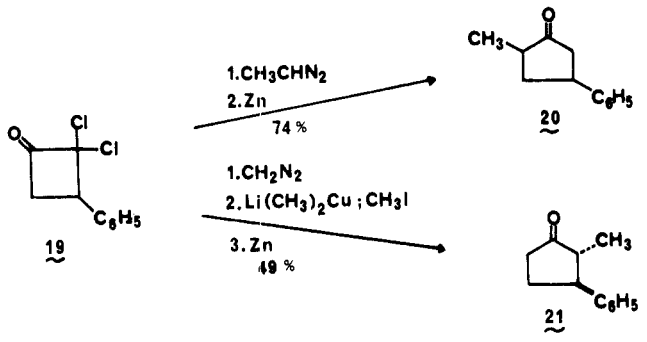
with cyclopentanones.[6d] Thus the addition of MeI in HMPA to the solution of the α-chloro enolate afforded the α-chloro-α-methyl ketone **4** (R = CH_3) in 78% yield after purification. Similarly, addition of allyl bromide provided chloro ketone **4** (R = allyl) in 71% yield. In spite of the steric congestion, alkylation could also be successfully carried out with dichloro ketone **17**, leading to **18** in 70% yield. This ability to introduce α-alkyl substituents complements the diazoalkane procedure for introducing α′ substituents.[3] Thus, for example, the pure regioisomers **20**[3] and **21**[8] become readily available from a common precursor.



Prompted by the simplicity of this reduction–protonation or alkylation method, we have also examined various means of converting the chloro ketones to the corresponding enones. The solution in most cases examined proved to be surprisingly simple, reflecting the favorable trans stereochemistry for elimination in the reduction products,[9] viz., in the case of nonalkylated chloro ketones, the enone is produced in situ through addition of $LiI{\cdot}2H_2O$ and HMPA to the reaction mixture (**2** → **5**,[1f] 60%); with α-alkyl-α-chloro ketones the mixture is merely stirred at room temperature overnight [**2** → **6** (R = CH_3),[1f] 86%; **2** → **6** (R = allyl), 68%].[10] In that α-methylcyclopentenones of this type are common to many naturally occurring hydroazulenes,[11] it is of potential synthetic importance that this simple one-step protocol also served to convert ketone **22** to the corresponding α-methyl enone **23**[1f] in 65% yield after chromatography.

22 **23**

The versatile[12] chloro enone **10** can be readily secured in excellent yield from the α,α-dichloro ketone **2** (DMF, Li_2CO_3, 85 °C, 30 min, 96%) and, importantly, also from the α,α-dichloro-β-[(trimethylsilyl)oxy]cyclopentanone **9**[13] (Zn, AcOH, room temperature, 30 min, 90%). *Direct* treatment of **9** with (a) H_2 and Pd/C in MeOH afforded the cis-fused bicyclic ketone **7**[7,14] in 80% yield (also available from **2** by using Zn in AcOH, 90%). Treatment with (b) Li in NH_3 followed by Zn in AcOH, or Ca in NH_3–MeOH followed by pyridinium chlorochromate in CH_2Cl_2, yielded the trans-fused bicyclic ketone **11**[7,14,15] in 55–60% yield.[16] (c) Excess lithium dimethylcuprate in Et_2O–hexane gave the angularly substituted cis-fused chloro ketone **12**,[3] mp 85–7 °C, in 50–60% yield. Of course, chloro enone **10**, an intermediate in a–c, would be expected to react similarly.

The mild, high-yield transformations of α,α-dichlorocyclopentanones described in this paper add to the value of this three-carbon annelation process, especially for use in the construction of complex natural products. We anticipate pursuing such goals.

Acknowledgment. The authors thank Professor P. Crabbé and Dr. J. L. Luche for their interest in this program. This work was supported by the CNRS (Equipe de Recherche Associée No. 478).

Registry No. 2, 72952-33-1; **3**, 72952-34-2; **4** (R = CH_3), 72952-35-3; **4** (R = allyl), 72952-36-4; **5**, 39163-29-6; **6** (R = CH_3), 24730-98-1; **6** (R = allyl), 72952-37-5; **7**, 5689-04-3; **9**, 72952-38-6; **10**, 72952-39-7; **11**, 16484-17-6; **12**, 72952-40-0; **13**, 72952-41-1; **14**, 72952-42-2; **15**, 72952-43-3; **16**, 72952-44-4; **17**, 72952-45-5; **18**, 72952-46-6; **22**, 72952-47-7; **23**, 67722-29-6.

(8) A. M. El-Abbady and S. H. Doss, *Can. J. Chem.*, **43**, 2408 (1965); T. Shomo, M. Okawa, and I. Nishiguchi, *J. Am. Chem. Soc.*, **97**, 6144 (1975).

(9) The stereochemistry of compounds **3** and **4** in Figure 1 has been assigned on the basis of attack of the electrophile from the less hindered side of the chloro enolate intermediate. The facile loss of HCl [**4** (R = CH_3) was totally converted to **6** (R = CH_3) on standing at 0 °C for a few weeks] and the kinetic formation[6d] of the chloro ketone **3** (δ_{CCl_4} 4.30, d, J = 7.5 Hz), which upon epimerization (Al_2O_3, $CHCl_3$) affords predominently the isomeric product (δ_{CCl_4} 3.90, d, J = 6.0 Hz), support the assignments.

(10) Of course, the commonly used techniques can also be applied. See C. Djerassi, "Steroid Reactions", Holden-Day, San Francisco, 1963, Chapter 4, and references cited therein. In the case of **2** → **6** (R = allyl) allyl iodide was used, and the conversion was incomplete.

(11) See T. K. Devon and A. I. Scott, "Handbook of Naturally Occuring Compounds", Academic Press, New York, 1972.

(12) G. Stork and T. L. Macdonald, *J. Am. Chem. Soc.*, **97**, 1264 (1975); G. Stork and V. Nair, *ibid.*, **101**, 1315 (1979); T. L. Macdonald, *J. Org. Chem.*, **43**, 4241 (1978). See also: T. Kametani, K. Sazuki, H. Nemoto, and K. Fukumoto, *ibid.*, **44**, 1036 (1979); Y. Tamura, T. Kawasaki, N. Gohda, and Y. Kita, *Tetrahedron Lett.*, 1129 (1979); P. Blatcher and S. Warren, *ibid.*, 1247 (1979).

(13) We have found that these compounds can be synthesized in excellent yield by treatment of the corresponding dichloroketene–trimethyl silyl enol ether adducts[2b,d] with diazomethane [**9**, 92%, mp 62–64 °C (hexane)]. This extends considerably the scope of the annelation process making it now applicable to ketones (i.e., enol ethers) as well as olefins. Silyl enol ethers are available *regioselectively* through a variety of procedures. See: J. K. Rasmussen, *Synthesis*, 91 (1977); E. W. Colvin, *Q. Rev., Chem. Soc.*, **7**, 15 (1978), and references cited therein.

(14) A. Kandiah, *J. Chem. Soc.*, 922 (1931).

(15) R. S. Thakur, *J. Chem. Soc.*, 1485 (1933).

(16) The cis-fused hydrindanone **7** was also formed in approximately 5% yield in these reactions.

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A Synthesis of Moenocinol[1]

Summary: The fluoride-induced elimination of a β-silyl sulfone and the reductive elimination of a β-acyloxy sulfone are key olefin-forming reactions in a new synthesis of moenocinol [(2*Z*,6*E*,13*E*)-3,8,8,14,18-pentamethyl-11-methylenenonadeca-2,6,13,17-tetraen-1-ol].

Sir: The moenomycins and prasinomycin are members of a group of relatively nontoxic phosphorus-containing antibiotics which have the remarkable property of long duration of action in vivo against Gram-positive bacteria.[2,3]

(1) Reprints of this paper will not be available.

(2) W. A. Slusarchyk, J. A. Osband, and F. L. Weisenborn, *Tetrahedron*, **29**, 1465 (1973).

(3) Witteler et al. [F.-J. Witteler, P. Welzel, H. Duddeck, G. Höfle, W. Riemer, and H. Budzikiewicz, *Tetrahedron Lett.*, 3493 (1979)] have proposed a complete structure for moenomycin A.

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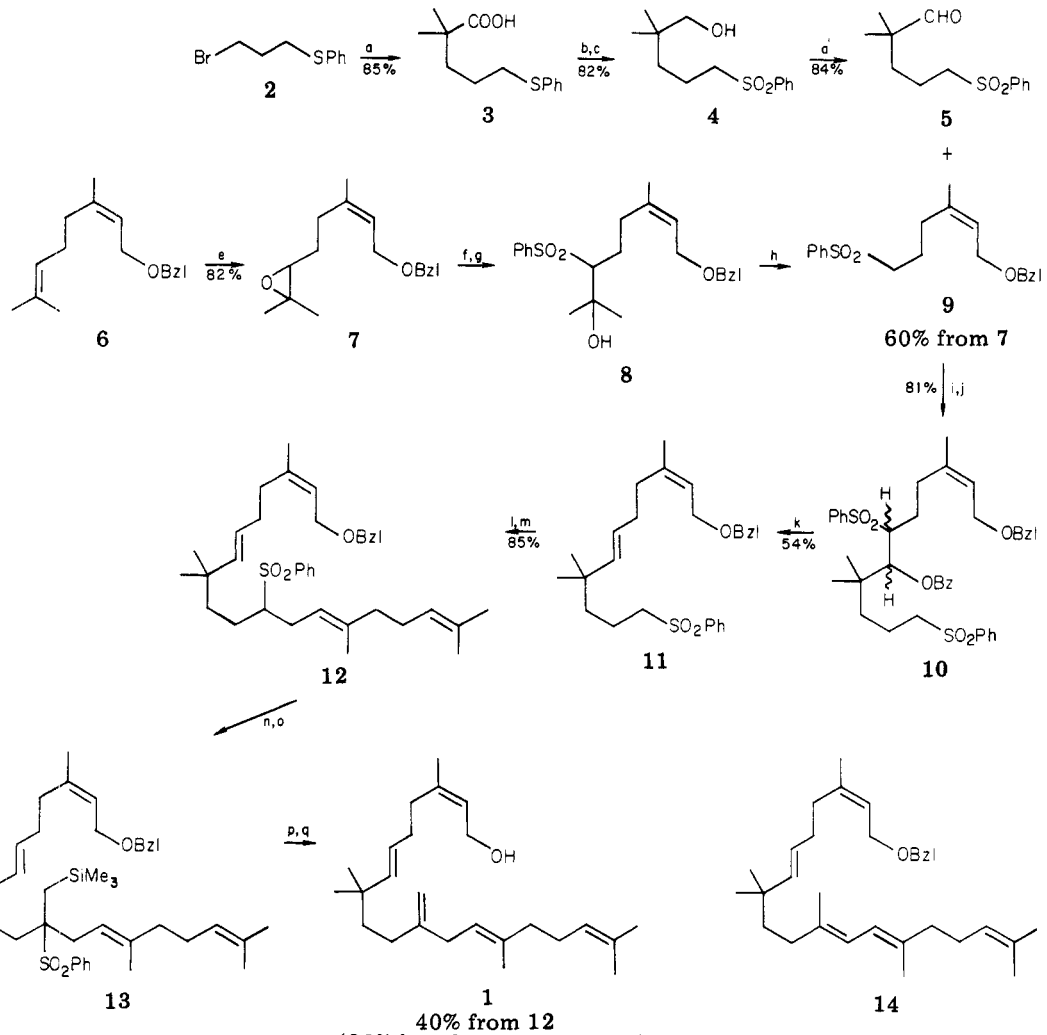
Scheme I[a]



[a] (a) $[Me_2C^-COO^-]2Li^+$/THF, 0 °C, 1 h; (b) LAH/Et_2O, reflux, 3 h; (c) H_2O_2/HOAc, 80 °C, 1 h; (d) Pyr·$HCrO_3Cl$, 25 °C, 3 h; (e) MCPBA/CH_2Cl_2, 0 °C; (f) PhSNa/EtOH, reflux, 3 h; (g) MCPBA/CH_2Cl_2, −78 °C, 2 h; (h) 2 equiv of KOH/MeOH, reflux, 30 min; (i) *n*-BuLi/THF, −78 °C to form a lithio derivative of **9**, followed by addition of **5**; (j) 2 equiv of BzCl, −78 → +25 °C, 20 h; (k) 2.5 equiv of Na(Hg)/3:1 THF-MeOH, −20 °C, 2 h; (l) *n*-BuLi/THF, −78 °C, 15 min; (m) geranyl chloride (2 equiv)/THF, −78 → +25 °C, 2 h; (n) (*i*-Pr)$_2$NLi/THF, −78 °C, 1 h; (o) 4 equiv each of ICH_2SiMe_3 and HMPA/THF, −78 → −20 °C, 4 h; (p) 2 equiv of *n*-$Bu_4NF·3H_2O$/THF, reflux, 1 h; (q) excess Li/NH_3, −78 °C, 30 min.

Hydrolysis of the moenomycins[4a] and prasinomycin[5] gives a biogenetically novel C_{25} lipid, moenocinol (**1**), in which the nonisoprenoid pattern from C_5 to C_{11} suggests that not all of the carbon atoms are derived from mevalonate. We report herein a new synthesis[4] of moenocinol in which the fluoride-induced elimination of a β-trimethylsilyl sulfone[6] to introduce the methylene group at C_{11} and the reductive elimination of a β-benzoyloxy sulfone to introduce the C_6–C_7 trans double bond are key steps.

Alkylation of 3-(phenylthio)-1-bromopropane[7] with the lithio dianion of isobutyric acid gave the acid **3**[8] which was converted by standard transformations to the aldehyde **5**.[9]

The sulfone **9**[10] was obtained in four steps from nerol benzyl ether (**6**)[4b] as shown in Scheme I. A more orthodox four-step preparation of **9** from **6** was abandoned when the initial ozonolysis of the terminal three carbons of **6** could not be made to surpass yields of 25–30%. The transformation of **6** to **9** reported herein was clean and efficient except for the unsatisfactory chemospecificity in the oxidation of the thioether derived from **7** to the sulfone **8**. Competing oxidation of the trisubstituted double bond in **8** diminished the yield of **9** to 60%; nonetheless, 10-g quantities of **9** were accessible by this route.

The diastereomeric mixture (ca. 1:1) of the benzoyloxy sulfones **10**, obtained by conjunction of the fragments **5** and **9**, underwent reductive elimination to give the diene **11**[11] containing the C_6–C_7 double bond of moenocinol. The

(4) (a) R. Tschesche and J. Reden, *Justus Liebigs Ann. Chem.*, 853 (1974), and references cited therein. (b) See Grieco et al. [P. Grieco, Y. Masaki, and D. Boxler, *J. Am. Chem. Soc.*, **97**, 1597 (1975)] and Johnson, [M. W. Johnson, *Diss. Abstr.*, **40**, 24813 (1979)] for previous syntheses.

(5) W. A. Slusarchyk and F. L. Weisenborn, *Tetrahedron Lett.*, 659 (1969).

(6) P. J. Kocienski, *Tetrahedron Lett.*, 2649 (1979).

(7) P. Bakuzis, M. L. F. Bakuzis, C. C. Fortes, and R. Santos, *J. Org. Chem.*, **41**, 2769 (1976).

(8) Mp 40–41 °C; IR (film) 3500–2500, 1700 (COOH) cm^{-1}; NMR ($CDCl_3$) δ 7.1–7.4 (m, 5 H, ArH), 2.8–3.0 (m, 2 H, SCH_2), 1.6–1.8 (m, 4 H, CH_2CH_2), 1.18 (s, 6 H, Me_2C).

(9) Mp 92–94 °C; IR (film) 1710 (CHO), 1310, 1145 (SO_2) cm^{-1}; NMR ($CDCl_3$) δ 9.39 (s, 1 H, CHO), 7.85–7.97 and 7.55–7.70 (m, 2 H and 3 H, ArH), 3.0–3.2 (m, 2 H, SO_2CH_2), 1.57–1.85 (m, 4 H, CH_2CH_2), 1.03 (s, 6 H, Me_2C).

(10) IR (film) 1320, 1305, 1150 ($ArSO_2$) cm^{-1}; NMR ($CDCl_3$) δ 7.8–7.95 and 7.45–7.65 (m, 2 H and 3 H, $ArHSO_2$), 7.27 (s, 5 H, ArH), 5.45 (t with further fine splitting, J = 8 Hz, $=CHCH_2$), 4.43 (s, 2 H, OCH_2), 3.9 (d, 2 H, J = 8 Hz, $=CHCH_2$), 3.0 (m, 2 H, $ArSO_2CH_2$), 1.65 (s, 3 H, $CH_3C=$).

high E stereoselectivity (by TLC and NMR) of the reductive elimination was not unexpected: a recent study of the Julia olefin synthesis[12] has shown that the olefin stereochemistry is independent of the stereochemistry of the acyloxy sulfone[13] precursor and sensitive to proximate alkyl branching.[14] It is noteworthy that isolated sulfones are cleaved only very slowly under the conditions for reductive elimination of β-benzoyloxy sulfones.

Alkylation of **11** by geranyl chloride followed by (iodomethyl)trimethylsilane gave the β-silyl sulfone **13**. Attempts to separate **13** from unreacted **12** on silica gel led to decomposition; of the several products, moenocinol benzyl ether and the diene **14** were identified.[15] However, treatment of the mixture (ca. 1:1) of **12** and **13** with n-$Bu_4NF{\cdot}3H_2O$ in refluxing THF cleanly converted **13** to moenocinol benzyl ether which was then easily separated from **12** by chromatography. Finally, reductive debenzylation gave moenocinol (**1**), having IR and NMR spectra identical with those of natural **1** obtained by degradation of prasinomycin.[16]

Registry No. **1**, 19953-93-6; **2**, 3238-98-0; **3**, 73199-51-6; **4**, 73199-52-7; **5**, 73199-53-8; **6**, 55802-98-7; **7**, 73199-54-9; **8**, 73199-55-0; **9**, 73199-56-1; **10**, isomer 1, 73199-57-2; **10**, isomer 2, 73199-58-3; **11**, 73199-59-4; **12**, 73199-60-7; **13**, 73199-61-8; **14**, 73199-62-9; geranyl chloride, 5389-87-7; isobutyric acid lithium dianion, 57344-34-0.

(11) IR (film) 1320, 1305, 1150 ($ArSO_2$) cm^{-1}; NMR ($CDCl_3$) δ 7.8–7.98 and 7.5–7.7 (m, 2 H and 3 H, $ArHSO_2$), 7.3 (s, 5 H, ArH), 5.4 (t with further fine splitting, J = 7 Hz, $=CHCH_2$), 5.15–5.30 (m, 2 H, CH=CH), 4.50 (s, 2 H, CH_2O), 4.00 (2 H, d, J = 7 Hz, $=CHCH_2$), 3.03 (t, 2 H, J = 7 Hz, $ArSO_2CH_2$), 2.07 (app d, 4 H, $=CCH_2CH_2C=$), 1.73 (d, 3 H, J = 1 Hz, $CH_3C=$), 0.91 (s, 6 H). Homogeneity was established by TLC and NMR. No evidence for the presence of the cis isomer could be adduced.

(12) M. Julia and J.-M. Paris, *Tetrahedron Lett.*, 4833 (1973).

(13) P. J. Kocienski, B. Lythgoe, and S. Ruston, *J. Chem. Soc., Perkin Trans. 1*, 829 (1978).

(14) P. J. Kocienski, B. Lythgoe, and I. Waterhouse, *J. Chem. Soc., Perkin Trans. 1*, in press.

(15) Moenocinol benzyl ether does not isomerize to **14** on chromatography. It is likely that the confluence of carbonium ion stabilizing features (the sulfone group occupies a position which is tertiary, homoallylic, and β to silicon) is responsible for the observed lability of **13**.

(16) We thank Dr. William A. Slusarchyk, Squibb Institute for Medical Research, for spectra of natural **1**.

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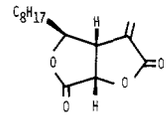
Efficient Synthesis of a Bislactone Skeleton Leading to *dl*-Avenaciolide

Summary: Treatment of 2-halodecanal and potassium ethyl malonate under phase-transfer catalysis condition gave ethyl tetrahydro-4-(ethoxycarbonyl)-2-octyl-5-oxo-3-furanacetate in one step. This compound was successfully converted into dihydro-4-octylfuro[3,4-*b*]furan-2,6-(3*H*,4*H*)-dione, which is an important key intermediate for the synthesis of *dl*-avenaciolide.

Sir: Considerable attention[1-4] has been focussed on avenaciolide (**1**), a unique antifungal bislactone, which was first isolated from *Aspergillus avenaceaus* by Turner.[1]

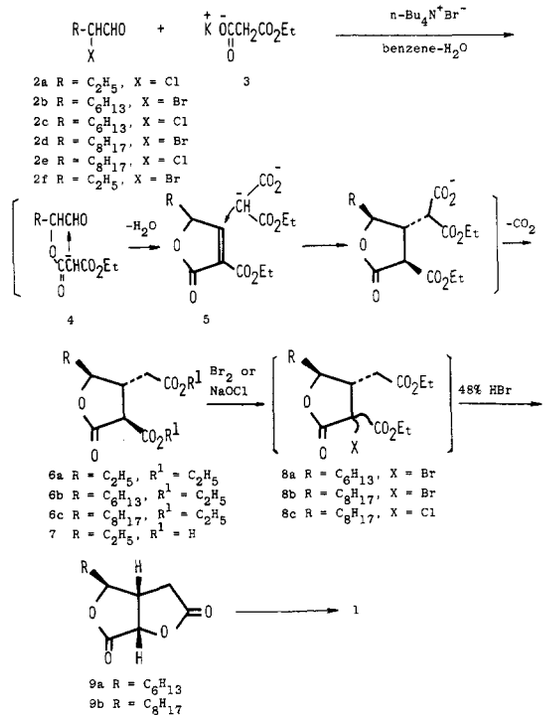


1

trans-Tetrahydro-2-octyl-5-oxo-3-furanacetic acid derivatives, known key intermediates for the synthesis of *dl*-**1**, have been independently prepared via several steps by Johnson[3a] and by Schlessinger.[3b] We now report a one-step synthesis of ethyl *trans,trans*-tetrahydro-2-alkyl-4-(ethoxycarbonyl)-5-oxo-3-furanacetate (**6**) by the reaction of α-halo aldehyde and potassium ethyl malonate (**3**) in a two-phase system consisting of water and benzene in the presence of tetra-*n*-butylammonium bromide (TBAB). Furanone **6c** was conveniently converted into bislactone **9b**, precursor of *dl*-**1**.[3a]

A mixture (1:2) of 2-bromodecanal (**2d**) and **3** was stirred vigorously in a benzene–H_2O (55:45) system containing 0.05 equiv of TBAB for 40 h under reflux. Workup in the usual manner gave **6c**[5] in 66% yield. The yield of **6c** was de-

Scheme I



(1) Isolation: (a) D. Brookes, B. K. Tidd, and W. B. Turner, *J. Chem. Soc.*, 5385 (1963); (b) J. J. Ellis, F. H. Stodola, R. F. Vesonder, and C. A. Glass, *Nature (London)*, **203**, 1382 (1964).

(2) Structure assignment: D. Brookes, S. Sternhell, B. K. Tidd, and W. B. Turner, *Aust. J. Chem.*, **18**, 373 (1967).

(3) Syntheses of *dl*-avenaciolide: (a) W. L. Parker and F. Johnson, *J. Am. Chem. Soc.*, **91**, 2708 (1969); W. L. Parker and F. Johnson, *J. Org. Chem.*, **38**, 2489 (1973); (b) J. L. Herrmann, M. H. Berger, and R. H. Schlessinger, *J. Am. Chem. Soc.*, **95**, 7923 (1973); J. L. Herrmann, M. H. Berger, and R. H. Schlessinger, *ibid.*, **101**, 1544 (1979); (c) H. Takei, Y. Fukuda, H. Mizutani, K. Sugaya, and T. Taguchi, Abstracts, 36th Symposium on Synthetic Organic Chemistry, Tokyo, June 1975, p 39. (d) E. Fujita, Y. Nagao, and K. Kaneko, Abstracts III, 26th meeting of the International Union of Pure and Applied Chemistry, Sept 1977, Tokyo, Japan, p 1019.

(4) Syntheses of optically active avenaciolide: (a) R. C. Anderson and B. Fraser-Reid, *J. Am. Chem. Soc.*, **97**, 3870 (1975); (b) M. Niwa, M. Iguchi, and S. Yamamura, *Tetrahedron Lett.*, 3661 (1975).

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