

Short Note

# (E)-1,1,1-Trifluoro-6,6-bis(4-methoxyphenyl)hexa-3,5-dien-2-one

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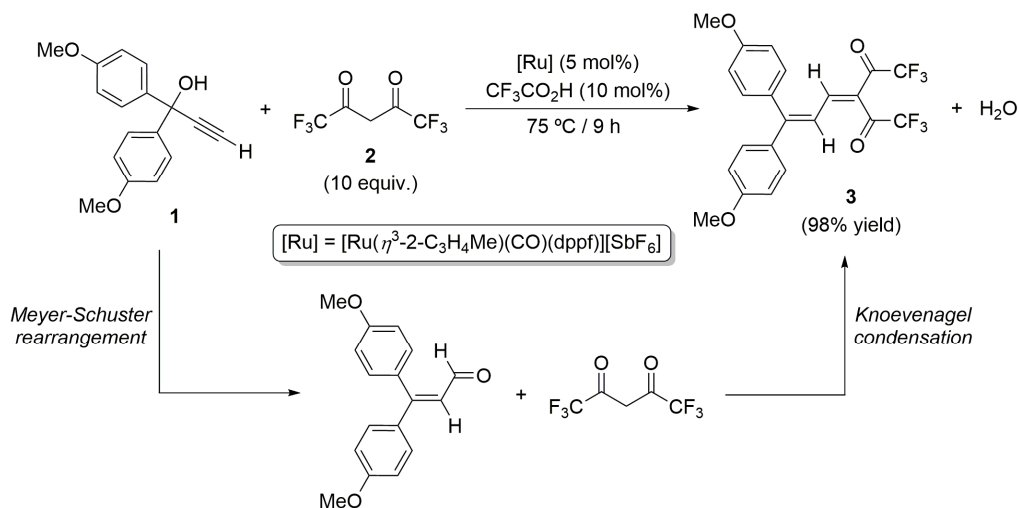
**Abstract:** The title compound was obtained in high yield (84%) via the deacetylation of 3-(3,3-bis(4-methoxyphenyl)allylidene)-1,1,1,5,5,5-hexafluoro-2,4-pentanedione with  $K_2CO_3$  in refluxing methanol. This previously unreported compound has been fully characterized by  $^{19}F\{^1H\}$ ,  $^1H$  and  $^{13}C\{^1H\}$  NMR, IR, UV-Vis, and HRMS.

**Keywords:** trifluoromethyl ketones; conjugated dienones; 1,3-butadienes; deacetylation reactions

## 1. Introduction

Trifluoromethyl ketones represent a fascinating class of molecules with application in a wide range of fields [1]. In particular, taking advantage of the activating effect of the trifluoroacetyl group on the conjugated C=C bond, trifluoromethyl enones  $R^1R^2C=C(R^3)C(=O)CF_3$  have been extensively employed for the construction of 3- to 7-membered fluorinated heterocycles through different cycloaddition processes [2–5]. On the contrary, despite their enormous synthetic potential, the chemistry of related trifluoromethyl dienones has been comparatively much less developed due to their more difficult access [6–9].

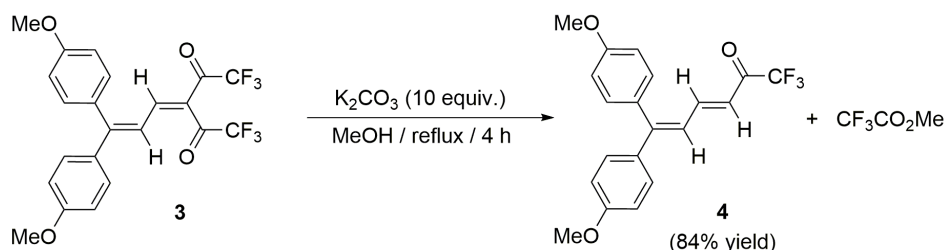
In the context of our studies on the preparation of conjugated diene-dione derivatives by metal-catalyzed dehydrative couplings between propargylic alcohols and  $\beta$ -diketones [10–13], we reported a few years ago the synthesis and structural characterization of the push-pull dye 3-(3,3-bis(4-methoxyphenyl)allylidene)-1,1,1,5,5,5-hexafluoro-2,4-pentanedione (**3**), which showed remarkable solvatochromic properties, through the coupling of 1,1-bis(4-methoxyphenyl)prop-2-yn-1-ol (**1**) with 1,1,1,5,5,5-hexafluoropentanedione (**2**) (Scheme 1) [11]. The formation of **3** involves the initial Meyer–Schuster rearrangement of propargylic alcohol **1**, catalyzed by the allyl-ruthenium(II) complex  $[Ru(\eta^3-2-C_3H_4Me)(CO)(dppf)][SbF_6]$  (dppf = 1,1'-bis(diphenylphosphino)ferrocene), and a subsequent Knoevenagel condensation of the resulting  $\alpha,\beta$ -unsaturated aldehyde with the perfluorinated  $\beta$ -diketone **2**. Herein, we describe that compound **3** can be easily deacetylated upon treatment with  $K_2CO_3$  in refluxing methanol, leading to the novel trifluoromethyl dienone (E)-1,1,1-trifluoro-6,6-bis(4-methoxyphenyl)hexa-3,5-dien-2-one (**4**) in a completely stereoselective manner.



**Scheme 1.** Route employed for the preparation of the diene-dione **3**.

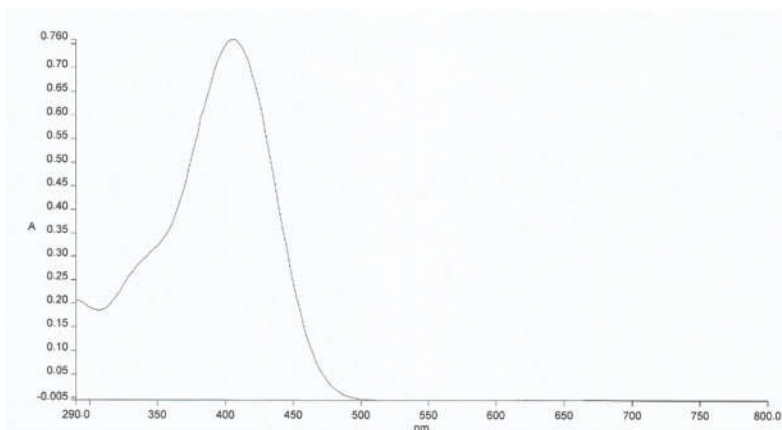
## 2. Results and Discussion

Base-promoted deacetylation reactions of  $\beta$ -diketones are well documented in the literature [14–17]. Accordingly, we found that the treatment of a methanolic solution of diene-dione **3** with an excess of  $\text{K}_2\text{CO}_3$  (10 equiv.) under refluxing conditions leads to the clean formation of the dienone **4**, which was isolated as a yellow oil in 84% yield after appropriate chromatographic work-up (Scheme 2). In the reaction, the volatile ester  $\text{CF}_3\text{CO}_2\text{Me}$  is also formed, as confirmed by recording the  $^{19}\text{F}\{^1\text{H}\}$  NMR spectrum of the reaction mixture prior to vacuum evaporation. Thus, in addition to the signal of compound **4** (a singlet at  $\delta_{\text{F}} -77.3$  ppm), a second singlet at  $\delta_{\text{F}} -75.7$  ppm [18] was present in the spectrum.



**Scheme 2.** Synthesis of the dienone **4** by deacetylation of the diene-dione **3**.

Compound **4** was characterized by means of HRMS, IR, and multinuclear NMR spectroscopy, the data obtained being fully in accord with the proposed formulation (details are given in the Materials and Methods section; copies of the NMR spectra are provided as Supplementary Materials). In this regard, key spectroscopic features are the following: (i) (IR) the presence of a characteristic absorption band at  $1699\text{ cm}^{-1}$  for the carbonyl group, (ii) ( $^1\text{H}$  NMR) typical signals for the olefinic protons of the butadiene chain at  $\delta_{\text{H}}$  6.59 (d,  $^3J_{\text{HH}} = 15.0$  Hz), 6.82 (d,  $^3J_{\text{HH}} = 11.7$  Hz), and 7.75 (dd,  $^3J_{\text{HH}} = 15.0$  and  $11.7$  Hz) ppm, with the coupling constant of  $15.0$  Hz confirming the *E* stereochemistry of the  $\text{CH}=\text{CH}$  bond, and (iii) ( $^{13}\text{C}\{^1\text{H}\}$  NMR) characteristic quartet resonances for the  $\text{CF}_3$  and  $\text{C}=\text{O}$  carbons at  $\delta_{\text{C}}$  116.6 ( $^1J_{\text{CF}} = 291.0$  Hz) and 179.9 ( $^2J_{\text{CF}} = 34.6$  Hz) ppm, respectively. On the other hand, as previously observed for **3**, the UV-Vis spectrum of **4** in  $\text{CH}_2\text{Cl}_2$  also displayed an intense absorption band in the visible region ( $\lambda_{\text{max}} = 406$  nm; Figure 1).



**Figure 1.** UV-Vis spectrum of compound **4** recorded in dichloromethane solution.

Compared to **3**, a large hypsochromic shift ( $\Delta\lambda_{\max} = -41$  nm), as a consequence of the replacement of one of the electron-acceptor trifluoroacetyl groups by hydrogen, is observed. Finally, it is also worth mentioning that the trifluoromethyl dienone **4** also features a solvatochromic behavior, its absorption maximum undergoing a red shift by increasing the solvent polarity, i.e.,  $\lambda_{\max}$  changes from 389 to 410 nm on going from hexane to *N,N*-dimethylformide (DMF). However, the bathochromic shift of the absorption band observed for **4** ( $\Delta\lambda_{\max} = 21$  nm) is smaller in comparison to that of parent diene-dione **3** ( $\Delta\lambda_{\max} = 42$  nm when going from hexane to DMF) [11].

### 3. Materials and Methods

The diene-dione **3** was synthesized as described in the literature [11]. NMR measurements (all the spectra were recorded at room temperature) were performed with a Bruker DPX-300 instrument (Billerica, MA, USA). The chemical shift values ( $\delta$ ) are given in part per million and are referred to the residual peak of the deuterated solvent that was employed ( $^1\text{H}$  and  $^{13}\text{C}$ ) or to the  $\text{CFCl}_3$  standard ( $^{19}\text{F}$ ). The PerkinElmer 1720-XFT and Lambda 25 spectrometers (Waltham, MA, USA) were employed for IR and UV-Vis measurements, respectively. HRMS data (QTOF Bruker Impact II mass spectrometer) were provided by the General Services of the University of Oviedo). Merck silica gel 60 (230–400 mesh) was employed for the chromatographic work-up.

#### (*E*)-1,1,1-Trifluoro-6,6-bis(4-methoxyphenyl)hexa-3,5-dien-2-one (**4**)

To a solution of compound **3** (0.230 g, 0.5 mmol) in methanol (15 mL),  $\text{K}_2\text{CO}_3$  (0.691 g, 5 mmol) was added, and the resulting mixture heated under reflux for 4 h. A color change from orange to yellow was observed. After elimination of the volatiles under vacuum, the oily residue was purified by column chromatography using a mixture EtOAc/hexane (1:10 *v/v*) as eluent. Compound **4** was isolated as a yellow oil in 84% yield (0.152 g). The characterization data for **4** are as follows:  $^{19}\text{F}\{^1\text{H}\}$  NMR (282 MHz,  $\text{CDCl}_3$ ):  $\delta = -77.3$  (s) ppm.  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta = 7.75$  (dd, 1H,  $^3J_{\text{HH}} = 15.0$  and 11.7 Hz,  $\text{CH}=\text{CHC}(=\text{O})\text{CF}_3$ ), 7.32, 7.17, 6.98 and 6.90 (d, 2H each,  $^3J_{\text{HH}} = 8.7$  Hz,  $\text{CH}_{\text{arom}}$ ), 6.82 (d, 1H,  $^3J_{\text{HH}} = 11.7$  Hz,  $\text{CH}=\text{CH}=\text{CHC}(=\text{O})\text{CF}_3$ ), 6.59 (d, 1H,  $^3J_{\text{HH}} = 15.0$  Hz,  $=\text{CHC}(=\text{O})\text{CF}_3$ ), 3.90 and 3.86 (s, 3H each, OMe) ppm.  $^{13}\text{C}\{^1\text{H}\}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta = 179.9$  (q,  $^2J_{\text{CF}} = 34.6$  Hz, C=O), 161.1, 160.5 and 148.7 (2C) (s,  $\text{C}_{\text{arom}}$ ), 157.0 (s, =C), 133.5, 123.2, 118.0 (s, =CH), 132.1, 130.4, 113.9 and 113.8 (s,  $\text{CH}_{\text{arom}}$ ), 116.6 (q,  $^1J_{\text{CF}} = 291.0$  Hz,  $\text{CF}_3$ ), 55.4 and 55.3 (s, OMe) ppm. IR (neat):  $\nu = 3006$  (w), 2959 (w), 2934 (w), 2839 (w), 1699 (m), 1603 (s), 1562 (s), 1511 (s), 1463 (m), 1420 (w), 1341 (w), 1287 (m), 1253 (s), 1195 (s), 1173 (s), 1140 (s), 1121 (m), 1059 (s), 1032 (s), 992 (w), 913 (w), 857 (m), 837 (m), 806 (w), 734 (w), 837 (m), 806 (w), 734 (w), 721 (m), 601 (m)  $\text{cm}^{-1}$ . UV-vis ( $\text{CH}_2\text{Cl}_2$ ):  $\lambda_{\max} 406$  nm ( $\epsilon 20,850 \text{ M}^{-1} \text{ cm}^{-1}$ ). HRMS (ESI): *m/z* 363.120281,  $[\text{M} + \text{H}^+]$  (calcd. for  $\text{C}_{20}\text{H}_{18}\text{F}_3\text{O}_3$ : 363.120256).

### 4. Conclusions

In summary, a novel trifluoromethyl dienone has been synthesized in high yield and in a complete stereoselective manner through a deacetylation procedure, a route of access scarcely applied to date to obtain this type of fluorinated molecules [19].

**Supplementary Materials:** The following are available online at [www.mdpi.com/xxx/s1](http://www.mdpi.com/xxx/s1), Figures S1–S3:  $^{19}\text{F}\{^1\text{H}\}$ ,  $^1\text{H}$  and  $^{13}\text{C}\{^1\text{H}\}$  NMR spectra of compound 4.

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**Conflicts of Interest:** The author declares no conflict of interest.

## References

1. Kelly, C.B.; Mercadante, M.A.; Leadbeater, N.E. Trifluoromethyl ketones: Properties, preparation, and application. *Chem. Commun.* **2013**, *49*, 11133–11148.
2. Nenajdenko, V.G.; Sanin, A.V.; Balenkova, E.S. Methods for the synthesis of  $\alpha,\beta$ -unsaturated trifluoromethyl ketones and their use in organic synthesis. *Russ. Chem. Bull.* **1999**, *68*, 437–458.
3. Druzhinin, S.V.; Balenkova, E.S.; Nenajdenko, V.G. Recent advances in the chemistry of  $\alpha,\beta$ -unsaturated trifluoromethylketones. *Tetrahedron* **2007**, *63*, 7753–7808.
4. Nenajdenko, V.G.; Balenkova, E.S.  $\alpha,\beta$ -Unsaturated trifluoromethyl ketones in the synthesis of fluorinated heterocycles. *Targets Heterocycl. Syst.* **2010**, *14*, 213–265.
5. Nenajdenko, V.G.; Balenkova, E.S. Preparation of  $\alpha,\beta$ -unsaturated trifluoromethyl ketones and their application in the synthesis of heterocycles. *Arkivoc* **2011**, (i), 246–328.
6. Jiang, B.; A stereocontrolled synthesis of conjugated dienyl trifluoromethyl ketones via the Claisen rearrangement of allyl 2-phenylsulfanyl-1-(trifluoromethyl) vinyl ethers. *Chem. Commun.* **1996**, 861–862.
7. Xiao, J.; Feng, Y.; Yuan, C. A new and facile stereocontrolled synthesis of conjugated dienyl trifluoromethyl ketones. *Perkin 1* **2000**, 4240–4241.
8. Peng, W.; Zhu, S. The synthesis of 2,4-dienyl fluoroalkyl ketones by a tandem three-stage sequence of propargyl 2-fluoroalkylvinyl ether formation, Claisen rearrangement, and allene-to-conjugated diene isomerization. *Tetrahedron* **2003**, *59*, 4641–4649.
9. Kohn, B.L.; Rovis, T. Cobaltate anion couples terminal dienes with trifluoroacetic anhydride: A direct fluoroacylation of 1,3-dienes. *Chem. Sci.* **2014**, *5*, 2889–2892.
10. Cadierno, V.; Díez, J.; García-Garrido, S.E.; Gimeno, J.; Nebra, N. Efficient Access to conjugated dienones and diene-diones from propargylic alcohols and enolizable ketones: A tandem isomerization/condensation process catalyzed by the sixteen-electron allyl-ruthenium(II) complex  $[\text{Ru}(\eta^3\text{-C}_3\text{H}_4\text{Me})(\text{CO})(\text{dppf})][\text{SbF}_6]$ . *Adv. Synth. Catal.* **2006**, *348*, 2125–2132.
11. Borge, J.; Cadierno, V.; Díez, J.; García-Garrido, S.E.; Gimeno, J. Novel push-pull butadienes derived from 1,1-diaryl-2-propyn-1-ols and 1,1,1,5,5,5-hexafluoro-2,4-pentanedione: Synthesis, absorption spectra and solvatochromic behaviour. *Dyes Pigm.* **2010**, *87*, 209–217.
12. Francos, J.; Borge, J.; Díez, J.; García-Garrido, S.E.; Cadierno, V. Easy entry to donor/acceptor butadiene dyes through a MW-assisted  $\text{InCl}_3$ -catalyzed coupling of propargylic alcohols with indan-1,3-dione in water. *Catal. Commun.* **2015**, *63*, 10–14.
13. Francos, J.; García-Garrido, S.E.; Borge, J.; Suárez, F.J.; Cadierno, V. Butadiene dyes based on 3-(dicyanomethylidene)indan-1-one and 1,3-bis(dicyanomethylidene)indane: Synthesis, characterization and solvatochromic behaviour. *RSC Adv.* **2016**, *6*, 6858–6867.
14. Rezgui, F.; El Gaïed, M.M. Réaction régiospécifique des carbanions stabilisés avec la 2-(acétoxyméthyl)cyclohex-2-én-1-one: Synthèse de diénones bicycliques. *Tetrahedron* **1997**, *53*, 15711–15716.
15. Bray, D.J.; Jolliffe, K.A.; Lindoy, L.F.; McMurtrie, J.C. Tris- $\beta$ -diketones and related keto derivatives for use as building blocks in supramolecular chemistry. *Tetrahedron* **2007**, *63*, 1953–1958.
16. Amijs, C.H.M.; López-Carrillo, V.; Raducan, M.; Pérez-Galán, P.; Ferrer, C.; Echavarrén, A.M. Gold(I)-catalyzed intermolecular addition of carbón nucleophiles to 1,5- and 1,6-enynes. *J. Org. Chem.* **2008**, *73*, 7721–7730.
17. Ahumada, G.; Soto, J.P.; Carrillo, D.; Manzur, C.; Roisnel, T.; Hamon, J.-R. Deacetylation of chiral ferrocenyl containing  $\beta$ -diketones promoted by ethylene diamine: Spectroscopic and structural characterization of the fragmentation products. *J. Organomet. Chem.* **2014**, *770*, 14–20.

18. Pellerite, M.J. Unusual reaction chemistry in thermal decomposition of alkali metal 2-alkoxy-2,3,3,3-tetrafluoropropionate salts. *J. Fluor. Chem.* **1990**, *49*, 43–66.
19. Hojo, M.; Masuda, R.; Okada, E. A facile and convenient synthetic route to 1-amino-4,4-bis(trifluoroacetyl)- and 1-amino-4-trifluoroacetyl-1,3-butadienes. *Synthesis* **1990**, 425–427.

**Sample Availability:** Samples of the compounds **3** and **4** are not available from the author.



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