

5,13-DIETHYL-10-METHYL-8-HEPTADECANONE: A COMPONENT OF POST-1976 KELEX 100

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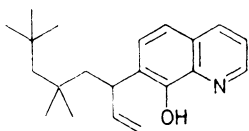
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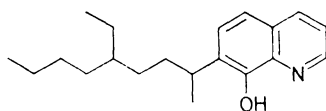
Dedicated with warm regards to Professor E. Mutschler on the occasion of his 60th birthday.

The title compound was prepared by mixed aldol condensation of 2-ethylhexanal and acetone, double bond hydrogenation, aldol autocondensation of the resulting saturated ketone and final double bond hydrogenation. It is identical with the ketone $C_{22}H_{44}O$ previously isolated from new Kelex 100 which was erroneously assigned a furoquinoline structure.

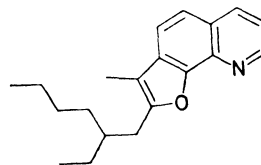
Kelex 100 is a commercial chelating solvent extraction reagent (Ashland Oil Inc./ Sherex Chemical Co. Dublin, Ohio, U.S.A.). It was shown¹ that Kelex 100 consisted of approximately 77.7% of 7-(1-ethenyl-3,3,5,5-tetramethylhexyl)-8-quinolinol (*I*) and 3.7% of 8-quinolinol while the remainder was an unknown viscous fluorescent material. This Kelex 100 was prepared by Claisen rearrangement of the allylic ether of 8-quinolinol².



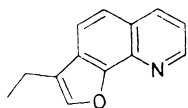
I



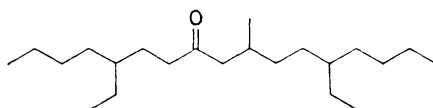
II



III



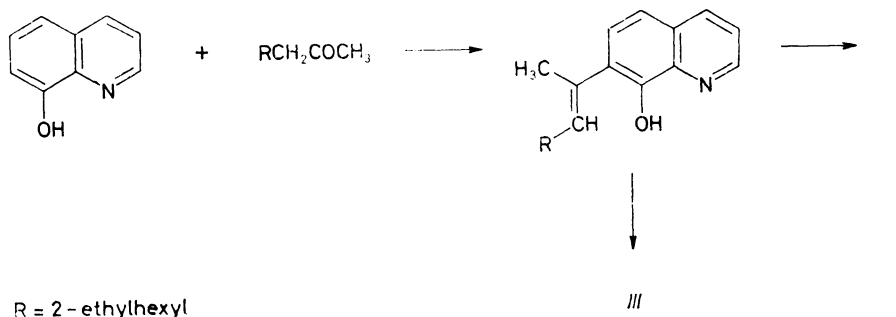
IV



V

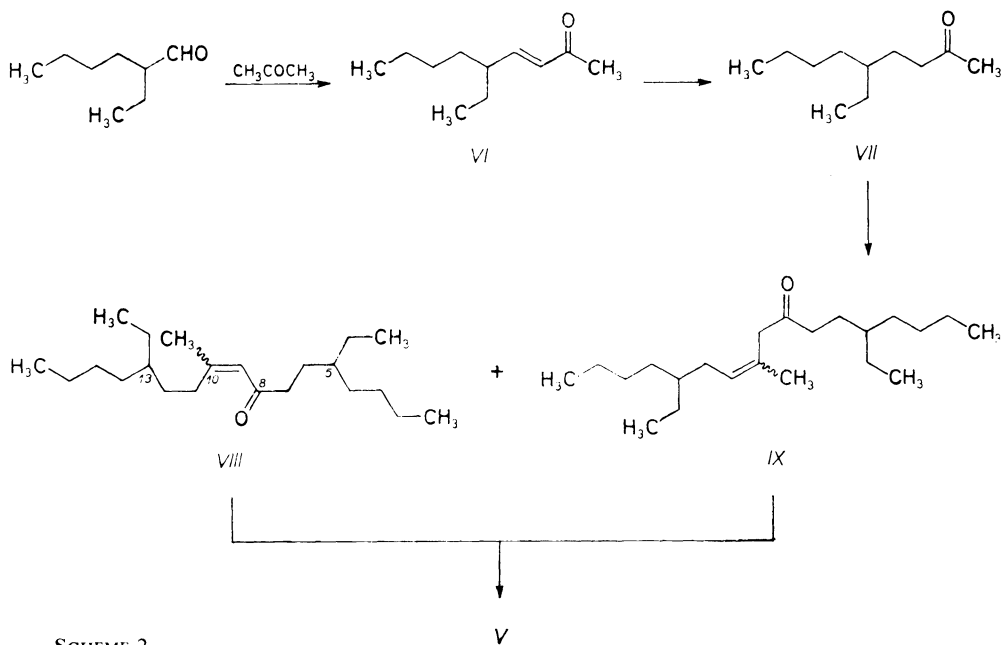
Since 1976 so called post-1976 Kelex 100 has contained again mainly alkenyl-

quinolinols, which are, however, prepared³ by base-catalyzed addition of 8-quinolinol to branched aliphatic aldehydes (e.g. 2-ethylhexanal) and ketones (e.g. 5-ethyl-2-nonanone *VII* in Scheme 2). Finally, in 1982 the stability of the mixture was improved by hydrogenation⁴.



SCHEME 1

Concerning the composition of the new Kelex 100 our investigations largely confirm the published results⁵: 7-(4-ethyl-1-methyloctyl)-8-quinolinol (*II*) is the main component, furoquinoline *III* being a further component (*III* may be formed ac-



SCHEME 2

cording to Scheme 1). A third, minority component (8 wt. %) was regarded to be another furoquinoline.

The composition of post-1976 Kelex 100 was studied⁵ by GC-MS and FT-IR spectrometry. Unfortunately, there are no NMR data and no fragmentation patterns quoted in this publication. The strong signal near 1700 cm^{-1} in the IR spectrum of a purified sample of Kelex 100 was omitted by the authors, they attributed peak No. 2 in their GC-MS diagram (TIC mode) and the corresponding ion at m/z 197 to structure *IV*. However, structure *IV* for the minority component seems to be unlikely. This substance could arise in analogy to *III* by addition of butanone to 8-quinolinol (Scheme 1), but the main hydrogenation product of this process was not detected. In our opinion, *IV* cannot be obtained by the process described in literature³. More recent GC-MS results⁶ revealed a branched ketone $\text{C}_{22}\text{H}_{44}\text{O}$ to be an impurity in post-1976 Kelex 100. It seemed to be a "dimer" of the ketone employed^{3,4,7,8} in the synthesis of Kelex, $\text{C}_{11}\text{H}_{22}\text{O}$.

Here we describe preparation and spectral properties of ketone *V* (5,13-diethyl-10-methylheptadecan-8-one) whose mass spectrum is identical with that of the ketone $\text{C}_{22}\text{H}_{44}\text{O}$ found in Kelex⁶. Moreover, the structure of *V* explains the MS signal⁵ at m/z 197 which is not a molecular ion of compound *IV* but a fragment ion of *V* resulting from its α -cleavage. Finally, the presence of *V* in Kelex 100 can easily be explained by self-condensation of 5-ethyl-2-nonanone (*VII*) leading to the unsaturated ketone *VIII* and its subsequent hydrogenation⁴. In fact, we prepared ketone *V* in that way (Scheme 2).

The dimerisation of ketone *VII* to the unsaturated ketone *VIII* is strongly dependent on the reaction conditions. Mostly, ketones are heated to reflux in a Soxhlet or Thielepape apparatus in the presence of basic catalysts such as $\text{Ba}(\text{OH})_2 \cdot 8\text{H}_2\text{O}$, anion exchange resins and Al_2O_3 . With the exception of Al_2O_3 (ref.⁹) all the reagents mentioned above proved to be unfavourable for our problem. *Z*- and *E*-isomers of *VIII* could be separated from isomeric β,γ -unsaturated ketones (*IX*) by column chromatography.

However, the crude mixture of *VIII* and *IX* was used for hydrogenation. Although the crude hydrogenation product did not contain any more *VIII* (TLC), it appeared again after distillation of crude *V* owing to the presence of the corresponding aldol in the product. This can be overcome by a new hydrogenation and distillation. Product *V* so obtained contains 1–2% of impurities (GC). Its IR, ^1H NMR, and MS data are in accordance with the suggested structure, there are no hints for diastereomers.

EXPERIMENTAL

EI-MS: Varian MAT CH5 (70/12 eV). ^1H NMR: Varian EM 390 (90 MHz, 26°C) and Bruker Spectrospin (250 MHz). IR: Nicolet 510 FT-IR, data acquisition by Mac II ci (Apple Mac-

intosh). UV: Uvikon 810 (Kontron). TLC: CH_2Cl_2 or benzene-hexane (1 : 1) on SiO_2 (Merck 5554), detection: 2,4-dinitrophenylhydrazine 0.2% in ethanolic HCl, then $\text{K}_3[\text{Fe}(\text{CN})_6]$ 0.2% in 2M-HCl. GC: a) Carlo Erba Fractovap 2450, FID, carrier gas N_2 , filled glass column 2.0 mm \times 1.5 m, 3% OV 17 on Chromosorb G AW DMCS 80/100 mesh, injector 275°C, programme: 170°C (2 min) – 230°C (3°C/min); b) Hewlett-Packard HP 5890 I, FID, carrier gas H_2 4 ml/min (90 kPa), split 100 ml/min, capillary column 40 m \times 0.32 mm, OV101 crosslinked on fused silica, 0.17 μm , injector 245°C, detector 250°C, oven 170°C. GC-MS: a) HP 5890 I, capillary column 40 m \times 0.32 mm, OV101 crosslinked on fused silica, 0.17 μm , carrier H_2 , 1.5 ml/min (40 kPa), oven temperature 170°C (isothermal), injector 250°C, transfer line 170°C, probe: 0.2 μl 1% in CH_2Cl_2 , cool on column-system, split 75 ml/min (1 : 50), septum purge: 3 ml/min, detector MAT 90 EI-MS (70 eV), delay 13.0 min, B-scan (exp.) 35–400 u, scan rate 1 s/dec., interscan time 0.10 s, resolution 1 130, 8 samples per peak, 20.833 Hz sampling frequency, dynamic: 2.65 $\cdot 10^6$; b) HP MS 5970, inlet GC: 25 m column SE 54 (5%), carrier gas He, injector 250°C, programme: 80°C (30 s)–290°C (10°C/min), 290°C (2 min), detector MS (EI – 70 eV, CI), TIC (ref.⁶).

Materials

(*E*)-5-Ethyl-3-nonen-2-one¹⁰ (VI). To a well stirred boiling mixture of acetone (348.0 g) and 10% aqueous NaOH (20 ml) 2-ethylhexanal (207.0 g) was added over a 16 h period, the last 25% being added more slowly. After complete addition heating was continued for 4 h. Ether was added (200 ml) and the separated aqueous layer was drained off. After washing with several portions of water, drying and stripping, the residual oil was fractionated, yielding 250 g VI, b.p._{1 kPa} 90°C (ref.¹⁰; b.p._{1.3 kPa} 98°C; $n_D^{16} = 1.4571$).

5-Ethyl-2-nonanone¹¹ (VII). Hydrogenation at 2.0–2.5 MPa and room temperature of a magnetically stirred suspension of Pd/C (1.2 g, 5%) in VI (120.0 g) in an 500 ml autoclave afforded complete reaction after 64 h, yield 98%. Several runs have been made with the recovered catalyst. The oily product was distilled over a 30 cm Vigreux column, b.p._{1.5 kPa} 93°C or b.p._{0.3 kPa} 67°C (ref.¹¹; b.p._{0.67 Pa} 36°C, $n_D^{21} = 1.4340$).

(*E*)- and (*Z*)-5,13-Diethyl-10-methyl-9-heptadecen-8-one (VIII). In a Soxhlet apparatus the extractor thimble was filled with basic alumina (for CC, Woelm, activity 0; 25 g) covered with glasswool. Compound VII (100 g) was refluxed in vacuo (0.3 kPa) over the basic catalyst until the boiling temperature in the bottom climbed from 65°C to 80°C. After about 72 h the reaction was stopped. The crude condensation product (bottom) (76 g) was combined with an ether extract of the catalyst (20 g). After evaporation of the ether unreacted VII was removed by column distillation. (*E*)- and (*Z*)-VIII (2.5 g) were separated by column chromatography on SiO_2 (250 g Geduran 60 Merck 7734), with benzene-hexane (1 : 1) (fractions 20 ml). The order of elution: (*Z*)-VIII, mixture of (*E*)- and (*Z*)-IX, (*E*)-VIII. After stripping off the solvent the pure isomers were obtained by bulb-to-bulb distillation (Büchi) yielding: 0.2 g (*Z*)-VIII, 0.2 g (*E*)-VIII, and 0.1 g (*E*)-(*Z*)-IX.

5,13-Diethyl-10-methyl-8-heptadecanone (V). The crude mixture of VIII and IX (60 g) in 150 ml MeOH was hydrogenated on 5% Pd/C (1.0 g) in an autoclave under magnetic stirring at room temperature and 2.0 $\cdot 10^3$ kPa. Uptake of H_2 was complete after 48 h. After removing low boiling fractions (up to 127°C/5 Pa) distillation first afforded fractions up to 155°C/5 Pa, which still contained VIII and IX. The mixture was again hydrogenated in the same way. Then distillation afforded the main fraction boiling at 145°C/5 Pa, which consisted of rather pure V (38 g) with less than 2% of impurities (GC).

Characteristics of the new products are given in Table I.

TABLE I
Characteristics of ketones *V*, *VIII* and *IX*

Compound	R_F n_D^{20}	IR, cm^{-1}	$^1\text{H NMR}^a$ δ , ppm	MS m/z (rel. intensity ^b , %)
<i>(Z)</i> - <i>VIII</i>	0.85 1.4680	2 961, 2 930, 2 874, 2 860, 1 691, 1 620 ^c	6.03 s, 1 H (H-9); 2.58—2.51 m, 2 H (H-11); 2.39—2.32 m, 2 H (H-7); 1.86 d, 3 H ($^4J = 1.29$, C-10 Me); 1.56—1.20 m, 22 H; 0.91—0.81 m, 12 H	322 (62/100), 223 (94/68), 210 (22/37), 205 (26/12), 195 (59/31), 155 (11/7), 152 (53/44), 137 (20/5), 111 (62/8), 98 (100/50), 95 (42/3), 93 (84/15), 83 (41/-), 81 (38/-), 69 (75/-), 57 (61/-), 55 (59/-), 43 (59/-), 41 (47/-)
<i>(E)</i> - <i>VIII</i>	0.65	^d	6.06 d, 1 H ($^4J = 1.15$, H-9); 2.41—2.35 m, 2 H (H-7); 2.13 d, 3 H ($^4J = 1.15$, C-10 Me); 2.09—2.05 m, 2 H (H-11); 1.61—1.20 m, 22 H; 0.95—0.82 m, 12 H	322 (8/11), 223 (17/12), 210 (66/100), 195 (74/32), 155 (28/17), 152 (44/35), 137 (35/7), 111 (52/13), 98 (100/61), 97 (23/2), 95 (31.2), 83 (30/1), 81 (25/2), 69 (46/-), 57 (43/-), 55 (43/), 43 (40/-), 41 (32/-)
<i>(E/Z)</i> - <i>IX</i>	0.80/0.70 1.4698	2 961, 2 930, 2 874, 2 860, 1 717, 1 644, 1 461	5.30/5.36 m, 1 H (H-11); 3.03/3.10 s, 2 H (H-9); 2.40/2.40 m, 2 H (H-7); 1.95/2.00 m, 2 H (H-12); 1.72/1.62 d, 3 H ($^4J = 1.2$, C-10 Me); 1.57—0.7 m, 32 H	322 (8/31), 223 (8/17), 210 (9/23), 195 (5/7), 155 (78/48), 152 (81/100), 137 (100/40), 97 (15/5), 95 (52/10), 85 (14/1), 83 (17/3), 81 (43/7), 71 (24/-), 69 (39/-), 57 (60/-), 55 (35/-), 43 (45/-), 41 (28/-)
<i>V</i>	1.4517	2 959, 2 928, 2 874, 2 860, 1 716, 1 461, 1 379	2.50—2.15 m, 4 H (H-7, H-9); 1.7—1.4 m, 3 H (H-10, H-5, H-13); 1.4—1.05 m, 22 H; 1.05—0.7 m, 15 H	324 ^e (7/45), 213 (14/32), 197 (71/85), 171 (25/30), 155 (34/58), 154 (27/37), 153 (15/17), 152 (41/47), 112 (100/100), 85 (85/47), 71 (61/8), 57 (88/-), 43 (52/-)

^a In CDCl_3 at 90 MHz (*VIII* at 250 MHz); ^b at 70/12 eV; ^c UV: λ_{max} 239 nm ($\log \epsilon$ 4.49) in CHCl_3 ; ^d IR and UV spectra identical with those of *(Z)*-*VIII*; ^e HR-MS found: 324.3398, $\text{C}_{22}\text{H}_{44}\text{O}$ requires 324.3392.

REFERENCES

1. Ashbrook A. W.: *J. Chromatogr.* *105*, 151 (1975).
2. Budde W. M., Jr., Hartlage J. A.: U.S. 3 637 711 (1972); *Chem. Abstr.* *76*, 99531 (1972).
3. Richards H. J., Trivedi B. C.: U.S. 4 045 441 (1977); *Chem. Abstr.* *87*, 201341 g (1977).
4. Gefvert D. L., Richards H. J.: *PCT Int. Appl. WO 82 01 369* (1982); *Chem. Abstr.* *97*, 201231c (1982).
5. Demopoulos G. P., Distin P. A.: *Hydrometallurgy* *11*, 389 (1983).
6. Loßmann G.: Private communication (1987).
7. Loewenberg K., Smeykal K.: U.S. 2 200 216 (1940); *Chem. Abstr.* *34*, 5855³ (1940).
8. Röhm and Haas Co.: U.S. 2 148 103 (1938); *Chem. Zentralbl.* *1939* II, 2990.
9. Seebald H. J., Schunack W.: *Arch. Pharm.* *305*, 406 (1972).
10. Häusermann M.: *Helv. Chim. Acta* *34*, 2172 (1951).
11. Bharucha K. R., Weedon B. C. L.: *J. Chem. Soc.* *1953*, 1578.