[4] Under the conditions chosen *(vide infra)*, the thermodynamically more stable of the two enolate anions of the D ring component adds, in extremely regioselective manner, to *(12)*. The $(CH_3)_3Si$ ligand ensures that the reaction also produces *rac-(10)* in extremely high stereoselectivity.

[5] *m*-Cresol methyl ether (3-methylanisole) is brominated analogously to 3-ethylanisole: *D. J. Nelson, E. A. Uschak*, J. Org. Chem. *42*, 3308 (1977).

[6] *A. Ottolenghi, M. Friedkin, A. Zilkha*, Can. J. Chem. *41*, 2977 (1963).

[7] *rac-(8)*, $R = C_2H_5$, was synthesized by *R. W. Kierstead, R. P. Linstead, B. C. L. Weedon*, J. Chem. Soc. *1952*, 3613; we adopted to procedure of *J. M. Stewart, G. K. Pagenkopf*, J. Org. Chem. *34*, 7 (1969), but used *(6)*, $R = CH_3$. Concerning nucleophilic ring opening of cyclopropane derivatives activated by electron acceptors, see *S. Danishefsky*, Acc. Chem. Res. *12*, 66 (1979).

[8] The diastereomer of *rac-(5)* having *Z*-configurated 9,10-double bond traverses mainly that transition structure in which the dienophilic vinyl group approaches the *o*-quinonoid dienic moiety from the β-side, from the *exo* orientation: this affords *rac-(3)*. A competition reaction, of admittedly subordinate proportions, proceeds *via* that transition structure in which the vinyl group approaches the diene unit from the α-side, from the *endo* orientation: this gives *rac-(14)*. *rac-(3)* and *rac-(14)* are separated only for identification.

[9] *rac-(2)* and *rac-(15)* are separated only for identification.

[10] The mixture *rac-(2)* + *rac-(15)* is reduced by potassium in liquid ammonia in the presence of aniline and then oxidized by chromic acid to give *rac-(1)*, $R = CH_3$: *G. H. Douglas, J. M. H. Graves, D. Hartley, G. A. Hughes, B. J. McLoughlin, J. Siddall, H. Smith*, J. Chem. Soc. *1963*, 5072. *rac-(1)*, $R = CH_3$, is transformed, on heating with pyridine hydrochloride to 210 °C, into *rac-(1)*: *W. S. Johnson, D. K. Banerjee, W. P. Schneider, C. D. Gutsche, W. E. Shelberg, L. V. Chinn*, J. Am. Chem. Soc. *74*, 2832 (1952).

[11] The mixture *rac-(2)* + *rac-(15)* is reduced by potassium in liquid ammonia in the presence of aniline and then treated with diisobutylaluminum hydride *rac-(16)*; R = H: *J.-C. Hilscher*, DBP 2409991 (1976); Schering; Chem. Abstr. *84*, 59862v (1976).

[12] The mixture *rac-(2)* + *rac-(15)* is converted by Birch reduction into *rac-(17)* [by analogy with the procedure of *W. S. Johnson, W. A. Vredenburgh, J. E. Pike*, J. Am. Chem. Soc. *82*, 3409 (1960)].

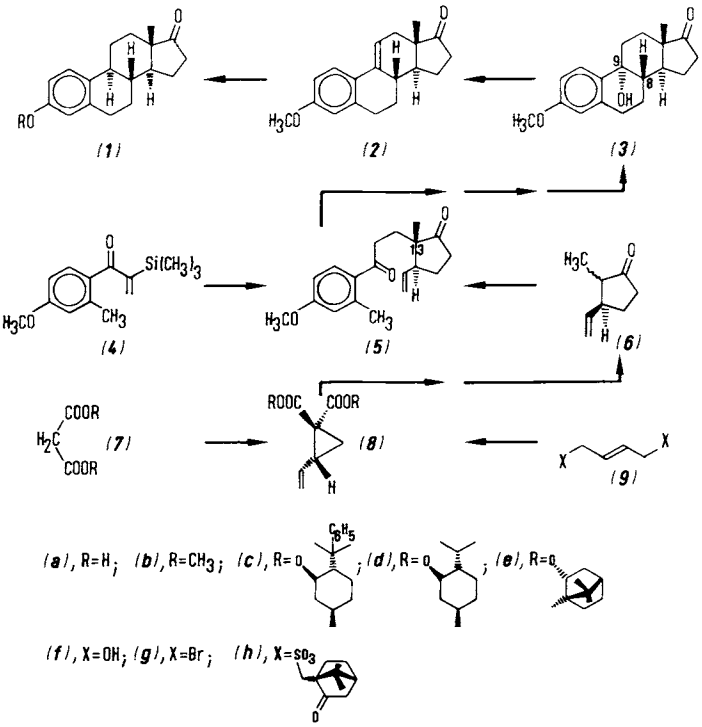
[13] Since *rac-(10)* undergoes at least 61% conversion into [*rac-(2)* + *rac-(15)*], the overall yield of this mixture is 22% for *m*-cresol methyl ether and 12% for (*E*)-1,4-dibromo-2-butene or dimethyl malonate.

Asymmetric Total Synthesis of (+)-Estrone[**]

By *Gerhard Quinkert, Ulrich Schwartz, Herbert Stark, Wolf-Dietrich Weber, Helmut Baier, Friedheld Adam*, and *Gerd Dürner*[*]

Dedicated to Professor Rolf Huisgen on the occasion of his 60th birthday

We have reported a steroid total synthesis which can be directed towards various racemic synthetic target compounds in considerable overall yield[1]. This synthesis contains a photochemical key reaction, starts from inexpensive chemicals, and proceeds largely regio- and stereoselectively. Of the four asymmetric C atoms of the title compound *(1a)*, three have been introduced with high diastereoselectivity: C-13 by a Michael addition, leading to the photo-enolizable key compound *rac-(5)*, C-8 and C-9 *via* an *o*-quinodimethanoid phototransient whose intramolecular Diels-Alder reaction[2] completes the steroid skeleton [of *rac-(3)*]. If the chiral dextrorotatory D ring component is used instead of the racemate (2Ξ,3*RS*)-*(6)*, then stereoselection is complete: natural (+)-estrone *(1a)* and its relatives thus become accessible by enantiomer selection (Scheme 1).

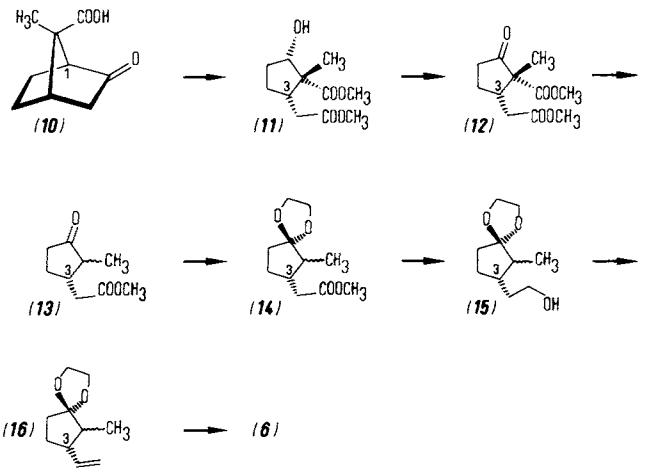


Scheme 1

The chiral, dextrorotatory D ring component has been obtained in three ways:

- According to Scheme 1, by ring expansion of the dextrorotatory three-membered ring compound *(R)-(8b)*, which is accessible from *(RS)-(8a)* by resolution with brucine[3,4];
- according to Scheme 2, by ring opening of the levorotatory bicyclic compound *(1S)-(10)*, obtained from *(1RS)-(10)* by resolution with (+)-1-phenylethylamine[5];
- according to Scheme 1, by ring expansion of the three-membered ring enantiomers *(R)-(8b)*/*(S)-(8b)* = 9:1, which are obtainable in this composition by asymmetric induction during diastereoselective cyclopropanation of *(7c)* and subsequent transesterification[6].

Table 1 indicates the extent of asymmetric induction, and shows (i) that the chiral substituent R greatly influences the



Scheme 2

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[**] Light Induced Reactions, Communication 22. This work was supported by the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie, and Hoechst AG. We are indebted to Prof. *R. Wiechert*, Schering AG, for kindly supplying large amounts of valuable steroids. *Marlies Dürr, Gabriele Stracke*, and *Sabine Beck* contributed greatly to optimization of the various reaction steps.—Communication 21: [1].

transformation of the malonic diesters *(7c)*, *(7d)*, and *(7e)* into products of type *(8)* and (ii) that the diastereoselective-asymmetric step of the synthesis is superior to the enantioselective-asymmetric alkylation [of *(7b)* by chiral *(9h)*[7] or by achiral *(9g)* in the presence of a chiral phase transfer catalyst[8]].

Table 1. Extent of asymmetric induction in the synthesis of *(8b)*.

Synthesis	Asymm. induction [%]
Diastereoselectively asymmetric	
(7c) + *(9g)*	76—80
(7d) + *(9g)*	52—54
(7e) + *(9g)*	39
Enantioselectively asymmetric	
(7b) + *(9h)*	13
(7b) + *(9g)*	<2

(*R*)-*(8b)* and (1*S*)-*(10)*, both obtained by resolution of racemates, represent reference compounds for the corresponding species from the chiral branch; *(5)* and *(2)*[9], which are obtained after introduction of (*R*)-*(8b)* and (1*S*)-*(10)* into the synthetic procedure (Scheme 1), are reference compounds for the corresponding species from the chiral trunk.

Table 2 shows that the optical yield of the diastereoselective-asymmetric synthesis is 80% on use of *(7c)*.

Table 2. Optical yield of the diastereoselectively asymmetric synthesis of *(2)* and intermediates [starting from *(7c)*] relative to reference compounds.

Opt. act. cpd.	$[\alpha]_D$ From the diastereoselectively asymmetric synthesis	Reference cpd.	Opt. yield [%]
(2)	+231.8 (dioxane)	+288.6	80
(5)	+ 21.2 ($CHCl_3$)	+ 27.1	80
(6)	+112.7 (CH_2Cl_2)	+149.0	76
(8b)	+ 43.9 (CCl_4)	+ 55.0	80

Table 3 contains some selected physical data of the compounds discussed above.

Table 3. Selected physical data of the identified chiral compounds. All formerly undescribed compounds and those synthesized by new methods exhibit correct molecular compositions and were characterized by IR and ^{1}H-NMR spectra.

(1a): m.p. 259 °C (ethanol); $[\alpha]_D^{20} = 164.8$ ($c = 0.501$ in dioxane)
(2): m.p. 143—144 °C (pentane); $[\alpha]_D^{20} = 288.6$ ($c = 0.506$ in dioxane).—*(2)* and *rac-(2)* [1] have similar IR spectra (KBr) but identical UV (methanol) and ^{1}H-NMR spectra ($CDCl_3$)
(5): $[\alpha]_D^{20} = 27.1$ ($c = 1.007$ in $CHCl_3$).—UV- (*n*-hexane), IR- (Film) and ^{1}H-NMR spectra ($CDCl_3$) of *(5)* and *rac-(5)* [1] were identical
cis-(6) + *trans-(6)* (8:92): $[\alpha]_D^{20} = 149.0$ ($c = 0.963$ in CH_2Cl_2)
(8b): $[\alpha]_D^{25} = 55.0$ ($c = 0.96$ in CCl_4)
(1*S*)-*(10)*: m.p. 206 °C (acetone, dec.); $[\alpha]_D^{20} = -76.1$ ($c = 0.992$ in ethanol)
(3*S*)-*(11)*: b.p. 120 °C/0.09 torr; $[\alpha]_D^{20} = -20.7$ ($c = 1.016$ in $CHCl_3$)
(3*S*)-*(12)*: b.p. 120 °C/0.06 torr; $[\alpha]_D^{20} = 67.9$ ($c = 0.960$ in $CHCl_3$)
(3*S*)-*(13)*: b.p. 90 °C/0.07 torr; $[\alpha]_D^{20} = 78.3$ ($c = 0.937$ in $CHCl_3$)
(3*S*)-*(14)*: b.p. 90 °C/0.05 torr; $[\alpha]_D^{20} = -38.1$ ($c = 1.004$ in $CHCl_3$)
(3*S*)-*(15)*: $[\alpha]_D^{20} = -49.5$ ($c = 1.000$ in $CHCl_3$)
(3*S*)-*(16)*: b.p. 90 °C/14 torr; $[\alpha]_D^{20} = -24.1$ ($c = 0.947$ in $CHCl_3$)

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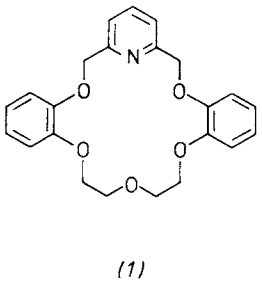
[1] *G. Quinkert, W.-D. Weber, U. Schwartz, G. Dürner*, Angew. Chem. 92, 1060 (1980); Angew. Chem. Int. Ed. Engl. *19*, 1027 (1980).
[2] Review: *R. G. Carlson*, Annu. Rep. Med. Chem. 9, 270 (1974); *W. Oppolzer*, Angew. Chem. *89*, 10 (1977); Angew. Chem. Int. Ed. Engl. *16*, 10 (1977); *W. Oppolzer*, Synthesis *1978*, 793; *R. L. Funk, K. P. C. Vollhardt*, Chem. Soc. Rev. 9, 41 (1980); *G. Brieger, J. N. Bennett*, Chem. Rev. *80*, 63 (1980).
[3] *S. Danishefsky, G. Rovnyak*, J. Chem. Soc. Chem. Commun. *1972*, 821: $[\alpha]_D = +55.2$ for *(8b)* in CCl_4; *N. A. Abraham*, Tetrahedron Lett. *1974*, 1393: $[\alpha]_D = -54.7$ for *ent-(8b)* in CCl_4; *F. Adam*, unpublished: $[\alpha]_D^{25} = +55.0$ for *(8b)* in CCl_4.
[4] Assuming the configuration at C-2 to invert on ring expansion and on the basis of the conversion into (+)-*(1a)*, *R* chirality is assigned to (+)-*(8b)*.
[5] Since the chirality center C-4 is unaffected on transformation of (−)-*(10)* into (2Ξ,3*S*)-*(6)* and because (−)-*(10)* can be converted into (+)-*(1a)*, *S* chirality is assigned to C-4.
[6] In fact, the compound was first hydrolyzed to the dicarboxylic acid (*R*)-*(8a)* and then esterified with diazomethane to give (*R*)-*(8b)*.
[7] *G. Quinkert, K. R. Schmieder, G. Dürner, K. Hache, A. Stegk, D. H. R. Barton*, Chem. Ber. *110*, 3582 (1977), see Section 5.2.1.3.
[8] (−)-*N,N*-Dimethylephedrinium bromide was used as chiral phase transfer catalyst; see *H. B. Kagan, J. C. Fiaud*, Top. Stereochem. *10*, 236 (1978); *E. V. Dehmlow*, Angew. Chem. *89*, 521 (1977); Angew. Chem. Int. Ed. Engl. *16*, 493 (1977), see Section 4.8.
[9] *(2)* has also been obtained by dehydrogenation of *(1b)* according to *C. G. Pitt, D. H. Rector, C. E. Cook, M. C. Wani*, J. Med. Chem. *22*, 966 (1979), the crude product contains, in addition to 97% of *(2)*, the isomer 3-methoxy-1,3,5(10),8-estratetraen-17-one, which was removed by preparative HPLC.

Selective Inclusion of Alcohols with a New Pyridino Crown[**]

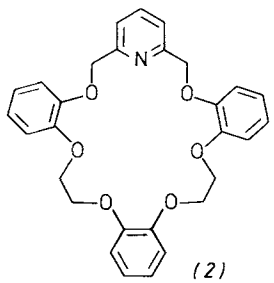
By *Edwin Weber* and *Fritz Vögtle*[*]

Dedicated to Professor David Ginsburg on the occasion of his 60th birthday

Although several host/guest complexes of crown compounds with CH- and NH-acidic neutral molecules such as acetonitrile, nitromethane, and dimethyl sulfone have already been described[1], alcohols have so far defied all attempts at inclusion by compounds of this kind. Spurred on by the surprising complexation of uncharged guest molecules by the hexadentate dibenzopyridino crown *(1)*[1], our systematic study has now culminated in the discovery of the heptadentate tribenzopyridino crown *(2)* as a new host substance of this type. It is the first crown to form inclusion compounds—selectively—with aliphatic alcohols. Alcohol inclusion compounds of any kind were formerly very rare[2].



(1)



(2)

Our synthesis of *(2)* started from pyrocatechol monobenzyl ether *(3)*[3]; cyclization *(7)* + *(8)* → *(2)* could be accomplished by the dilution principle[4].

Compound *(2)* is obtained as a complex of exact 2:1 stoichiometry (ligand:guest) with *methanol* on recrystallization

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[**] Part 8 of Complexes between Neutral Molecules.—Part 7: [1].

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