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Tetrahedron Letters 45 (2004) 4935–4938
Tetrahedron Letters

Synthesis of new halo-containing acetylenes and their application to the synthesis of azoles

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Received 6 September 2003; revised 17 April 2004; accepted 20 April 2004

Abstract—The convenient synthesis of ten halo- and an isoxazole-containing acetylenes from the reaction of acetylenes with *n*-butyl lithium and subsequent reaction with an electrophile agent (ethyl trichloroacetate, ethyl dichloroacetate, trifluoroacetic anhydride, 3-methylisoxazol-5-carbonyl chloride, carbon tetrachloride and 1,1,1-trifluoro-4-ethoxy-3-buten-2-one) in moderated to good yields is reported. The application of 1,1,1-trichloro-4-phenyl-3-butyn-2-one on the synthesis of two azoles is also showed.

Recently, a variety of important biological activities of acetylenic compounds have been published. For example, Efavirenz exhibits nonnucleoside HIV-1 reverse transcriptase inhibition and acetylenic heterocycles are used as muscarinic M_1 agonists for the treatment of Alzheimer's disease.[1,2] Acetylenic derivatives are also useful precursor in synthetic organic chemistry,[3,4] in special, for the preparation of 1,2,3-triazoles from the 1,3-dipolar cycloaddition with organic and inorganic azides.[5]

One of the most efficient methods for the preparation of acylacetylenes is the direct acylation of metal-acetylenides. The literature reports the reaction of activated acylating reagents such as acid chlorides or anhydrides with various types of metal-acetylenides such as lithium-,[6] magnesium-,[7] copper-,[8] cadmium-,[9] silicium-,[10] silver-[11] and tin-acetylenides[12] that have been used to obtain the corresponding acylacetylenes.

In recent years, we have developed a general synthesis of a large number of 1,1,1-trihalo-4-methoxy-alken-2-ones,[13,14] important halogen-containing building blocks, and demonstrated their usefulness in heterocyclic preparations, for example, isoxazoles,[13,15,16] pyrazoles,[14b,17] pyrazolium chlorides,[18] pyrrolidinones,[19] pyrimidines,[20] pyridines,[21] thiazines[22] and diazepines.[23]

In continuation of our research program to develop new halo-heterocyclic precursors, we are reporting the methodology to synthesize a series of halo- and isoxazole-containing acetylenes. Thus, the aim of this work is to report the synthesis of acetylenes **2**–**8** from the reaction of acetylene **1** with *n*-butyl lithium and subsequent reaction with an electrophile, often in the presence of boron trifluoride etherate (Scheme 1).

Ziegler et al.[24] demonstrated the preparation of a series of halo alkynes, where the compound **7a** was prepared by shaking the alkyne with a large excess of sodium hydroxide and chlorine. Zweifel et al.[3] proposed the preparation of the same compound from the reaction of the alkyne in *n*-butyl lithium in the presence of *n*-chlorosuccinimide. In a recent paper, Andrew and Mellor[25] reported the synthesis of a novel series of acetylenes, including the 6-phenyl-1,1,1-trifluoro-3-hexen-5-yne-2-one (**8a**) in low yield (37%), using Grignard and organolithium reagents. So far, phenyl acetylenes **2**–**6** have not been reported. In this work, phenyl acetylenes were obtained in moderate to good yields.

The synthesis of compounds **2**–**4**, **8** were carried out from the reaction of lithium acetylenide with the

Keywords: Acetylenes; Heterocycles; Pyrazoles; Isoxazoles.
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URL: http://www.ufsm.br/nuquimhe

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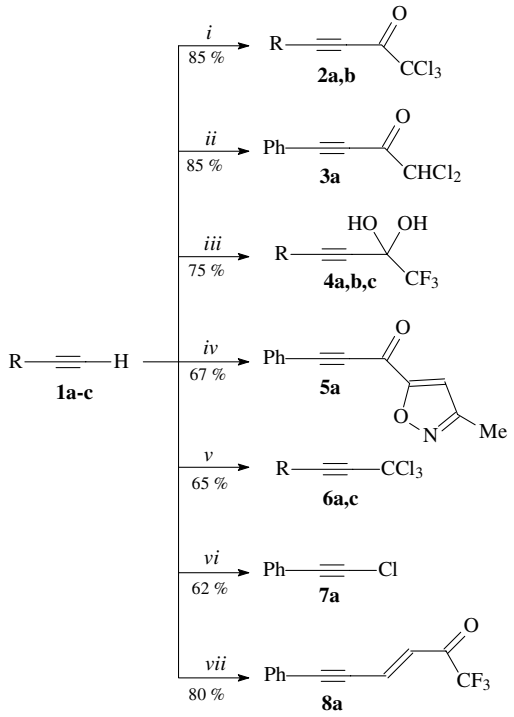
doi:10.1016/j.tetlet.2004.04.106

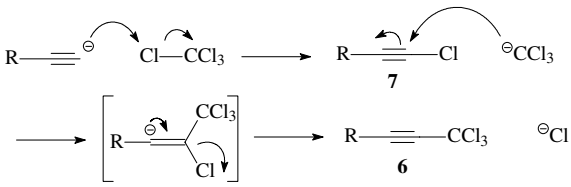


Scheme 1. Reagents and conditions: (i) (1) *n*-BuLi, THF, 30 min, −78 °C; (2) $Cl_3CC(O)OEt$, 2 equiv BF_3·OEt, rt, 2 h. (ii) (1) *n*-BuLi, THF, 30 min, −78 °C; (2) $Cl_2CHC(O)OEt$, 2 equiv BF_3·OEt, rt, 2 h. (iii) (1) *n*-BuLi, THF, 30 min, −78 °C; (2) $(F_3CCO)_2O$, 3 equiv BF_3·OEt, rt, 1.5 h (iv) (1) *n*-BuLi, THF, 30 min, −78 °C; (2) isoxazol-5-carbonyl chloride, rt, 45 min. (v) (1) *n*-BuLi, THF, 30 min, −78 °C; (2) CCl_4 (excess), −78 °C to rt, 45 min. (vi) (1) *n*-BuLi (excess), THF, 30 min, −78 °C; (2) CCl_4, rt, 1 h. (vii) (1) *n*-BuLi, THF, 30 min, −78 °C; (2) $CF_3C(O)CH{=}CHOEt$, 2 equiv BF_3·OEt, rt, 2 h.

corresponding electrophile agent, in the presence of 2 equiv of boron trifluoride diethyl etherate. The use of 2 equiv of boron trifluoride diethyl etherate was required to improve the product yields. In the synthesis of compounds **5**–**7** the use of Lewis acid was not necessary.

The preparation of compounds **6** and **7** from the same reagents with modification in the reaction conditions was unexpected. To obtain **7a** a solution of carbon tetrachloride in THF was added to an excess of lithium acetylenide (molar ratio of 3:5) at −78 °C, whereas, in the synthesis of **6a**–**c**, a solution of lithium acetylenide in THF was added to an excess of carbon tetrachloride (molar ratio of 1:3) at −78 °C. The preparation of **7** is in accordance with analogous results obtained by Zweifel et al.[3] and Ziegler et al.[24] that reacted acetylenides with electrophilic chlorine compounds to obtain chloroalkynes. On the other hand, the reaction mechanism for preparation of **6** remains unclear. A possible explanation is that the product **6** was obtained from compound **7** due to the attack of the trichloromethyl anion on **7** and subsequent elimination of a chlorine anion (Scheme 2).

Considering the importance of isoxazoles and pyrazoles as biological active compounds,[26–28] Linderman and Lonicar[29] prepared trifluoromethyl functionalized acetylenes with the objective to obtain a series of perfluoroalkyl substituted azoles. However, the synthetic route



Scheme 2.

used by these authors for the synthesis of isoxazoles, from the reaction of trifluoromethyl acetylenes with hydroxylamine, furnished a mixture of oxime and isoxazoline. Also, the reaction of acetylenes with hydrazine in acetonitrile at room temperature, lead to a mixture of pyrazole and pyrazoline.[29]

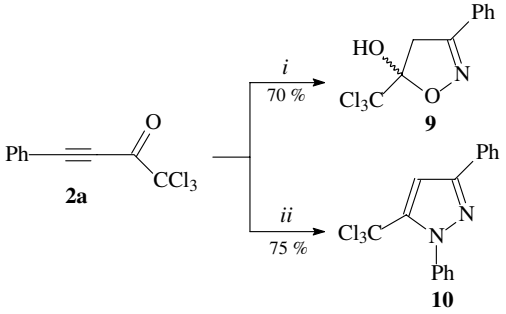
In this work, **2a** was used to show the synthetic potential of this compound towards reactions with hydroxylamine and phenyl hydrazine (Scheme 3). From a similar procedure reported by Linderman et al.,[29] in this work only 4,5-dihydroisozazole (**9**) and the pyrazole (**10**), respectively, were obtained, instead of the mixture of products. The physical and spectral data of compounds **9**, **10** obtained are in accordance with the literature.[15c,17b,30]

Unless otherwise indicated, all common reagents and solvents were used as obtained from commercial supplies without further purifications. 1,1,1-Trifluoro-4-ethoxy-3-buten-2-one was synthesized using the methodology developed in our laboratory.[13a] The melting points were taken on a melting point microscope Reichert Thermovar and are uncorrected. ^1H and ^{13}C NMR spectra were recorded on a Bruker DPX 400 (1H at 400.13 MHz and 13C at 100.62 MHz) in 5 mm sample tubes at 298 K (digital resolution ±0.01 ppm) in $CDCl_3$/TMS solutions.

1. Synthesis of 1,1,1-trichloro-4-phenyl-3-butyn-2-one 2a

1.1. Typical procedure

To a stirred solution of phenyl acetylene (0.204 g, 2 mmol) in dry THF (10 mL) was added dropwise 1.6 M solution of *n*-butyl lithium in hexane (1.5 mL) at −78 °C and under nitrogen. After stirring for 30 min, was added to the mixture a solution of ethyl trichloroacetate



Scheme 3. Reagents and conditions: (i) NH_2OH·HCl, pyridine, methanol, reflux, 12 h. (ii) NH_2NHPh, benzene, rt, 4 h.

(0.28 mL, 2 mmol) and trifluoride diethyl etherate (0.5 mL) in dry THF (5 mL). The reaction was allowed to warm to room temperature and the resulting mixture was stirred at room temperature for 2 h. After this time, a saturated solution of NH_4Cl (10 mL) was added and the organic layer was extracted with dichloromethane (3×15 mL). The organic phase was dried (Na_2SO_4) and the solvent was evaporated. The residue was purified by column chromatography on silica gel 230–400 mesh, hexane/ethyl acetate (10:1). Selected physical and spectral data of compounds **2**–**8** are presented in Ref. 31.

2. Synthesis of 1,1,1-trichloro-3-phenyl-2-propyne 6a

To a stirred solution of phenyl acetylene (0.510 g, 5 mmol) in dry THF (10 mL) was added dropwise 1.6 M solution of *n*-butyl lithium in hexane (5 mmol, 3.12 mL) at −78 °C and under nitrogen. After stirring for 30 min, the phenyl acetylenide obtained was added to the carbon tetrachloride (15 mmol, 1.43 mL) at −78 °C. The reaction was allowed to warm to room temperature and the resulting mixture was stirred at room temperature for 45 min. The isolation of the product was similar to that used in the synthesis of **2a**. Selected physical and spectral data of compound **6a** are presented in Ref. 31.

3. Synthesis of 1-chloro-2-phenylethyne 7a

To a stirred solution of phenyl acetylene (0.510 g, 5 mmol) in dry THF (10 mL) was added dropwise 1.6 M solution of *n*-butyl lithium in hexane (5 mmol, 3.12 mL) at −78 °C and under nitrogen. After stirring for 30 min, a solution of carbon tetrachloride (3 mmol, 0.28 mL) in dry THF (5 mL) at −78 °C, was added. The reaction was allowed to warm to room temperature and the resulting mixture was stirred at room temperature for 1 h. The isolation of the product was similar to that used in the synthesis of **2a**. Selected physical and spectral data of compound **7a** are presented in Ref. 31.

Acknowledgements

The authors thank the Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq/PADCT), Fundação de Amparo à pesquisa do Estado do Rio Grande do Sul (FAPERGS) for financial support. The fellowships from CNPq, CAPES and FAPERGS are also acknowledged.

References and notes

1. Pierce, M. E.; Parsoms, R. L., Jr.; Radesca, L. A.; Lo, Y. S.; Silvermamn, S.; Moore, J. R.; Islan, Q.; Choudhury, A.; Fortunak, J. M. D.; Nguyen, D.; Luo, C.; Morgan, S. J.; Davis, W. P.; Conalone, P. N. *J. Org. Chem.* **1998**, *63*, 8536.
2. Rodriguez-Franco, M. I.; Dorronso, I.; Castro, A.; Martínez, A.; Badía, A.; Bãnos, J. E. *Bioorg. Med. Chem.* **2003**, *11*, 2263.
3. Zweifel, G.; Lewis, W.; On, H. P. *J. Am. Chem. Soc.* **1979**, *101*, 5101.
4. (a) Legros, J.; Crousse, B.; Delpon, D.-B.; Bégué, J.-P. *J. Fluorine Chem.* **2001**, *107*, 121; (b) Tykwinski, R. R.; Zhao *Synlett* **2002**, *12*, 1939; Brown, H. C.; Racherla, U. S.; Sing, S. M. *Tetrahedron Lett.* **1984**, *25*, 2411.
5. Degl'lnnocenti, A.; Scafato, P.; Capperucci Bartoletti, L. A.; Mordini, A.; Reginato, G. *Tetrahedron Lett.* **1995**, *36*, 9031.
6. Kroeger, J. W.; Niewland, J. A. *J. Am. Chem. Soc.* **1936**, *58*, 1861.
7. Normant, J. F.; Bourgain, M. *Tetrahedron Lett.* **1970**, *11*, 2659.
8. Yashina, G.; Zarva, T. V.; Kaigordova, T. D.; Vereshchagin, L. I. *Zh. Org. Khim.* **1968**, *4*, 2104.
9. Utimoto, K.; Tanaka, M.; Kitai, M.; Nozaki, H. *Tetrahedron Lett.* **1978**, *18*, 405.
10. Davis, R. B.; Scheiber, D. H. *J. Am. Chem. Soc.* **1956**, *78*, 1675.
11. Himbert, G. *Angew. Chem.* **1979**, *91*, 432; *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 405.
12. Kroeger, J. W.; Nieuwland, J. A. J. *J. Am. Chem. Soc.* **1936**, *58*, 1861.
13. (a) Colla, A.; Martins, M. A. P.; Clar, G.; Krimmer, S.; Fischer, P. *Synthesis* **1991**, *6*, 483; (b) Martins, M. A. P.; Zoch, A. N.; Flores, A. F. C.; Clar, G.; Zanatta, N.; Bonacorso, H. G. *J. Heterocycl. Chem.* **1995**, *32*, 739.
14. (a) Martins, M. A. P.; Bastos, G. P.; Bonacorso, H. G.; Zanatta, N.; Flores, A. F. C.; Siqueira, G. M. *Tetrahedron Lett.* **1999**, *40*, 4309; (b) Bonacorso, H. G.; Martins, M. A. P.; Bittencourt, S. R. T.; Lourega, R. V.; Zanatta, N.; Flores, A. F. C. *J. Fluorine Chem.* **1999**, *99*, 177.
15. (a) Martins, M. A. P.; Flores, A. C.; Freitag, R.; Zanatta, N. *J. Heterocycl. Chem.* **1995**, *32*, 731; (b) Martins, M. A. P.; Flores, A. C.; Freitag, R. A.; Zanatta, N. *J. Heterocycl. Chem.* **1996**, *33*, 1223; (c) Martins, M. A. P.; Siqueira, G. M.; Bastos, G. P.; Bonacorso, H. G.; Zanatta, N. *J. Heterocycl. Chem.* **1996**, *33*, 1619; (d) Martins, M. A. P.; Flores, A. F. C.; Bastos, G. P.; Zanatta, N.; Bonacorso, H. G. *J. Heterocycl. Chem.* **1999**, *36*, 837; (e) Martins, M. A. P.; Neto, M.; Sinhorin, A. P.; Bastos, G. P.; Zimmermann, N. E. K.; Rosa, A.; Bonacorso, H. G.; Zanatta, N. *Synth. Commun.* **2002**, *32*, 425.
16. Martins, M. A. P.; Sinhorin, A. P.; Zimmermann, N. E. K.; Zanatta, N.; Bonacorso, H. G.; Bastos, G. P. *Synthesis* **2001**, *13*, 1959.
17. (a) Braibante, M. E. F.; Martins, M. A. P.; Clar, G. *J. Heterocycl. Chem.* **1993**, *30*, 1159; (b) Flores, A. C. F.; Martins, M. A. P.; Rosa, A.; Flores, D. C.; Zanatta, N.; Bonacorso, H. G. *Synth. Commun.* **2002**, *32*, 1585.
18. (a) Martins, M. A. P.; Pereira, C. M. P.; Sinhorin, A. P.; Bastos, G. P.; Zimmermann, N. E. K.; Rosa, A.; Bonacorso, H.; Zanatta, N. *Synth. Commun.* **2002**, *32*, 419; (b) Martins, M. A. P.; Blanco, R. F.; Pereira, C. M. P.; Beck, P.; Brondani, S.; Cunico, W.; Zimmermann, N. E. K.; Bonacorso, H. G.; Zanatta, N. *J. Fluorine Chem.* **2002**, *118*, 69.
19. Zanatta, N.; Rosa, L. S.; Loro, E.; Bonacorso, H. G.; Martins, M. A. P. *J. Fluorine Chem.* **2001**, *107*, 149.
20. (a) Madruga, C. C.; Clerici, E.; Martins, M. A. P.; Zanatta, N. *J. Heterocycl. Chem.* **1995**, *32*, 735; (b) Zanatta, N.; Cortelini, M. F. M.; Carpes, M. J. S.; Bonacorso, H. G.; Martins, M. A. P. *J. Heterocycl. Chem.* **1997**, *34*, 509; (c) Zanatta, N.; Madruga, C. C.; Marisco, P. C.; Flores, D. C.; Bonacorso, H. G.; Martins, M. A. P. *J. Heterocycl. Chem.* **2000**, *37*, 1213; (d) Zanatta, N.;

Pacholski, I. L.; Faoro, D.; Bonacorso, H. G.; Martins, M. A. P. *Synth. Commun.* **2001**, *31*, 2855.
21. Zanatta, N.; Barichello, R.; Bonacorso, H. G.; Martins, M. A. P. *Synthesis* **1999**, *5*, 765.
22. Bonacorso, H. G.; Bittencourt, S. R. T.; Lourega, R. V.; Flores, A. F. C.; Zanatta, N.; Martins, M. A. P. *Synthesis* **2000**, 1.
23. (a) Bonacorso, H. G.; Bittencourt, S. R. T.; Wastowski, A. D.; Wentz, A. P.; Zanatta, N.; Martins, M. A. P. *Tetrahedron Lett.* **1996**, *37*, 9155; (b) Bonacorso, H. G.; Bittencourt, S. R. T.; Wastowski, A. D.; Wentz, A. P.; Zanatta, N.; Martins, M. A. P. *J. Heterocycl. Chem.* **1999**, *36*, 45.
24. Ziegler, G. R.; Welch, C. A.; Orzech, C. E.; Kikkawa, S.; Miller, S. I. *J. Am. Chem. Soc.* **1963**, *85*, 1648.
25. Andrew, R. J.; Mellor, J. M. *Tetrahedron* **2000**, *56*, 7261.
26. (a) Ishii, S.; Yagi, K.; Umehara, T.; Kudo, M.; Nawamaki, T.; Watanabe, S. Japan Kokai, Tokkyo Koho JP 02, *129*, 171. *Chem. Abstr.* **1990**, *113*, 17201a; (b) Buntain, I. G.; Hatton, L. R.; Hawkins, D. W.; Pearson, C. J.; Roberts, D. A. Eur. Pat. Appl. EP 295, 117. *Chem. Abstr.* **1990**, *112*, 35845n; (c) Moser, H.; Bohner, B.; Foery, W. Eur. Pat. Appl. EP 268, 554; *Chem. Abstr.* **1988**, *110*, 23879; (d) Ishii, T.; Shimotori, H.; Tanaka, Y.; Ishikawa, K. Japan Kokai, Tokkyo Koho JP 01, 168, 675. *Chem. Abstr.* **1989**, *112*, 35854; (e) Okada, I.; Yoshida, K.; Sekine, K. Japan Kokai, Tokkyo Koho, JP 02, 292, 263. *Chem. Abstr.* **1990**, *114*, 185497; (f) Sohn, E.; Handle, R.; Mildenberger, H.; Buerstell, H.; Bauer, K.; Bieringer, H. German Patent 3, 633, 840. *Chem. Abstr.* **1988**, 110, 8202.
27. (a) Casida, J. E.; Pulman, D. A. In Advances in the Chemistry of Insect Control III; Briggs, G. G., Ed.; Proc 3rd Int. Symp. Adv. Chem. of Insect Control, Spec. Publ. **1994**, 147, p 36; (b) Bloomquist, J. R. In *Biochemical Sites of Insecticide Action and Resistance*; Ishaaya, I., Ed.; Springer: Berlin, 2001; p 17; (c) Colliot, F.; Kukorowski, K. A.; Hawkins, D. W.; Roberts, D. A. In Brighton Crop Protection Conference—Pests and Diseases; British Crop Protection Council: Farnham, UK, **1992**; Vol. 1, p 29.
28. Penning, T. D.; Talley, J. J.; Bertenshaw, S. R.; Carter, J. S.; Collins, P. W.; Docter, S.; Graneto, M. J.; Lee, L. F.; Malecha, J. W.; Miyashiro, J. M.; Rogers, R. S.; Rogier, D. J.; Yu, S. S.; Anderson, G. D.; Burton, E. G.; Cogburn, J. N.; Gregory, S. A.; Koboldt, C. M.; Perkins, W. E.; Seibert, K.; Veenhuizen, A. W.; Zhang, Y. Y.; Isakson, P. C. *J. Med. Chem.* **1997**, *40*, 1347.
29. Linderman, R. J.; Lonicar, M. S. *J. Org. Chem.* **1988**, *53*, 6013.
30. Martins, M. A. P.; Beck, P.; Cunico, W.; Pereira, C. M. P.; Sinhorin Blanco, R. F.; Peres; Bonacorso, H. G.; Zanatta, N. *Tetrahedron Lett.* **2002**, *43*, 7005.
31. Compounds **2**–**8**, were fully characterized by spectroscopy methods, and satisfactory elemental analysis were obtained: C ± 0.30, H ± 0.20; selected physical and spectral data of the compounds **9**, **10**, are according to literature.[15c,17b,30]

Compounds **2a**,**b** and **3a** did not show any IR bands on the ν_{OH} region but presented $\nu_{C=O}$ at 1690, 1694 and 1697 cm^{-1}, respectively.

Compound **2a**, $C_{10}H_5Cl_3O$ (M. wt 247.51); bp 120 °C/2.3 mbar; CG-MS (EI 70 eV) *m*/*z* (%): 246 (M^+, 10), 212 (2), 129 (100), 101 (90), 77 (99), 51 (90);
^1H NMR ($CDCl_3$, 400 MHz) δ 7.66–7.24 (m, 5H, Ph);
^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.5 (C2), 133.6, 132.1, 128.8, 118.6 (Ph), 99.8 (C3), 95.3 (C1), 81.9 (C4).

Compound **2b**, C_4HCl_3O (M. wt 171.41); oil; CG-MS (EI 70 eV) *m*/*z* (%): 171 (MH^+, 5), 117 (100), 63 (85), 53 (20);
^1H NMR ($CDCl_3$, 400 MHz) δ 2.09 (s, 1H, H4);
^{13}C NMR ($CDCl_3$, 100 MHz) δ 164.3 (C2), 89.7 (C1), 71.7 (C3), 64.0 (C4).

Compound **3a**, $C_{10}H_6Cl_2O$ (M. wt 213.06); bp 85 °C/2.3 mbar; CG-MS (EI 70 eV) *m*/*z* (%): 212 (M^+, 5), 129 (100), 101 (23), 77 (57), 51 (8);
^1H NMR ($CDCl_3$, 400 MHz) δ 7.59–7.17 (m, 5H, Ph), 5.85 (s, 1H, H1);
^{13}C NMR ($CDCl_3$, 100 MHz) δ 173.8 (C2), 133.5, 132.0, 128.7, 118.8 (Ph), 97.9 (C3), 83.4 (C4), 70.0 (C1).

Compound **4a**, $C_{10}H_7F_3O_2$ (M. wt 216.15); oil; CG-MS (EI 70 eV) *m*/*z* (%): 216 (M^+, 32), 187 (95), 129 (100), 108 (17), 77 (10);
^1H NMR ($CDCl_3$, 400 MHz) δ 7.45–7.22 (m, 5H, Ph);
^{13}C NMR ($CDCl_3$, 100 MHz) δ 133.7–128.1 (Ph); 123.8 (C1, q, $^1J_{C-F} = 289$ Hz), 84.0 (C4), 82.1 (C3), 65.2 (C2, q, $^2J_{C-F} = 37$ Hz).

Compound **4b**, $C_4H_3F_3O_2$ (M. wt 140.05); oil; CG-MS (EI 70 eV) *m*/*z* (%): 140 (M^+, 2), 136 (14), 108 (5), 55 (100);
^1H NMR ($CDCl_3$, 400 MHz) δ 2.63 (s, 1H, H4);
^{13}C NMR ($CDCl_3$, 100 MHz) δ 126.8 (C1, q, $^1J_{C-F} = 285$ Hz), 77.3 (C3), 75.9 (C2, q, $^2J_{C-F} = 26$ Hz), 65.8 (C4).

Compound **4c**, $C_9H_{13}F_3O_2$ (M. wt 210.19); oil; CG-MS (EI 70 eV) *m*/*z* (%): 210 (M^+, 2), 153 (65), 141 (75), 71 (100);
^1H NMR ($CDCl_3$, 400 MHz) δ 2.42 (t, 2H, H5), 2.19 (m, 2H, H6), 1.78 (m, 2H, H7), 1.43 (m, 2H, H8), 0.84 (t, 3H, H9);
^{13}C NMR ($CDCl_3$, 100 MHz) δ 124.1 (C1, q, $^1J_{C-F} = 285$ Hz), 105.1 (C3), 91.6 (C4), 65.8 (C2, q, $^2J_{C-F} = 26$ Hz), 30.8 (C5), 26.7 (C6), 21.9 (C7), 18.4 (C8), 13.5 (C9).

Compound **5a**, $C_{13}H_9O_2N$ (M. wt 211.21); oil; CG-MS (EI 70 eV) *m*/*z* (%): 211 (M^+, 33), 129 (100), 101 (9), 75 (19);
^1H NMR ($CDCl_3$, 400 MHz) δ 7.43–7.25 (m, 5H, Ph), 6.35 (s, 1H, H4), 2.22 (s, 3H, Me);
^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.2 (C6), 160.8 (C5), 160.0 (C3), 132.3–128.2 (Ph), 109.8 (C4), 84.8 (C7), 65.8 (C8), 18.9 (Me).

Compound **6a**, $C_9H_5Cl_3$ (M. wt 219.50); oil; CG-MS (EI 70 eV) *m*/*z* (%): 218 (M^+, 43), 203 (100), 101 (57), 144 (36), 107 (19), 77 (17);
^1H NMR ($CDCl_3$, 400 MHz) δ 7.35–7.11 (5H, m, Ph);
^{13}C NMR ($CDCl_3$, 100 MHz) δ 132.0, 130.4, 128.3, 122.1 (Ph), 90.2 (C3), 86.7 (C2); 82.3 (C1).

Compound **6c**, $C_8H_{11}Cl_3$ (M. wt 213.54); oil; CG-MS (EI 70 eV) *m*/*z* (%): 213 (MH^+, 5), 141 (35), 129 (52), 95 (100), 71 (72);
^1H NMR ($CDCl_3$, 400 MHz) δ 2.41 (t, 2H, H4), 2.19 (m, 2H, H5), 1.58 (m, 2H, H6), 1.35 (m, 2H, H7), 0.89 (t, 3H, H8);
^{13}C NMR ($CDCl_3$, 100 MHz) δ 93.4 (C1), 82.6 (C2), 69.6 (C3), 31.0 (C4), 27.1 (C5), 22.1 (C6), 18.7 (C7), 13.8 (C8).

Compound **7a**, C_8H_5Cl (M. wt 136.58); bp 42 °C/4 mbar; CG-MS (EI 70 eV) *m*/*z* (%): 136 (M^+, 100), 101 (43), 77 (38), 51 (29);
^1H NMR ($CDCl_3$, 400 MHz) δ 7.66–7.27 (5H, m, Ph);
^{13}C NMR ($CDCl_3$, 100 MHz) δ 132.9, 128.5, 128.3, 122.0 (Ph), 69.3 (C2), 67.3 (C1).

Compound **8a**, $C_{12}H_7F_3O$ (M. wt 224.18); oil; CG-MS (EI 70 eV) *m*/*z* (%): 224 (M^+, 100), 155 (72), 102 (54), 77 (71), 51 (70);
^1H NMR ($CDCl_3$, 400 MHz) δ 7.54–7.28 (m, 5H, Ph), 7.24 (d, 1H, H4, $^3J_{H-H} = 16$ Hz), 6.83 (d, 1H, H3, $^3J_{H-H} = 16$ Hz);
^{13}C NMR ($CDCl_3$, 100 MHz) δ 179.4 (C2, q, $^2J_{C-F} = 35$ Hz), 132.8 (C3), 132.4–121.1 (Ph), 121.4 (C4), 115.5 (C1, q, $^1J_{C-F} = 289$ Hz), 104.8 (C5), 87.1 (C6).