyl)cyclopentane-1,1,3,3-tetracarboxylate* **4i**. Yield, 50%. IR (CHCl$_3$, $\nu$/cm$^{-1}$): 3023, 2955, 1732 (br., O=CO), 1599, 1515, 1435, 1255, 1227. $^1$H NMR, $\delta$: 2.83 (s, 3H, C$^3$O$_2$Me), 2.85 (dd, 1H, H$_a$-5, $^2J$ 13.7 Hz, $^3J$ 10.7 Hz), 2.92 (ddd, 1H, H$_b$-5, $^2J$ 13.7 Hz, $^3J$ 7.9 Hz, $^4J$ 1.6 Hz), 3.08 (dd, 1H, H$_a$-2, $^2J$ 14.4 Hz, $^4J$ 1.6 Hz), 3.40 (d, 1H, H$_b$-2, $^2J$ 14.4 Hz), 3.72, 3.80 and 3.81 (all s, 3×3H, 3OMe), 5.21 (dd, 1H, H-4, $^3J$ 10.7 and 7.9 Hz), 7.36–7.44 (m, 2H, 1-naphthyl), 7.46 (ddd, 1H, 1-naphthyl, $^3J$ 8.0 and 6.9 Hz, $^4J$ 1.0 Hz), 7.55 (ddd, 1H, 1-naphthyl, $^3J$ 8.5 and 6.8 Hz, $^4J$ 1.4 Hz), 7.72 (br. dd, 1H, 1-naphthyl, $^3J$ 6.9 Hz, $^4J$ 2.2 Hz), 7.81 (br. d, 1H, 1-naphthyl, $^3J$ 8.1 Hz), 8.50 (br. d, 1H, 1-naphthyl, $^3J$ 8.6 Hz). $^{13}$C NMR, $\delta$: 41.7, 42.0 and 43.0 (C$^5$H$_2$, C$^2$H$_2$ and C$^4$H), 52.0, 53.17 and 53.23 (1C, 1C and 2C, 4OMe), 59.4 (C$^1$), 65.5 (C$^3$), 124.5, 125.1, 125.4, 125.7, 126.2, 128.1 and 128.7 (7CH, 1-naphthyl), 132.7, 133.9 and 136.2 (3C, 1-naphthyl), 170.0, 171.3, 171.8 and 172.2 (4COO). MS, *m/z* (%): 428 (13) [M]$^+$, 397 (0.1) [M–OMe]$^+$, 368 (3) [M–HCO$_2$Me]$^+$, 337 (10), 277 (31), 224 (22), 220 (19), 219 (19), 217 (31), 189 (66), 179 (21), 165 (100), 152 (34), 145 (20), 128 (15), 113 (25), 59 (97). HRMS, *m/z*: 451.1346 (calc. for C$_{23}$H$_{24}$O$_8$, *m/z*: 451.1346 [M+Na]$^+$).

For characteristics of compounds **4d**,**e**,**g**,**h**,**j**, see Online Supplementary Materials.



**Scheme 3**

the fragmentation of the resulting dimeric intermediate **III** (see Scheme 3) with elimination of the arylidene moiety as azomethineimine.

This work was supported by the Russian Federation President Council for Grants (Program for State Support of Leading Scientific Schools of the Russian Federation, grant no. NSh-8242.2010.3) and the Division of Chemistry and Materials Sciences of the Russian Academy of Sciences (Program for Basic Research 'Theoretical and Experimental Study of the Nature of Chemical Bonds and Mechanisms of Important Chemical Reactions and Processes').

*Online Supplementary Materials*

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.mencom.2012.06.002.

## References

1 (*a*) Yu. V. Tomilov, R. A. Novikov and O. M. Nefedov, *Tetrahedron*, 2010, **66**, 9151; (*b*) R. A. Novikov, E. V. Shulishov and Yu. V. Tomilov, *Mendeleev Commun*., 2012, **22**, 87.

2 M. Ya. Mel'nikov, E. M. Budynina, O. A. Ivanova and I. V. Trushkov, *Mendeleev Commun.*, 2011, **21**, 293.

3 R. A. Novikov, V. A. Korolev, V. P. Timofeev and Yu. V. Tomilov, *Tetrahedron Lett*., 2011, **52**, 4996.

4 A. O. Chagarovskiy, O. A. Ivanova, E. M. Budynina, I. V. Trushkov and M. Ya Melnikov, *Tetrahedron Lett*., 2011, **52**, 4421.

5 (*a*) O. A. Ivanova, E. M. Budynina, A. O. Chagarovskiy, I. V. Trushkov and M. Ya. Melnikov, *J. Org. Chem.*, 2011, **76**, 8852; (*b*) O. A. Ivanova, E. M. Budynina, A. O. Chagarovskiy, E. R. Rakhmankulov, I. V. Trushkov, A. V. Semeykin, N. L. Shimanovskii and M. Ya. Melnikov, *Chem. Eur. J.*, 2011, **17**, 11738.

6 R. A. Novikov, D. N. Platonov, V. A. Dokichev, Yu. V. Tomilov and O. M. Nefedov, *Izv. Akad. Nauk, Ser. Khim.*, 2010, 963 (*Russ. Chem. Bull., Int. Ed*., 2010, **59**, 984).

7 (*a*) H. U. Reissig and R. Zimmer, *Chem. Rev.*, 2003, **103**, 1151; (*b*) M. Yu and B. L. Pagenkopf, *Tetrahedron*, 2005, **61**, 321; (*c*) F. de Simone and J. Waser, *Synthesis*, 2009, **20**, 3353.

*Received: 5th March 2012; Com. 12/3887*