Organic &
Biomolecular
Chemistry

Cite this: *Org. Biomol. Chem.*, 2012, **10**, 966

www.rsc.org/obc

**PAPER**

# Asymmetric synthesis of *ethano*-Tröger bases using CuTC-catalyzed diazo decomposition reactions†

**Ankit Sharma,[a] Céline Besnard,[b] Laure Guénée[b] and Jérôme Lacour*[a]**

***Received 18th October 2011, Accepted 24th October 2011***
**DOI: 10.1039/c1ob06751f**

Nonracemic *ethano*-bridged Tröger bases are prepared using CuTC-catalyzed decompositions of diazo compounds. Excellent levels of diastereo- and enantio-control (*dr* and *ee* up to 12 : 1 and 95% respectively) are now obtained with aryl diazoketone precursors.

*Ethano*-Tröger bases **1**,[1] which are structural analogues of the important *methano*-Tröger derivatives **2**,[2,3] present the advantage of being, unlike their congeners, configurationally stable under acidic conditions.[1a,1c,1f,4,5] Recently, new routes to these compounds have been made available through the use of nitrogen ylide chemistry.[1f,6] In particular, $Rh_2(OAc)_4$-catalyzed reactions of aryl diazoesters and *methano*-Tröger bases **2** afforded functionalized derivatives of type **3** (Fig. 1). In a single step, the *ethano*-bridge was constructed, a new carbon quaternary stereogenic center was introduced,[7] and enantiopure derivatives **2** were transformed into **3** with very high levels of chirality transfer (*ee* up to 99%).[6] Herein, we extend the scope of this chemistry as we report that CuTC (copper(I) thiophene-2-carboxylate) is an excellent catalyst.[8,9] A rather large range of diazocarbonyl reagents can be used. Aryl diazoketones provide good levels of diastereo- and enantio-control (*dr* and *ee* up to 12 : 1 and 95% respectively) in particular.

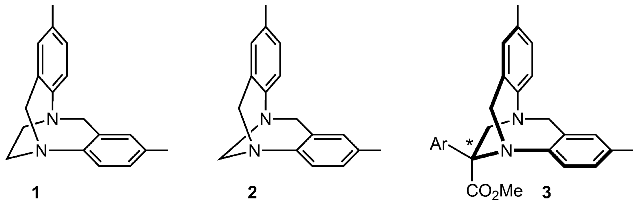
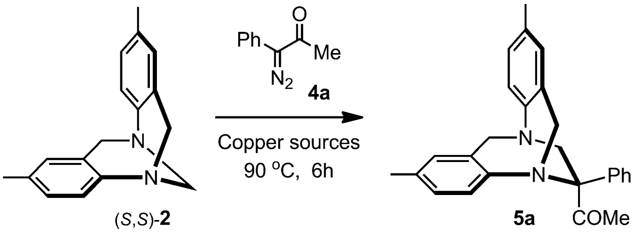


**Fig. 1** Traditional *ethano*- and *methano*-Tröger bases (**1** and **2**) and arylester functionalized *ethano*-derivatives **3**.

As mentioned previously, nitrogen ylide chemistry can be considered for the transformation of *methano*-Tröger bases into *ethano*-derivatives. Given the fact that copper sources, metal or salts, are used more frequently than Rh(II) complexes in this context,[10] we were keen on studying the decomposition of a large variety of diazocarbonyls under copper catalysis in the presence of compounds **2**.

**Table 1** Screening of copper sources[a]



| Entry | Catalyst | Yield (%)[b,c] | *dr*[c] | *ee*[d] |
|---|---|---|---|---|
| 1 | Cu powder | 60 | 1.0 : 1 | 25 |
| 2 | $Cu(OTf)_2$ | 89 | 3.5 : 1 | 10 |
| 3 | $[Cu(CH_3CN)_4][BF_4]$ | 85 | 12 : 1 | 15 |
| 4 | $Cu_2(OTf)_2\cdot$Toluene | 72 | 3.0 : 1 | 36 |
| 5 | CuBr | 91 | 5.1 : 1 | 81 |
| 6 | $Cu_2(OAc)_2$ | 82 | 5.5 : 1 | 81 |
| 7 | CuCl | 89 | 8.7 : 1 | 82 |
| 8 | $Cu(hfacac)_2\cdot H_2O$ | 85 | 5.0 : 1 | 82 |
| 9 | $Cu(acac)_2$ | 90 | 4.3 : 1 | 83 |
| 10 | CuI | 87 | 10 : 1 | 87 |
| 11 | CuTC | 85 | 11 : 1 | 90 |

[a] Conditions (+)-(*S*,*S*)-**2** (0.1 mmol), diazo reagent **4** (0.2 mmol), 5 mol% of catalyst, 0.25 mL of toluene, 90 °C, 6 h. [b] Combined yield for both diastereoisomers using 1,3,5-trimethoxybenzene as the internal standard. [c] Determined by $^1$H-NMR analysis (400 MHz). [d] Of the major diastereoisomer; determined by CSP-HPLC analysis.

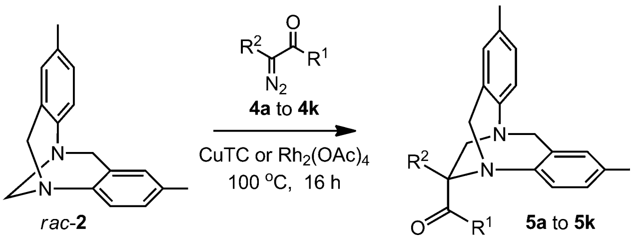
The reaction of (+)-(*S*,*S*)-**2** with diazo arylketone **4a** (Table 1) was used to select the best possible copper catalyst.[11] More than ten sources of copper were used (Table 1). Satisfactorily, all of them afforded the desired product **5a** in moderate to excellent yields (60–91%). Interestingly, strong differences were noticed in terms of diastereoselectivity and enantiospecificity. CuI and CuTC salts were the most effective (Table 1, entries 10 and 11), with a slight preference for the latter in terms of selectivity. As CuTC, to our knowledge, had never been reported in diazo decomposition chemistry,[12] a broader comparison was performed with 10 diazo

---

[a] *Department of Organic Chemistry, Quai Ernest Ansermet 30, CH-1211, Geneva 4. E-mail: jerome.lacour@unige.ch; Fax: +41 22 379 3215*
[b] *Laboratoire de Cristallographie, University of Geneva, Quai Ernest Ansermet 24, CH-1211, Geneva 4, Switzerland*

† Electronic supplementary information (ESI) available: Synthetic procedures and spectral characterization of the major diastereoisomers of products **5**. Crystal structure determinations of **5a**, **5c** and **5i**. CCDC reference numbers [840414–840416]. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c1ob06751f

**Table 2** Copper *vs.* rhodium catalysis[a]



| Entry | Diazo | $R^1$ | $R^2$ | Product | CuTC | | $Rh_2(OAc)_4$ | |
|---|---|---|---|---|---|---|---|---|
| | | | | | Yield[b] | *dr*[c] | Yield[b] | *dr*[c] |
| 1 | **4a** | Me | Ph | **5a** | 80 | 11 : 1 | 70 | 5 : 1 |
| 2 | **4b** | Me | COMe | **5b** | 70 | — | np | — |
| 3 | **4c** | Me | $CO_2Me$ | **5c** | 80 | 4.3 : 1 | 78 | 2.2 : 1 |
| 4 | **4d** | Me | $CO_2Et$ | **5d** | 82 | 5.5 : 1 | 80 | 2.0 : 1 |
| 5 | **4e** | Et | $CO_2Et$ | **5e** | 91 | 5.0 : 1 | 19 | 2.4 : 1 |
| 6 | **4f** | *n*Pr | $CO_2Et$ | **5f** | 80 | 5.0 : 1 | 25 | 2.7 : 1 |
| 7 | **4g** | *i*Pr | $CO_2Et$ | **5g** | 78 | 6.0 : 1 | np | — |
| 8 | **4h** | Ph | $CO_2Et$ | **5h** | 80 | 4.3 : 1 | 49 | 3.3 : 1 |
| 9 | **4i** | Me | $CO_2$*i*Pr | **5i** | 85 | 3.9 : 1 | 20 | 1.2 : 1 |
| 10 | **4j** | Me | $CO_2$*t*Bu | **5j** | 87 | 4.0 : 1 | 25 | 1 : 1 |
| 11 | **4k** | OEt | $CO_2Et$ | **5k** | 40 | — | 85 | — |

[a] Conditions: *rac*-**2** (0.4 mmol), diazo reagent **4** (0.8 mmol), CuTC (5 mol%) or $Rh_2(OAc)_4$) (5 mol%), 1.0 mL of toluene, 100 °C, 16 h; reported results are the average of at least two experiments. The relative configuration displayed is that of the major diastereoisomers of compounds **5**. np stands for no product of type **5**. [b] Isolated yield (%, both diastereoisomers). [c] *dr* ratios determined by $^1$H-NMR analysis (400 MHz) of the crude reaction mixtures.

reagents (Table S1, ESI†). In all cases, better yields and selectivity ratios were obtained with CuTC over CuI. CuTC was thus selected for the remainder of the study.

A series of α-diazo reagents (**4b** to **4k**) were then tested and the results were directly compared to reactions performed with $Rh_2(OAc)_4$. 5 mol% amounts of CuTC and $Rh_2(OAc)_4$ were used throughout the study. The results are presented in Table 2. First, α-diazo-β-diketone **4b** ($R^1$ = Me, $R^2$ = COMe) was reacted with *rac*-**2** at 100 °C in toluene.[18] To our satisfaction, product **5b** was isolated with a 70% yield (Table 2, entry 2); the analogous reaction with $Rh_2(OAc)_4$ being to the contrary totally unproductive. Encouraged by this result, non-symmetrically substituted α-diazo-β-ketoester derivatives were used. Compounds **4c** and **4d** reacted equally well ($R^1$ = Me, $R^2$ = $CO_2Me$ and $CO_2Et$, 80 and 82% respectively). Under copper catalysis, better diastereoselectivity ratios were obtained (*dr* 4.3 : 1 and 5.5 : 1) in comparison with that established with $Rh_2(OAc)_4$ (2.2 : 1 and 2.0 : 1 respectively, Table 2, entries 3 and 4). The diastereoisomers that predominate with CuTC are also the major components of the crude reaction mixtures with $Rh_2(OAc)_4$.

This better selectivity with CuTC was confirmed with more sterically demanding reactants **4e** to **4j**. Excellent yields and better *dr* values were obtained (**5e** to **5j**: 78 to 91%, *dr* up to 6.0 : 1, Table 2, entries 5 to 10) and this was irrespective of the size increase of $R^1$ or $R^2$. These results contrast sharply with that obtained in the presence of $Rh_2(OAc)_4$ for which products, **5**, are isolated on average with a maximum yield of 49%. In the case of **4g**, no product was formed. Only in the reaction of α-diazo β-diester **4k**, $Rh_2(OAc)_4$ outperformed CuTC (85 *vs.* 40%, Table 2, entry 11).

For **5a**, **5c** and **5i**, monocrystals were afforded for the major (racemic) diastereoisomers either after separation from the minor isomers or directly from crude reaction mixtures. The relative configuration of these adducts was established by X-ray diffraction analysis (Fig. 2, **5a** and **5c** only). In all cases, it was found that the ketone functional groups occupy the more hindered position on the ethane bridge.[13] All data indicate that this relative configuration is conserved for the major diastereoisomers within the series of products **5c** to **5r** (Tables 2 and 3).

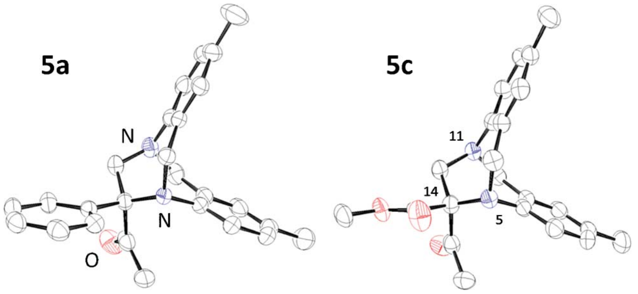
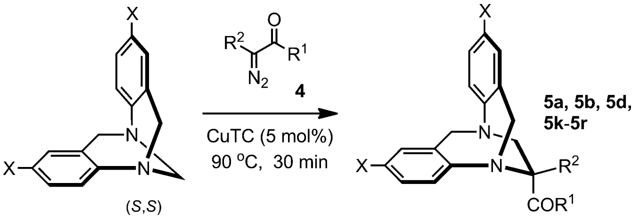


**Fig. 2** ORTEP views of the major diastereoisomers of **5a** and **5c** crystal structures; enantiomers ($5R_N$,$11S_N$,$14S_C$) are shown. Hydrogen atoms are omitted for clarity and thermal ellipsoids are drawn at 50% probability.

Finally, the scope of the chirality transfer was investigated under CuTC catalysis.[14] For this series of reactions, enantiopure (+)-(*S*,*S*)-**2** was used as the substrate (Table 3, entries 1 to 9). Whereas moderate enantiomeric purity levels were noticed for products **5b** and **5d** made using diazo compounds derived from β-diketones or ketoesters (*ee* 64 and 50% respectively), results were better with diazo reactants made from arylketones (**4a**, and **4l** to **4q**).[15] In all cases, the major diastereoisomers of products **5** were obtained with good diastereoselectivity (11 : 1 > *dr* > 8 : 1)

**Table 3** Efficient chirality transfer[a]



| Entry | diazo | $R^1$ | $R^2$ | X | Product | Yield[b] | *dr*[c] | *ee*[d] |
|---|---|---|---|---|---|---|---|---|
| 1 | **4a** | Me | Ph | Me | **5a** | 73 | 11 : 1 | 90 |
| 2 | **4b** | Me | COMe | Me | **5b** | 70 | — | 64 |
| 3 | **4d** | Me | $CO_2Et$ | Me | **5d** | 67 | 5.5 : 1 | 50 |
| 4 | **4l** | Et | Ph | Me | **5l** | 83 | 11 : 1 | 90 |
| 5 | **4m** | Ph | Ph | Me | **5m** | 85 (80)[f] | 8 : 1 | 90 (95)[f] |
| 6 | **4n** | Me | *p*-MePh | Me | **5n** | 80 | 9 : 1 | 82 |
| 7 | **4o** | Me | *m*-MePh | Me | **5o** | 83 | 10 : 1 | 84 |
| 8 | **4p** | Me | *p*-ClPh | Me | **5p** | 83 (75)[f] | 10 : 1 | 93 (99)[f] |
| 9 | **4q** | Me | *p*-$NO_2$Ph | Me | **5q** | 85 | 11 : 1 | 95 |
| 10 | **4a** | Me | Ph | OMe[e] | **5r** | 80 | 12 : 1 | 92 |

[a] Conditions: (+)-(*S*,*S*)-*methano*-Tröger bases (0.1 mmol), 5 mol% CuTC, 0.25 mL of dry toluene, 90 °C, 30 min; major diastereoisomer of **5** shown. Reported results are the average of at least two experiments. [b] Isolated yield (%) of the major diastereoisomer. [c] *dr* ratios determined by $^1$H-NMR spectroscopy (400 MHz) on the crude reactions mixtures. [d] *ee* values determined by CSP-HPLC. [e] *ee* 98%. [f] After crystallization.

and isolated yields (80–85%). In terms of enantioselectivity, the substitution of methyl by ethyl or phenyl substituents α to the carbonyl group had little effect in comparison with **5a**; products **5l** and **5m** (Table 3, entries 4 and 5) being afforded with the same 90% *ee* value than **5a**. In the case of **5m**, a simple recrystallization in acetone by slow evaporation of the solvent afforded the adduct in 95% *ee* (Table 3, entry 5). Increased steric hindrance on the reactants does not seem to be a factor under CuTC catalysis.

A series of diazoketones carrying different substituents on the aryl moiety was also utilized, namely reagents **4n** to **4q** ($R^2$ = *p*-MePh, *m*-MePh, *p*-ClPh, *p*-$NO_2$Ph). Very similar yields and diastereoselectivity ratios were obtained (Table 3, entries 6 to 9), which are in line with those previously discussed. Reasonably better enantiomeric purity values (*ee* ≥93%) were however, obtained with reagents carrying electron-withdrawing groups (*p*-Cl and *p*-$NO_2$: **4p** and **4q** respectively) in place of electron-donating ones (*ee* ≤84%, *p*- and *m*-Me: **4n** and **4o**).[16] Clearly, within this series of diazo reagents derived from arylketones, the highest levels of enantioselectivity are observed with the most reactive electrophilic carbenoids.[17] More generally, the more reactive diazo compounds, *i.e.* those derived from aryl ketones, give better results than stable derivatives made from β-diketones and β-ketoesters (*ee* 50–64%). Non-racemic 2,8-dimethoxy *methano*-Tröger base (*ee* 98%) was also treated with diazo **4a** under the new conditions, good yield (80%), *dr* (12 : 1) and *ee* (92%) values were obtained.

In conclusion, in the context of nitrogen ylide chemistry, we have shown that CuTC is a particularly effective source of copper for the decomposition of diazo reagents. A rather large scope of reactivity was obtained for the preparation of functionalized *ethano*-bridged Tröger bases; aryl diazoketones providing good levels of diastereo- and enantio-control (*dr* and *ee* up to 12 : 1 and 95% respectively) in particular.

## Experimental

### Representative preparation of racemic *ethano*-Tröger base: 5a

In a 10 mL 2 neck round bottom flask equipped with a magnetic stirring bar, 100.0 mg of Tröger base **2** (0.399 mmol) was introduced along with 1 mL of dry toluene and 3.8 mg CuTC (0.02 mmol, 5 mol%), all under a dinitrogen atmosphere. To this solution, diazo compound **4a** (64 mg, 0.4 mmol) was added in one portion. The reaction mixture was placed in an already heated oil bath (100 °C) and was stirred for 30 min at this temperature. Then, 0.4 mmol of the same diazo compound **4a** was added in one portion to the reaction mixture at 100 °C. The reaction was monitored by ESI-MS. The solution was then allowed to cool to 25 °C and the solvent was removed under reduced pressure. Purification by column chromatography ($SiO_2$, 3 × 30 cm, acetone/pentane 5 : 95) afforded the major diastereoisomer {(5*S*,11*R*,14*R*) and (5*R*,11*S*,14*S*)} of the desired product **5a** (111.5 mg, 73%) as a white solid. M.p.: 215–217 °C; IR: (neat): $\nu^{-1}$ = 2923, 1706, 1495, 1260, 1220 cm$^{-1}$. $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ = 7.61 (b, 2H), 7.38 (t, *J* = 7.8 Hz, 2H), 7.34–7.26 (m, 2H), 7.00 (d, *J* = 8.0 Hz, 1H), 6.96 (d, *J* = 8.0 Hz, 1H), 6.85 (d, *J* = 8.0 Hz, 1H), 6.64 (s, 2H), 5.28 (d, *J* = 14.6 Hz, 1H), 4.73 (d, *J* = 17.6 Hz, 1H), 4.60 (d, *J* = 17.4 Hz, 1H), 4.41 (d, *J* = 17.6 Hz, 1H), 4.31 (d, *J* = 17.4 Hz, 1H), 3.52 (d, *J* = 14.6 Hz, 1H), 2.18 (s, 3H), 2.14 (s, 3H), 1.66 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ = 205.5, 147.5, 144.7, 141.5, 136.2, 135.9, 135.8, 134.4, 130.5, 129.8, 129.0, 128.8, 128.7, 128.3, 128.1, 127.8, 127.4, 82.3, 59.6, 59.4, 56.4, 25.3, 21.2, 21.1. HRMS (ESI) for ($C_{26}H_{26}N_2O$ + H)$^+$: 383.2117, found: 383.2129.

### Representative preparation of enantio-enriched *ethano*-Tröger base: 5a

The method is the same as above, using enantiopure (+)-(*S*,*S*)-**2** (25 mg, 0.1 mmol) as the substrate in place of *rac*-**2** and **4a** (32 mg, 0.2 mmol) and 0.95 mg of CuTC (5 mol%) as the catalyst. The reaction was kept at 90 °C instead of 100 °C (Table 3). The major diastereoisomer (5*S*,11*R*,14*R*)-**5a** was isolated in 73% yield (28 mg, *ee* 90%), $[\alpha]_D^{20}$ = +198 (c 0.02, $CH_2Cl_2$). CSP-HPLC separation: (*S*,*S*)-Whelk-O 1 column, *n*-hexane/*i*-PrOH 99 : 1, 0.7 mL $min^{-1}$, 23 °C, $\lambda = 254$ nm; $t_R$ (5*S*,11*R*,14*R*) = 9.0 min, $t_R$ (5*R*,11*S*,14*S*) = 10.2 min.

## Acknowledgements

We thank the University of Geneva and the Swiss NSF for financial support. We also acknowledge the contributions of the Sciences Mass Spectrometry (SMS) platform at the Faculty of Sciences, University of Geneva.

## Notes and references

1 (*a*) Y. Hamada and S. Mukai, *Tetrahedron: Asymmetry*, 1996, **7**, 2671; (*b*) Y. Ishida, H. Ito, D. Mori and K. Saigo, *Tetrahedron Lett.*, 2005, **46**, 109; (*c*) D. A. Lenev, D. G. Golovanov, K. A. Lyssenko and R. G. Kostyanovsky, *Tetrahedron: Asymmetry*, 2006, **17**, 2191; (*d*) M. Faroughi, A. C. Try, J. Klepetko and P. Turner, *Tetrahedron Lett.*, 2007, **48**, 6548; (*e*) M. Faroughi, A. C. Try and P. Turner, *Acta Cryst.*, 2008, **E64**, o39; (*f*) C. Michon, A. Sharma, G. Bernardinelli, E. Francotte and J. Lacour, *Chem. Commun.*, 2010, **46**, 2206; (*g*) B. Bhayana and M. R. Ams, *J. Org. Chem.*, 2011, **76**, 3594.

2 (*a*) J. Tröger, *J. Prakt. Chem.*, 1887, **36**, 225; (*b*) S. Sergeyev, *Helv. Chim. Acta*, 2009, **92**, 415; (*c*) B. Dolensky, J. Elguero, V. Kral, C. Pardo and M. Valik, *Adv. Heterocycl. Chem.*, 2007, **93**, 1; (*d*) M. Demeunynck and A. Tatibouet, *Prog. Heterocycl. Chem.*, 1999, **11**, 1; (*e*) C. Pardo, I. Alkorta and J. Elguero, *Tetrahedron: Asymmetry*, 2006, **17**, 191; (*f*) V. Galasso, D. Jones and A. Modelli, *Chem. Phys.*, 2003, **288**, 33; (*g*) A. Aamouche, F. J. Devlin and P. J. Stephens, *J. Am. Chem. Soc.*, 2000, **122**, 2346; (*h*) S. H. Wilen, J. Z. Qi and P. G. Williard, *J. Org. Chem.*, 1991, **56**, 485; (*i*) T. R. Miller and E. C. Wagner, *J. Am. Chem. Soc.*, 1941, **63**, 832; (*j*) M. A. Spielman, *J. Am. Chem. Soc.*, 1935, **57**, 583.

3 (*a*) A. Lutzen, T. Weilandt, U. Kiehne, J. Bunzen and G. Schnakenburg, *Chem.–Eur. J.*, 2010, **16**, 2418; (*b*) S. Sergeyev, D. Didier, V. Boitsov, A. Teshome, I. Asselberghs, K. Clays, C. M. L. V. Velde, A. Plaquet and B. Champagne, *Chem.–Eur. J.*, 2010, **16**, 8181; (*c*) K. Warnmark, C. S. Arribas, O. F. Wendt, A. P. Sundin, C. J. Carling, R. Y. Wang and R. P. Lemieux, *Chem. Commun.*, 2010, **46**, 4381; (*d*) W. Wang, X. Du, Y. L. Sun, B. Tan, Q. F. Teng, X. J. Yao and C. Y. Sue, *Chem. Commun.*, 2010, **46**, 970; (*e*) B. Dolensky, A. Tatar, J. Cejka and V. Kral, *Org. Lett.*, 2010, **12**, 1872; (*f*) H. Wu, Y. Wan, R. Yuan, W. C. Zhang, Y. H. Shi, W. Lin, W. Yin, R. C. Bo and J. J. Shi, *Tetrahedron*, 2010, **66**, 3405; (*g*) A. C. Try, M. D. H. Bhuiyan, K. X. Zhu and P. Jensen, *Eur. J. Org. Chem.*, 2010, 4662; (*h*) E. B. Veale and T. Gunnlaugsson, *J. Org. Chem.*, 2010, **75**, 5513; (*i*) S. Satishkumar and M. Periasamy, *Tetrahedron: Asymmetry*, 2009, **20**, 2257; (*j*) D. Schroder, A. Revesz, T. A. Rokob, M. Havlik and B. Dolensky, *Angew. Chem. Int. Ed.*, 2011, **50**, 2401; (*k*) A. Corma, E. P. Poli, E. E. Merino, U. Diaz and D. Brunel, *J. Phys. Chem. C*, 2011, **115**, 7573; (*l*) R. Abonia, F. Cuenu, A. Bolanos and A. Cabrera, *J. Organomet. Chem.*, 2011, **696**, 1834; (*m*) B. Dolensky, V. Parchansky, P. Matejka, M. Havlik, P. Bour and V. Kral, *J. Mol. Struct.*, 2011, **996**, 69; (*n*) A. C. Try, Q. M. Malik, S. Ijaz and D. C. Craig, *Tetrahedron*, 2011, **67**, 5798.

4 (*a*) O. Trapp, G. Trapp, J. W. Kong, U. Hahn, F. Vögtle and V. Schurig, *Chem.–Eur. J.*, 2002, **8**, 3629; (*b*) O. Trapp and V. Schurig, *J. Am. Chem. Soc.*, 2000, **122**, 1424.

5 Configurationally stable *methano*-Tröger bases can be obtained upon double protonation or introduction of substituents on the aromatic framework. See: A. Greenberg, N. Molinaro and M. Lang, *J. Org. Chem.*, 1984, **49**, 1127; A. Tatibouët, M. Demeunynck, C. Andraud, A. Collet and J. Lhomme, *Chem. Commun.*, 1999, 161; D. A. Lenev, K. A. Lyssenko, D. G. Golovanov, V. Buss and R. G. Kostyanovsky, *Chem.–Eur. J.*, 2006, **12**, 6412.

6 A. Sharma, L. Guenée, J. V. Naubron and J. Lacour, *Angew. Chem., Int. Ed.*, 2011, **50**, 3677.

7 The presence of two different substituents around the diazo moiety leads to the formation of a carbon stereocenter on the *ethano*-bridge, and hence the formation of diastereomers.

8 (*a*) G. D. Allred and L. S. Liebeskind, *J. Am. Chem. Soc.*, 1996, **118**, 2748; (*b*) I. Paterson and J. Man, *Tetrahedron Lett.*, 1997, **38**, 695; (*c*) S. Zhang, D. Zhang and L. S. Liebeskind, *J. Org. Chem.*, 1997, **62**, 2312.

9 (*a*) M. Perez, M. Fananas-Mastral, P. H. Bos, A. Rudolph, S. R. Harutyunyan and B. L. Feringa, *Nat. Chem.*, 2011, **3**, 377; (*b*) H. Li, A. He, J. R. Falck and L. S. Liebeskind, *Org. Lett.*, 2011, **13**, 3682; (*c*) H. Li, A. He, R. Falck John and S. Liebeskind Lanny, *Org. Lett.*, 2011, **13**, 3682; (*d*) J.-B. Langlois and A. Alexakis, *Angew. Chem., Int. Ed.*, 2011, **50**, 1877; (*e*) W.-W. Jin, W.-M. Du, Q. Yang, H.-F. Yu, J.-P. Chen and Z.-K. Yu, *Org. Lett.*, 2011, **13**, 4272; (*f*) D. Hobuss, A. Baro, K. V. Axenov, S. Laschat and W. Frey, *Eur. J. Inorg. Chem.*, 2011, 384; (*g*) J. B. Feltenberger and R. P. Hsung, *Org. Lett.*, 2011, **13**, 3114; (*h*) M. Welker, S. Woodward, L. F. Veiros and M. J. Calhorda, *Chem.–Eur. J.*, 2010, **16**, 5620; (*i*) M. Wang and Z. Lin, *Organometallics*, 2010, **29**, 3077; (*j*) M. Tissot, D. Muller, S. Belot and A. Alexakis, *Org. Lett.*, 2010, **12**, 2770; (*k*) A. Guzman-Martinez and A. H. Hoveyda, *J. Am. Chem. Soc.*, 2010, **132**, 10634; (*l*) L. M. Bishop, R. E. Roberson, R. G. Bergman and D. Trauner, *Synthesis*, 2010, 2233.

10 (*a*) J. A. Vanecko, H. Wan and F. G. West, *Tetrahedron*, 2006, **62**, 1043; (*b*) M. P. Doyle, M. A. McKervey and T. Ye, *Modern catalytic methods for organic synthesis with diazo compounds: from cyclopropanes to ylides*, Wiley, New York, 1998; (*c*) J. S. Clark, *Nitrogen, Oxygen and Sulfur Ylide Chemistry: A Practical Approach*, Oxford University Press, Oxford, 2002, pp. 1; (*d*) A. Padwa and S. F. Hornbuckle, *Chem. Rev.*, 1991, **91**, 263; (*e*) E. Nakamura, N. Yoshikai and M. Yamanaka, *J. Am. Chem. Soc.*, 2002, **124**, 7181.

11 For information, this reaction had afforded **5a** (70%) with a moderate diastereoselectivity (*dr* 5 : 1) using 1 mol% of $Rh_2(OAc)_4$. The transfer of chirality had been low in this case (*ee* 10%). No change was observed with 5 mol% of catalyst (Table 2).

12 CuTC was mentioned once in the context of carbene self-dimerization. Fischer complexes were used as the substrates and a transmetalation from Cr to Cu was evinced: J. C. del Amo, M. J. Mancheno, M. Gomez-Gallego and M. A. Sierra, *Organometallics*, 2004, **23**, 5021.

13 At the new carbon stereogenic centers, results indicate that large and small substituents replace preferentially the pro-(*S*) and pro-(*R*) hydrogen atoms of the parent (*S*,*S*)-**1**, respectively (and *vice versa* for (*R*,*R*)-**1**).

14 In the presence of either 1 or 5 mol% of $Rh_2(OAc)_4$, the reaction of enantiopure **2** provides no product with **4b** or essentially racemic material with diazo **4a** and **4d** ($ee_{max}$ 10%).

15 In all likelihood, the chirality transfer occurs with retention of configuration as in the case of $Rh_2(OAc)_4$.

16 A single recrystallization of **5p** in acetone afforded the adduct in 99% *ee*.

17 Interestingly, this trend is opposite to that observed with arylester diazo derivatives under $Rh_2(OAc)_4$ catalysis. See reference 6 for further information.

18 For the Rh(II)-catalyzed reactions, 1 mol% of $Rh_2(OAc)_4$ is actually sufficient to reach full conversion. 5 mol% of catalyst was used to allow a direct comparison with copper-mediated reactions.